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Laurie Herviou, Sara Ovejero, Fanny Izard, Ouissem Karmous-Gadacha, Claire Gourzones, Celine Bellanger, Eva de Smedt, Anqi Ma, Laure Vincent, Guillaume Cartron, et al.

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Clinical Epigenetics

Targeting the methyltransferase SETD8 impairs tumor cell survival and overcomes drug resistance independently of p53 status in multiple myeloma

--Manuscript Draft--

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	Fondation Française pour la Recherche contre le Myélome et les Gammopathies monoclonales	Dr Laurie Herviou
Abstract:	<p>Background: Multiple myeloma (MM) is a malignancy of plasma cells that largely remains incurable. The search for new therapeutic targets is therefore essential. In addition to a wide panel of genetic mutations, epigenetic alterations also appear as important players in the development of this cancer, thereby offering the possibility to reveal novel approaches and targets for effective therapeutic intervention.</p> <p>Results: Here, we show that a higher expression of the lysine methyltransferase SETD8, which is responsible for the mono-methylation of histone H4 at lysine 20, is an adverse prognosis factor associated with a poor outcome in two cohorts of newly diagnosed patients. Primary malignant plasma cells are particularly addicted to the activity of this epigenetic enzyme. Indeed, the inhibition of SETD8 by the chemical compound UNC-0379 and the subsequent decrease in histone H4 methylation at lysine 20 are highly toxic in MM cells compared to normal cells from the bone marrow microenvironment. At the molecular level, RNA sequencing and functional studies revealed that SETD8 inhibition induces a mature non-proliferating plasma cell signature and, as observed in other cancers, triggers an activation of the tumor suppressor p53, which together cause an impairment of myeloma cell proliferation and survival. However, a deadly level of replicative stress was also observed in p53-deficient myeloma cells treated with UNC-0379, indicating that the cytotoxicity associated with SETD8 inhibition is not necessarily dependent on p53 activation. Consistent with this, UNC-0379 triggers a specific p53-independent nucleolar stress characterized by nucleolin delocalization and reduction of nucleolar RNA synthesis. Finally, we showed that SETD8 inhibition is strongly synergistic with melphalan and may overcome resistance to this alkylating agent widely used in MM treatment.</p> <p>Conclusions: Altogether, our data indicate that the up-regulation of the epigenetic enzyme SETD8 is associated with a poor outcome and the deregulation of major signaling pathways in MM. Moreover, we provide evidences that myeloma cells are dependent on SETD8 activity and its pharmacological inhibition synergizes with melphalan, which could be beneficial to improve MM treatment in high-risk patients whatever their status for p53.</p>	

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Response to Reviewers:	<p>Dear Dr. LICHT,</p> <p>Please find the revised version of the manuscript CLEP-D-20-00523 entitled "Targeting the methyltransferase SETD8 impairs tumor cell survival and overcomes drug resistance independently of p53 status in multiple myeloma". We have performed several additional experiments in order to address all the issues raised by the reviewers. Notably, as requested, we provide additional mechanistic information underlining how SETD8 inhibitor is working in myeloma cells. Regardless of the status of p53 and in addition to induce DNA damage, we now reveal that the treatment of malignant myeloma cells with the SETD8 inhibitor triggers a specific nucleolar stress characterized by the delocalization of the pool of Nucleolin and a strong decrease in nucleolar RNA synthesis.</p> <p>We thank the reviewers for their valuable comments. Please find our point-by-point response below:</p> <p>Reviewer 1</p> <p>Overall the studies are relatively clear and straightforward, however it remains unclear what the mechanism by which SETD8 inhibition results in cell death. The authors have ruled out changes in total H4K20me so its not clear how they can conclude that gene expression changes are direct effects of SETD8 inhibition. It seems equally plausible that they are changes that are associated with any event that would result in</p>

decreased proliferation. They authors also ruled out TP53. So why do the cells stop growing and die?

Regarding the concern raised by reviewer 1, we have performed additional experiments shown in a new figure 5. The obtained results indicate that, in addition to induce DNA damage, the SETD8 inhibitor leads to a nucleolar dysfunction, in myeloma cells, independently of the p53 status. This nucleolar impairment is notably characterized by the delocalization of the nucleolin and a strong decrease in nucleolar RNA synthesis, which are known to contribute to growth inhibition and cell death regardless of the p53 status (see James A et al., 2014 Nucleus, 402-426). These data have been included in the manuscript lines 492 to 523.

SETD8 inhibition is SET8 up-regulation in multiple myeloma is not associated with global changes in H4K20me1 levels. However, we cannot exclude that some local changes can occur. Since H4K20me1 is critical for the maintenance of genome integrity, the loss of H4K20me1 upon UNC0379 treatment may also impact cell proliferation and survival. We clarify this point in the discussion section (lines 626 to 641). Regarding gene expression changes upon SETD8 inhibition and as indicated in lanes 424 to 427, RNAseq analysis after SETD8 inhibition was performed when H4K20me1 was reduced but before the appearance of cell-proliferation defects in order to minimize gene expression changes resulting indirectly from proliferation decreased.

Reviewer 2.

1- In line 318, the authors stated that malignant plasma cells are particularly addicted to SETD8 activity. The conclusion was driven by the increased toxicity of the inhibitor in CD138+ cells. The authors did not compare cytotoxicity between malignant plasma cells and normal plasma cells isolated from healthy donors. Thus, the authors cannot rule out preferential cytotoxicity towards mature plasma cells regardless of their malignant status.

As requested by reviewer 2, we now compare the cytotoxicity of the SETD8 inhibitor between malignant plasma cells and normal plasma cells from healthy donors. We also examine the cytotoxicity of the inhibitor in normal plasma cells generated in vitro by differentiation of memory B cells. These new results are described in lines 396 to 410 and shown in Figure 2C and supplementary Figure S5. We demonstrated that SETD8 inhibition is toxic for malignant plasma cells and not to normal ones.

2- The authors need to compare melphalan sensitivity between SETD8 knockdown and control cells to confirm that the synergistic effect of the inhibitor with melphalan is due to SETD8 inhibition.

As suggested by reviewer 2, we used a doxycycline-inducible shRNA lentiviral vector to silence SETD8 expression in XG7 cells and we measured melphalan sensitivity between SETD8 depleted and control cells. The results are shown in new supplementary Figure 12A-C and described in lanes 534 to 540. We validated that SETD8 depletion sensitizes MM cells to melphalan toxicity.

3- In figure 5E, I think that the melphalan and UNC-0379 label colors are switched?! The cells should be resistant to melphalan not UNC-0379.

To avoid confusion, we modified the panel of Figure 6E (previously Figure 5E) and added the percentage of annexin-positive cells in the sensitive cell line treated with melphalan. Thus, we can clearly observe the therapeutic interest of SETD8 inhibition to overcome Melphalan resistance in the XG7 MelR cell line.

4- Did the authors observe an increase in SETD8 levels in melphalan-resistant cells? Such an observation would support the evidence that SETD8 inhibition increases melphalan sensitivity.

By performing RT-qPCR and immunoblots, a significant increase in SETD8 expression was not observed in melphalan resistant cells. We did not include these results in the revised manuscript.

	<p>We have answered all comments and we hope that our manuscript could be published in Clinical Epigenetics.</p> <p>With our best regards,</p> <p>Eric JULIEN and Jérôme MOREAUX</p>
Additional Information:	
Question	Response
<p>Is this study a clinical trial?</p> <p>A clinical trial is defined by the World Health Organisation as 'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.</p>	No
<p>If you would like to do so, please enter text to be used to Tweet about your manuscript from our Twitter account.</p>	

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Targeting the methyltransferase SETD8 impairs tumor cell survival and overcomes drug resistance independently of p53 status in multiple myeloma

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33

34 **ABSTRACT**

1 35
2 36 **Background:** Multiple myeloma (MM) is a malignancy of plasma cells that largely remains
3
4 37 incurable. The search for new therapeutic targets is therefore essential. In addition to a
5
6 38 wide panel of genetic mutations, epigenetic alterations also appear as important players
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8 39 in the development of this cancer, thereby offering the possibility to reveal novel
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10 40 approaches and targets for effective therapeutic intervention.

11 41 **Results:** Here, we show that a higher expression of the lysine methyltransferase SETD8,
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15 43 prognosis factor associated with a poor outcome in two cohorts of newly diagnosed
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21 46 0379 and the subsequent decrease in histone H4 methylation at lysine 20 are highly toxic
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23 47 in MM cells compared to normal cells from the bone marrow microenvironment. At the
24
25 48 molecular level, RNA sequencing and functional studies revealed that SETD8 inhibition
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27 49 induces a mature non-proliferating plasma cell signature and, as observed in other
28
29 50 cancers, triggers an activation of the tumor suppressor p53, which together cause an
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31 51 impairment of myeloma cell proliferation and survival. However, a deadly level of
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33 52 replicative stress was also observed in p53-deficient myeloma cells treated with UNC-
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35 53 0379, indicating that the cytotoxicity associated with SETD8 inhibition is not necessarily
36
37 54 dependent on p53 activation. Consistent with this, UNC-0379 triggers a specific p53-
38
39 55 independent nucleolar stress characterized by nucleolin delocalization and reduction of
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41 56 nucleolar RNA synthesis. Finally, we showed that SETD8 inhibition is strongly synergistic
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43 57 with melphalan and may overcome resistance to this alkylating agent widely used in MM
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45 58 treatment.

46 59 **Conclusions:** Altogether, our data indicate that the up-regulation of the epigenetic
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48 60 enzyme SETD8 is associated with a poor outcome and the deregulation of major signaling
49
50 61 pathways in MM. Moreover, we provide evidences that myeloma cells are dependent on
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52 62 SETD8 activity and its pharmacological inhibition synergizes with melphalan, which could
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54 63 be beneficial to improve MM treatment in high-risk patients whatever their status for p53.
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INTRODUCTION

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68 Multiple Myeloma (MM) is a cancer of terminally differentiated plasma cells[1] and
69 is the second most common hematological malignancy[2]. Over the past 15 years, several
70 advances in treatments have led to a significantly higher survival of intensively treated
71 patients[3]. Unfortunately, despite the recent progress in MM treatments, most patients
72 will ultimately relapse and develop drug resistance.

73 In addition to a wide panel of genetic mutations, recent studies have pinpointed
74 that epigenetic alterations, including aberrant DNA and histone methylation, might be also
75 important players in MM development[4]. These recent findings could illuminate new
76 mechanisms central to the genesis of MM and offer the possibility to reveal novel
77 approaches and targets for effective therapeutic intervention. For example, the inhibition
78 of the histone H3K27 methyltransferase EZH2 has recently emerged as a potential
79 strategy for the treatment of myeloma[5]. Moreover, classic epigenetic modulating agents,
80 such as histone deacetylase and DNA methyltransferase inhibitors, are already tested as
81 monotherapy or in combination with conventional anti-MM agents[6, 7]. However, the
82 occurrence of important side effects and the appearance of resistance to these drugs
83 increase the need to identify novel epigenetic targets in MM and evaluate their pre-clinical
84 perspective.

85 SETD8 (also known as SET8, PR-Set7, KMT5A) has been identified as the
86 epigenetic enzyme responsible for the mono-methylation of histone H4 at lysine 20
87 (H4K20me1) [8]. SETD8 and H4K20me1 are naturally increased during mitosis and play
88 a critical role in chromatin compaction, gene regulation and cell-cycle progression[8–
89 10][10]. In addition, SETD8 could induce the methylation of non-histone proteins, such as
90 the replication factor PCNA and the tumor suppressor p53[11, 12]. While SETD8-

1 mediated methylation of p53 inhibits apoptosis[12], PCNA methylation by SETD8 might
2 enhance the interaction with the Flap endonuclease FEN1 and promote cell
3 proliferation[11]. Consistent with this, the overexpression of SETD8 has been reported in
4
5 93 many different solid tumors[14–17] and pharmacological inhibition of SETD8 is sufficient
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7 94 to activate the p53 pro-apoptotic program in neuroblastoma cell lines[18]. This has
8
9 95 suggested that this enzyme could be an attractive target to rescue p53 functions in
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11 96 cancers displaying a low incidence of *TP53* genetic alterations, as it is the case at early
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13 97 stages in MM[19]. However, the role of SETD8 and its incidence in the development of
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15 98 MM or any hematological malignancies is not known.
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22 100 Here, we provide evidence that malignant plasma cells are addicted to SETD8
23
24 101 expression, which is associated with a poor outcome independently of changes in the
25
26 102 steady state level of histone H4K20me1. Although inducing p53 canonical pathway, we
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28 103 show that the pharmacological inhibition of SETD8 by the chemical compound UNC-0379
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30 104 causes specific nucleolar alterations and cytotoxic effects independently of p53 status.
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32
33 105 Finally, the combination of UNC-0379 with the cytotoxic agent melphalan strongly
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35 106 enhances DNA damage and overcomes drug resistance, suggesting that targeting
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37 107 SETD8 activity could be beneficial to improve MM treatment in high-risk patients
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39 108 independently of their mutational status for p53.
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MATERIALS AND METHODS

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112 **Primary multiple myeloma cells**

113 Patients' MMCs were purified using anti-CD138 MACS microbeads (Miltenyi Biotec,
114 Bergisch Gladbach, Germany) and their gene expression profile (GEP) obtained using
115 Affymetrix U133 plus 2.0 microarrays as described[20, 21][22]. We also used publicly
116 available Affymetrix GEP (Gene Expression Omnibus, accession number GSE2658) of a
117 cohort of 345 purified MMC from previously untreated patients from the University of
118 Arkansas for Medical Sciences (UAMS, Little Rock, AR), termed in the following UAMS-
119 TT2 cohort. These patients were treated with total therapy 2 including high-dose
120 melphalan (HDM) and autologous stem cell transplantation (ASCT)[23]. We also used
121 Affymetrix data from total therapy 3 cohort (UAMS-TT3; n=158; E-TABM-1138)[24].
122 Mouse 5T33MMv cells originated spontaneously in aging C57BL/KaLwRij mice and have
123 since been propagated *in vivo* by intravenous transfer of diseased marrow in young
124 syngeneic mice as described[25, 26].

125 **Treatment of primary MM cells**

126 Bone marrow of patients with previously untreated MM (n = 8) at the university hospital of
127 Montpellier was obtained after patients' written informed consent in accordance with the
128 Declaration of Helsinki and agreement of the Montpellier University Hospital Centre for
129 Biological Resources (DC-2008-417). Mononuclear cells were treated with or without
130 UNC-0379 (1µM, 2.5µM or 5µM) and MMC cytotoxicity was evaluated using anti-CD138-
131 phycoerythrin monoclonal antibody (Immunotech, Marseille, France) as described[27].

132 **Apoptosis assays**

133 Cells were cultured in 24-well, flat-bottomed microtiter plates at 10⁵ cells per well in
134 RPMI1640–10% FCS or X-VIVO 20 culture media with or without IL-6 (3ng/mL) and

135 appropriate concentration of chemical drugs. After 4 days of culture, cells were washed
1
2 136 twice in PBS and apoptosis was assayed with PE-conjugated Annexin V labeling (BD
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5 137 Biosciences) using a Fortessa flow cytometer (BD) following manufacturer protocols.
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7 138 **Human Myeloma Cell Lines (HMCLs)**

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10 139 XG human myeloma cell lines (HMCLs) were cultured in the presence of recombinant IL-
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12 140 6 as previously described[28]. XG7 Melphalan-resistant cell line was derived from the
13
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15 141 sensitive parental XG7 cells[29]. JJN3 was kindly provided by Dr Van Riet (Brussels,
16
17 142 Belgium), JIM3 by Dr MacLennan (Birmingham, UK) and MM1S by Dr S. Rosen (Chicago,
18
19 143 USA). AMO-1, LP1, L363, U266, OPM2, and SKMM2 were purchased from DSMZ
20
21
22 144 (Braunschweig, Germany) and RPMI8226 from ATTC (Rockville, MD, USA). HMCLs were
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24 145 authenticated according to their short tandem repeat profiling and their gene expression
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27 146 profiling using Affymetrix U133 plus 2.0 microarrays deposited in the ArrayExpress public
28
29 147 database under accession numbers E-TABM-937 and E-TABM-1088[28].
30

31 148 **Establishment of shRNA expressing HMCLs**

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34 149 Control and p53 shRNA sequences were cloned in the pLenti4-EZ-miR plasmid as
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36 150 previously described[30]. SETD8 and associated control shRNA sequences were cloned
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39 151 into a puromycin retroviral vector RNAi Ready pSiren as described[31]. Retroviral
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41 152 particles were produced in 293FT cells. Briefly, 293FT cell line was cultured in Dulbecco's
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44 153 modified Eagle's medium and supplemented with 10% defined fetal bovine serum,
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46 154 500µg/mL geneticin, 4mM L-glutamine, and 1mM MEM sodium pyruvate. The day before
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49 155 transfection, cells were plated into a 10cm tissue culture plate to 90%-95% confluence.
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51 156 9µg of ViraPower packaging mix (Invitrogen) and 9µg of lentiviral plasmids were co-
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54 157 transfected into 293FT cells using 36µL Lipofectamine 2000 reagent (Invitrogen). Forty-
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56 158 eight hours later, culture supernatants were collected, concentrated 100-fold by
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58 159 ultracentrifugation (20,000 g; 4 hours) and viral titers determined. Corresponding HMCLs
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160 were transduced with virus and stable transduced cells were obtained by adding zeocin
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2 161 (10 µg/mL) for pLenti4-EZ-miR and puromycin (2.5 µg/mL) for pSIREN viral particles.
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4 162 **Growth assays and cell cycle analysis**

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7 163 Cells were cultured for 4 days in 96-well flat-bottom microtiter plates in RPMI 1640
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9 164 medium, 10% FCS, and 2 ng/ml IL-6 (control medium) in the presence of UNC-0379. Cell
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11 165 growth was evaluated by quantifying intracellular ATP amount with a Cell Titer Glo
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13 166 Luminescent Assay (Promega, Madison, WI) using a Centro LB 960 luminometer
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15 167 (Berthold Technologies, Bad Wildbad, Germany). For cell cycle analysis, cells were
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17 168 cultured in 24-well flat-bottomed microtiter plates at 10⁵ cells per well in RPMI1640–10%
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19 169 FCS or X-VIVO 20 culture media with or without IL-6 (3ng/mL). The cell cycle was
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21 170 assessed using DAPI staining (Sigma-Aldrich, Saint-Louis, MO, USA) and cells in the S
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23 171 phase using incubation with bromodeoxyuridine (BrdU) for 1 h and labeling with an anti-
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25 172 BrdU antibody (APC BrdU flow kit, BD Biosciences, San Jose, CA, USA) according to the
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27 173 manufacturer's instructions. Flow cytometry analysis was done on a Fortessa flow
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29 174 cytometer (BD, Mountain View, CA, USA).
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34 175 **RNA sequencing**

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36 176 HMCLs were cultured for 16 hours with or without 5 µM of UNC-0379, or infected with
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38 177 shControl or shRNA SETD8 pSIREN vectors for 48h. RNA samples were collected as
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40 178 previously described. The RNA sequencing (RNA-seq) library preparation was done with
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42 179 150ng of input RNA using the Illumina TruSeq Stranded mRNA Library Prep Kit. Paired-
43
44 180 end RNA-seq were performed with Illumina NextSeq sequencing instrument (Helixio,
45
46 181 Clermont-Ferrand, France). RNA-seq read pairs were mapped to the reference human
47
48 182 GRCh37 genome using the STAR aligner[32]. All statistical analyses were performed with
49
50 183 the statistics software R (version 3.2.3; available from <https://www.r-project.org>) and R
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52 184 packages developed by BioConductor project (available from
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185 <https://www.bioconductor.org/>)[33]. The expression level of each gene was summarized
1
2 186 and normalized using DESeq2 R/Bioconductor package[34]. Differential expression
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5 187 analysis was performed using DESeq2 pipeline. P values were adjusted to control the
6
7 188 global FDR across all comparisons with the default option of the DESeq2 package. Genes
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10 189 were considered differentially expressed if they had an adjusted p-value of 0.05 and a fold
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12 190 change of 1.5. Pathway enrichment analyses were performed using online the curated
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14
15 191 gene set collection on the Gene Set Enrichment Analysis software
16
17 192 (<http://software.broadinstitute.org/gsea/msigdb/index.jsp>)[35, 36].
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19 193 **Gene expression profiling and statistical analyses**

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22 194 Gene expression data were normalized with the MAS5 algorithm and analyses processed
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24 195 with GenomicScape (<http://www.genomicscape.com>)[37] the R.2.10.1 and bioconductor
25
26
27 196 version 2.5 programs[33]. Gene Set Expression Analysis (GSEA) was used to identify
28
29 197 genes and pathways differentially expressed between populations. Univariate and
30
31
32 198 multivariate analysis of genes prognostic for patients' survival was performed using the
33
34 199 Cox proportional hazard model. Difference in overall survival between groups of patients
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36 200 was assayed with a log-rank test and survival curves plotted using the Kaplan-Meier
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38
39 201 method (Maxstat R package)[38].
40

41 202 **53BP1 Staining-immunofluorescence microscopy**

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44 203 After deposition on slides using a Cytospin centrifuge (600 r.p.m. for 10 minutes), cells
45
46 204 were fixed with 4% PFA, permeabilized with 0.5% Triton in PBS and saturated with 5%
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48
49 205 bovine milk in PBS. The rabbit anti-53BP1 (Novus Biologicals - Littleton, CO, USA –
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51 206 NB100304) antibody was diluted 1/300 in 5% bovine milk in PBS, and deposited on
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54 207 cytopins for 60 minutes at room temperature. Slides were washed twice and anti-rabbit
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56 208 alexa 488-conjugated antibody (diluted 1/500 in 5% bovine milk in PBS) was added for
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58 209 60 minutes at room temperature. Slides were washed and mounted with Vectashield and
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210 1% DAPI. Images and fluorescence were captured with a ZEISS Axio Imager Z2
211 microscope (X63 objective) (Oberkochen, Germany), analyzed with Omero
212 (omero.mri.cnrs.fr) server and ImageJ software.

213 **Nucleolar proteins staining-immunofluorescence microscopy**

214 After indicated treatments and deposition on slides as described above, cells were fixed
215 with 4% PFA for 10 minutes at RT, permeabilized with 0.1% Triton in PBS-0.5% BSA for
216 10 minutes, and saturated with PBS-1% BSA for 20 minutes. Anti-nucleolin (ab22758,
217 Abcam) and anti-fibrillarin (ab5821, Abcam) antibodies were diluted 1/200 in saturation
218 buffer, and incubated for 90 minutes in a humid chamber at room temperature. Slides
219 were washed 3 times with PBS-0.01% Tween-20 and anti-rabbit Alexa Texas Red-
220 conjugated antibody (diluted 1/500 in saturation buffer) was added for 45 minutes in a
221 humid chamber at room temperature protected from light. Slides were washed 3 times (5
222 minutes each) as previously, incubated with DAPI (20 µg/ml in water) for 5 minutes
223 protected from light, washed 3 times with water, air dried and mounted with ProLong
224 (Invitrogen). Images and fluorescence were captured with a ZEISS Axio Imager Z1
225 microscope (X40 objective) (Oberkochen, Germany), and analyzed with Omero
226 (omero.mri.cnrs.fr) server. Quantification of cells with nucleolin delocalization was visually
227 performed.

228 **5-Ethynyl Uridine (EU) staining-immunofluorescence microscopy**

229 Cells were treated with UNC-0379 3 µM or the vehicle DMSO (0.0003%) for 24h. EU (0.2
230 mM) was added during the last 5 minutes of treatment. Cells were deposited on slides as
231 described above, fixed with 4% PFA for 10 minutes at RT, permeabilized with 0.5% Triton
232 in PBS-0.5% BSA for 10 minutes, saturated with PBS-1% BSA for 20 minutes and Click-
233 it reaction was performed. Briefly, for 10 slides, a mix of 438 µl PBS 1X + 15 µl CuSO₄
234 (0.1 M) + 2.5 µl Azide AF555 + 50 µl Vitamine C (100 mM) was prepared by adding the

235 reagents in the mentioned order. Slides were incubated in a humid chamber protected
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2 236 from light for 15 minutes at RT, washed 3 times with PBS-0.01% Tween-20, and
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5 237 subsequently incubated with DAPI and mounted as described above. Image acquisition
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7 238 was performed with a ZEISS Axio Imager Z1 microscope (X40 objective) (Oberkochen,
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10 239 Germany), and analyzed with Omero (omero.mri.cnrs.fr) server. Quantification of EU
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12 240 intensity was performed with CellProfiler™ “Human Cell” pipeline.

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14 241 **Immunoblot analysis.** Cells washed with phosphate-buffered saline (PBS) were lysed in
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17 242 SDS buffer and boiled at 94°C for 5 minutes. After measuring protein quantity by Bradford,
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19 243 equal amounts of protein were resolved by SDS-PAGE, transferred to a nitrocellulose
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22 244 membrane (Millipore) and probed with one of the following antibodies: mouse anti-Chk1
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24 245 (1:1000, abcam), rabbit anti-p21 (1:500, Cell signaling), rabbit anti- p53 (1:1000, Cell
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27 246 Signaling), rabbit anti-SETD8 (1:1000, Cell Signaling), mouse anti-β-actin (1:20000,
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29 247 Sigma), rabbit anti-H2A.X and anti-phospho-H2A.X-Ser139 (1:1000, Cell signaling),
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32 248 rabbit anti-H4-K20me1 (1:1000 Cell Signaling), and rabbit anti-Histone H4 (1:1000, Cell
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34 249 Signaling), rabbit anti-tubulin (1:1000, Cell signaling). Membranes were then incubated
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36
37 250 with the appropriate horseradish peroxidase (HRP)-conjugated secondary antibodies.
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39 251 The immunoreactive bands were detected by chemiluminescence (Pierce).

40 41 252 **Drug combination study**

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44 253 The interaction between the drugs tested in vitro was investigated with a concentration
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46 254 matrix test, in which increasing concentration of each single drug were assessed with all
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49 255 possible combinations of the other drugs. For each combination, the percentage of
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51 256 expected growing cells in the case of effect independence was calculated according to
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53
54 257 the Bliss equation (Combes et al., 2019; Greco et al., 1995):

$$55
56 258 \quad fuC = fuA.fuB$$

259 where fuC is the expected fraction of cells unaffected by the drug combination in the case
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2 260 of effect independence, and fuA and fuB are the fractions of cells unaffected by treatment
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4 261 A and B, respectively. The difference between the fraction of living cells in the cytotoxicity
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7 262 test and the fuC value was considered as an estimation of the interaction effect, with
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10 263 positive values indicating synergism and negative values antagonism.

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12 264 Synergy matrix was built with the R package “SynergyFinder”.

14 265 ***In vitro* Plasma Cell differentiation**

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17 266 Peripheral blood cells from healthy donors were purchased from the French Blood Center
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19 267 (Toulouse, France) and CD19+ CD27+ MBCs purified (>95% purity) using “MBC isolation
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21
22 268 kit” (Order no. 130-093-546, Miltenyi) according to manufacturer’s instructions.
23
24 269 Preplasmablasts (prePB), plasmablasts (PB) and plasma cells (PC) were generated as
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26
27 270 reported[39, 40], by a 3-step *in vitro* protocol. At day 7 of differentiation, when PB was the
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29 271 most abundant population in the culture, UNC-0379 (at 1, 2.5 or 5 μ M) or the vehicle
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32 272 DMSO (=mock, at 0.0005%) were added, and cells were incubated for the next 3 days
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34 273 during their differentiation into PC. At the end of this treatment, all cells were collected,
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37 274 visually counted with Trypan Blue to assess viability, apoptosis was analyzed as described
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39 275 above, and PCs (CD38+ CD138+ cells) were quantified by cytometry. Data are expressed
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41
42 276 as percentage of CD38+ CD138+ cells compared to the mock sample (100%).
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RESULTS

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5 284 **SETD8 up-regulation in myeloma is associated with a poor outcome.** In order to
6
7 285 identify epigenetic factors potentially involved in MM, we used public Affymetrix
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9 286 microarrays gene expression data sets to identify which genes encoding histone-
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11 287 modifying enzymes are differentially expressed between normal bone marrow plasma
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13 288 cells (BMPCs, n=22), purified primary MM cells from newly diagnosed patients (MMCs, n
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15 289 = 345) and human myeloma cell lines (HMCLs, N=42)¹⁹. As shown in Figure 1A,
16
17 290 significantly higher levels of mRNAs encoding the histone H4K20 mono-
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19 291 methyltransferase SETD8 were found in HMCLs compared to BMPCs and MMCs (**Figure**
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21 292 **1A**). Furthermore, although we did not observe a statistical difference with BMPCs,
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23 293 *SETD8* mRNA levels appeared heterogeneous in MMCs (**Figure 1A**) ranging from 65 to
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25 294 63338 in Affymetrix signal. These contrasted *SETD8* mRNA levels were not restrained to
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27 295 a particular MM molecular sub-type (**Supplementary Figure S1A**). Immunoblot analysis
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29 296 with a specific SETD8 antibody showed that HMCLs and some MMCs displayed higher
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31 297 SETD8 protein levels compared with normal plasma cells (PC) (**Figure 1B**). These higher
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33 298 SETD8 protein levels were independent of the natural cell-cycle fluctuation of the
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35 299 enzyme[9], as the levels of the mitotic marker histone H3-S10 phosphorylation were
36
37 300 relatively similar in all tested samples (**Figure 1B**). SETD8 is known as the unique enzyme
38
39 301 responsible for the mono-methylation of histone H4 at lysine 20 (H4K20me1)[8]. Yet,
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41 302 levels of H4K20me1 remained roughly unchanged in HMCLs and MMCs displaying higher
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43 303 SETD8 levels and similar levels of the G2/M marker histone H3-S10 phosphorylation
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45 304 (**Figure 1B**), indicating that SETD8 up-regulation is not accompanied by a significant
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47 305 increase in the steady state level of histone H4K20me1 in MM.
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306 We next investigated the prognostic value of SETD8 up-regulation in two
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2 307 independent cohorts of previously untreated MM patients (UAMS-TT2 n=256 and UAMS-
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4 308 TT3 n=158 cohorts), using Maxstat R algorithm. High *SETD8* mRNA levels were
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7 309 predictive of both shorter event free survival and overall survival in the two cohorts (**Figure**
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9
10 310 **1C**). Consistent with these results, *SETD8* mRNA levels were significantly increased in
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12 311 patients harboring Chr1q21 gain (**Supplementary Figure S1B**) or presenting a high gene
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14 312 expression-based proliferation index (GPI) (**Supplementary Figure S1C**), molecular
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16 313 features being associated with a poor outcome in MM patients. However, *SETD8*
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19 314 expression did not correlate with MMC plasma cell labeling index (PCLI) in a cohort of
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22 315 101 newly diagnosed patients (**Supplementary Figure S1D**), suggesting that SETD8 up-
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24 316 regulation is likely not a hallmark of MMC proliferation status. Gene set expression
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26 317 analysis (GSEA) of patients with high *SETD8* expression highlighted a significant
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29 318 enrichment of genes involved in IRF4 targets, MYC-MAX targets, MAPK pathway and
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31 319 DNA repair (**Supplementary Figure S2**, $P < 0.001$), suggesting that SETD8 up-regulation
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34 320 correlates with changes in signaling pathways involved in MM pathophysiology.
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36 321 Furthermore, SETD8 expression is significantly higher in MM cells from relapsed patients
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39 322 compared to newly diagnosed patients, underlining a potential role of SETD8 in drug
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41 323 resistance (**Supplementary Figure S3**). Altogether, these data reveal that the epigenetic
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44 324 enzyme SETD8 is overexpressed in myeloma and this up-regulation is associated with a
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46 325 poor outcome and deregulation of major signaling pathways in MM patients.
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51 327 **UNC-0379-mediated SETD8 inhibition leads to cell-cycle defects and apoptosis in**
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53 328 **MMCs.** To determine the biological significance of SETD8 up-regulation in MM
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56 329 pathophysiology, the effects of the small-molecule SETD8 inhibitor UNC-0379 were
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58 330 examined in eight different HMCLs representative of the disease. UNC-0379 is a well-
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331 characterized substrate-competitive inhibitor selective for SETD8 [15, 18, 42]. As shown
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2 332 in Figure 2A, UNC-0379 treatment was sufficient to inhibit the growth of all HMCLs in a
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5 333 dose dependent manner with an average half maximal inhibitory concentration (IC₅₀)
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7 334 ranging from 1.25 to 6.3 μM (**Figure 2A**). To determine the molecular mechanisms of this
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10 335 HMCL growth inhibition, the effects of UNC-0379 treatment on SETD8 activity, cell
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12 336 proliferation and survival were examined using immunoblot and flow cytometry assays in
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14 337 XG7 and XG25 MM cell lines, which displayed similar IC₅₀ values for UNC-0379. Analysis
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17 338 of whole cell extracts after 24 hours of treatment showed a strong decrease in H4K20me1,
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19 339 thereby demonstrating the rapid and efficient inhibition of SETD8 activity
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22 340 (**Supplementary Figure S4A**). In the following hours, this SETD8 inhibition was
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24 341 associated with cell-cycle defects, as shown in both cell lines by an accumulation in G1
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26 342 phase and a decrease in DNA replication (S) phase 48 hours after treatment (**Figure 2B**
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29 343 and **Supplementary Figure S4B**). At later time points, these cell cycle defects were
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31 344 followed by the activation of apoptosis, as measured by the appearance of 33% and 26%
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34 345 of annexin-V positive cells in XG7 and XG25 cell lines respectively (**Figure 2B** and
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36 346 **Supplementary Figure S4C**).

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39 347 To demonstrate that SETD8 is indeed required for growth and viability of malignant
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41 348 plasma cells, bone marrow (BM) cells isolated from two healthy donors and from eight
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44 349 MM patients were cultured with recombinant interleukin 6 in presence or not of UNC-0379.
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46 350 Four days after treatment, the percentage of plasma cells was measured by flow
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49 351 cytometry after staining with anti-CD138 and anti-CD38 antibodies. As shown in Figure
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51 352 2C, the viability of normal mature plasma cells remained roughly unaffected by UNC-0379
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53 353 treatment except at the highest dose for one donor. In contrast, the median number of
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56 354 malignant plasma cells in MM patient samples was decreased in a dose-dependent
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58 355 manner with 50% and 63% of reduction with 2.5 μM and 5 μM of UNC-0379 respectively
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356 ($P = 0.001$ and $P < 0.0001$; $N=8$), whereas non-tumoral CD138-negative BM cells
357 displayed less sensitivity, like normal plasma cells (Figure 2D). Consistent with a
358 cytotoxicity of UNC-0379 preferentially in malignant plasma cells, normal plasma cells
359 generated *in vitro* by differentiation of memory B cells remained largely unaffected by
360 SETD8 inhibitor, even at high doses (**Supplementary figure S5**). In the perspective of
361 potential preclinical studies with SETD8 inhibitors, primary 5T33vv murine MM models
362 [25] were also treated with growing concentrations of UNC-0379 for 24h hours before cell
363 viability analysis. As observed with human primary MM cells, UNC-0379 treatment results
364 in a significant reduction of 5T33vv viability in a dose dependent manner (**Supplementary
Figure S6**). Altogether, these results indicate that malignant plasma cells are particularly
addicted to SETD8 activity and that UNC0379 treatment is highly toxic to these tumor
cells, leading rapidly to their growth inhibition and death.

**SETD8 inhibition impairs MM cell proliferation together with activation of p53-target
gene pathways.** SETD8 has been involved in all nuclear processes that use DNA as a
matrix, including a critical role in the regulation of gene expression [8]. In order to gain
insights into the mechanisms contributing to SETD8-mediated MM cell growth inhibition
and death, we performed transcriptome analysis in XG7 and XG25 HMCLs after SETD8
inhibition using RNA sequencing (**Figure 3A**). To identify gene expression alterations
caused by SETD8 inhibition in HMCLs, we isolated total RNAs 18 hours after UNC-0379
treatment or 48 hours after shRNA-induced SETD8 silencing, when H4K20me1 decrease
had not yet triggered DNA replication defects [31, 43]. A common signature of 820 up-
regulated genes and 360 down-regulated genes was found in UNC-0379-treated and
SETD8-depleted cell lines compared to the untreated and shRNA control cell lines (Fold
change > 2 ; $FDR \leq 0.05$) (**Supplementary Figure S7A** and **Supplementary Table 1**).

381 Gene Set Enrichment Analysis (GSEA) identified, as the most down-regulated pathways,
382 genes involved in cell-cycle, stem cells, proliferating plasmablasts and MM proliferating
383 molecular subgroup together with genes repressed upon loss of the histone H3K27
384 methyltransferase EZH2 (**Figures 3B** and **Supplementary Figure S7B**). Conversely and
385 consistent with the presence of a functional p53 in XG7 and XG25 cell lines [41], a
386 significant positive enrichment was found for p53 target genes, including *p21* and
387 *GADD45A* genes, and genes overexpressed in mature BMPCs versus plasmablasts
388 (**Figures 3B** and **Supplementary Figure S7C**). A positive enrichment for genes normally
389 down-regulated by c-MYC, EZH2, DNA methylation or histone deacetylases (HDAC) was
390 also observed (**Figure 3B**), which might suggest some impairment of chromatin silencing
391 pathways upon SETD8 inhibition in MM cells. As shown in figure 3C, immunoblot analysis
392 of UNC-0379-treated XG7 HMCLs confirmed the increased levels of p53 and p21 proteins
393 upon UNC-0379 treatment. However, we did not observe a significant phosphorylation of
394 the histone variant H2A.X (**Figure 3C**), suggesting p53 activation in XG7 MM cells treated
395 with UNC-0379 likely occurs in absence or low level of DNA damage. Altogether, these
396 data indicate that the cytotoxic effects of SETD8 inhibition in p53-proficient HMCLs are
397 associated with activation of the p53 canonical pathway and a mature non-proliferating
398 plasma cell transcriptional signature.

The cytotoxicity of UNC-0379 treatment is not dependent on p53 in malignant plasma cells. Previous studies showed that UNC-0379-induced cell death depends on the activation of p53 in neuroblastoma cancer models (NB), thereby rendering p53-deficient NB cells more resistant to SETD8 inhibition [41]. To determine whether the cytotoxic effects of the pharmacological inhibition of SEDT8 mediated by UNC-0379 were also dependent on p53 activation in MM cells, we compared the UNC-0379 response in p53

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406 wild-type HMCLs (n=7) and p53-deficient HMCLs (n=5) [28, 41] that displayed similar
407 *SETD8* expression levels (**supplementary figure S8A**). Of note, there was no significant
408 correlation between *SETD8* and *TP53* expression in HMCLs (**Supplementary Figure**
409 **S8B**). Although IC₅₀ values for p53-deficient HMCLs following UNC-0379 treatment were
410 more heterogeneous, we found no statistical difference with the group of p53 wild-type
411 HMCLs (**Figure 4A**). We also observed no statistical difference in the IC₅₀ values of UNC-
412 0379 according to the expression levels of p53 in HMCLs, whatever their mutational p53
413 status (**Supplementary Figure S9**). Altogether, these results suggested that the absence
414 of a functional p53 did not alter significantly the sensitivity of malignant plasma cells to
415 the pharmacological inhibition of SETD8 activity. To verify this hypothesis, we examined
416 by immunoblot and flow cytometry analysis the cytotoxic effects of UNC-0379 treatment
417 on p53-proficient XG7 HMCL transduced with high-titer of lentivirus encoding either a p53
418 shRNA or an irrelevant control shRNA. Both cell lines showed relatively similar IC₅₀ values
419 for UNC-0379 (3.7 μM in control shRNA and 4.8 μM in p53 shRNA expressing cells).
420 Immunoblot analysis confirmed the efficient p53 depletion in p53 shRNA XG7 HMCL
421 compared to control cells (**Figure 4B**). Consistent with results in Figure 3C, UNC-0379
422 treatment led to an up-regulation of p53 without detectable DNA damage in shRNA control
423 XG7 cells (**Figure 4B**). In contrast, higher levels of DNA damage and replicative stress
424 were observed in UNC-0379-treated XG7 cells depleted for p53, as evidenced by the
425 increased levels of both phosphorylated histone variant H2A.X and checkpoint protein
426 Chk1 (**Figure 4B**) and by an accumulation of cells in G2/M phase of the cell cycle (**Figure**
427 **4C**). Accordingly, an increase in DNA damage and replicative stress was also observed
428 in XG1 HMCL naturally harboring a mutated inactive p53 (**Supplementary Figure S10A**).
429 In XG1, as well as in XG7 inactive for p53, this was followed by changes in cell cycle
430 distribution (**Supplementary Figure S10B**) and the appearance of a high percentage of

431 apoptotic cells (**Figure 4C** and **Supplementary Figure S10C**). Thus, these results
432 indicated that UNC-0379-induced cytotoxicity in MM cells is independent on p53 status
433 and that a high level of SETD8 likely protects MM cells from DNA damage and excessive
434 replicative stress.

435 **UNC-0379 induces nucleolar stress independently of p53 activation**

437 Nucleolar stress can lead to cell-cycle defects and apoptosis with and without p53[44].
438 Since SETD8 interacts with nucleolar proteins and has been involved in the regulation of
439 nucleoli structure and function[45, 46], we asked whether the cytotoxicity of UNC-0379
440 treatment might be related to nucleolar dysfunction independently of p53 activation in
441 myeloma cells. To address this question, we first examined, by immunofluorescence, the
442 localization of the major nucleolar proteins fibrillarin and nucleolin in control and p53-
443 depleted XG7 cells untreated or treated with 3 μ M of UNC-0379 for 24 hours. Whereas
444 the steady-state levels of nucleolar proteins and the localization of fibrillarin remained
445 largely unaltered in all experimental conditions (**Supplementary figure S11**), a massive
446 delocalization of the nucleolin pool from nucleoli to the nucleoplasm was observed in
447 control and p53-depleted XG7 cells upon UNC-0379 treatment (**Figure 5A**). Nucleolin is
448 required for the transcription of ribosome DNA (rDNA) and alteration of its nucleolar
449 transcriptional function can lead to apoptosis in cancer cells[47]. Therefore, to determine
450 whether nucleolin delocalization upon UNC-0379 is associated with defective nucleolar
451 transcription, cells were pulsed labeled with 5-Ethynyl Uridine (EU) for 5 minutes and
452 nascent RNAs incorporating EU were detected *in situ* by click chemistry. Consistent with
453 nucleoli being the sites of the most active RNA synthesis, short EU pulse labeling resulted
454 in an intense granular staining specifically in nucleoli of untreated control and p53-
455 depleted XG7 cells (**Figure 5B**). Upon UNC-0379 treatment, this intense nucleolar EU

1 456 staining was almost abolished in both control and p53 depleted cells, indicating a strong
2 457 decrease of rDNA transcription independently of p53 activation. Taken together, these
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4 458 results show that, prior to p53 activation, treatment with UNC-0379 leads to specific
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7 459 nucleolar alterations characterized by massive nucleolin delocalization and a strong
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10 460 decrease in nucleolar RNA synthesis, thus providing an explanation for the cytotoxic
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12 461 effects of this SETD8 inhibitory compound on malignant plasma cells regardless of p53
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14 462 status.

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18 463 **UNC-0379-mediated inhibition of SETD8 synergizes with melphalan.** The results
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20 464 presented above indicate that the pharmacological inhibition of SETD8 by UNC-0379
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23 465 could constitute a promising strategy to improve MM treatment by genotoxic agents. To
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25 466 gain further insights into this possibility, we investigated whether SETD8 inhibition could
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28 467 enhance the cytotoxicity of melphalan and overcome resistance to this alkylating agent
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30 468 widely used in MM treatment. To this end, we first measured the viability of XG7 and XG1
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33 469 cells continuously treated for 4 days with different concentrations of each compound alone
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35 470 or in combination. The synergy score of each combination dose was then evaluated using
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38 471 bliss model. As shown in Figures 6A and 6B, we observed a significant synergism of the
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40 472 combination compared to the individual treatments in XG7 cell line and, to a lesser extent,
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42 473 in XG1 for the highest melphalan doses (**Figures 6A and 6B**). Importantly, the higher
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45 474 sensitivity to melphalan was also observed in XG7 cells depleted for SETD8 after lentiviral
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47 475 shRNA expression (Supplementary figure S12A-C) and, consistent with results in Figure
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50 476 4C, XG7 cells depleted for p53 displayed a similar sensitivity to the combination than the
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52 477 shRNA-control XG7 cells (**Supplementary Figure S12D**). These data demonstrate that
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55 478 the lethal synergy between UNC-0379 and melphalan is indeed related to SETD8
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57 479 inhibition and does not depend on p53 activation. As shown in **Figure 6C**, the lethality
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60 480 induced by the co-treatment of melphalan and UNC-0379 was preceded by high levels of
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481 DNA breaks, as measured by the significant increase in the number of DNA damage-
482 induced 53BP1 foci in combined versus single agent therapy, in both XG7 and XG1 cell
483 lines. This was also observed in melphalan-resistant XG7 clones [29] (**Figure 6D**), which
484 coincided with higher levels of γ H2AX signal upon melphalan/UNC-0379 combination
485 (**Supplementary Figure S13**). At later time points, we observed a significant increase in
486 apoptotic cell death as measured by annexin V staining (**Figure 6E**). Altogether, these
487 results indicate that UNC-0379-mediated SETD8 inhibition enhances the cytotoxic effects
488 of melphalan in MM cells in a p53 independent manner. This demonstrates the potential
489 therapeutic interest to target SETD8-mediated lysine methylation in MM regardless of p53
490 status (**Figure 7**).

DISCUSSION

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496 This study unveils for the first time a role of the histone H4K20 mono-
497 methyltransferase SETD8 in MM pathophysiology. We have shown that elevated levels
498 of SETD8 are associated with a poor prognosis and correlate with the deregulation of
499 regulatory nodes involved in MM, including IRF4, MYC/MAX, MAPK and DNA repair
500 pathways (**Figure 1 and Supplementary Figure S2**). Moreover, patients displaying
501 higher SETD8 expression are associated with specific molecular features, such as
502 increased copy of Chr1q21 or a high GPI index (**Supplementary Figure S1**). Consistent
503 with this, primary MM cells are particularly addicted to SETD8 activity and the recently
504 developed small-molecule inhibitor of SETD8, UNC-0379, demonstrated a higher toxicity
505 in MM cells compared to normal cells from the bone marrow microenvironment and

506 normal plasma cells (**Figure 2**). From a mechanistic point of view, our RNA-seq results
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2 507 show that genetic or pharmacological inhibition of SETD8 in MM cell lines results in the
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4 508 activation of a mature non-proliferating plasma cell signature and of the p53 canonical
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7 509 pathway (**Figure 3**). However, UNC-0379-induced cytotoxicity does not necessarily
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10 510 require p53 activation as p53 wild-type and deficient MM cells display similar sensitivity
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12 511 to SETD8 inhibition (**Figures 3 and 4**). Indeed, we provide evidence that UNC-0379 is an
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14 512 inhibitor of nucleolar RNA synthesis independently of p53 activation (**Figure 5**). Finally,
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17 513 we have shown that UNC-0379 treatment leads to a significant lethal synergy with the
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19 514 DNA-damaging agent melphalan and can overcome the resistance associated with this
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22 515 cytotoxic drug in both p53 wild-type and deficient MM cells (**Figure 6**). Altogether, these
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24 516 results provide evidence for SETD8 inhibition as a potential novel therapeutic strategy in
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27 517 MM independently from the mutational p53 status of these tumors (**Figure 7**).

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29 518 An up-regulation of SETD8 is not specific to MM, as it has also been observed in
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31 519 different types of solid tumors [11], such as papillary thyroid cancer [16], breast carcinoma
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34 520 [14, 48], and childhood tumors of the nervous system [15, 18]. However, the mechanisms
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36 521 that contribute to elevated levels of SETD8 in cancer still remained unclear. In
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39 522 neuroblastoma, a higher level of SETD8 could be due in part to DNA copy-number gains
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41 523 at chr12q24, the region that encompasses *SETD8* encoding gene²⁶. Another non-
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44 524 exclusive mechanism is related to the deregulation of oncogenic c-MYC pathway, since
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46 525 *SETD8* encoding gene has been found as a transcriptional target of c-MYC[49] and
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49 526 functionally required to mediate MYC-induced cell growth [15]. It is widely established that
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51 527 c-MYC is a key regulator in MM with deregulations related to translocations, gains and
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53 528 amplification, mutations in RAS genes and MYC transcription or translation activation [50].
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56 529 Interestingly, while chr12q24 gains are not present in myeloma, we identified here a
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58 530 significant enrichment of c-MYC/MAX target genes in MM patients characterized by high
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531 *SETD8* expression, thereby supporting a potential role of this oncogenic pathway in
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2 532 *SETD8* deregulation. Furthermore, *SETD8* depletion or inhibition results in up-regulation
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5 533 of genes repressed upon c-MYC expression (**Figure 3C**) suggesting that *SETD8* might
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7 534 also participate in deregulation of c-MYC functions in MM.

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10 535 A striking result of our study is that the up-regulation of *SETD8* in malignant plasma
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12 536 cells is not associated with visible changes in the global levels of the histone H4K20 mono-
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14 537 methylation (H4K20me1), the primary target of *SETD8* [8], although we cannot rule out
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17 538 that some local changes can occur at specific loci. This result is independent from cell-
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19 539 cycle progression, since changes in the levels of *SETD8* do not correlate with cell
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22 540 proliferation (**Figure 1B and Supplementary Figure S2**). One hypothesis is that the
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24 541 overexpression of the H4K20me1-specific demethylase PHF8, observed in many cancers
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27 542 including hematopoietic malignancies [51, 52], could attenuate the impact of *SETD8* up-
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29 543 regulation on histone H4K20 [53]. Nevertheless, H4K20me1 is critical in the maintenance
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32 544 of genome integrity [8] and its decrease upon UNC-0379 treatment would most likely
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34 545 contribute to the cytotoxic effects of this *SETD8* inhibitor in myeloma cells.

36 546 Recent studies have suggested that the role of *SETD8* in cancer might also involve
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39 547 the methylation of other substrates than histone H4. Thus, Takawa et al. proposed that
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41 548 *SETD8* can methylate the proliferating cell nuclear antigen PCNA and thus favor HeLa
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44 549 cell proliferation [11]; but this result was never further confirmed in other cell types.
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46 550 Additionally, *SETD8* can induce the mono-methylation of the tumor suppressor p53 at
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49 551 lysine 382 (p53K382me1), which attenuates its pro-apoptotic and growth arrest functions
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51 552 [12, 18]. Hence, in neuroblastoma, inhibition of *SETD8* by UNC-0379 leads to cell death
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54 553 in a p53-dependent manner and p53K382me1 is important for this phenotype [18]. Our
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56 554 RNA-seq and functional studies in MM cells show that the genetic or pharmacological
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58 555 inhibition of *SETD8* leads to the activation of p53 conventional pathways, which correlates
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556 with an increased in p53 and p21 protein levels, and cell cycle arrest followed by cell
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2 557 death. However, in contrast to neuroblastoma [18], UNC-0379-induced cytotoxicity in MM
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4 558 cells is not necessarily dependent on p53 activation and, despite several attempts, we
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7 559 were unable to detect p53K382me1. Since the appearance of nucleolar stress or DNA
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10 560 damage is sufficient to activate p53 functions [54, 55] and occurs independently of p53
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12 561 upon UNC-0379 (**Figures 4 and 5**), we propose that the activation of p53 upon SETD8
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14 562 inhibition is mainly caused by these stress signals rather than the potential loss of SETD8-
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17 563 induced p53 methylation in MM cells. Since nucleolar dysfunction can lead to apoptosis
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19 564 without p53[44], the induction of these cellular stress prior to p53 activation provides an
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22 565 explanation of the cell-growth inhibition and apoptotic effects of UNC-0379 in p53-
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24 566 deficient cells. While the appearance of DNA damage might be related to SETD8
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27 567 functions in chromatin structure [50], the reasons of nucleolar alterations upon UNC-0379-
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29 568 mediated SETD8 inhibition remain unclear. Future work will be necessary to unravel the
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32 569 SETD8 nucleolar functions, which could be related to the apparent ability of SETD8 to
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34 570 interact directly with ribosomal proteins or regulate their expression[45, 46]. Altogether,
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37 571 our findings are consistent with a model in which UNC-0379-mediated cell death is
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39 572 triggered by multiple cellular stress signals followed by p53 activation in p53-proficient
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41 573 MM cells and deadly cell-cycle progression in absence of p53, thereby rendering multiple
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44 574 myeloma sensitive to SETD8 inhibition whatever the status of p53.

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46 575 In spite of effective therapeutic protocols developed in MM, drug resistance
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49 576 remains a major concern. In this regard, we report here that high *SETD8* expression is
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51 577 associated with a poor prognosis in patients treated by high-dose of melphalan and
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53 578 autologous stem cell transplantation (**Figure 1**). *SETD8* expression is also significantly
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56 579 up-regulated in patients at relapse compared to newly diagnosed patients
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58 580 (**Supplementary Figure S3**). In agreement with this, UNC-0379 treatment potentiates the
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581 cytotoxicity of melphalan and overcomes melphalan drug resistance in MM cells,
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2 582 underlining the interest to target SETD8 to improve the treatment of MM patients.
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5 583 Deletion of the short arm of chromosome 17 (del 17p) is associated with a poor
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7 584 outcome in MM independently of treatment regimen [56–60]. Interestingly, MM cell toxicity
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9 585 mediated by SETD8 inhibitor is mainly p53-independent. The frequency of events
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11 586 targeting p53 (del 17p, *TP53* mutation or double hits) increases during the progression of
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13 587 MM and consecutive relapses underlining a selection of cells harboring *TP53*
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15 588 abnormalities in association with resistance to treatment. *TP53* bi-allelic events are also
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17 589 associated with a dramatic impact on MM patients' survival after relapse [61]. Therapies
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19 590 inducing significant toxicity of p53 defective-MM cells are needed. Our results
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21 591 demonstrate the therapeutic interest of SETD8 inhibitor to target p53 deficient MM cells
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23 592 by increasing replicative stress and DNA breaks. Accordingly, the use of this epigenetic
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25 593 drug in combination with cytotoxic agents, such as melphalan, could be of clinical interest,
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27 594 notably in newly diagnosed patients presenting del17p and/or *SETD8* overexpression and
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29 595 eligible to high dose melphalan and ASCT (**Figure 6**). Thus, SETD8 inhibition appears of
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31 596 therapeutic interest to overcome drug resistance and improve the treatment of MM
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33 597 patients at relapse independently of the p53 status.
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41 598 **Conclusion**

42 599
43 600 Our data reveal that the up-regulation of the histone H4K20 mono-methyltransferase
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45 601 SETD8 is associated with a poor prognosis and the deregulation of major signaling
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47 602 pathways in multiple myeloma patients. The inhibition of this enzyme leads to deadly
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49 603 cellular stress in multiple myeloma cells and a lethal synergy was identified when SETD8
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51 604 inhibition is combined with melphalan alkylating agent. Altogether, these results
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53 605 demonstrate that SETD8 is a novel epigenetic target in multiple myeloma and that its
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606 pharmacological inhibition could be beneficial in high-risk MM patients whatever their p53

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FIGURE LEGENDS

Figure 1. SETD8 expression is a prognosis value in MM. (A) SETD8 gene expression in BMPCs, patients' MMCs and HMCLs. Data are MAS5-normalized Affymetrix signals (U133 plus 2.0 microarrays). Statistical difference was assayed using a student t-test. **(B)** Immunoblot analysis of indicated proteins in total lysates from normal plasma cells, MMCs and HMCLs (XG1, XG7, XG25). β -actin and histone H4 were used as loading controls. **(C)** Overall survival and of newly diagnosed MM patients (UAMS-TT2, N=345; and UAMS-TT3, N=158) who's MMCs highly expressed *SETD8* gene. The splitting of the patients into two groups according to SETD8 expression in MMCs was done using the Maxstat algorithm.

Figure 2. SETD8 inhibitor UNC-0379 is highly toxic to malignant plasma cells. (A) Graphical representation of HMCLs viability upon exposure to various concentrations of UNC-0379. Color scale represents cell viability, from the highest (blue) to the lowest (red) values. The IC50 value of each tested HMCL is indicated. Data are mean values \pm standard deviation (SD) of five experiments determined on sextuplet culture wells. **(B)** The first bar graph results from the quantitation of cellcycle distribution of control (untreated) and UNC-0379-treated XG7 and XG25 HMCLs 48 hours after treatment. After short-pulse of BrdU incorporation, cellcycle was analyzed by FACS using DAPI and anti-BrdU antibody. Second bar graph represents the results from the quantitation of apoptosis in control and UNC-0379-treated XG7 and XG25 HMCLs by flow cytometry with AnnexinV-PE staining at 96h after UNC-0379 treatment. Data shown are mean values \pm SD of 4 separate experiments. Statistical analysis was done with a paired t-test. (*)

635 indicates a significant difference compared to control cells using a Wilcoxon test for pairs
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2 636 ($P \leq 0.05$). (C) Percentage of normal mature plasma cells (CD38+ CD138+) from two
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4 637 different donors and quantified by FACS after *in vitro* treatment with increasing
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6 638 concentrations of UNC-0379 or the vehicle DMSO at the highest concentration (MOCK)
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9 639 for 4 days. Samples were treated and analyzed in duplicates. (D) Percentage of *in vitro*
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11 640 cultivated primary MM cells (CD138+ tumor cells) and bone marrow microenvironment
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13 641 (CD138- non-malignant cells) upon increasing concentrations of UNC-0379 treatment for
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15 642 4 days. Data shown are mean values of 8 patient samples. (*) indicates a significant
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17 643 difference compared to control cells using a Wilcoxon test for pairs ($P \leq 0.05$).
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24 645 **Figure 3. Gene expression changes in HMCLs upon genetic or pharmacological**
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26 646 **inhibition of SETD8. (A)** Diagram of the experimental plan. **(B)** Molecular signatures of
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28 647 UNC-0379 and shSETD8 downregulated (blue bar plot) and up-regulated (red bar plot)
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30 648 genes compared to control were investigated using GSEA Database (all curated gene
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32 649 sets), and relevant pathways are presented (FDR q-value ≤ 0.05). **(C)** Immunoblot
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34 650 analysis of indicated proteins in total lysates from UNC-0379-treated or untreated XG7
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36 651 HMCL. β -actin and H2A.X were used as loading controls.
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43 653 **Figure 4. UNC-0379 toxicity is independent of p53. (A)** Comparison of UNC-0379 IC₅₀
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45 654 (μ M) according to HMCLs *TP53* status. **(B)** Immunoblot analysis of indicated proteins in
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47 655 total lysates from UNC-0379-treated (5 μ M) or untreated XG7-shControl and XG7-shp53
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49 656 HMCLs. β -actin and H2A.X were used as loading controls. **(C)** First bar plot represents
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51 657 cell cycle of control and 48h UNC-0379-treated (5 μ M) XG7-shp53 analyzed by flow
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53 658 cytometry using DAPI, BrdU incorporation and labelling with an anti-BrdU antibody.
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55 659 Results are representative of three independent experiments. Second bar plot represents
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660 apoptosis induction in control and UNC-0379-treated (5 μ M) XG7-shControl and XG7-
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2 661 shp53 analyzed by AnnexinV-PE staining and flow cytometry after 96h treatment. Data
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5 662 shown are mean values \pm SD of 4 separate experiments. Statistical analysis was done
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7 663 with a paired t-test. * indicates a significant difference compared to control cells using a
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10 664 Wilcoxon test for pairs ($P \leq 0.05$).

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14 666 **Figure 5: UNC-0379 treatment causes similar nucleolar alterations in wild-type and**
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17 667 **p53 depleted-myeloma cells. (A)** immunofluorescence microscopy of nucleolin
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19 668 localization and DNA (DAPI staining) in XG7 cells depleted or not for p53 and treated with
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22 669 3 μ M of UNC-0379 or the vehicle DMSO (mock) for 24 hours. Scale bar: 10 μ m. Visual
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24 670 quantification of percentage of cells with nucleolin diffusion out of the nucleolus. A
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27 671 minimum of 300 cells were quantified per condition. N = 3. Statistical significance between
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29 672 conditions was assessed using Student paired t-test (*: pvalue<0.05, ** pvalue<0.01, ns:
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32 673 not significant). **(B)** Analysis of RNA synthesis by 5 minutes 5-Ethynyl Uridine (EU)
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34 674 pulse-labeling in XG7 cells depleted or not for p53 and treated with 3 μ M of UNC-0379 or
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37 675 the vehicle DMSO (mock) for 24 hours. Scale bar: 10 μ m. EU intensity was quantified
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39 676 using CellProfiler "Human cell" pipeline. A minimum of 200 cells were quantified per
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42 677 condition. Graph shows the quantification of one representative experiment of 3.

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46 679 **Figure 6: UNC-0379 treatment sensitizes HMCLs to Melphalan-induced DNA**
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49 680 **damage. (A)** Dose-response matrix inhibition and landscape representation for
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52 681 experimentally measured drug synergy in XG7 cells treated with increased concentration
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54 682 of the combination of melphalan and SETD8 inhibitor (UNC-0379). Synergy scores are
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56 683 displayed using a continuous pseudo-color scale ranging from dark-green=antagonistic
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59 684 to dark-red=synergistic **(B)** Landscape and 3-D matrix representation for experimentally

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685 measured drug synergy in XG1 cells. **(C)** Number of 53BP1 foci in XG7 and XG1 HMCLs,
686 treated with melphalan (3 μ M), UNC-0379 (3 μ M) or the combination of the two drugs for
687 6h or 24h as indicated. Number of foci per cell was quantified using ImageJ software
688 (mean number of cells counted: 300). Statistical significance between conditions was
689 assessed using Student paired t-test (*: pvalue<0.05). **(D)** Measure of 53BP1 foci in
690 melphalan-resistant XG7 cells treated with melphalan (15 μ M), UNC-0379 (3 μ M) or the
691 combination of the two drugs for 24h. Number of foci per cell was quantified using ImageJ
692 software (mean number of cells counted: 300). Statistical significance between conditions
693 was assessed using Student paired t-test (*: pvalue<0.05). **(E)** Measure of AnnexinV-
694 positive cells in the same drug concentrations as in D. AnnexinV-PE staining was
695 analyzed by flow cytometry 96h after drug treatment. Statistical significance between
696 conditions was assessed using Student paired t-test (*: pvalue<0.05).

Figure 7: SETD8 inhibition is of therapeutic interest in MM independently of p53 status and could overcome melphalan resistance. High *SETD8* expression is associated with a poor outcome in MM and represent a therapeutic target independently of p53 status. In p53 WT patients SETD8 inhibition results in MM cell cytotoxicity mediated by p53 pathway activation. In p53 deficient MM cells, SETD8 inhibition increases replicative stress in association with MM cell death. Furthermore, SETD8 inhibition overcomes melphalan resistance in MM.

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718 **Author contributions**

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721 EJ and JM designed the project, supervised the research, and wrote the paper. LH, FI,
722 EJ and SO designed, performed the research and analyzed the data. LH and SO
723 contributed to paper writing. OKC, CG, CB participated to the research. LV and GC
724 participated to clinical data analysis. AM and JJ contributed to design and production of
725 SETD8 inhibitor. ED and EDB contributed to experiments with primary murine models.

727 **Conflict of interest**

728 The authors declare that they have no competing interests.

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Supplementary Table 1: Genes regulated by SETD8 in p53wt myeloma cell lines

name	description	chromosome	baseMean	log2FoldChar	padj	XG7_Control	XG25_Contro	XG7_UNC037	XG25_UNC0379	XG7_shContr	XG25_shCont	XG7_shSETD8	XG25_shSETD8
ENSG000001 MYCT1	myc target 1 [Source:HGNC Symbol;Acc:HGNC:23172]	6	470.004813	-2.0772084	6.35E-29	822.86	551.59	127.78	158.98	984.71	783.06	186.67	144.39
ENSG000001 TNIK	TRAF2 and NCK interacting kinase [Source:HGNC Symbol;Acc:HGNC:30765]	3	335.124717	-1.6301799	4.86E-20	473.05	473.06	149.07	122.45	635.64	501.35	147.14	179.24
ENSG000001 SAPCD2	suppressor APC domain containing 2 [Source:HGNC Symbol;Acc:HGNC:28055]	9	2976.06009	-1.5634575	1.24E-26	2799.44	7234.1	690.6	2378.85	2315.61	5727.78	902.6	1759.51
ENSG000001 CXCR4	chemokine (C-X-C motif) receptor 4 [Source:HGNC Symbol;Acc:HGNC:2561]	2	592.380667	-1.4993983	2.09E-12	1507.32	683.1	398.54	280.45	884.7	551.96	329.41	103.56
ENSG000000 SLC9A3R2	solute carrier family 9, subfamily A (NHE3, cation proton antiporter 3), member 3 regulator 2 [Source:HGNC Symbol;Acc:HGNC:11076]	16	645.482238	-1.4577266	8.42E-08	590.6	1278.22	250.48	544.1	777.96	1394.22	146.04	182.22
ENSG000001 FBXL16	F-box and leucine-rich repeat protein 16 [Source:HGNC Symbol;Acc:HGNC:14150]	16	107.326929	-1.329717	3.49E-09	107.12	196.79	36.51	65.17	128.86	206.27	36.24	81.65
ENSG000001 PBX1	pre-B-cell leukemia homeobox 1 [Source:HGNC Symbol;Acc:HGNC:8632]	1	46.0772904	-1.3048634	5.13E-06	55.93	70.01	17.24	25.67	80.78	78.31	19.76	20.91
ENSG000002 SNORD17	small nucleolar RNA, C/D box 17 [Source:HGNC Symbol;Acc:HGNC:32713]	20	506.313451	-1.2487099	7.97E-15	671.18	755.96	281.92	321.92	705.84	767.78	216.32	329.6
ENSG000001 C14orf37	chromosome 14 open reading frame 37 [Source:HGNC Symbol;Acc:HGNC:19846]	14	98.3677876	-1.2284139	3.25E-06	135.56	104.07	38.54	22.71	198.1	142.29	77.96	67.71
ENSG000000 WNT8B	wingless-type MMTV integration site family, member 8B [Source:HGNC Symbol;Acc:HGNC:12789]	10	54.5849478	-1.2143173	1.73E-05	70.15	100.29	21.3	24.69	70.2	87.86	26.35	35.85
ENSG000001 KLF15	Kruppel-like factor 15 [Source:HGNC Symbol;Acc:HGNC:14536]	3	1281.56816	-1.1917397	4.39E-07	1997.43	1489.21	886.33	323.89	2390.61	1354.12	1396.72	414.24
ENSG000001 THRA	thyroid hormone receptor, alpha [Source:HGNC Symbol;Acc:HGNC:11796]	17	830.15798	-1.1837178	1.57E-24	966.01	1469.34	395.5	637.91	910.66	1310.19	402.98	548.66
ENSG000001 MYB	v-myb avian myeloblastosis viral oncogene homolog [Source:HGNC Symbol;Acc:HGNC:7545]	6	2476.37062	-1.1655856	1.88E-10	3604.29	4224.46	1601.27	2404.52	2956.05	3041.51	1039.85	939
ENSG000001 ST6GALNAC3	ST6 (alpha-N-acetylneuraminy)l-2,3-beta-galactosyl-1,3)-N-acetylglucosaminide alpha-2,6-sialyltransferase 3 [Source:HGNC Symbol;Acc:HGNC:19343]	1	69.6525547	-1.1399998	1.19E-05	121.34	65.28	49.69	28.64	147.13	71.62	51.61	21.91
ENSG000000 ARG2	arginase 2 [Source:HGNC Symbol;Acc:HGNC:664]	14	229.25385	-1.1324358	1.10E-07	348.86	229.91	141.97	66.16	367.34	342.83	196.55	140.4
ENSG000001 PLK1	polo-like kinase 1 [Source:HGNC Symbol;Acc:HGNC:9077]	16	8077.8006	-1.1315618	2.61E-26	11616.78	13231.61	4956.94	6650.71	8972.01	10781.36	3878.31	4534.69
ENSG000001 RNF150	ring finger protein 150 [Source:HGNC Symbol;Acc:HGNC:23138]	4	101.078156	-1.1303241	1.29E-05	118.5	94.61	48.68	44.44	222.14	155.66	54.9	69.7
ENSG000001 BCL11A	B-cell CLL/lymphoma 11A (zinc finger protein) [Source:HGNC Symbol;Acc:HGNC:13221]	2	86.9996793	-1.1198638	0.00030924	83.42	140.03	32.45	22.71	156.75	134.65	91.14	34.85
ENSG000001 RUNDC3B	RUN domain containing 3B [Source:HGNC Symbol;Acc:HGNC:30286]	7	116.849491	-1.117064	3.89E-07	151.68	158.95	57.8	62.21	155.78	196.72	77.96	73.69
ENSG000001 CDH2	cadherin 2, type 1, N-cadherin (neuronal) [Source:HGNC Symbol;Acc:HGNC:1759]	18	402.116368	-1.1167466	6.38E-08	945.16	565.78	306.26	194.53	497.16	283.62	290.98	133.43
ENSG000001 ARHGAP29	Rho GTPase activating protein 29 [Source:HGNC Symbol;Acc:HGNC:30207]	1	18.7673923	-1.1109556	0.00128923	16.12	35.01	3.04	8.89	23.08	54.43	6.59	2.99
ENSG000001 FLNB	filamin B, beta [Source:HGNC Symbol;Acc:HGNC:3755]	3	1246.09414	-1.0961266	4.12E-05	1448.54	1850.63	328.57	437.46	1737.67	1975.79	1020.09	1170.02
ENSG000001 EFNA3	ephrin-A3 [Source:HGNC Symbol;Acc:HGNC:3223]	1	216.97817	-1.0660094	5.56E-05	253.12	389.8	84.17	90.85	269.26	321.82	162.51	164.3
ENSG000001 CDC20	cell division cycle 20 [Source:HGNC Symbol;Acc:HGNC:1723]	1	6515.63766	-1.0569801	1.79E-24	10446.95	10834.12	4667.92	4757.7	7185.3	7103.86	3672.97	3456.28
ENSG000000 TRIP13	thyroid hormone receptor interactor 13 [Source:HGNC Symbol;Acc:HGNC:12307]	5	2958.0372	-1.056581	4.43E-07	4664.16	4575.48	2830.36	2506.23	3413.79	3474.1	1106.83	1093.34

ENSG000001	GSR	glutathione reductase [Source:HGNC Symbol;Acc:HGNC:4623]	8	797.128414	-1.0487558	2.74E-15	1280.75	1325.53	656.13	639.89	796.23	931.07	370.04	377.39
ENSG000001	RAB3A	RAB3A, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:9777]	19	385.519044	-1.0471124	3.82E-05	477.79	526.99	111.55	179.72	573.13	564.37	345.89	304.7
ENSG000001	MRAP2	melanocortin 2 receptor accessory protein 2 [Source:HGNC Symbol;Acc:HGNC:21232]	6	30.9887187	-1.0312478	0.00248562	66.36	55.82	16.23	8.89	35.58	33.42	18.67	12.94
ENSG000002	HSPA1A	heat shock 70kDa protein 1A [Source:HGNC Symbol;Acc:HGNC:5232]	6	14929.6974	-1.029148	1.73E-12	26719.36	22983.35	9577.2	11838.95	16128.47	15817.76	8190.34	8182.16
ENSG000002	CDC20P1	cell division cycle 20 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:29487]	9	454.057487	-1.0224125	5.93E-14	718.58	762.58	334.65	352.53	506.78	479.38	234.98	242.97
ENSG000002	HSPA1B	heat shock 70kDa protein 1B [Source:HGNC Symbol;Acc:HGNC:5233]	6	10718.5866	-1.0121263	6.52E-12	19668.14	16451.28	7109.88	8540.75	11199.15	11144.24	5802.09	5833.16
ENSG000001	DNMBP	dynamitin binding protein [Source:HGNC Symbol;Acc:HGNC:30373]	10	1159.93944	-0.9830533	8.01E-16	1552.82	1818.46	723.06	994.4	1101.07	1742.78	552.32	794.62
ENSG000001	KIF20A	kinesin family member 20A [Source:HGNC Symbol;Acc:HGNC:9787]	5	3562.72148	-0.9703921	1.09E-09	5340.08	5831.94	2051.53	2573.38	3695.55	4378.44	2208.18	2422.68
ENSG000001	GNAI1	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 1 [Source:HGNC Symbol;Acc:HGNC:4384]	7	48.7886954	-0.968013	0.00167457	60.67	69.07	24.34	20.74	59.62	89.77	36.24	29.87
ENSG000001	PIK3R5	phosphoinositide-3-kinase, regulatory subunit 5 [Source:HGNC Symbol;Acc:HGNC:30035]	17	289.991627	-0.9657414	0.00247109	1170.78	11.35	295.1	7.9	538.51	8.59	287.69	0
ENSG000001	SLPI	secretory leukocyte peptidase inhibitor [Source:HGNC Symbol;Acc:HGNC:11092]	20	95.669511	-0.9655863	0.0010969	108.07	17.98	53.75	6.91	372.15	66.85	98.82	40.83
ENSG000001	FAM102B	family with sequence similarity 102, member B [Source:HGNC Symbol;Acc:HGNC:27637]	1	226.349661	-0.960181	0.0006222	312.84	325.47	183.55	197.5	276.95	335.19	107.61	71.69
ENSG000001	SUSD4	sushi domain containing 4 [Source:HGNC Symbol;Acc:HGNC:25470]	1	34.9308645	-0.9552226	0.00361701	28.44	65.28	9.13	16.79	55.77	53.48	29.65	20.91
ENSG000001	NEUROD4	neuronal differentiation 4 [Source:HGNC Symbol;Acc:HGNC:13802]	12	23.0213632	-0.9530498	0.00679054	40.76	49.2	5.07	17.77	23.08	28.65	7.69	11.95
ENSG000001	PRR15	proline rich 15 [Source:HGNC Symbol;Acc:HGNC:22310]	7	77.3430814	-0.9494305	0.00142616	178.22	65.28	43.61	28.64	125.01	72.58	62.59	42.82
ENSG000001	SIPA1L2	signal-induced proliferation-associated 1 like 2 [Source:HGNC Symbol;Acc:HGNC:23800]	1	779.763465	-0.9403289	1.25E-05	816.23	1065.34	512.12	660.63	844.31	1483.03	278.9	577.54
ENSG000002	ARHGAP19	Rho GTPase activating protein 19 [Source:HGNC Symbol;Acc:HGNC:23724]	10	1992.19149	-0.9345192	1.29E-09	2287.52	2803.38	1295.01	1690.57	2564.67	2939.33	1123.3	1233.75
ENSG000002	FBXW4P1	F-box and WD repeat domain containing 4 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:13609]	22	91.5156555	-0.9323486	0.00061761	88.16	104.07	55.78	46.41	138.47	178.58	65.88	54.77
ENSG000001	HK2	hexokinase 2 [Source:HGNC Symbol;Acc:HGNC:4923]	2	10169.8905	-0.9222028	1.13E-11	14572.64	14052.85	6963.85	6101.66	12573.32	12636.82	7755.52	6702.46
ENSG000001	MAP2K6	mitogen-activated protein kinase kinase 6 [Source:HGNC Symbol;Acc:HGNC:6846]	17	34.6435537	-0.9219371	0.00548654	43.61	62.44	25.35	24.69	50.97	42.97	13.18	13.94
ENSG000001	ATP1A3	ATPase, Na ⁺ /K ⁺ transporting, alpha 3 polypeptide [Source:HGNC Symbol;Acc:HGNC:801]	19	2199.1031	-0.9193865	0.00041685	2301.74	3878.18	720.01	1088.21	2620.44	3075.89	1891.94	2016.41
ENSG000000	MATK	megakaryocyte-associated tyrosine kinase [Source:HGNC Symbol;Acc:HGNC:6906]	19	463.317619	-0.9112315	0.00444611	171.59	1289.57	33.47	259.71	255.79	910.07	199.84	586.5
ENSG000001	DOK5	docking protein 5 [Source:HGNC Symbol;Acc:HGNC:16173]	20	1332.16662	-0.9080956	0.00022944	2612.69	534.56	1625.61	400.92	3614.77	551	1126.6	191.19
ENSG000000	DEPDC1	DEP domain containing 1 [Source:HGNC Symbol;Acc:HGNC:22949]	1	1484.31832	-0.9027547	1.76E-14	2218.32	1843.06	1173.32	950.95	1805.94	1925.17	856.48	1101.31
ENSG000001	ALDH5A1	aldehyde dehydrogenase 5 family, member A1 [Source:HGNC Symbol;Acc:HGNC:408]	6	3206.32008	-0.9027473	4.88E-11	4372.17	5135.59	2510.92	3056.26	3361.86	3900.01	1516.41	1797.35

ENSG000000	TFAP4		transcription factor AP-4 (activating enhancer binding protein 4) [Source:HGNC Symbol;Acc:HGNC:11745]	16	1500.32298	-0.8941881	7.48E-14	2074.22	2568.74	1024.24	1254.1	1430.91	1825.86	836.71	987.79
ENSG000001	ADAMTS1		ADAM metalloproteinase with thrombospondin type 1 motif, 1 [Source:HGNC Symbol;Acc:HGNC:217]	21	1057.48194	-0.8818022	1.33E-09	1697.87	1206.31	743.34	607.3	1623.23	1023.7	980.56	577.54
ENSG000001	CACYBP		calyculin binding protein [Source:HGNC Symbol;Acc:HGNC:30423]	1	17835.9407	-0.8768749	5.70E-16	27707.17	24824.52	15476.24	14442.94	21078.94	19064.58	10921.19	9171.94
ENSG000001	FGFBP3		fibroblast growth factor binding protein 3 [Source:HGNC Symbol;Acc:HGNC:23428]	10	64.2193827	-0.8739392	0.00136725	95.75	67.18	39.55	31.6	119.24	67.8	53.8	38.83
ENSG000001	CENPF		centromere protein F, 350/400kDa [Source:HGNC Symbol;Acc:HGNC:1857]	1	8511.72812	-0.871588	3.30E-18	9151.04	13649.8	4701.39	7951.22	8033.46	13298.6	4141.84	7166.48
ENSG000001	DOCK4		dedicator of cytokinesis 4 [Source:HGNC Symbol;Acc:HGNC:19192]	7	861.530385	-0.8673157	1.96E-09	842.77	1185.5	388.4	574.72	1040.48	1410.46	599.53	850.38
ENSG000001	SETD8		SET domain containing (lysine methyltransferase) 8 [Source:HGNC Symbol;Acc:HGNC:29489]	12	2145.29659	-0.8661355	0.00373377	3107.54	2984.09	2412.55	2101.37	2507.93	2764.57	639.06	645.25
ENSG000001	FZD4		frizzled class receptor 4 [Source:HGNC Symbol;Acc:HGNC:4042]	11	285.606518	-0.8661338	0.00024311	258.8	310.33	147.05	216.26	408.69	551.96	132.86	258.9
ENSG000001	EPHB3		EPH receptor B3 [Source:HGNC Symbol;Acc:HGNC:3394]	3	24.9827559	-0.8622221	0.01606774	9.48	52.98	2.03	20.74	30.77	53.48	5.49	24.89
ENSG000001	CACYBPP2		calyculin binding protein pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:45123]	2	1406.79165	-0.8591881	1.95E-13	2133.95	1935.78	1208.81	1103.02	1688.62	1535.56	893.81	754.79
ENSG000001	MLF1		myeloid leukemia factor 1 [Source:HGNC Symbol;Acc:HGNC:7125]	3	423.581098	-0.8556271	1.21E-07	532.78	526.99	297.13	237.98	620.25	532.86	314.04	326.61
ENSG000000	TSR3		TSR3, 20S rRNA accumulation, homolog (S, cerevisiae) [Source:HGNC Symbol;Acc:HGNC:14175]	16	1129.20004	-0.8538262	0.00032133	1624.87	1413.52	1095.23	1004.27	1595.34	1284.4	558.91	457.05
ENSG000000	ASPM		asp (abnormal spindle) homolog, microcephaly associated (Drosophila) [Source:HGNC Symbol;Acc:HGNC:19048]	1	7641.42373	-0.8537	2.13E-07	6768.71	12242.9	3853.59	8268.21	7811.32	12713.22	3172.26	6301.17
ENSG000002	ADM5		adrenomedullin 5 (putative) [Source:HGNC Symbol;Acc:HGNC:27293]	19	133.617077	-0.8512023	0.00037228	151.68	158.95	68.96	111.59	192.33	208.18	85.65	91.61
ENSG000001	CR2		complement component (3d/Epstein Barr virus) receptor 2 [Source:HGNC Symbol;Acc:HGNC:2336]	1	65.5428723	-0.8501566	0.01519876	89.11	63.39	53.75	47.4	150.98	75.44	26.35	17.92
ENSG000001	MT2A		metallothionein 2A [Source:HGNC Symbol;Acc:HGNC:7406]	16	166.468168	-0.8467353	0.00774771	296.72	410.62	59.83	210.33	90.39	128.92	80.16	54.77
ENSG000002	GRIN2B		glutamate receptor, ionotropic, N-methyl D-aspartate 2B [Source:HGNC Symbol;Acc:HGNC:4586]	12	25.2842703	-0.8412319	0.01957478	64.46	19.87	26.37	1.97	35.58	27.69	15.37	10.95
ENSG000001	TSPAN7	X	tetraspanin 7 [Source:HGNC Symbol;Acc:HGNC:11854]		502.432927	-0.8404335	8.89E-07	406.69	616.88	173.41	399.93	801.04	780.19	405.18	436.14
ENSG000001	MPP7		membrane protein, palmitoylated 7 (MAGUK p55 subfamily member 7) [Source:HGNC Symbol;Acc:HGNC:26542]	10	81.1742926	-0.8382394	0.01173617	100.49	123.94	68.96	76.04	108.66	114.59	20.86	35.85
ENSG000001	OCLN		occludin [Source:HGNC Symbol;Acc:HGNC:8104]	5	329.269844	-0.8375317	0.00091799	565.96	414.4	193.69	158	436.58	337.1	274.51	253.92
ENSG000001	POLR3G		polymerase (RNA) III (DNA directed) polypeptide G (32kD) [Source:HGNC Symbol;Acc:HGNC:30075]	5	2229.96049	-0.8352444	0.00218309	3557.84	3627.46	1108.42	1141.53	2486.78	2271.82	2163.16	1482.69
ENSG000001	HRK		harakiri, BCL2 interacting protein [Source:HGNC Symbol;Acc:HGNC:5185]	12	105.398696	-0.8273054	0.02108768	66.36	221.39	9.13	31.6	120.2	191.94	90.04	112.52
ENSG000002	PALM2		paralemmin 2 [Source:HGNC Symbol;Acc:HGNC:15845]	9	397.754637	-0.8204655	6.38E-08	408.59	428.6	251.5	214.28	580.82	640.77	312.94	344.53
ENSG000001	SLC19A1		solute carrier family 19 (folate transporter), member 1 [Source:HGNC Symbol;Acc:HGNC:10937]	21	3150.89284	-0.8202449	0.00183468	4376.91	4915.14	1209.83	1957.19	3745.55	3581.05	2924.1	2497.36
ENSG000001	PPP6R1		protein phosphatase 6, regulatory subunit 1 [Source:HGNC Symbol;Acc:HGNC:29195]	19	4155.01227	-0.8199038	0.0032237	4796.88	6308.79	3663.96	4810.04	5101.45	5440.34	1506.52	1612.13

ENSG000001	EHD4		EH-domain containing 4 [Source:HGNC Symbol;Acc:HGNC:3245]	15	4270.04038	-0.8181421	8.52E-16	4867.03	5028.67	2870.93	2823.22	6182.32	5858.6	3488.5	3041.05
ENSG000001	PGRMC1	X	progesterone receptor membrane component 1 [Source:HGNC Symbol;Acc:HGNC:16090]		4374.35854	-0.8171596	0.00220922	6149.67	5409.96	4429.61	4242.23	5955.38	5256.99	1754.68	1796.35
ENSG000001	UBE2S		ubiquitin-conjugating enzyme E2S [Source:HGNC Symbol;Acc:HGNC:17895]	19	4033.57713	-0.8154822	4.68E-07	5427.3	6645.61	2397.34	3233.02	3691.7	5202.56	2557.36	3113.74
ENSG000001	KIF14		kinesin family member 14 [Source:HGNC Symbol;Acc:HGNC:19181]	1	3376.44907	-0.8127666	5.71E-12	4426.21	5212.22	2150.91	2930.85	3514.76	4194.13	2063.23	2519.27
ENSG000001	CHORDC1		cysteine and histidine-rich domain (CHORD) containing 1 [Source:HGNC Symbol;Acc:HGNC:14525]	11	6767.12421	-0.8109266	1.22E-05	9435.44	9146.22	6034.93	6398.9	8268.1	7868.77	3296.34	3688.29
ENSG000001	SH3GL2		SH3-domain GRB2-like 2 [Source:HGNC Symbol;Acc:HGNC:10831]	9	448.834455	-0.8103372	0.00261019	587.76	479.69	369.13	403.88	670.26	636	222.9	221.06
ENSG000001	IL6R		interleukin 6 receptor [Source:HGNC Symbol;Acc:HGNC:6019]	1	10115.8408	-0.8096998	3.18E-06	14644.69	18152.42	10573.05	9610.2	8356.57	10620.93	4661.22	4307.66
ENSG000001	PLEKHB2		pleckstrin homology domain containing, family B (evectins) member 2 [Source:HGNC Symbol;Acc:HGNC:19236]	2	4927.23566	-0.8084975	6.18E-07	8215.36	7820.7	5257.11	5160.59	4334.07	4563.7	1963.31	2103.04
ENSG000002	UBE2SP1		ubiquitin-conjugating enzyme E2S pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:30864]	17	1166.12094	-0.8076997	2.72E-06	1630.56	1949.97	752.46	882.81	1025.1	1465.84	696.16	926.06
ENSG000001	NDUFB9		NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 9, 22kDa [Source:HGNC Symbol;Acc:HGNC:7704]	8	3501.58518	-0.8070112	0.00047211	4872.72	4950.14	3673.08	3326.83	4326.38	3812.15	1479.07	1572.3
ENSG000001	CENPE		centromere protein E, 312kDa [Source:HGNC Symbol;Acc:HGNC:1856]	4	2715.49429	-0.8058232	1.45E-07	3523.71	3919.81	2139.76	2529.93	2895.47	3544.77	1250.68	1919.82
ENSG000001	COL1A1		collagen, type I, alpha 1 [Source:HGNC Symbol;Acc:HGNC:2197]	17	166.960438	-0.8058183	0.00671142	116.6	144.76	53.75	31.6	268.29	336.14	151.53	233.01
ENSG000002	UBE2SP2		ubiquitin-conjugating enzyme E2S pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:32196]	17	468.582824	-0.8054449	1.54E-05	645.59	791.91	285.98	375.24	455.81	544.32	273.41	376.4
ENSG000001	ANKRD16		ankyrin repeat domain 16 [Source:HGNC Symbol;Acc:HGNC:23471]	10	469.919463	-0.8036623	3.16E-06	607.67	587.55	263.67	320.93	608.71	617.85	397.49	355.49
ENSG000000	FARP2		FERM, RhoGEF and pleckstrin domain protein 2 [Source:HGNC Symbol;Acc:HGNC:16460]	2	1668.39713	-0.8033721	9.57E-12	2166.18	2399.38	1329.49	1357.79	1973.27	1999.66	1105.73	1015.67
ENSG000001	GPLD1		glycosylphosphatidylinositol specific phospholipase D1 [Source:HGNC Symbol;Acc:HGNC:4459]	6	285.237566	-0.8000084	2.60E-06	310.94	469.28	159.21	276.5	299.07	386.75	147.14	233.01
ENSG000001	NPM3		nucleophosmin/nucleoplamin 3 [Source:HGNC Symbol;Acc:HGNC:7931]	10	3260.79877	-0.7970503	0.00014666	5026.29	5457.27	2069.79	2224.8	3383.02	3223.9	2515.63	2185.69
ENSG000001	RIMKLA		ribosomal modification protein rimK-like family member A [Source:HGNC Symbol;Acc:HGNC:28725]	1	350.29726	-0.7943938	1.48E-05	414.28	526.05	185.58	272.55	366.38	502.3	251.45	283.79
ENSG000000	ANLN		anillin actin binding protein [Source:HGNC Symbol;Acc:HGNC:14082]	7	3673.50093	-0.7883166	4.94E-08	4740.94	4696.58	2830.36	3155.01	4636.02	4685.93	2147.78	2495.37
ENSG000001	TOMM20		translocase of outer mitochondrial membrane 20 homolog (yeast) [Source:HGNC Symbol;Acc:HGNC:20947]	1	10611.9323	-0.7840722	2.01E-14	14948.05	14043.39	8921.07	7882.1	13832.09	11202.49	7281.16	6785.1
ENSG000002	TOMM20P4	X	TOMM20 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:50522]		195.308997	-0.7837893	3.66E-05	260.7	264.92	145.02	154.05	263.49	218.68	125.18	130.44
ENSG000001	CORO2A		coronin, actin binding protein, 2A [Source:HGNC Symbol;Acc:HGNC:2255]	9	42.9394317	-0.7832351	0.03390136	59.72	49.2	9.13	2.96	73.08	73.53	45.02	30.87
ENSG000001	CCNB1		cyclin B1 [Source:HGNC Symbol;Acc:HGNC:1579]	5	9500.74436	-0.7831575	4.65E-10	13679.63	14101.1	6867.51	7387.37	9857.67	10984.76	6090.88	7037.03
ENSG000001	MAPT		microtubule-associated protein tau [Source:HGNC Symbol;Acc:HGNC:6893]	17	353.868662	-0.7810595	0.02442375	245.53	677.43	35.49	158.98	291.37	692.34	244.86	484.93
ENSG000002	TRIM52-AS1		TRIM52 antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HGNC:49006]	5	202.14518	-0.7803811	7.98E-05	258.8	254.51	167.33	146.15	266.37	262.61	122.98	138.41

ENSG000002	HK2P1	hexokinase 2 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:4924]	X	32.6224262	-0.7800028	0.02053513	42.66	47.31	22.31	15.8	47.12	42.02	20.86	22.9	
ENSG000002	PEG10	paternally expressed 10 [Source:HGNC Symbol;Acc:HGNC:14005]		7	563.344865	-0.7782776	0.00054312	899.65	343.44	381.3	299.21	1276.08	466.97	595.14	244.96
ENSG000001	FAM182B	family with sequence similarity 182, member B [Source:HGNC Symbol;Acc:HGNC:34503]		20	42.0868645	-0.777222	0.02266073	21.8	68.12	15.21	39.5	65.39	78.31	27.45	20.91
ENSG000001	MYRIP	myosin VIIA and Rab interacting protein [Source:HGNC Symbol;Acc:HGNC:19156]		3	64.1266154	-0.7769359	0.00674002	118.5	32.17	58.82	13.82	163.48	26.74	84.55	14.94
ENSG000001	NEK2	NIMA-related kinase 2 [Source:HGNC Symbol;Acc:HGNC:7745]		1	2085.68369	-0.7711374	2.60E-06	2671.46	2637.81	1778.74	1745.87	2526.2	2782.72	1127.7	1414.97
ENSG000000	PRKAR2B	protein kinase, cAMP-dependent, regulatory, type II, beta [Source:HGNC Symbol;Acc:HGNC:9392]		7	482.54955	-0.7676416	0.00675766	560.27	967.89	171.38	344.63	407.73	607.35	305.26	495.89
ENSG000002	HSPA8P8	heat shock 70kDa protein 8 pseudogene 8 [Source:HGNC Symbol;Acc:HGNC:44923]		7	28.460297	-0.7659686	0.02597719	36.97	55.82	16.23	21.72	35.58	28.65	19.76	12.94
ENSG000002	TMEFF1	transmembrane protein with EGF-like and two follistatin-like domains 1 [Source:HGNC Symbol;Acc:HGNC:11866]		9	42.0896112	-0.7655237	0.02235773	76.79	45.41	29.41	33.57	47.12	60.16	15.37	28.88
ENSG000000	AP3D1	adaptor-related protein complex 3, delta 1 subunit [Source:HGNC Symbol;Acc:HGNC:568]		19	15440.6389	-0.7626372	0.0108565	19382.79	19677.58	16649.56	15708.9	19893.25	20764.39	5562.71	5885.93
ENSG000002	HMG1P10	high mobility group box 1 pseudogene 10 [Source:HGNC Symbol;Acc:HGNC:4994]		22	992.841908	-0.7594333	4.62E-10	1429.58	1603.69	898.5	883.8	967.4	1026.57	534.75	598.45
ENSG000001	HSPA8	heat shock 70kDa protein 8 [Source:HGNC Symbol;Acc:HGNC:5241]		11	141686.279	-0.7592888	4.39E-05	226416.35	239567.32	98214.94	111985.64	132253.04	135512.82	92005.49	97534.63
ENSG000001	CMTM7	CKLF-like MARVEL transmembrane domain containing 7 [Source:HGNC Symbol;Acc:HGNC:19178]		3	3144.86821	-0.7592049	2.58E-08	3641.27	4337.05	1943.02	3048.36	3418.6	4506.4	1896.33	2367.92
ENSG000001	PLD6	phospholipase D family, member 6 [Source:HGNC Symbol;Acc:HGNC:30447]		17	1675.74444	-0.7579756	0.00570477	2706.54	2701.2	923.85	905.52	1796.33	1607.18	1540.56	1224.78
ENSG000001	MYC	v-myc avian myelocytomatosis viral oncogene homolog [Source:HGNC Symbol;Acc:HGNC:7553]		8	27891.7582	-0.7578926	0.00560856	32077.45	37398.57	9509.25	13721.09	36723.71	35928.96	33158.87	24616.17
ENSG000000	PIR	pirin (iron-binding nuclear protein) [Source:HGNC Symbol;Acc:HGNC:30048]	X		646.274362	-0.7563959	0.00051209	892.07	853.41	385.36	363.39	858.74	699.02	673.1	445.1
ENSG000001	ERCC6L	excision repair cross-complementation group 6-like [Source:HGNC Symbol;Acc:HGNC:20794]	X		1833.66291	-0.7546245	1.09E-06	2364.31	3060.73	1056.7	1821.91	1743.44	2139.08	1055.22	1427.92
ENSG000001	HEY2	hes-related family bHLH transcription factor with YRPW motif 2 [Source:HGNC Symbol;Acc:HGNC:4881]		6	43.5225736	-0.7535176	0.01766744	48.35	56.77	30.42	30.61	75.01	53.48	29.65	23.9
ENSG000001	TRMT12	tRNA methyltransferase 12 homolog (S, cerevisiae) [Source:HGNC Symbol;Acc:HGNC:26091]		8	845.532425	-0.7531883	3.44E-08	1099.68	909.23	654.1	552.99	1366.48	925.34	681.89	574.55
ENSG000001	MSRB1	methionine sulfoxide reductase B1 [Source:HGNC Symbol;Acc:HGNC:14133]		16	2868.36924	-0.7511791	0.00017664	3557.84	2851.63	2614.36	2002.62	4433.12	3845.57	2023.7	1618.11
ENSG000001	CEP55	centrosomal protein 55kDa [Source:HGNC Symbol;Acc:HGNC:1161]		10	4578.91798	-0.7504865	0.0006222	6165.79	6016.43	4511.75	4456.52	5165.88	5795.58	1995.15	2524.25
ENSG000001	HMG1P5	high mobility group box 1 pseudogene 5 [Source:HGNC Symbol;Acc:HGNC:4997]		3	4848.50246	-0.7503139	3.34E-13	6892.9	7696.76	4347.46	4507.87	4828.35	4981.96	2653.98	2878.74
ENSG000000	DEPDC1B	DEP domain containing 1B [Source:HGNC Symbol;Acc:HGNC:24902]		5	2424.08384	-0.7498736	3.23E-08	3351.18	3447.69	1634.74	1946.33	2675.26	2817.1	1682.21	1838.17
ENSG000001	BSPRY	B-box and SPRY domain containing [Source:HGNC Symbol;Acc:HGNC:18232]		9	27.6313002	-0.7485836	0.03533678	30.34	30.28	18.25	9.87	49.04	42.97	26.35	13.94
ENSG000000	SLC7A2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2 [Source:HGNC Symbol;Acc:HGNC:11060]		8	360.715557	-0.7484618	0.03447698	1042.8	1.89	233.24	3.95	964.52	2.86	632.48	3.98
ENSG000001	RCC1	regulator of chromosome condensation 1 [Source:HGNC Symbol;Acc:HGNC:1913]		1	7609.82863	-0.7454115	0.00032676	10585.36	13671.56	4462.06	6003.9	7178.57	7873.54	5247.57	5856.06

ENSG000001	SGTA	small glutamine-rich tetratricopeptide repeat (TPR)-containing, alpha [Source:HGNC Symbol;Acc:HGNC:10819]	19	5406.65707	-0.7434668	5.84E-14	6635.05	7668.37	4010.78	4733.01	6727.57	6157.5	3849.76	3471.22
ENSG000002	SNORD89	small nucleolar RNA, C/D box 89 [Source:HGNC Symbol;Acc:HGNC:32750]	2	26.5291455	-0.7433448	0.0338479	36.02	36.9	15.21	13.82	30.77	42.02	17.57	19.92
ENSG000000	GNA11	guanine nucleotide binding protein (G protein), alpha 11 (Gq class) [Source:HGNC Symbol;Acc:HGNC:4379]	19	494.763978	-0.7418227	0.00461705	277.76	951.81	90.26	409.81	323.11	995.06	280	630.32
ENSG000001	TNFRSF19	tumor necrosis factor receptor superfamily, member 19 [Source:HGNC Symbol;Acc:HGNC:11915]	13	32.0132041	-0.7414817	0.04639144	68.26	34.06	24.34	22.71	53.85	26.74	24.16	1.99
ENSG000001	AVP1	arginine vasopressin-induced 1 [Source:HGNC Symbol;Acc:HGNC:30898]	10	497.617109	-0.7395906	1.46E-06	478.74	620.66	280.91	381.17	708.72	710.48	349.18	451.08
ENSG000000	SYT13	synaptotagmin XIII [Source:HGNC Symbol;Acc:HGNC:14962]	11	24.6700343	-0.7394701	0.04621763	7.58	52.98	1.01	4.94	14.42	77.35	13.18	25.89
ENSG000001	MIS18A	MIS18 kinetochore protein A [Source:HGNC Symbol;Acc:HGNC:1286]	21	1465.76915	-0.7390752	0.00025777	2118.78	2205.43	1568.82	1502.95	1557.84	1445.79	643.46	683.09
ENSG000000	PRR11	proline rich 11 [Source:HGNC Symbol;Acc:HGNC:25619]	17	2475.18222	-0.7378512	0.00055327	3068.67	3849.8	2021.11	2831.12	2342.53	3129.36	831.22	1727.64
ENSG000001	SPC24	SPC24, NDC80 kinetochore complex component [Source:HGNC Symbol;Acc:HGNC:26913]	19	1517.22327	-0.7370862	0.00010582	1934.87	2466.56	1178.39	1824.87	1403.98	1777.16	594.04	957.92
ENSG000002	RBM14	RNA binding motif protein 14 [Source:HGNC Symbol;Acc:HGNC:14219]	11	5560.17921	-0.736068	6.31E-10	7419.04	8016.55	3779.56	4799.17	6268.87	6303.61	3968.35	3926.28
ENSG000001	GALNT18	polypeptide N-acetylgalactosaminyltransferase 18 [Source:HGNC Symbol;Acc:HGNC:30488]	11	3619.32963	-0.7358259	0.00129334	5029.14	5287.91	2051.53	2148.77	4240.79	3948.71	3424.81	2822.98
ENSG000001	FGFR4	fibroblast growth factor receptor 4 [Source:HGNC Symbol;Acc:HGNC:3691]	5	1063.14742	-0.7332232	0.00355715	1192.58	1077.64	433.02	450.29	1544.38	1499.27	1419.78	888.22
ENSG000001	NUDT11	nudix (nucleoside diphosphate linked moiety X)-type motif 11 [Source:HGNC Symbol;Acc:HGNC:18011]	X	1143.29479	-0.7330411	1.26E-08	1287.38	1630.18	677.42	970.7	1288.58	1547.02	849.89	895.19
ENSG000001	HBA2	hemoglobin, alpha 2 [Source:HGNC Symbol;Acc:HGNC:4824]	16	151.834997	-0.7322933	0.00469249	136.51	304.65	89.24	177.75	95.2	255.93	64.78	90.61
ENSG000001	WNT10B	wingless-type MMTV integration site family, member 10B [Source:HGNC Symbol;Acc:HGNC:12775]	12	974.389691	-0.7322395	0.02950449	1313.93	1743.71	314.37	409.81	914.51	1204.19	872.95	1021.65
ENSG000001	GPRC5B	G protein-coupled receptor, class C, group 5, member B [Source:HGNC Symbol;Acc:HGNC:13308]	16	279.295568	-0.7318122	0.03968494	320.42	510.91	58.82	114.55	247.14	430.68	280	271.84
ENSG000001	TNFRSF11A	tumor necrosis factor receptor superfamily, member 11a, NFkB activator [Source:HGNC Symbol;Acc:HGNC:11908]	18	67.9820092	-0.7309393	0.02044934	57.83	82.31	37.52	58.26	104.82	116.5	31.84	54.77
ENSG000001	ULBP3	UL16 binding protein 3 [Source:HGNC Symbol;Acc:HGNC:14895]	6	138.004779	-0.7269808	0.00482221	148.84	219.5	58.82	100.72	146.17	193.85	97.73	138.41
ENSG000001	PAX1	paired box 1 [Source:HGNC Symbol;Acc:HGNC:8615]	20	40.72199	-0.7267282	0.03021155	10.43	65.28	5.07	28.64	30.77	110.77	12.08	62.73
ENSG000000	FKBP7	FK506 binding protein 7 [Source:HGNC Symbol;Acc:HGNC:3723]	2	106.049833	-0.726596	0.00345168	153.58	163.68	102.42	76.04	91.35	137.51	57.1	66.72
ENSG000001	C2orf88	chromosome 2 open reading frame 88 [Source:HGNC Symbol;Acc:HGNC:28191]	2	225.064222	-0.7264597	0.0005644	334.64	269.65	147.05	179.72	266.37	276.93	176.79	149.36
ENSG000001	LARP1	La ribonucleoprotein domain family, member 1 [Source:HGNC Symbol;Acc:HGNC:29531]	5	27917.3811	-0.7264011	3.46E-14	38778.86	41636.28	24761.37	24356.3	29288.38	29977.72	16859.44	17680.7
ENSG000001	CENPA	centromere protein A [Source:HGNC Symbol;Acc:HGNC:1851]	2	1231.05591	-0.7259194	9.63E-08	1582.21	1787.24	907.62	1212.63	1364.55	1433.38	710.44	850.38
ENSG000000	SEMA3G	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3G [Source:HGNC Symbol;Acc:HGNC:30400]	3	997.367104	-0.72529	0.01606774	1292.12	1694.52	333.64	638.9	1071.26	1122.06	932.24	894.19

ENSG000001	ENAH	enabled homolog (Drosophila) [Source:HGNC Symbol;Acc:HGNC:18271]	1	2474.93466	-0.725145	1.22E-06	3203.29	2812.84	2095.14	1383.47	3509.95	2912.59	1867.78	2014.42
ENSG000001	SLC16A1	solute carrier family 16 (monocarboxylate transporter), member 1 [Source:HGNC Symbol;Acc:HGNC:10922]	1	5889.42622	-0.7245096	7.25E-13	8295.94	8293.76	4930.57	5328.46	6501.58	6357.09	3725.68	3682.32
ENSG000001	SSSCA1	Sjogren syndrome/scleroderma autoantigen 1 [Source:HGNC Symbol;Acc:HGNC:11328]	11	2090.25968	-0.723688	3.93E-07	2800.39	2289.63	1728.03	1597.75	3186.84	2223.12	1792.02	1104.3
ENSG000001	GCDH	glutaryl-CoA dehydrogenase [Source:HGNC Symbol;Acc:HGNC:4189]	19	2393.05414	-0.7227024	0.00015515	3136.93	2711.6	2303.03	1914.73	3648.43	2563.08	1708.56	1158.07
ENSG000001	YWHAH	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta [Source:HGNC Symbol;Acc:HGNC:12853]	22	6498.45385	-0.7185269	0.00142309	8987.98	8807.51	6889.82	6669.47	7568.99	7041.79	3150.3	2871.77
ENSG000001	ADGRB3	adhesion G protein-coupled receptor B3 [Source:HGNC Symbol;Acc:HGNC:945]	6	33.8223577	-0.7164145	0.04981939	33.18	44.47	7.1	16.79	51.93	54.43	20.86	41.82
ENSG000001	CRYZ	crystallin, zeta (quinone reductase) [Source:HGNC Symbol;Acc:HGNC:2419]	1	831.676126	-0.714562	1.12E-07	1075.98	923.42	649.03	582.62	1128.95	1038.98	713.73	540.7
ENSG000001	ACADSB	acyl-CoA dehydrogenase, short/branched chain [Source:HGNC Symbol;Acc:HGNC:91]	10	1475.90963	-0.7141585	7.69E-08	2257.19	1826.03	1329.49	997.36	1808.83	1515.5	1012.4	1060.48
ENSG000001	NOTUM	notum pectinacetyltransferase homolog (Drosophila) [Source:HGNC Symbol;Acc:HGNC:27106]	17	282.313111	-0.7131592	0.00558944	249.32	461.71	96.34	201.45	283.68	445.01	248.16	272.84
ENSG000001	UBE2C	ubiquitin-conjugating enzyme E2C [Source:HGNC Symbol;Acc:HGNC:15937]	20	4260.05258	-0.7130338	5.30E-05	5857.69	6602.09	2595.09	3523.34	3807.09	5282.77	2722.06	3690.28
ENSG000002	SNORD14E	small nucleolar RNA, C/D box 14E [Source:HGNC Symbol;Acc:HGNC:30354]	11	73.6011135	-0.7119354	0.03985946	188.65	116.37	42.59	59.25	49.04	54.43	40.63	37.84
ENSG000001	CKS2	CDC28 protein kinase regulatory subunit 2 [Source:HGNC Symbol;Acc:HGNC:2000]	9	4456.49788	-0.7114972	2.06E-11	6537.4	6032.52	3853.59	3971.66	5107.22	4540.78	3021.83	2586.98
ENSG000000	AASS	aminoadipate-semialdehyde synthase [Source:HGNC Symbol;Acc:HGNC:17366]	7	944.68099	-0.7108255	0.00978522	949.9	801.37	808.24	656.68	1466.49	1720.82	554.51	599.45
ENSG000001	RCN3	reticulocalbin 3, EF-hand calcium binding domain [Source:HGNC Symbol;Acc:HGNC:21145]	19	187.733245	-0.7103707	0.01896402	139.36	290.46	45.63	97.76	179.82	339.96	124.08	284.79
ENSG000001	FRAT2	frequently rearranged in advanced T-cell lymphomas 2 [Source:HGNC Symbol;Acc:HGNC:16048]	10	1353.38277	-0.7093726	8.85E-08	1859.97	1734.25	968.47	1030.93	1607.85	1577.57	980.56	1067.45
ENSG000001	DFFB	DNA fragmentation factor, 40kDa, beta polypeptide (caspase-activated DNase) [Source:HGNC Symbol;Acc:HGNC:2773]	1	1022.12347	-0.7092073	0.00681121	1437.17	1463.66	522.26	570.77	1104.91	1213.74	934.44	930.04
ENSG000001	KDM1B	lysine (K)-specific demethylase 1B [Source:HGNC Symbol;Acc:HGNC:21577]	6	944.756213	-0.7089545	1.95E-07	1198.27	981.14	695.68	522.38	1331.86	1201.32	901.5	725.91
ENSG000001	CCNB2	cyclin B2 [Source:HGNC Symbol;Acc:HGNC:1580]	15	2309.22877	-0.705256	2.07E-07	2701.8	3064.51	1680.37	2141.85	2525.24	3220.08	1307.78	1832.2
ENSG000001	NBPF3	neuroblastoma breakpoint family, member 3 [Source:HGNC Symbol;Acc:HGNC:25076]	1	230.822233	-0.7051857	0.00478184	189.6	400.21	80.11	167.87	259.64	322.77	194.35	232.01
ENSG000001	H2AFX	H2A histone family, member X [Source:HGNC Symbol;Acc:HGNC:4739]	11	2071.89977	-0.7041806	0.0001909	2459.11	2868.66	1066.84	1532.58	2319.45	2743.57	1798.6	1786.39
ENSG000000	WDR3	WD repeat domain 3 [Source:HGNC Symbol;Acc:HGNC:12755]	1	3649.54592	-0.7027821	4.52E-09	5002.59	5716.51	3366.82	3089.84	3797.48	3700.42	2201.59	2321.12
ENSG000001	PIK3CG	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma [Source:HGNC Symbol;Acc:HGNC:8978]	7	14289.6934	-0.7023724	1.80E-08	9821.27	25587.1	5155.7	17666.09	11741.51	23158.44	6794.72	14392.71
ENSG000001	PDE5A	phosphodiesterase 5A, cGMP-specific [Source:HGNC Symbol;Acc:HGNC:8784]	4	149.247204	-0.7016338	0.00604187	153.58	117.32	76.06	95.79	249.06	248.29	149.33	104.55
ENSG000001	HSPH1	heat shock 105kDa/110kDa protein 1 [Source:HGNC Symbol;Acc:HGNC:16969]	13	9185.03253	-0.7010208	1.07E-08	14292.98	13394.34	8587.43	9203.35	8999.9	8874.33	4735.88	5392.04
ENSG000001	PRMT1	protein arginine methyltransferase 1 [Source:HGNC Symbol;Acc:HGNC:5187]	19	6711.06909	-0.7007511	1.85E-09	8794.59	10329.83	5670.87	5507.2	7153.57	7245.19	4666.71	4320.6

ENSG000000	PAFAH1B3	platelet-activating factor acetylhydrolase 1b, catalytic subunit 3 (29kDa) [Source:HGNC Symbol;Acc:HGNC:8576]	19	1419.37579	-0.7004477	0.00061379	1479.83	1967.95	630.77	959.83	1762.67	1874.56	1291.31	1388.09
ENSG000002	MIR4444-2	microRNA 4444-2 [Source:HGNC Symbol;Acc:HGNC:43481]	3	194.305865	-0.699538	0.01287309	229.42	222.34	83.16	198.48	239.45	302.72	150.43	128.45
ENSG000001	MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast) [Source:HGNC Symbol;Acc:HGNC:6763]	4	2692.5962	-0.6983651	1.10E-10	3691.51	3855.47	2170.18	2225.79	2799.31	3080.66	1845.82	1872.03
ENSG000001	HPDL	4-hydroxyphenylpyruvate dioxygenase-like [Source:HGNC Symbol;Acc:HGNC:28242]	1	1492.10376	-0.6978574	0.00769925	2046.73	1881.85	751.45	723.83	2008.85	1588.08	1673.43	1262.62
ENSG000000	TCOF1	Treacher Collins-Franceschetti syndrome 1 [Source:HGNC Symbol;Acc:HGNC:11654]	5	14162.2981	-0.6972068	3.90E-12	16880.07	22002.22	10931.02	13815.89	14278.29	17132.72	8229.87	10028.29
ENSG000000	KCNN2	potassium channel, calcium activated intermediate/small conductance subfamily N alpha, member 2 [Source:HGNC Symbol;Acc:HGNC:6291]	5	62.453607	-0.6948951	0.02321824	95.75	62.44	52.73	48.39	101.93	65.89	40.63	31.86
ENSG000001	TC2N	tandem C2 domains, nuclear [Source:HGNC Symbol;Acc:HGNC:19859]	14	248.347264	-0.6946069	0.01285972	283.45	316.01	111.55	113.56	272.14	381.02	205.34	303.71
ENSG000001	SLC19A2	solute carrier family 19 (thiamine transporter), member 2 [Source:HGNC Symbol;Acc:HGNC:10938]	1	1790.58902	-0.6942768	7.24E-08	2193.67	2445.74	1433.94	1387.42	2183.86	2090.38	1461.5	1128.2
ENSG000001	CCDC88A	coiled-coil domain containing 88A [Source:HGNC Symbol;Acc:HGNC:25523]	2	110.459759	-0.6938349	0.02378553	167.8	114.48	123.72	32.59	156.75	126.05	74.67	87.63
ENSG000001	FZD8	frizzled class receptor 8 [Source:HGNC Symbol;Acc:HGNC:4046]	10	484.000024	-0.6934611	0.00207727	615.25	632.96	224.12	431.53	565.44	618.81	376.63	407.27
ENSG000002	LINC01003	long intergenic non-protein coding RNA 1003 [Source:HGNC Symbol;Acc:HGNC:48957]	7	122.912396	-0.692798	0.0075387	134.62	146.65	56.79	73.07	143.28	195.76	86.75	146.38
ENSG000001	EXT1	exostosin glycosyltransferase 1 [Source:HGNC Symbol;Acc:HGNC:3512]	8	897.123214	-0.6919385	0.01936251	943.26	983.97	770.72	894.66	1160.69	1528.87	412.87	481.95
ENSG000001	AJAP1	adherens junctions associated protein 1 [Source:HGNC Symbol;Acc:HGNC:30801]	1	949.359966	-0.6880734	0.0154343	1557.56	1344.45	532.4	522.38	987.59	978.82	1002.52	669.15
ENSG000001	NCR3LG1	natural killer cell cytotoxicity receptor 3 ligand 1 [Source:HGNC Symbol;Acc:HGNC:42400]	11	88.314346	-0.6880331	0.00536081	79.63	111.64	47.66	64.19	115.4	143.24	68.08	76.67
ENSG000001	MTDH	metadherin [Source:HGNC Symbol;Acc:HGNC:29608]	8	36853.3238	-0.6866209	1.43E-05	58893.51	43579.63	40407.98	31738.73	44481.18	35176.46	21921.44	18627.67
ENSG000001	GABRB2	gamma-aminobutyric acid (GABA) A receptor, beta 2 [Source:HGNC Symbol;Acc:HGNC:4082]	5	243.759892	-0.6861997	0.00162473	174.43	144.76	129.81	75.05	483.7	433.55	224	284.79
ENSG000001	CDCA8	cell division cycle associated 8 [Source:HGNC Symbol;Acc:HGNC:14629]	1	3743.85789	-0.685707	1.97E-10	5074.64	5610.54	3196.46	3654.68	3848.45	3979.27	2163.16	2423.68
ENSG000001	GPD1L	glycerol-3-phosphate dehydrogenase 1-like [Source:HGNC Symbol;Acc:HGNC:28956]	3	1856.44384	-0.6850951	0.00025221	2372.84	2682.27	1106.39	1349.89	2132.9	2105.66	1494.44	1607.16
ENSG000000	KDM1A	lysine (K)-specific demethylase 1A [Source:HGNC Symbol;Acc:HGNC:29079]	1	8677.54344	-0.6822127	5.71E-12	10444.11	11762.27	6437.53	6994.35	10250.02	10513.98	6098.56	6919.53
ENSG000000	RPU5D1	RNA pseudouridylylate synthase domain containing 1 [Source:HGNC Symbol;Acc:HGNC:14173]	16	2993.03183	-0.6797685	0.00020363	3655.49	3872.5	1599.24	2230.73	3882.1	3451.18	2975.71	2277.3
ENSG000001	RAB3C	RAB3C, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:30269]	5	52.4796646	-0.6793983	0.03847183	95.75	106.91	40.56	42.46	38.47	39.15	29.65	26.89
ENSG000001	NUP35	nucleoporin 35kDa [Source:HGNC Symbol;Acc:HGNC:29797]	2	1640.98943	-0.678936	0.01313437	1899.79	2286.79	1715.86	1760.68	1937.69	2065.55	713.73	747.82
ENSG000002	BCYRN1	brain cytoplasmic RNA 1 [Source:HGNC Symbol;Acc:HGNC:1022]	2	250.737514	-0.6778613	0.00091387	364.03	232.75	238.31	111.59	325.03	326.59	174.59	233.01
ENSG000002	HBA1	hemoglobin, alpha 1 [Source:HGNC Symbol;Acc:HGNC:4823]	16	76.5160888	-0.6762253	0.03118608	70.15	147.6	47.66	85.91	50.97	131.78	36.24	41.82

ENSG000001: MT1X	metallothionein 1X [Source:HGNC Symbol;Acc:HGNC:7405]	16	72.5005146	-0.6761156	0.0312452	158.32	91.77	61.86	42.46	68.28	62.07	60.39	34.85
ENSG000001: INCENP	inner centromere protein antigens 135/155kDa [Source:HGNC Symbol;Acc:HGNC:6058]	11	5402.25607	-0.6746225	3.66E-09	6289.98	7710.95	3542.26	5311.68	5638.04	7020.78	3497.28	4207.08
ENSG000000: KARS	lysyl-tRNA synthetase [Source:HGNC Symbol;Acc:HGNC:6215]	16	10906.9426	-0.6733078	0.04389184	14840.93	15295.11	14142.69	12994.3	13125.29	10971.4	2852.73	3033.08
ENSG000001: UCK2	uridine-cytidine kinase 2 [Source:HGNC Symbol;Acc:HGNC:12562]	1	12210.1089	-0.6722393	1.50E-13	15138.6	18116.47	9518.38	10987.74	13465.71	13567.9	8337.48	8548.59
ENSG000001: ANKRD27	ankyrin repeat domain 27 (VPS9 domain) [Source:HGNC Symbol;Acc:HGNC:25310]	19	3646.7915	-0.6707723	1.86E-07	4307.71	5951.15	2461.23	3404.85	3411.86	4454.83	2488.18	2694.52
ENSG000000: BIRC5	baculoviral IAP repeat containing 5 [Source:HGNC Symbol;Acc:HGNC:593]	17	2220.50391	-0.670216	4.19E-07	3215.61	3309.56	2059.64	2322.56	2101.16	2286.15	1152.95	1316.39
ENSG000001: ADRA2C	adrenoceptor alpha 2C [Source:HGNC Symbol;Acc:HGNC:283]	4	136.363641	-0.6698784	0.0223225	69.2	345.34	27.38	143.19	60.58	235.87	56	153.35
ENSG000001: CSPP1	centrosome and spindle pole associated protein 1 [Source:HGNC Symbol;Acc:HGNC:26193]	8	2223.05078	-0.6696735	8.29E-10	2897.09	2794.86	1792.94	1841.66	2624.29	2657.62	1522.99	1652.96
ENSG000001: BCRP2	breakpoint cluster region pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:1015]	22	117.557147	-0.6696349	0.01219837	122.29	177.87	51.72	98.75	128.86	162.34	69.18	129.45
ENSG000001: ELMOD1	ELMO/CED-12 domain containing 1 [Source:HGNC Symbol;Acc:HGNC:25334]	11	248.9283	-0.6679627	0.00402233	218.99	303.71	90.26	162.93	320.22	389.62	222.9	282.8
ENSG000001: AHSA1	AHA1, activator of heat shock 90kDa protein ATPase homolog 1 (yeast) [Source:HGNC Symbol;Acc:HGNC:1189]	14	11410.0614	-0.6670267	2.31E-05	15194.53	16200.56	11091.25	11339.28	11671.31	12974.88	6298.41	6510.28
ENSG000001: DBN1	drebrin 1 [Source:HGNC Symbol;Acc:HGNC:2695]	5	8372.93865	-0.6664109	0.00205181	10444.11	11310.02	4610.12	5160.59	9964.41	9905.67	8209.01	7379.57
ENSG000001: HMGNS5	high mobility group nucleosome binding domain 5 [Source:HGNC Symbol;Acc:HGNC:8013]	X	2118.63597	-0.6660767	1.56E-05	2424.03	2149.6	1813.22	1375.57	3045.48	2906.86	1529.58	1704.74
ENSG000002: FAM195B	family with sequence similarity 195, member B [Source:HGNC Symbol;Acc:HGNC:28007]	17	221.130828	-0.6651244	0.00990786	229.42	222.34	150.09	191.57	342.34	329.46	172.39	131.44
ENSG000001: CCNA2	cyclin A2 [Source:HGNC Symbol;Acc:HGNC:1578]	4	2619.99859	-0.6647383	1.25E-07	3836.55	3884.8	2050.52	2424.27	2554.09	2711.1	1673.43	1825.23
ENSG000001: SLC39A3	solute carrier family 39 (zinc transporter), member 3 [Source:HGNC Symbol;Acc:HGNC:17128]	19	920.534681	-0.6633258	1.13E-05	849.41	1142.92	435.05	681.36	1166.46	1368.44	790.59	930.04
ENSG000001: PSD3	pleckstrin and Sec7 domain containing 3 [Source:HGNC Symbol;Acc:HGNC:19093]	8	879.186361	-0.6631489	9.81E-05	1203.01	1098.46	711.9	525.34	1099.14	959.72	737.89	698.03
ENSG000002: VPS9D1-AS1	VPS9D1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:48915]	16	782.151413	-0.6628606	1.09E-06	941.36	998.17	523.28	594.47	970.29	953.99	642.36	633.3
ENSG000001: NR1D1	nuclear receptor subfamily 1, group D, member 1 [Source:HGNC Symbol;Acc:HGNC:7962]	17	686.667019	-0.6621984	0.02848662	994.45	1150.49	363.05	371.29	730.84	649.36	685.18	548.66
ENSG000001: CDCA3	cell division cycle associated 3 [Source:HGNC Symbol;Acc:HGNC:14624]	12	2544.39344	-0.6612559	7.82E-05	3203.29	3617.05	1492.76	2169.5	2347.34	3448.32	1712.96	2363.93
ENSG000000: NCAPD2	non-SMC condensin I complex, subunit D2 [Source:HGNC Symbol;Acc:HGNC:24305]	12	13542.2417	-0.6611705	2.38E-10	15266.58	19763.68	9035.66	13262.9	12666.6	18752.31	7467.83	12122.38
ENSG000001: TRPM6	transient receptor potential cation channel, subfamily M, member 6 [Source:HGNC Symbol;Acc:HGNC:17995]	9	513.091597	-0.6605008	0.0003102	643.69	670.81	410.71	317.97	679.87	555.78	410.67	415.23
ENSG000001: PHOSPHO1	phosphatase, orphan 1 [Source:HGNC Symbol;Acc:HGNC:16815]	17	94.6056293	-0.6601324	0.04766826	50.24	112.59	16.23	34.56	122.13	186.21	73.57	161.31
ENSG000001: DCPS	decapping enzyme, scavenger [Source:HGNC Symbol;Acc:HGNC:29812]	11	1112.27627	-0.6600884	5.61E-07	1517.75	1564.9	850.83	978.6	1173.19	1242.39	825.73	744.83
ENSG000001: DLGAP5	discs, large (Drosophila) homolog-associated protein 5 [Source:HGNC Symbol;Acc:HGNC:16864]	14	5340.53335	-0.6584812	2.42E-05	6757.34	7138.54	4859.59	5096.41	6176.55	6179.47	3154.69	3361.68

ENSG000001	GCAT	glycine C-acetyltransferase [Source:HGNC Symbol;Acc:HGNC:4188]	22	2006.60506	-0.6584595	0.00155824	2554.86	2303.82	1200.7	1086.23	2859.89	2151.5	2431.08	1464.76
ENSG000000	MRPS34	mitochondrial ribosomal protein S34 [Source:HGNC Symbol;Acc:HGNC:16618]	16	5122.78043	-0.6582928	4.81E-11	6706.15	6669.26	4225.77	4266.92	6187.13	5618.91	4000.19	3307.91
ENSG000001	TMEM109	transmembrane protein 109 [Source:HGNC Symbol;Acc:HGNC:28771]	11	6832.35375	-0.6575023	5.07E-09	8541.47	10370.52	5356.5	6785.99	6996.82	7679.69	4659.02	4268.82
ENSG000001	SELPLG	selectin P ligand [Source:HGNC Symbol;Acc:HGNC:10722]	12	12433.3026	-0.6574789	1.34E-06	14892.12	17298.07	7909	12556.85	13228.19	15727.04	8745.96	9109.21
ENSG000001	DMRTA1	DMRT-like family A1 [Source:HGNC Symbol;Acc:HGNC:13826]	9	133.759156	-0.6572624	0.00482221	150.73	161.79	87.21	89.86	186.56	170.94	95.53	127.46
ENSG000001	CHN1	chimerin 1 [Source:HGNC Symbol;Acc:HGNC:1943]	2	208.674143	-0.6566706	0.00304419	206.66	372.77	154.14	235.02	216.37	243.51	95.53	145.38
ENSG000001	PYCR1	pyrroline-5-carboxylate reductase-like [Source:HGNC Symbol;Acc:HGNC:25846]	8	1623.00927	-0.6565744	0.01484756	1987.01	1796.7	679.45	770.24	2336.76	1874.56	2067.63	1471.73
ENSG000001	CCDC106	coiled-coil domain containing 106 [Source:HGNC Symbol;Acc:HGNC:30181]	19	498.943098	-0.6563978	0.00345916	472.1	536.45	199.78	266.62	699.11	736.26	532.55	548.66
ENSG000002	PPT2	palmitoyl-protein thioesterase 2 [Source:HGNC Symbol;Acc:HGNC:9326]	6	457.058835	-0.6558694	3.25E-05	558.37	666.07	313.36	376.23	475.05	563.42	309.65	394.32
ENSG000002	RPL7P21	ribosomal protein L7 pseudogene 21 [Source:HGNC Symbol;Acc:HGNC:36762]	5	335.596746	-0.655614	0.0002007	445.56	458.87	256.57	337.72	377.92	376.25	210.83	221.06
ENSG000001	NAV1	neuron navigator 1 [Source:HGNC Symbol;Acc:HGNC:15989]	1	354.198776	-0.6554161	0.04193065	319.48	428.6	141.97	96.77	461.58	554.82	362.36	468.01
ENSG000001	POLR3K	polymerase (RNA) III (DNA directed) polypeptide K, 12,3 kDa [Source:HGNC Symbol;Acc:HGNC:14121]	16	1970.96749	-0.6552108	3.25E-07	2721.71	3013.42	1533.32	1825.86	1927.11	2080.83	1387.93	1277.56
ENSG000002	TUBAP2	tubulin, alpha pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:14531]	11	1046.51173	-0.6550531	3.29E-07	1402.09	1576.25	896.47	1008.22	1033.75	1133.52	570.99	750.8
ENSG000001	DNAAF3	dynein, axonemal, assembly factor 3 [Source:HGNC Symbol;Acc:HGNC:30492]	19	82.4810649	-0.6545397	0.04122732	55.93	161.79	27.38	52.34	50.97	156.61	37.33	117.5
ENSG000001	GSPT1	G1 to S phase transition 1 [Source:HGNC Symbol;Acc:HGNC:4621]	16	17048.5812	-0.6509416	3.93E-07	23790.04	23253	16788.49	15799.75	18484.46	17842.24	10386.44	10044.23
ENSG000001	ARHGAP11A	Rho GTPase activating protein 11A [Source:HGNC Symbol;Acc:HGNC:15783]	15	13156.9468	-0.6509044	6.73E-11	16831.73	19420.23	9968.64	11986.08	13486.87	14925.83	8685.56	9950.62
ENSG000001	WWC1	WW and C2 domain containing 1 [Source:HGNC Symbol;Acc:HGNC:29435]	5	1293.69771	-0.6493889	3.82E-05	1671.32	1999.17	993.82	1026.98	1349.17	1394.22	1026.68	888.22
ENSG000000	HMMR	hyaluronan-mediated motility receptor (RHAMM) [Source:HGNC Symbol;Acc:HGNC:5012]	5	4555.18507	-0.648694	2.73E-11	5343.87	5891.54	3366.82	3694.18	4848.54	6244.4	2962.54	4089.58
ENSG000000	ATP5D	ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit [Source:HGNC Symbol;Acc:HGNC:837]	19	3801.48237	-0.6473432	1.10E-05	3941.78	4239.6	2396.33	3117.49	5425.52	5108.97	3586.23	2595.94
ENSG000001	GAR1	GAR1 homolog, ribonucleoprotein [Source:HGNC Symbol;Acc:HGNC:14264]	4	1775.63219	-0.6472009	1.17E-05	2977.67	2326.53	1641.83	1276.82	1911.72	1594.76	1317.66	1158.07
ENSG000001	DNAJB1	DnaJ (Hsp40) homolog, subfamily B, member 1 [Source:HGNC Symbol;Acc:HGNC:5270]	19	4677.60459	-0.6468663	4.98E-05	7150.76	7361.83	3698.44	4035.85	4384.07	4403.26	3033.91	3352.72
ENSG000000	HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2) [Source:HGNC Symbol;Acc:HGNC:5035]	14	40204.3625	-0.6460367	2.37E-11	56273.24	58625.91	37214.57	38244.27	40849.1	40803.01	24597.39	25027.42
ENSG000001	GDPD1	glycerophosphodiester phosphodiesterase domain containing 1 [Source:HGNC Symbol;Acc:HGNC:20883]	17	162.106816	-0.6457181	0.00152201	145.99	177.87	87.21	106.65	215.41	266.43	144.94	152.35
ENSG000001	ALDH4A1	aldehyde dehydrogenase 4 family, member A1 [Source:HGNC Symbol;Acc:HGNC:406]	1	426.812435	-0.644873	0.00083841	411.43	437.11	288.01	328.83	737.57	540.5	405.18	265.87
ENSG000001	UBQLN1	ubiquilin 1 [Source:HGNC Symbol;Acc:HGNC:12508]	9	14855.6712	-0.6442163	8.17E-05	20349.75	18358.68	14081.84	14192.12	17020.86	16991.39	9125.88	8724.84
ENSG000002	CENPW	centromere protein W [Source:HGNC Symbol;Acc:HGNC:21488]	6	1292.32249	-0.6433399	0.01233965	1533.86	1588.55	1229.09	1373.59	1565.53	1704.58	599.53	743.83

ENSG000001	PRC1	protein regulator of cytokinesis 1 [Source:HGNC Symbol;Acc:HGNC:9341]	15	5602.56127	-0.6430495	0.00011911	6116.49	6867	4348.48	5246.5	6690.06	7920.34	3432.5	4199.12
ENSG000001	POLR1C	polymerase (RNA) I polypeptide C, 30kDa [Source:HGNC Symbol;Acc:HGNC:20194]	6	2764.41164	-0.6405977	1.46E-06	3488.64	3559.34	1948.09	2046.07	3336.86	3187.62	2320.18	2228.51
ENSG000001	MEI1	meiotic double-stranded break formation protein 1 [Source:HGNC Symbol;Acc:HGNC:28613]	22	502.109977	-0.639806	0.00108239	558.37	577.14	266.71	314.02	774.11	553.87	564.4	408.26
ENSG000001	TRAF3	TNF receptor-associated factor 3 [Source:HGNC Symbol;Acc:HGNC:12033]	14	3564.49641	-0.6393384	1.81E-08	4830.06	4305.83	2752.28	2700.77	4600.44	3742.44	3077.83	2506.33
ENSG000001	RRP9	ribosomal RNA processing 9, small subunit (SSU) processome component, homolog (yeast) [Source:HGNC Symbol;Acc:HGNC:16829]	3	3677.65378	-0.6390722	0.00056015	4959.93	5946.42	2771.55	2751.13	3774.4	3633.58	2864.81	2719.42
ENSG000001	AURKB	aurora kinase B [Source:HGNC Symbol;Acc:HGNC:11390]	17	3306.38547	-0.6390118	8.72E-08	3861.2	5007.86	2195.53	3038.49	3274.35	4070.94	2180.72	2821.98
ENSG000001	P2RY6	pyrimidineric receptor P2Y, G-protein coupled, 6 [Source:HGNC Symbol;Acc:HGNC:8543]	11	2380.38428	-0.6390068	0.00034224	2527.37	2344.51	1246.33	1842.65	3646.5	3212.44	1958.92	2264.36
ENSG000001	RABL3	RAB, member of RAS oncogene family-like 3 [Source:HGNC Symbol;Acc:HGNC:18072]	3	848.855069	-0.6379479	6.41E-07	1097.78	1128.73	714.94	713.95	996.25	939.67	573.18	626.33
ENSG000002	CPSF1P1	cleavage and polyadenylation specific factor 1, 160kDa pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:19251]	22	186.974312	-0.6370581	0.04354185	220.88	289.52	70.99	112.57	216.37	217.73	163.61	204.13
ENSG000001	TBL3	transducin (beta)-like 3 [Source:HGNC Symbol;Acc:HGNC:11587]	16	3595.73213	-0.636942	2.12E-06	4478.35	4471.4	2759.38	2628.68	4573.51	4063.3	3462.15	2329.08
ENSG000001	TTC39B	tetratricopeptide repeat domain 39B [Source:HGNC Symbol;Acc:HGNC:23704]	9	128.829545	-0.6349832	0.02649593	135.56	131.51	76.06	49.37	216.37	159.48	121.88	140.4
ENSG000001	CD55	CD55 molecule, decay accelerating factor for complement (Cromer blood group) [Source:HGNC Symbol;Acc:HGNC:2665]	1	1115.59925	-0.6348646	0.01175441	2394.65	1331.2	1115.51	556.94	1042.41	865.18	1045.34	573.56
ENSG000001	YARS	tyrosyl-tRNA synthetase [Source:HGNC Symbol;Acc:HGNC:12840]	1	10449.797	-0.6330199	1.91E-09	12891.84	13332.84	7967.81	8494.34	12731.03	12080.09	8861.25	7239.17
ENSG000001	TCP1	t-complex 1 [Source:HGNC Symbol;Acc:HGNC:11655]	6	23301.9453	-0.6328413	6.34E-09	32462.34	31745.45	22776.77	20631.51	25218.76	24069.46	14932.36	14578.91
ENSG000000	C3orf18	chromosome 3 open reading frame 18 [Source:HGNC Symbol;Acc:HGNC:24837]	3	250.363274	-0.6325103	0.00177743	307.15	226.12	157.19	130.35	346.19	351.42	262.43	222.05
ENSG000002	HNRNPCP2	heterogeneous nuclear ribonucleoprotein C pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:48814]	2	2742.78739	-0.6319201	1.48E-09	3787.26	4028.62	2421.68	2714.59	2766.61	2789.4	1718.45	1715.69
ENSG000001	BAG4	BCL2-associated athanogene 4 [Source:HGNC Symbol;Acc:HGNC:940]	8	1679.42714	-0.6315123	1.73E-08	2275.2	2296.25	1505.94	1508.88	1802.1	1823	1138.68	1085.38
ENSG000001	BUB1B	BUB1 mitotic checkpoint serine/threonine kinase B [Source:HGNC Symbol;Acc:HGNC:1149]	15	7061.73081	-0.6314232	7.78E-06	8663.77	9399.79	5452.84	7129.64	7769.01	8593.58	4122.07	5363.16
ENSG000001	NUDCD1	NudC domain containing 1 [Source:HGNC Symbol;Acc:HGNC:24306]	8	2476.06627	-0.63105	0.0039169	3371.09	3300.1	2741.12	2564.5	2756.99	2603.19	1197.97	1273.58
ENSG000000	PHF7	PHD finger protein 7 [Source:HGNC Symbol;Acc:HGNC:18458]	3	272.818382	-0.6310382	0.00349127	289.14	280.05	217.02	205.4	401.96	387.71	192.16	209.11
ENSG000001	STX10	syntaxin 10 [Source:HGNC Symbol;Acc:HGNC:11428]	19	1894.90032	-0.6306438	0.000997	2363.36	2442.9	1685.44	1975.96	2115.59	2339.62	1110.13	1126.2
ENSG000002	FAM72D	family with sequence similarity 72, member D [Source:HGNC Symbol;Acc:HGNC:33593]	1	4852.46998	-0.6299678	3.92E-09	5792.28	6369.34	3944.86	4224.46	5528.41	5991.34	3364.42	3604.65
ENSG000001	DDI2	DNA-damage inducible 1 homolog 2 [Source:HGNC Symbol;Acc:HGNC:24578]	1	5473.74225	-0.629255	8.54E-10	7763.17	7724.19	4839.3	5277.12	5385.13	5801.31	3276.58	3723.14
ENSG000001	TMEM74	transmembrane protein 74 [Source:HGNC Symbol;Acc:HGNC:26409]	8	101.905768	-0.6290853	0.01321632	116.6	130.57	57.8	94.8	127.9	132.74	80.16	74.68
ENSG000001	UBE2E2	ubiquitin-conjugating enzyme E2E 2 [Source:HGNC Symbol;Acc:HGNC:12478]	3	969.429851	-0.6282697	1.47E-06	1138.55	1367.16	778.83	906.51	1077.99	1151.67	613.81	720.93

ENSG000001.LYAR	Ly1 antibody reactive [Source:HGNC Symbol;Acc:HGNC:26021]	4	4871.80854	-0.6282212	4.83E-09	7350.79	7129.08	5091.81	4566.13	4699.49	4505.44	2947.16	2684.57
ENSG000001.ANP32E	acidic (leucine-rich) nuclear phosphoprotein 32 family, member E [Source:HGNC Symbol;Acc:HGNC:16673]	1	29960.7533	-0.6265933	4.39E-12	40074.77	44973.27	25238	29153.5	27957.48	33035.46	18296.78	20956.75
ENSG000001.GAS2L3	growth arrest-specific 2 like 3 [Source:HGNC Symbol;Acc:HGNC:27475]	12	1516.21752	-0.626277	1.19E-05	1672.27	1992.55	1204.76	1387.42	1623.23	2125.71	906.99	1216.82
ENSG000000.DSP	desmoplakin [Source:HGNC Symbol;Acc:HGNC:3052]	6	10223.363	-0.6258828	9.56E-08	12436.8	13494.63	8433.29	7563.14	9727.85	14338.54	6690.41	9102.24
ENSG000001.YWHAE	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon [Source:HGNC Symbol;Acc:HGNC:12851]	17	37540.4384	-0.6257538	0.01463935	49463.76	50155.22	44013.12	40938.13	42206.92	40098.26	16499.28	16948.82
ENSG000001.HMGB1	high mobility group box 1 [Source:HGNC Symbol;Acc:HGNC:4983]	13	18638.9696	-0.6253484	1.09E-10	26619.82	27901.33	18120.01	17775.7	17600.72	18527.9	10832.25	11734.03
ENSG000001.RPL7L1	ribosomal protein L7-like 1 [Source:HGNC Symbol;Acc:HGNC:21370]	6	17917.1484	-0.6252451	1.37E-08	23117.91	26047.87	16218.56	17140.75	18545.04	19415.04	10853.11	11998.9
ENSG000001.KCNS3	potassium voltage-gated channel, modifier subfamily S, member 3 [Source:HGNC Symbol;Acc:HGNC:6302]	2	903.876529	-0.6243955	0.00229357	910.08	1046.42	595.28	897.62	1105.88	1384.67	508.4	782.67
ENSG000001.UQCR11	ubiquinol-cytochrome c reductase, complex III subunit XI [Source:HGNC Symbol;Acc:HGNC:30862]	19	567.08368	-0.6240642	4.29E-06	657.91	832.59	442.15	515.47	624.1	659.87	406.28	398.3
ENSG000000.NDC1	NDC1 transmembrane nucleoporin [Source:HGNC Symbol;Acc:HGNC:25525]	1	7200.42523	-0.6238684	6.25E-10	9674.33	9968.41	6139.38	6005.88	7848.83	7649.13	5188.28	5129.16
ENSG000001.ICE1	interactor of little elongation complex ELL subunit 1 [Source:HGNC Symbol;Acc:HGNC:29154]	5	6111.34213	-0.6236952	0.01758106	7661.73	8042.09	6304.68	7120.75	7151.65	6904.27	2563.94	3141.62
ENSG000001.MAST1	microtubule associated serine/threonine kinase 1 [Source:HGNC Symbol;Acc:HGNC:19034]	19	601.085009	-0.6236324	0.01606082	603.88	750.28	258.6	316.98	685.64	902.43	634.67	656.21
ENSG000001.TUBA1B	tubulin, alpha 1b [Source:HGNC Symbol;Acc:HGNC:18809]	12	21180.9312	-0.6215281	4.43E-11	27849.37	30375.46	18590.55	19541.32	21052.01	23764.83	13664.12	14609.78
ENSG000001.FAM72B	family with sequence similarity 72, member B [Source:HGNC Symbol;Acc:HGNC:24805]	1	2894.61779	-0.6213467	1.52E-08	3393.84	3782.62	2273.62	2548.7	3363.78	3555.27	2000.64	2238.47
ENSG000000.DHX33	DEAH (Asp-Glu-Ala-His) box polypeptide 33 [Source:HGNC Symbol;Acc:HGNC:16718]	17	4624.54976	-0.6212042	1.38E-06	5913.62	6392.99	4067.57	4584.89	5034.14	5122.34	2981.2	2899.65
ENSG000001.C10orf2	chromosome 10 open reading frame 2 [Source:HGNC Symbol;Acc:HGNC:1160]	10	2962.04137	-0.6208593	0.00066716	4308.66	4891.48	2323.31	2428.22	2771.42	2746.43	2178.53	2048.28
ENSG000001.SLRP	SRA stem-loop interacting RNA binding protein [Source:HGNC Symbol;Acc:HGNC:20495]	14	2872.19289	-0.6204294	0.00243989	4133.28	3594.34	3608.18	2474.64	3454.18	2690.09	1739.31	1283.53
ENSG000001.PSRC1	proline/serine-rich coiled-coil 1 [Source:HGNC Symbol;Acc:HGNC:24472]	1	330.290991	-0.6194821	0.0005178	366.88	482.53	218.03	273.53	320.22	456.47	244.86	279.81
ENSG000001.SLCO3A1	solute carrier organic anion transporter family, member 3A1 [Source:HGNC Symbol;Acc:HGNC:10952]	15	6210.4452	-0.6194437	2.37E-06	8305.42	9464.12	5153.68	7016.08	5612.08	6745.75	3665.29	3721.15
ENSG000001.NR2F6	nuclear receptor subfamily 2, group F, member 6 [Source:HGNC Symbol;Acc:HGNC:7977]	19	681.662595	-0.6187281	0.00125549	828.55	750.28	550.66	619.15	909.7	860.41	454.59	479.96
ENSG000001.CDCA2	cell division cycle associated 2 [Source:HGNC Symbol;Acc:HGNC:14623]	8	3019.65893	-0.6186329	8.41E-06	3925.66	4322.86	2090.07	2713.61	3110.87	3409.16	2240.02	2345.01
ENSG000001.AFAP1	actin filament associated protein 1 [Source:HGNC Symbol;Acc:HGNC:24017]	4	613.816447	-0.6184336	0.02842474	565.96	806.1	220.06	308.1	750.07	869	632.48	758.77
ENSG000002.ILF3-AS1	ILF3 antisense RNA 1 (head to head) [Source:HGNC Symbol;Acc:HGNC:27115]	19	550.978478	-0.6180331	0.00033614	688.25	471.17	452.29	320.93	915.47	642.68	458.98	458.05
ENSG000001.TUBA1C	tubulin, alpha 1c [Source:HGNC Symbol;Acc:HGNC:20768]	12	16538.8398	-0.6174378	7.54E-09	23316.04	24483.91	15141.58	14274.08	15792.86	17117.44	10467.7	11717.1

ENSG000002	ALG3		ALG3, alpha-1,3- mannosyltransferase [Source:HGNC Symbol;Acc:HGNC:23056]	3	4530.42999	-0.6174	1.01E-06	5765.73	6189.57	3606.15	3460.14	5207.23	4950.45	3765.21	3298.95
ENSG000001	FGD6		FYVE, RhoGEF and PH domain containing 6 [Source:HGNC Symbol;Acc:HGNC:21740]	12	366.926345	-0.6170664	0.00217712	504.34	450.36	326.54	206.38	419.27	426.86	290.98	310.68
ENSG000000	KIF2A		kinesin heavy chain member 2A [Source:HGNC Symbol;Acc:HGNC:6318]	5	9022.69555	-0.6167469	0.00309822	12978.11	12504.04	10214.05	10049.63	9210.5	8690.98	4153.92	4380.35
ENSG000000	FRY		furry homolog (Drosophila) [Source:HGNC Symbol;Acc:HGNC:20367]	13	338.873285	-0.6161254	0.00861169	674.03	290.46	308.29	152.07	453.89	260.7	395.3	176.25
ENSG000001	SLC6A6		solute carrier family 6 (neurotransmitter transporter), member 6 [Source:HGNC Symbol;Acc:HGNC:11052]	3	3142.63783	-0.616037	1.92E-06	3591.97	4505.46	2026.18	2729.41	3583.04	3635.49	2438.77	2630.8
ENSG000001	TLE1		transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila) [Source:HGNC Symbol;Acc:HGNC:11837]	9	2059.94569	-0.6157689	0.00020959	2039.15	2209.21	1449.15	1712.3	2596.4	3292.66	1466.99	1713.7
ENSG000000	NTHL1		nth-like DNA glycosylase 1 [Source:HGNC Symbol;Acc:HGNC:8028]	16	1238.01974	-0.6156834	0.00652976	1567.04	1721.95	661.2	911.45	1461.68	1332.15	1274.83	973.85
ENSG000001	SEPT6		septin 6 [Source:HGNC Symbol;Acc:HGNC:15848]	X	6031.99419	-0.615488	0.00167185	7402.93	7087.45	5540.05	5774.81	7268.96	7682.56	3400.66	4098.55
ENSG000001	GPSM2		G-protein signaling modulator 2 [Source:HGNC Symbol;Acc:HGNC:29501]	1	646.329764	-0.614216	0.00012663	705.31	861.92	408.68	526.33	743.34	837.49	440.32	647.24
ENSG000000	NUBP2		nucleotide binding protein 2 [Source:HGNC Symbol;Acc:HGNC:8042]	16	2672.13703	-0.614086	1.72E-05	3051.61	3182.78	1589.1	2199.13	3460.91	3294.57	2454.14	2144.87
ENSG000000	RNF126		ring finger protein 126 [Source:HGNC Symbol;Acc:HGNC:21151]	19	2283.86496	-0.6126181	4.24E-07	2726.45	2693.63	1599.24	1757.72	2807	2876.3	2018.21	1792.37
ENSG000001	FAM72A		family with sequence similarity 72, member A [Source:HGNC Symbol;Acc:HGNC:24044]	1	4031.80723	-0.6123438	6.15E-09	4811.1	5122.34	3228.91	3482.86	4746.61	4900.79	2920.81	3041.05
ENSG000001	TOP2A		topoisomerase (DNA) II alpha 170kDa [Source:HGNC Symbol;Acc:HGNC:11989]	17	18974.4033	-0.6113584	1.64E-09	24605.32	30359.37	14879.94	20149.61	15567.84	21536.94	9902.2	14794
ENSG000000	TIMM13		translocase of inner mitochondrial membrane 13 homolog (yeast) [Source:HGNC Symbol;Acc:HGNC:11816]	19	3410.72454	-0.6105744	6.68E-07	4255.57	5165.86	2843.55	3495.69	3565.73	3549.54	2433.28	1976.58
ENSG000001	TUBA4A		tubulin, alpha 4a [Source:HGNC Symbol;Acc:HGNC:12407]	2	9746.06161	-0.6104383	4.17E-07	13272.94	12519.17	8074.29	7291.58	10425.04	11251.2	7586.42	7547.86
ENSG000001	RPTOR		regulatory associated protein of MTOR, complex 1 [Source:HGNC Symbol;Acc:HGNC:30287]	17	2420.78284	-0.6101153	0.00271843	2806.08	2968.01	2105.28	2479.57	3156.07	2877.26	1557.03	1416.97
ENSG000001	HOOK3		hook microtubule-tethering protein 3 [Source:HGNC Symbol;Acc:HGNC:23576]	8	8983.66094	-0.6098461	0.00196405	10811.93	13539.1	8758.81	10378.46	8408.5	10557.9	4101.21	5313.37
ENSG000000	NAALAD2		N-acetylated alpha-linked acidic dipeptidase 2 [Source:HGNC Symbol;Acc:HGNC:14526]	11	98.8314344	-0.609735	0.03377003	164	75.69	74.03	66.16	141.36	119.37	71.37	78.66
ENSG000000	DGKG		diacylglycerol kinase, gamma 90kDa [Source:HGNC Symbol;Acc:HGNC:2853]	3	397.946039	-0.6095752	0.00019482	666.44	551.59	444.18	376.23	321.18	393.44	174.59	255.91
ENSG000001	FAM78B		family with sequence similarity 78, member B [Source:HGNC Symbol;Acc:HGNC:13495]	1	1305.34688	-0.609385	0.04017996	1882.73	1377.56	1774.68	1172.14	1885.76	1206.1	755.46	388.35
ENSG000001	TNKS1BP1		tankyrase 1 binding protein 1, 182kDa [Source:HGNC Symbol;Acc:HGNC:19081]	11	1924.49122	-0.6088043	0.03967714	2315.96	2558.33	810.27	964.77	2288.68	2275.64	2331.16	1851.12
ENSG000000	NOP16		NOP16 nucleolar protein [Source:HGNC Symbol;Acc:HGNC:26934]	5	3672.10979	-0.6083648	1.06E-06	5259.5	5157.35	3612.24	2861.73	3887.87	3571.5	2577.12	2449.57
ENSG000001	MDC1		mediator of DNA-damage checkpoint 1 [Source:HGNC Symbol;Acc:HGNC:21163]	6	8810.10332	-0.608342	0.00051715	9290.39	10436.74	7397.89	7645.1	12030.96	11340.96	6096.37	6242.42
ENSG000001	C20orf27		chromosome 20 open reading frame 27 [Source:HGNC Symbol;Acc:HGNC:15873]	20	3087.38363	-0.6079657	5.27E-06	3625.15	4550.88	2048.49	2739.28	3532.07	3323.22	2605.67	2274.31
ENSG000001	C16orf59		chromosome 16 open reading frame 59 [Source:HGNC Symbol;Acc:HGNC:25849]	16	1306.59105	-0.6073531	0.00043858	1631.51	1798.59	846.78	1075.37	1442.45	1505.95	1189.19	962.9
ENSG000001	PODXL		podocalyxin-like [Source:HGNC Symbol;Acc:HGNC:9171]	7	6107.10978	-0.6070507	0.00019532	6154.41	9798.11	3130.54	5742.22	5890.95	7901.24	4521.76	5717.65

ENSG000001	PRPS1	phosphoribosyl pyrophosphate synthetase 1 [Source:HGNC Symbol;Acc:HGNC:9462] X family with sequence similarity 107, member B [Source:HGNC	14957.3016	-0.6051243	1.76E-08	16051.52	23307.88	10824.54	14184.22	15574.57	17795.45	10951.94	10968.29	
ENSG000000	FAM107B	Symbol;Acc:HGNC:23726] secreted frizzled-related protein 1	10	2109.62779	-0.6049187	0.006204	2520.73	2908.4	2083.98	2296.89	2495.43	2297.6	1076.09	1197.9
ENSG000001	SFRP1	[Source:HGNC Symbol;Acc:HGNC:10776] coenzyme Q3 methyltransferase	8	793.762234	-0.6025479	0.00351996	958.43	995.33	468.52	511.52	963.55	950.17	758.75	743.83
ENSG000001	COQ3	[Source:HGNC Symbol;Acc:HGNC:18175] WD repeat domain 12 [Source:HGNC	6	814.173804	-0.6025398	0.00117736	1112	889.36	848.8	660.63	1152.99	811.71	569.89	468.01
ENSG000001	WDR12	Symbol;Acc:HGNC:14098] RBPJ interacting and tubulin associated 1	2	5305.82138	-0.6017888	1.63E-05	8115.82	6525.45	4665.89	3762.31	6172.71	5035.44	4689.77	3479.18
ENSG000001	RITA1	[Source:HGNC Symbol;Acc:HGNC:25925] telomerase reverse transcriptase	12	1672.66429	-0.6013532	0.00350591	2002.17	2202.59	987.74	1097.09	1979.04	1965.28	1654.76	1492.64
ENSG000001	TERT	[Source:HGNC Symbol;Acc:HGNC:11730] hydroxyacylglutathione hydrolase-like	5	2366.52151	-0.6004865	0.03351434	2560.55	3221.57	878.21	1455.55	2728.15	3015.73	2790.14	2282.28
ENSG000001	HAGHL	[Source:HGNC Symbol;Acc:HGNC:14177] S-phase kinase-associated protein 2, E3 ubiquitin protein ligase [Source:HGNC	16	600.206145	-0.5999996	0.04676933	764.09	693.51	260.62	291.31	796.23	663.69	875.14	457.05
ENSG000001	SKP2	Symbol;Acc:HGNC:10901] NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10, 22kDa [Source:HGNC	5	1590.13713	-0.5987391	0.00030373	2245.81	2397.49	1215.91	1342.98	1555.92	1595.72	1190.28	1176.99
ENSG000001	NDUFB10	Symbol;Acc:HGNC:7696] leucine rich repeat and fibronectin type III domain containing 1 [Source:HGNC	16	5479.46252	-0.598561	0.00231222	6782.93	6733.6	5440.67	5250.45	6714.1	6306.48	3630.15	2977.32
ENSG000001	LRFN1	Symbol;Acc:HGNC:29290] solute carrier family 16 (monocarboxylate transporter), member 7 [Source:HGNC	19	869.15129	-0.5983305	0.00013256	897.76	1120.22	580.07	876.89	978.94	1218.51	558.91	721.93
ENSG000001	SLC16A7	Symbol;Acc:HGNC:10928] forkhead box J1 [Source:HGNC	12	1610.4052	-0.5976246	0.00041879	2242.97	1934.83	1605.33	1442.71	2142.51	1499.27	1049.73	965.89
ENSG000001	FOXJ1	Symbol;Acc:HGNC:3816] phosphatase domain containing, paladin 1	17	2206.38927	-0.5962671	0.00472193	2753.94	3347.4	1273.71	1795.25	2101.16	2621.33	1863.39	1894.93
ENSG000001	PALD1	[Source:HGNC Symbol;Acc:HGNC:23530] phosphatidylinositol-4-phosphate 5-kinase, type I, beta [Source:HGNC	10	2313.54135	-0.594433	0.00217712	2073.27	3330.37	1118.56	1658.97	2411.77	3421.58	2073.12	2420.69
ENSG000001	PIP5K1B	Symbol;Acc:HGNC:8995] coiled-coil domain containing 85B	9	486.994336	-0.5943996	0.02720123	490.12	686.89	369.13	645.81	474.08	713.35	189.96	326.61
ENSG000001	CCDC85B	[Source:HGNC Symbol;Acc:HGNC:24926] tight junction protein 1 [Source:HGNC	11	1149.83603	-0.5940552	0.01832734	1267.48	1224.29	493.87	643.84	1535.72	1506.91	1468.09	1058.49
ENSG000001	TJP1	Symbol;Acc:HGNC:11827] interferon stimulated exonuclease gene 20kDa-like 2 [Source:HGNC	15	1279.41695	-0.5935466	3.04E-05	1930.13	1216.72	1290.95	665.56	1598.23	1433.38	1050.83	1049.53
ENSG000001	ISG20L2	Symbol;Acc:HGNC:25745] family with sequence similarity 117, member B [Source:HGNC	1	14424.9879	-0.5935089	2.16E-07	19106.93	16887.45	12150.99	9972.6	18337.33	15449.15	12298.14	11197.31
ENSG000001	FAM117B	Symbol;Acc:HGNC:14440] leucine rich repeat containing 40	2	645.853206	-0.5934555	0.01331434	866.47	1071.02	385.36	531.27	551.98	707.62	444.71	608.41
ENSG000000	LRRC40	[Source:HGNC Symbol;Acc:HGNC:26004] coordinator of PRMT5, differentiation stimulator [Source:HGNC	1	3566.65482	-0.5932308	0.0393863	4222.39	3243.33	3763.34	3153.04	5680.35	4549.37	2064.33	1857.09
ENSG000001	COPRS	Symbol;Acc:HGNC:28848] REX4 homolog, 3'-5' exonuclease	17	1527.65632	-0.5919281	1.62E-05	1831.53	2380.46	1383.24	1581.95	1526.11	1634.87	931.15	951.95
ENSG000001	REXO4	[Source:HGNC Symbol;Acc:HGNC:12820] protocadherin gamma subfamily C, 3	9	3481.82126	-0.591839	1.76E-07	4520.06	5467.68	3041.3	3257.71	3314.74	3582.96	2341.04	2329.08
ENSG000002	PCDHGC3	[Source:HGNC Symbol;Acc:HGNC:8716] erythropoietin receptor [Source:HGNC	5	81.7078097	-0.5915556	0.04201757	57.83	119.21	30.42	67.15	79.82	144.2	39.53	115.51
ENSG000001	EPOR	Symbol;Acc:HGNC:3416] prothymosin, alpha [Source:HGNC	19	663.113349	-0.5912946	0.04149339	767.88	882.74	295.1	345.62	720.26	868.05	655.53	769.72
ENSG000001	PTMA	Symbol;Acc:HGNC:9623]	2	126259.671	-0.5911754	5.84E-11	189086.04	184801.61	124777.35	124565.2	118141.11	116439.65	77110.46	75155.94

ENSG000001	NHP2	NHP2 ribonucleoprotein [Source:HGNC Symbol;Acc:HGNC:14377]	5	2769.69916	-0.5906089	5.82E-09	3579.65	3687.06	2425.74	2357.12	3161.84	2944.1	2064.33	1937.75
ENSG000001	HNRNPA2B1	heterogeneous nuclear ribonucleoprotein A2/B1 [Source:HGNC Symbol;Acc:HGNC:5033]	7	90627.0265	-0.5903328	1.21E-09	127439.54	118785.49	86768.75	81143.55	96337.1	93915.3	62095.74	58530.74
ENSG000000	HSD3B7	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 7 [Source:HGNC Symbol;Acc:HGNC:18324]	16	5049.11672	-0.5887778	0.02046942	6197.07	6953.1	2538.3	3200.44	5946.72	5511	5473.77	4572.53
ENSG000002	FAM27E4	family with sequence similarity 27, member E4 [Source:HGNC Symbol;Acc:HGNC:44415]	9	143.564442	-0.5885462	0.00835842	224.68	208.15	133.86	140.22	149.05	120.32	106.51	65.72
ENSG000001	MDN1	midasin AAA ATPase 1 [Source:HGNC Symbol;Acc:HGNC:18302]	6	9385.22657	-0.5885401	4.38E-09	10311.39	11920.27	7090.61	8013.43	10693.33	12382.81	7027.51	7642.45
ENSG000001	HSPBP1	HSPA (heat shock 70kDa) binding protein, cytoplasmic cochaperone 1 [Source:HGNC Symbol;Acc:HGNC:24989]	19	1141.14971	-0.5880365	4.22E-06	1476.03	1596.12	980.64	1126.72	1253	1176.5	830.12	690.06
ENSG000001	NAA38	N(alpha)-acetyltransferase 38, NatC auxiliary subunit [Source:HGNC Symbol;Acc:HGNC:28212]	17	2106.66009	-0.5861806	4.00E-07	2315.01	2703.09	1513.04	1919.67	2613.71	2527.75	1730.52	1530.48
ENSG000001	WDR35	WD repeat domain 35 [Source:HGNC Symbol;Acc:HGNC:29250]	2	1972.41708	-0.585653	6.81E-05	3078.15	1799.54	2462.24	1057.6	2935.86	1629.14	1815.07	1001.73
ENSG000001	RNF125	ring finger protein 125, E3 ubiquitin protein ligase [Source:HGNC Symbol;Acc:HGNC:21150]	18	1825.47858	-0.585486	0.00014469	2186.09	2299.09	1360.93	1836.72	2121.36	2203.06	1385.74	1210.84
ENSG000001	PDE12	phosphodiesterase 12 [Source:HGNC Symbol;Acc:HGNC:25386]	3	4671.90567	-0.5853761	0.00766501	7095.77	6762.93	5876.73	5529.91	4067.7	4146.38	1939.15	1956.67
ENSG000001	SURF2	surfeit 2 [Source:HGNC Symbol;Acc:HGNC:11475]	9	872.864957	-0.5852343	3.92E-05	1276.96	1391.76	957.31	903.55	792.38	734.35	465.57	461.04
ENSG000001	S100BPB	S100P binding protein [Source:HGNC Symbol;Acc:HGNC:25768]	1	3708.35748	0.58588318	4.83E-09	2652.5	2777.83	4188.25	4109.91	3159.92	3200.99	4695.26	4882.21
ENSG000002	SCAMP1-AS1	SCAMP1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:50544]	5	301.119408	0.58657743	0.00028971	196.24	206.26	303.22	318.96	262.53	282.66	392	447.1
ENSG000001	LARP6	La ribonucleoprotein domain family, member 6 [Source:HGNC Symbol;Acc:HGNC:24012]	15	79.4355884	0.58678077	0.04205822	71.1	48.25	94.31	67.15	57.7	61.12	105.41	130.44
ENSG000001	INPPL1	inositol polyphosphate phosphatase-like 1 [Source:HGNC Symbol;Acc:HGNC:6080]	11	11178.8565	0.58734094	3.62E-05	7759.37	8042.09	10622.74	10776.41	9121.06	10005.94	16442.18	16661.05
ENSG000001	ZNF606	zinc finger protein 606 [Source:HGNC Symbol;Acc:HGNC:25879]	19	209.039502	0.58767837	0.0225619	175.38	190.17	243.38	216.26	134.63	140.38	262.43	309.68
ENSG000001	ACCS	1-aminocyclopropane-1-carboxylate synthase homolog (Arabidopsis)(non-functional) [Source:HGNC Symbol;Acc:HGNC:23989]	11	1893.59822	0.58788221	0.0023951	1074.08	885.58	1284.87	1204.73	1985.77	1738.01	3329.28	3646.47
ENSG000001	DMXL2	Dmx-like 2 [Source:HGNC Symbol;Acc:HGNC:2938]	15	978.288625	0.58800834	0.00016312	687.3	709.6	1211.85	1206.71	895.28	797.38	1155.15	1163.05
ENSG000001	PKD2	polycystic kidney disease 2 (autosomal dominant) [Source:HGNC Symbol;Acc:HGNC:9009]	4	876.806256	0.58913231	0.00026427	693.94	725.68	938.05	981.56	607.75	722.9	1074.99	1269.59
ENSG000001	GAB1	GRB2-associated binding protein 1 [Source:HGNC Symbol;Acc:HGNC:4066]	4	1241.63696	0.58970045	2.83E-05	1094.94	1254.57	1606.34	2274.18	687.57	827.94	960.79	1226.78
ENSG000001	CSGALNACT2	chondroitin sulfate N-acetylgalactosaminyltransferase 2 [Source:HGNC Symbol;Acc:HGNC:24292]	10	2781.20823	0.58990704	5.09E-06	2634.49	2362.48	4619.24	3331.77	1876.14	1855.46	2980.1	2589.97
ENSG000001	ELF4	E74-like factor 4 (ets domain transcription factor) [Source:HGNC Symbol;Acc:HGNC:3319]	X	3936.75581	0.59021719	0.00412352	3614.72	3706.93	4721.67	4450.59	2159.82	2897.31	4813.84	5129.16
ENSG000001	DMPK	dystrophia myotonica-protein kinase [Source:HGNC Symbol;Acc:HGNC:2933]	19	888.092681	0.591518	1.96E-05	580.18	756.9	964.41	1200.78	636.6	836.53	1009.11	1120.23
ENSG000001	C2	complement component 2 [Source:HGNC Symbol;Acc:HGNC:1248]	6	102.316082	0.59153712	0.02720338	90.06	45.41	191.67	60.24	104.82	64.94	165.81	95.59

ENSG000002	MF12-AS1		MF12 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:40373]	3	164.081955	0.59227673	0.03583952	99.54	105.02	106.48	148.12	121.17	153.75	299.77	278.81
ENSG000002	BTBD19		BTB (POZ) domain containing 19 [Source:HGNC Symbol;Acc:HGNC:27145]	1	87.5643012	0.59228111	0.02516252	87.22	62.44	136.9	84.92	62.51	54.43	117.49	94.6
ENSG000001	PRKAB2		protein kinase, AMP-activated, beta 2 non-catalytic subunit [Source:HGNC Symbol;Acc:HGNC:9379]	1	5114.9563	0.59443374	0.00066959	3358.76	3994.55	6190.09	7573.02	4117.7	4494.94	5176.2	6014.39
ENSG000001	ABCD1	X	ATP-binding cassette, sub-family D (ALD), member 1 [Source:HGNC Symbol;Acc:HGNC:61]		363.39572	0.59447083	0.00033377	281.56	248.83	419.84	368.33	275.99	331.37	496.32	484.93
ENSG000001	CPNE5		copine V [Source:HGNC Symbol;Acc:HGNC:2318]	6	165.110806	0.5955035	0.04249733	104.28	70.01	178.48	67.15	163.48	126.05	417.26	194.17
ENSG000001	SLMO1		slowmo homolog 1 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:24639]	18	114.412333	0.59556611	0.02390602	75.84	115.43	136.9	135.29	75.01	84.04	139.45	153.35
ENSG000001	RIPK1		receptor (TNFRSF)-interacting serine-threonine kinase 1 [Source:HGNC Symbol;Acc:HGNC:10019]	6	1721.3278	0.59659272	0.00417929	1565.15	1782.51	2118.46	2065.82	968.36	1099.14	1912.8	2258.38
ENSG000002	ANKRD10-IT1		ANKRD10 intronic transcript 1 [Source:HGNC Symbol;Acc:HGNC:39891]	13	142.666003	0.59834476	0.01848112	120.4	75.69	138.93	127.39	116.36	119.37	236.08	207.12
ENSG000001	JUNB		jun B proto-oncogene [Source:HGNC Symbol;Acc:HGNC:6205]	19	5108.09311	0.59910447	0.00195089	2983.35	2693.63	4970.12	5653.35	4952.4	5534.88	7845.56	6231.46
ENSG000001	ZNF84		zinc finger protein 84 [Source:HGNC Symbol;Acc:HGNC:13159]	12	895.932058	0.59929103	0.01173617	1007.72	506.18	1188.53	620.14	837.58	396.3	1700.88	910.12
ENSG000001	ARHGEF17		Rho guanine nucleotide exchange factor (GEF) 17 [Source:HGNC Symbol;Acc:HGNC:21726]	11	275.910657	0.59976142	0.03030102	157.37	227.07	163.27	297.23	153.86	267.39	364.55	576.54
ENSG000002	MTRNR2L12		MT-RNR2-like 12 [Source:HGNC Symbol;Acc:HGNC:37169]	3	181.217106	0.60010205	0.01864879	131.77	100.29	151.1	160.96	188.48	125.1	305.26	286.78
ENSG000001	TEP1		telomerase-associated protein 1 [Source:HGNC Symbol;Acc:HGNC:11726]	14	1147.36288	0.60024318	0.00034437	711.95	642.42	1387.29	1053.65	1194.35	1079.09	1532.88	1577.28
ENSG000001	ERMAP		erythroblast membrane-associated protein (Scianna blood group) [Source:HGNC Symbol;Acc:HGNC:15743]	1	457.562834	0.60080875	0.0006902	367.82	387.91	598.32	482.88	323.11	346.65	574.28	579.53
ENSG000001	GPR87		G protein-coupled receptor 87 [Source:HGNC Symbol;Acc:HGNC:4538]	3	145.677023	0.60243941	0.0458398	6.64	7.57	529.36	461.16	24.04	25.78	57.1	53.77
ENSG000001	GADD45A		growth arrest and DNA-damage-inducible, alpha [Source:HGNC Symbol;Acc:HGNC:4095]	1	4815.68274	0.60278231	0.01275962	3325.58	2300.98	7814.68	4942.36	4993.75	4234.24	6224.84	4689.03
ENSG000001	ZNF385A		zinc finger protein 385A [Source:HGNC Symbol;Acc:HGNC:17521]	12	166.366524	0.60416607	0.02627427	70.15	148.54	108.51	172.81	75.97	210.09	194.35	350.51
ENSG000001	TSPYL2	X	TSPY-like 2 [Source:HGNC Symbol;Acc:HGNC:24358]		913.268474	0.60489501	0.00600287	650.33	709.6	926.89	779.13	672.18	727.67	1351.7	1488.66
ENSG000001	RAB4B		RAB4B, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:9782]	19	95.4655132	0.6051586	0.02174398	50.24	45.41	100.4	75.05	96.16	99.31	164.71	132.44
ENSG000002	MYL5		myosin, light chain 5, regulatory [Source:HGNC Symbol;Acc:HGNC:7586]	4	265.048065	0.60521624	0.00125419	211.4	147.6	277.86	236.01	261.56	197.67	455.69	332.58
ENSG000001	NLRX1		NLR family member X1 [Source:HGNC Symbol;Acc:HGNC:29890]	11	1408.75103	0.60667979	0.00482221	820.02	1037.9	982.67	1305.45	1163.57	1172.68	2299.31	2488.4
ENSG000002	LINC00106	X	long intergenic non-protein coding RNA 106 [Source:HGNC Symbol;Acc:HGNC:31843]		80.5212638	0.60670038	0.03059416	36.97	37.85	51.72	53.32	73.08	87.86	146.04	157.33
ENSG000001	ITPR2		inositol 1,4,5-trisphosphate receptor, type 2 [Source:HGNC Symbol;Acc:HGNC:6181]	12	3145.53925	0.60729693	0.00266419	2371.89	2361.54	4589.83	4915.7	2354.07	2488.59	2817.59	3265.1
ENSG000000	SPAG4		sperm associated antigen 4 [Source:HGNC Symbol;Acc:HGNC:11214]	20	63.7646767	0.60751927	0.04778121	39.82	17.98	68.96	23.7	85.59	37.24	180.08	56.76
ENSG000001	MIR22HG		MIR22 host gene [Source:HGNC Symbol;Acc:HGNC:28219]	17	848.815323	0.60764378	0.00037956	957.48	508.07	1604.31	993.41	637.56	518.54	864.16	706.99
ENSG000001	HAS3		hyaluronan synthase 3 [Source:HGNC Symbol;Acc:HGNC:4820]	16	141.862782	0.60774943	0.00985769	106.18	141.92	189.64	177.75	102.89	84.99	181.18	150.36

ENSG000001: SYNM	synemin, intermediate filament protein [Source:HGNC Symbol;Acc:HGNC:24466]	15	1512.25509	0.60778951	0.02570631	1341.42	1376.62	1482.62	1602.69	835.66	998.88	2321.27	2138.89
ENSG000001: TUFT1	tuftelin 1 [Source:HGNC Symbol;Acc:HGNC:12422]	1	2791.39103	0.60861681	6.51E-08	2125.41	2148.66	3504.74	3029.6	2255.02	2233.62	3474.23	3559.84
ENSG000002: DENND6B	DENN/MADD domain containing 6B [Source:HGNC Symbol;Acc:HGNC:32690]	22	504.908528	0.60988066	0.00646412	238.9	386.02	484.74	802.82	370.23	572.01	519.38	665.17
ENSG000000: CDK17	cyclin-dependent kinase 17 [Source:HGNC Symbol;Acc:HGNC:8750]	12	1715.10133	0.61085694	0.01709453	1124.33	1336.88	2812.11	2858.77	1276.08	1324.51	1473.58	1514.55
ENSG000000: MTMR11	myotubularin related protein 11 [Source:HGNC Symbol;Acc:HGNC:24307]	1	560.299323	0.61110059	0.0002422	684.46	363.31	939.06	518.43	432.73	275.02	799.38	470
ENSG000001: GLIPR2	GLI pathogenesis-related 2 [Source:HGNC Symbol;Acc:HGNC:18007]	9	596.138766	0.61161601	0.01181447	382.04	608.36	417.81	823.56	284.64	512.81	601.73	1138.15
ENSG000001: FRMD4A	FERM domain containing 4A [Source:HGNC Symbol;Acc:HGNC:25491]	10	86.793173	0.61236079	0.03048942	53.09	55.82	78.09	76.04	59.62	87.86	139.45	144.39
ENSG000002: PTOV1-AS2	PTOV1 antisense RNA 2 [Source:HGNC Symbol;Acc:HGNC:51284]	19	105.983139	0.61304424	0.00970966	68.26	70.96	119.66	104.67	99.05	84.04	165.81	135.42
ENSG000001: HECA	hdc homolog, cell cycle regulator [Source:HGNC Symbol;Acc:HGNC:21041]	6	1490.00664	0.61343539	1.27E-08	945.16	1073.86	1451.18	1681.69	1127.99	1530.78	1773.35	2336.05
ENSG000002: FTH1P7	ferritin, heavy polypeptide 1 pseudogene 7 [Source:HGNC Symbol;Acc:HGNC:3994]	13	311.71749	0.61388008	0.04291691	402.9	356.69	492.85	431.53	92.32	127.96	320.63	268.86
ENSG000001: ARSA	arylsulfatase A [Source:HGNC Symbol;Acc:HGNC:713]	22	1859.44088	0.61479656	3.30E-06	939.47	840.16	1243.29	1409.14	1913.64	2058.87	3148.11	3322.85
ENSG000001: ZNF274	zinc finger protein 274 [Source:HGNC Symbol;Acc:HGNC:13068]	19	1079.97576	0.61630387	0.0006902	820.02	927.21	1127.68	1206.71	702.95	883.33	1438.44	1533.47
ENSG000000: PLEKHG2	pleckstrin homology domain containing, family G (with RhoGef domain) member 2 [Source:HGNC Symbol;Acc:HGNC:29515]	19	3456.01313	0.61681033	4.15E-06	2079.91	2083.38	3273.53	2748.17	3142.61	3335.63	5063.1	5921.78
ENSG000001: ACYP1	acylphosphatase 1, erythrocyte (common) type [Source:HGNC Symbol;Acc:HGNC:179]	14	837.460879	0.61684742	3.66E-07	739.44	735.14	1170.28	1165.23	591.4	550.05	882.83	865.31
ENSG000001: EFEMP2	EGF containing fibulin-like extracellular matrix protein 2 [Source:HGNC Symbol;Acc:HGNC:3219]	11	66.111048	0.61685301	0.04084445	35.08	39.74	54.76	96.77	45.2	75.44	71.37	110.53
ENSG000001: CCT6B	chaperonin containing TCP1, subunit 6B (zeta 2) [Source:HGNC Symbol;Acc:HGNC:1621]	17	59.2670408	0.61822875	0.04629162	43.61	44.47	99.38	60.24	48.08	36.29	71.37	70.7
ENSG000001: ODF3B	outer dense fiber of sperm tails 3B [Source:HGNC Symbol;Acc:HGNC:34388]	22	440.718204	0.61895027	0.03162749	307.15	236.53	337.7	286.37	339.46	345.69	1036.56	636.29
ENSG000001: GLT8D2	glycosyltransferase 8 domain containing 2 [Source:HGNC Symbol;Acc:HGNC:24890]	12	118.862506	0.61911801	0.00793578	125.14	77.58	191.67	111.59	90.39	68.76	160.32	125.47
ENSG000002: LUCAT1	lung cancer associated transcript 1 (non- protein coding) [Source:HGNC Symbol;Acc:HGNC:48498]	5	397.491193	0.61921948	0.0224671	338.44	81.37	586.15	257.73	600.06	226.32	807.07	282.8
ENSG000001: GNLY	granulysin [Source:HGNC Symbol;Acc:HGNC:4414]	2	2311.30996	0.61983738	0.01118309	1611.6	2699.3	1627.64	3920.31	768.34	1898.44	1712.96	4251.89
ENSG000002: SOD1P3	superoxide dismutase 1, soluble pseudogene 3 [Source:HGNC Symbol;Acc:HGNC:45136]	8	1737.96119	0.62197032	0.013828	1104.42	612.15	2266.52	1481.23	2259.83	1305.41	3622.46	1251.67
ENSG000001: GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N- acetylmannosamine kinase [Source:HGNC Symbol;Acc:HGNC:23657]	9	3394.14523	0.62300916	3.04E-06	2327.34	3098.57	3150.82	4853.48	2350.22	2720.65	3676.27	4975.81
ENSG000001: FAM129A	family with sequence similarity 129, member A [Source:HGNC Symbol;Acc:HGNC:16784]	1	10104.9907	0.62351357	0.00055253	6644.53	8541.65	13113.38	16404.09	6140.97	9503.64	7834.58	12657.1
ENSG000001: C21orf91	chromosome 21 open reading frame 91 [Source:HGNC Symbol;Acc:HGNC:16459]	21	8673.69527	0.62376525	1.47E-06	7397.24	8636.26	12571.84	11853.76	5057.21	6031.45	8976.55	8865.25
ENSG000001: TYMSOS	TYMS opposite strand [Source:HGNC Symbol;Acc:HGNC:29553]	18	143.320606	0.62398018	0.00384133	133.67	73.8	199.78	111.59	134.63	94.54	227.3	171.27
ENSG000002: MT-RNR1	mitochondrially encoded 12S RNA [Source:HGNC Symbol;Acc:HGNC:7470]	MT	21813.7875	0.62428699	0.0040881	18360.85	9677	22807.19	12022.62	23675.34	13137.22	42978.72	31851.36

ENSG000001	ABHD4	abhydrolase domain containing 4 [Source:HGNC Symbol;Acc:HGNC:20154]	14	1488.25539	0.62470201	0.00286785	1024.79	1005.73	1757.44	2374.9	1184.73	1306.37	1463.7	1788.38
ENSG000002	RUSC1-AS1	RUSC1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:26680]	1	1092.90812	0.62494002	0.00322653	660.76	526.05	752.46	764.31	937.59	1080.05	2086.29	1935.76
ENSG000001	ZNF720	zinc finger protein 720 [Source:HGNC Symbol;Acc:HGNC:26987]	16	691.086124	0.62575451	0.00015558	476.84	536.45	957.31	808.75	490.43	630.27	711.54	917.09
ENSG000002	SDCBP2-AS1	SDCBP2 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44314]	20	228.000293	0.62672412	0.00075469	181.07	149.49	316.4	208.36	191.36	175.71	311.85	289.77
ENSG000000	ITGB5	integrin, beta 5 [Source:HGNC Symbol;Acc:HGNC:6160]	3	933.051524	0.62769086	0.00425399	692.99	571.46	1390.34	597.43	806.81	686.61	1596.56	1122.22
ENSG000001	CDK19	cyclin-dependent kinase 19 [Source:HGNC Symbol;Acc:HGNC:19338]	6	727.272137	0.62833297	0.0004222	621.89	698.24	937.03	893.67	380.81	559.6	762.05	964.89
ENSG000001	PTBP3	polypyrimidine tract binding protein 3 [Source:HGNC Symbol;Acc:HGNC:10253]	9	4839.79425	0.6285129	4.24E-07	4625.29	4500.73	7922.18	6076.98	2973.36	2961.29	4817.14	4841.38
ENSG000001	CCDC64	coiled-coil domain containing 64 [Source:HGNC Symbol;Acc:HGNC:28095]	12	607.891737	0.62902514	0.00490875	455.99	677.43	605.42	827.51	336.57	399.17	723.61	837.43
ENSG000001	IL1RAP	interleukin 1 receptor accessory protein [Source:HGNC Symbol;Acc:HGNC:5995]	3	9615.60455	0.62954551	0.03870162	6077.62	5498.9	17222.52	16108.83	8785.46	6971.12	8355.05	7905.33
ENSG000001	CKB	creatine kinase, brain [Source:HGNC Symbol;Acc:HGNC:1991]	14	275.653846	0.63059408	0.01067671	188.65	150.43	370.15	301.18	295.22	179.53	535.85	184.22
ENSG000001	STAT2	signal transducer and activator of transcription 2, 113kDa [Source:HGNC Symbol;Acc:HGNC:11363]	12	6152.51196	0.63071163	0.00012348	3637.47	2926.38	6370.6	5856.77	6598.71	6242.49	8493.41	9094.27
ENSG000000	NTN1	netrin 1 [Source:HGNC Symbol;Acc:HGNC:8029]	17	214.591323	0.63093817	0.01420368	181.07	208.15	278.88	239.96	139.44	115.55	342.59	211.1
ENSG000001	FCER1G	Fc fragment of IgE, high affinity I, receptor for; gamma polypeptide [Source:HGNC Symbol;Acc:HGNC:3611]	1	47.8426062	0.63101852	0.04323457	30.34	34.06	54.76	57.27	36.54	37.24	75.77	56.76
ENSG000001	SLC16A3	solute carrier family 16 (monocarboxylate transporter), member 3 [Source:HGNC Symbol;Acc:HGNC:10924]	17	845.430793	0.63169962	0.00019616	350.76	795.69	566.88	1174.12	473.12	1028.48	967.38	1407.01
ENSG000001	IQSEC3	IQ motif and Sec7 domain 3 [Source:HGNC Symbol;Acc:HGNC:29193]	12	2459.24401	0.63182077	0.00961745	1329.09	1660.46	1602.28	1889.06	1370.32	2648.07	3118.46	6056.21
ENSG000001	NAT1	N-acetyltransferase 1 (arylamine N- acetyltransferase) [Source:HGNC Symbol;Acc:HGNC:7645]	8	208.234218	0.63184875	0.00283016	196.24	38.79	295.1	67.15	329.84	84.04	486.44	168.28
ENSG000001	CCNO	cyclin O [Source:HGNC Symbol;Acc:HGNC:18576]	5	164.963236	0.63249249	0.00429289	83.42	105.02	107.49	166.88	144.24	158.52	272.32	281.8
ENSG000001	RSPH3	radial spoke 3 homolog (Chlamydomonas) [Source:HGNC Symbol;Acc:HGNC:21054]	6	516.463616	0.63277854	0.02660304	311.89	300.87	880.24	635.94	483.7	419.22	454.59	645.25
ENSG000001	ZSCAN30	zinc finger and SCAN domain containing 30 [Source:HGNC Symbol;Acc:HGNC:33517]	18	549.396817	0.63402548	2.75E-05	370.67	349.12	670.32	579.65	491.39	491.8	709.34	732.88
ENSG000000	ATP1A2	ATPase, Na ⁺ /K ⁺ transporting, alpha 2 polypeptide [Source:HGNC Symbol;Acc:HGNC:800]	1	90.7471713	0.63431436	0.01932534	52.14	35.95	116.62	62.21	93.28	90.72	130.67	144.39
ENSG000001	PLCG2	phospholipase C, gamma 2 (phosphatidylinositol-specific) [Source:HGNC Symbol;Acc:HGNC:9066]	16	2030.08716	0.63495142	0.00145036	1396.4	1239.43	3374.94	1798.21	1830.94	1674.98	2488.18	2437.62
ENSG000001	SDCBP2	syndecan binding protein (syntenin) 2 [Source:HGNC Symbol;Acc:HGNC:15756]	20	50.8964467	0.63561788	0.03830138	42.66	50.14	65.92	83.94	25	30.56	47.22	61.74
ENSG000000	MAST4	microtubule associated serine/threonine kinase family member 4 [Source:HGNC Symbol;Acc:HGNC:19037]	5	376.982162	0.63579203	0.02748058	244.58	254.51	554.71	710	261.56	319.91	336	334.58
ENSG000002	LINC01239	long intergenic non-protein coding RNA 1239 [Source:HGNC Symbol;Acc:HGNC:49796]	9	112.552137	0.63583019	0.00691683	64.46	84.21	123.72	133.31	82.7	107.91	121.88	182.22
ENSG000001	GLIPR1	GLI pathogenesis-related 1 [Source:HGNC Symbol;Acc:HGNC:17001]	12	3502.47008	0.63592694	0.00220012	2665.77	2024.72	6019.72	3920.31	2949.32	2945.06	3738.86	3756

ENSG000001	TSNAXIP1		translin-associated factor X interacting protein 1 [Source:HGNC Symbol;Acc:HGNC:18586]	16	78.6921599	0.63622694	0.02077006	61.62	35.95	98.37	77.02	84.62	53.48	121.88	96.59
ENSG000001	IFNLR1		interferon, lambda receptor 1 [Source:HGNC Symbol;Acc:HGNC:18584]	1	1260.63473	0.63774737	4.39E-07	1021.94	1120.22	1578.96	1697.49	784.69	987.42	1407.7	1486.67
ENSG000001	GCH1		GTP cyclohydrolase 1 [Source:HGNC Symbol;Acc:HGNC:4193]	14	932.941852	0.63823053	0.001993	720.48	1010.47	954.27	1334.09	454.85	692.34	1056.32	1240.72
ENSG000002	ZNF630	X	zinc finger protein 630 [Source:HGNC Symbol;Acc:HGNC:28855]		85.7138187	0.63868929	0.02431555	52.14	62.44	99.38	73.07	62.51	72.58	125.18	138.41
ENSG000001	GOLGA1		golgin A1 [Source:HGNC Symbol;Acc:HGNC:4424]	9	1237.85512	0.63901656	0.00122554	1060.81	973.57	1336.59	1317.3	857.77	865.18	1726.13	1765.48
ENSG000001	ADAL		adenosine deaminase-like [Source:HGNC Symbol;Acc:HGNC:31853]	15	1288.46029	0.63988233	3.44E-08	972.65	1082.37	1566.79	1589.85	973.17	965.45	1591.07	1566.33
ENSG000001	MERTK		MER proto-oncogene, tyrosine kinase [Source:HGNC Symbol;Acc:HGNC:7027]	2	126.809485	0.63993557	0.01875938	88.16	56.77	140.96	70.11	139.44	84.04	222.9	212.1
ENSG000001	GSN		gelsolin [Source:HGNC Symbol;Acc:HGNC:4620]	9	610.000143	0.63997393	0.00026809	210.46	237.48	374.2	332.78	653.91	736.26	906.99	1427.92
ENSG000001	NECAB3		N-terminal EF-hand calcium binding protein 3 [Source:HGNC Symbol;Acc:HGNC:15851]	20	1485.80374	0.64007144	1.22E-05	1003.93	1146.71	1362.96	1886.09	1059.72	1350.3	2010.53	2066.2
ENSG000001	LMO7		LIM domain 7 [Source:HGNC Symbol;Acc:HGNC:6646]	13	559.495471	0.64148197	0.00929571	431.34	488.2	513.14	633.96	262.53	487.02	661.03	998.75
ENSG000001	TCTE1		t-complex-associated-testis-expressed 1 [Source:HGNC Symbol;Acc:HGNC:11693]	6	49.8693648	0.6415118	0.0444906	31.28	29.33	60.85	69.12	28.85	54.43	49.41	75.68
ENSG000001	ZNF79		zinc finger protein 79 [Source:HGNC Symbol;Acc:HGNC:13153]	9	958.282799	0.64206588	0.00024311	879.74	639.58	1486.68	1326.19	769.3	621.67	1115.62	827.48
ENSG000000	MMP25		matrix metalloproteinase 25 [Source:HGNC Symbol;Acc:HGNC:14246]	16	84.6554017	0.64237092	0.01932534	43.61	48.25	93.3	81.96	65.39	95.49	120.79	128.45
ENSG000002	ERV3-1		endogenous retrovirus group 3, member 1 [Source:HGNC Symbol;Acc:HGNC:3454]	7	244.949799	0.64451926	0.00250914	198.13	146.65	268.74	214.28	194.25	192.9	329.41	415.23
ENSG000001	LPIN3		lipin 3 [Source:HGNC Symbol;Acc:HGNC:14451]	20	1204.87068	0.64461413	6.67E-07	725.22	781.5	1214.9	1112.89	979.9	1222.33	1716.25	1885.97
ENSG000001	PMAIP1		phorbol-12-myristate-13-acetate-induced protein 1 [Source:HGNC Symbol;Acc:HGNC:9108]	18	930.365523	0.64521355	0.00452454	533.72	325.47	939.06	349.57	1379.94	504.21	2207.08	1203.87
ENSG000001	SNTB2		syntrophin, beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) [Source:HGNC Symbol;Acc:HGNC:11169]	16	310.28494	0.64541323	0.02086602	200.03	149.49	368.12	131.34	357.73	154.7	787.3	333.58
ENSG000001	RFX7		regulatory factor X, 7 [Source:HGNC Symbol;Acc:HGNC:25777]	15	3094.88147	0.64552189	1.15E-09	2449.63	3057.89	3794.78	5024.32	1815.56	2221.21	2703.4	3692.28
ENSG000001	NINJ2		ninjurin 2 [Source:HGNC Symbol;Acc:HGNC:7825]	12	96.2903922	0.64600525	0.0374625	81.53	62.44	162.26	178.73	50.97	73.53	59.29	101.57
ENSG000001	GTF2IRD2B		GTF2I repeat domain containing 2B [Source:HGNC Symbol;Acc:HGNC:33125]	7	1122.13278	0.64606036	1.49E-05	887.33	973.57	1741.22	1492.09	796.23	767.78	1140.87	1177.98
ENSG000001	SSUH2		ssu-2 homolog (C, elegans) [Source:HGNC Symbol;Acc:HGNC:24809]	3	117.21315	0.64670044	0.01397483	89.11	98.4	106.48	174.78	50.97	107.91	110.9	199.15
ENSG000001	DPY19L3		dpy-19-like 3 (C, elegans) [Source:HGNC Symbol;Acc:HGNC:27120]	19	2000.09623	0.64709139	0.00079392	1865.66	1859.14	2637.68	2303.8	1212.62	1208.96	2467.32	2445.59
ENSG000000	WWC3	X	WWC family member 3 [Source:HGNC Symbol;Acc:HGNC:29237]		1959.61849	0.64709688	6.79E-05	1364.17	1706.82	1970.4	2305.78	1050.1	1891.75	2125.82	3262.11
ENSG000001	C5orf42		chromosome 5 open reading frame 42 [Source:HGNC Symbol;Acc:HGNC:25801]	5	569.011831	0.64775497	0.00277198	552.68	386.02	715.96	505.59	429.85	338.05	949.81	674.13
ENSG000001	INPP1		inositol polyphosphate-1-phosphatase [Source:HGNC Symbol;Acc:HGNC:6071]	2	515.944559	0.64897867	0.00177262	284.4	427.65	587.17	864.05	350.03	495.62	485.34	633.3
ENSG000001	HIST1H4H		histone cluster 1, H4h [Source:HGNC Symbol;Acc:HGNC:4788]	6	182.847489	0.65053085	0.00204156	164	88.94	256.57	126.4	168.29	122.23	338.2	198.16
ENSG000001	ZNF658B		zinc finger protein 658B, pseudogene [Source:HGNC Symbol;Acc:HGNC:32033]	9	248.836749	0.65056185	0.00136857	169.69	163.68	252.51	237.98	242.33	172.85	383.22	368.43
ENSG000002	CCDC183-AS1		CCDC183 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44105]	9	187.464976	0.65105091	0.00116994	114.71	136.24	191.67	198.48	160.59	152.79	305.26	239.98

ENSG000002	DDX11 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44176]		12	66.6030992	0.65150835	0.04673396	49.3	41.63	61.86	56.29	56.74	36.29	125.18	105.55
ENSG000000	RHBD1 rhomboid 5 homolog 1 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:20561]		16	296.23577	0.65170551	0.00011461	136.51	172.2	244.4	277.48	278.87	319.91	411.77	528.75
ENSG000001	LRRC29 leucine rich repeat containing 29 [Source:HGNC Symbol;Acc:HGNC:13605]		16	52.6946632	0.65240268	0.03136557	25.6	23.65	42.59	49.37	63.47	39.15	112	65.72
ENSG000001	RGS3 regulator of G-protein signaling 3 [Source:HGNC Symbol;Acc:HGNC:9999]		9	1303.77971	0.65296152	1.78E-06	1298.76	889.36	1872.04	1340.02	911.63	911.98	1700.88	1505.59
ENSG000000	FOSL2 FOS-like antigen 2 [Source:HGNC Symbol;Acc:HGNC:3798]		2	2745.41167	0.6529691	1.53E-06	1751.9	2190.29	2829.35	3219.2	1885.76	2622.29	3626.85	3837.66
ENSG000001	FBXO4 F-box protein 4 [Source:HGNC Symbol;Acc:HGNC:13583]		5	327.138167	0.65360466	0.00035068	257.86	225.18	427.95	295.26	304.84	198.63	547.93	359.47
ENSG000001	BRMS1L breast cancer metastasis-suppressor 1-like [Source:HGNC Symbol;Acc:HGNC:20512]		14	524.639501	0.65447223	0.00032133	346.97	346.28	575	731.73	432.73	469.83	599.53	695.04
ENSG000001	CNTN5 contactin 5 [Source:HGNC Symbol;Acc:HGNC:2175]		11	72.1373998	0.65499925	0.03829296	41.71	38.79	116.62	84.92	54.81	70.67	77.96	91.61
ENSG000000	RCN1 reticulocalbin 1, EF-hand calcium binding domain [Source:HGNC Symbol;Acc:HGNC:9934]		11	917.380491	0.65560337	5.37E-06	1460.87	205.31	2536.27	304.15	946.24	106.95	1622.92	156.33
ENSG000001	SMAD3 SMAD family member 3 [Source:HGNC Symbol;Acc:HGNC:6769]		15	411.752056	0.6562674	0.03865823	251.22	264.92	877.2	647.79	217.33	388.66	263.53	383.37
ENSG000001	DCUN1D3 DCN1, defective in cullin neddylation 1, domain containing 3 [Source:HGNC Symbol;Acc:HGNC:28734]		16	681.718311	0.65638767	1.84E-06	469.26	614.98	837.65	900.59	448.12	559.6	710.44	913.11
ENSG000001	ZBTB4 zinc finger and BTB domain containing 4 [Source:HGNC Symbol;Acc:HGNC:23847]		17	759.495008	0.65644471	1.76E-07	738.49	749.33	1237.21	1184.98	421.19	417.31	642.36	685.08
ENSG000001	COLCA1 colorectal cancer associated 1 [Source:HGNC Symbol;Acc:HGNC:33789]		11	40.9359245	0.65647616	0.04870794	9.48	0.95	273.81	0	20.19	0	23.06	0
ENSG000000	RORA RAR-related orphan receptor A [Source:HGNC Symbol;Acc:HGNC:10258]		15	430.191613	0.65705879	0.01194768	320.42	245.05	686.55	633.96	406.77	289.35	439.22	420.21
ENSG000001	SERPINB8 serpin peptidase inhibitor, clade B (ovalbumin), member 8 [Source:HGNC Symbol;Acc:HGNC:8952]		18	97.9643873	0.65775121	0.00698833	79.63	64.34	140.96	99.74	84.62	62.07	132.86	119.49
ENSG000001	GFOD1 glucose-fructose oxidoreductase domain containing 1 [Source:HGNC Symbol;Acc:HGNC:21096]		6	1024.62811	0.65905683	0.00118764	785.89	860.98	1461.32	1933.49	701.99	654.14	875.14	924.06
ENSG000001	TNS2 tensin 2 [Source:HGNC Symbol;Acc:HGNC:19737]		12	90.1460242	0.66225192	0.01463935	58.78	60.55	86.2	85.91	62.51	78.31	140.55	148.37
ENSG000001	NAGK N-acetylglucosamine kinase [Source:HGNC Symbol;Acc:HGNC:17174]		2	3529.66311	0.66261309	1.42E-08	2460.06	2626.45	3553.42	4151.38	2733.92	2954.61	4521.76	5235.7
ENSG000001	COCH cochlin [Source:HGNC Symbol;Acc:HGNC:2180]		14	252.497224	0.66373259	0.01859618	241.74	130.57	276.85	167.87	199.06	144.2	506.2	353.49
ENSG000001	PPM1D protein phosphatase, Mg2+/Mn2+ dependent, 1D [Source:HGNC Symbol;Acc:HGNC:9277]		17	2640.02018	0.66425855	4.49E-09	2026.82	2192.18	3493.59	3708	1965.57	1889.84	2918.61	2925.54
ENSG000001	PTP4A1 protein tyrosine phosphatase type IVA, member 1 [Source:HGNC Symbol;Acc:HGNC:9634]		6	14116.9766	0.66472523	3.87E-06	15356.64	14270.46	21811.34	20395.5	7152.61	7197.44	13722.31	13029.51
ENSG000002	FADS3 fatty acid desaturase 3 [Source:HGNC Symbol;Acc:HGNC:3576]		11	3270.82639	0.66526186	1.64E-05	2994.73	1982.14	5121.22	3954.87	2857	2058.87	4483.33	2714.44
ENSG000001	CCSER2 coiled-coil serine-rich protein 2 [Source:HGNC Symbol;Acc:HGNC:29197]		10	1786.54926	0.66609564	0.00526404	1309.19	1382.29	3490.55	2609.92	1316.47	1109.65	1458.21	1616.12
ENSG000000	MBNL3 muscleblind-like splicing regulator 3 [Source:HGNC Symbol;Acc:HGNC:20564]	X		1090.81821	0.66673556	7.25E-05	1088.3	1200.64	1715.86	1566.15	519.28	569.15	993.73	1073.43
ENSG000001	CPD carboxypeptidase D [Source:HGNC Symbol;Acc:HGNC:2301]		17	3617.51436	0.6675564	3.39E-09	3582.49	3842.23	6073.47	6338.66	1607.85	1938.54	2314.69	3242.19
ENSG000002	MTCP1 mature T-cell proliferation 1 [Source:HGNC Symbol;Acc:HGNC:7423]	X		81.1582146	0.6678809	0.00933174	54.98	52.98	101.41	98.75	69.24	61.12	114.2	96.59

ENSG000001	DSE	dermatan sulfate epimerase [Source:HGNC Symbol;Acc:HGNC:21144]	6	157.650241	0.66828041	0.00157781	129.88	92.72	207.89	133.31	144.24	101.22	265.73	186.21
ENSG000001	FKBP10	FK506 binding protein 10, 65 kDa [Source:HGNC Symbol;Acc:HGNC:18169]	17	93.6788917	0.66953738	0.03996141	52.14	53.93	75.04	55.3	60.58	81.17	180.08	191.19
ENSG000001	SNX15	sorting nexin 15 [Source:HGNC Symbol;Acc:HGNC:14978]	11	67.0445877	0.66985187	0.02398786	40.76	25.55	67.94	68.14	61.54	66.85	101.02	104.55
ENSG000001	TRIM45	tripartite motif containing 45 [Source:HGNC Symbol;Acc:HGNC:19018]	1	204.929445	0.67035663	0.00264243	86.27	105.97	102.42	205.4	198.1	205.31	364.55	371.42
ENSG000001	THBS3	thrombospondin 3 [Source:HGNC Symbol;Acc:HGNC:11787]	1	934.206506	0.6714277	5.10E-07	630.42	551.59	1132.75	912.44	789.5	884.28	1300.09	1272.58
ENSG000000	FKBP6	FK506 binding protein 6, 36kDa [Source:HGNC Symbol;Acc:HGNC:3722]	7	49.7955182	0.67145793	0.04838196	27.49	25.55	76.06	68.14	41.35	42.02	66.98	50.78
ENSG000001	EMB	embigin [Source:HGNC Symbol;Acc:HGNC:30465]	5	2494.15981	0.67163914	0.0010969	1464.66	1765.48	3508.8	3307.08	2020.39	2222.16	2552.96	3111.75
ENSG000001	LONRF1	LON peptidase N-terminal domain and ring finger 1 [Source:HGNC Symbol;Acc:HGNC:26302]	8	2426.48943	0.67168823	0.0458398	2809.87	2160.01	3252.23	2070.75	895.28	994.1	4013.37	3216.3
ENSG000001	VSIG10	V-set and immunoglobulin domain containing 10 [Source:HGNC Symbol;Acc:HGNC:26078]	12	200.62765	0.67174626	0.01552662	123.24	142.87	232.23	141.21	164.44	133.69	397.49	269.85
ENSG000001	RIMS2	regulating synaptic membrane exocytosis 2 [Source:HGNC Symbol;Acc:HGNC:17283]	8	147.233739	0.67270776	0.00143752	136.51	118.27	221.07	180.71	83.66	102.18	159.22	176.25
ENSG000001	DLG4	discs, large homolog 4 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:2903]	17	49.2206546	0.67288355	0.04834772	24.65	22.71	37.52	35.55	34.62	47.75	115.3	75.68
ENSG000002	LINC01021	long intergenic non-protein coding RNA 1021 [Source:HGNC Symbol;Acc:HGNC:48995]	5	3197.0812	0.67502424	9.34E-05	2621.22	2110.81	4931.59	4355.79	2623.33	2225.98	3383.09	3324.84
ENSG000001	IDNK	idnK, gluconokinase homolog (E, coli) [Source:HGNC Symbol;Acc:HGNC:31367]	9	88.0850431	0.67502806	0.01285972	55.93	42.58	125.75	84.92	73.08	85.95	112	124.47
ENSG000001	HIST1H2BD	histone cluster 1, H2bd [Source:HGNC Symbol;Acc:HGNC:4747]	6	145.065625	0.67556464	0.03203831	71.1	52.98	211.95	146.15	149.05	145.15	232.79	151.36
ENSG000001	CCDC180	coiled-coil domain containing 180 [Source:HGNC Symbol;Acc:HGNC:29303]	9	94.1393824	0.67613764	0.00507172	63.52	53.93	107.49	91.84	77.89	81.17	143.84	133.43
ENSG000002	ZNF425	zinc finger protein 425 [Source:HGNC Symbol;Acc:HGNC:20690]	7	180.445161	0.67719805	0.00507172	110.92	158.95	248.46	320.93	108.66	144.2	138.35	213.09
ENSG000001	CARF	calcium responsive transcription factor [Source:HGNC Symbol;Acc:HGNC:14435]	2	331.224506	0.6803096	0.00042725	221.83	194.9	306.26	286.37	294.26	261.66	578.67	505.85
ENSG000001	IFIT3	interferon-induced protein with tetratricopeptide repeats 3 [Source:HGNC Symbol;Acc:HGNC:5411]	10	1256.80989	0.68036121	0.02084462	105.23	20.81	400.57	45.42	46.16	56.34	3782.78	5597.16
ENSG000001	SLC2A6	solute carrier family 2 (facilitated glucose transporter), member 6 [Source:HGNC Symbol;Acc:HGNC:11011]	9	312.905432	0.6804845	0.00017664	106.18	306.55	183.55	454.24	189.44	346.65	379.92	536.71
ENSG000001	RUNX2	runt-related transcription factor 2 [Source:HGNC Symbol;Acc:HGNC:10472]	6	827.474038	0.68073075	0.01478117	350.76	510.91	1112.47	1176.09	551.98	1032.3	730.2	1155.08
ENSG000001	SFN	stratifin [Source:HGNC Symbol;Acc:HGNC:10773]	1	153.14602	0.68223082	0.04140795	80.58	111.64	88.23	125.41	75.01	127.96	266.83	349.51
ENSG000001	PLAGL1	pleiomorphic adenoma gene-like 1 [Source:HGNC Symbol;Acc:HGNC:9046]	6	4372.19728	0.68282554	0.00843275	3862.15	3868.72	4724.71	4564.15	2336.76	2678.63	6558.64	6383.81
ENSG000001	ZNF135	zinc finger protein 135 [Source:HGNC Symbol;Acc:HGNC:12919]	19	101.426991	0.68347827	0.00383045	67.31	68.12	104.45	127.39	76.93	84.99	132.86	149.36
ENSG000001	ST8SIA2	ST8 alpha-N-acetyl-neuraminidase alpha-2,8-sialyltransferase 2 [Source:HGNC Symbol;Acc:HGNC:10870]	15	1336.27098	0.68353629	5.10E-07	1517.75	881.79	2479.48	1524.68	913.55	707.62	1674.52	990.78
ENSG000001	GTF2IRD2	GTF2I repeat domain containing 2 [Source:HGNC Symbol;Acc:HGNC:30775]	7	969.406924	0.68452705	2.07E-05	747.97	825.97	1580.99	1298.54	658.72	658.91	968.48	1015.67
ENSG000002	CCDC162P	coiled-coil domain containing 162, pseudogene [Source:HGNC Symbol;Acc:HGNC:21565]	6	133.461258	0.6845956	0.03302518	95.75	58.66	115.61	64.19	111.55	81.17	310.75	230.02

ENSG000001	ANKRD19P	ankyrin repeat domain 19, pseudogene [Source:HGNC Symbol;Acc:HGNC:22567]	9	701.345277	0.6852395	0.0002255	172.54	510.91	212.96	811.71	446.2	894.79	914.67	1646.99
ENSG000001	SPACA6P	sperm acrosome associated 6, pseudogene [Source:HGNC Symbol;Acc:HGNC:27113]	19	48.5605331	0.68592773	0.02833018	34.13	29.33	72	52.34	39.43	32.47	57.1	71.69
ENSG000001	PANK1	pantothenate kinase 1 [Source:HGNC Symbol;Acc:HGNC:8598]	10	69.7976539	0.68622075	0.02069467	40.76	62.44	94.31	93.81	51.93	42.97	73.57	98.58
ENSG000001	CCDC30	coiled-coil domain containing 30 [Source:HGNC Symbol;Acc:HGNC:26103]	1	54.0858706	0.68863488	0.02763674	40.76	35.95	105.47	65.17	37.5	34.38	52.71	60.74
ENSG000001	ANKRA2	ankyrin repeat, family A (RFXANK-like), 2 [Source:HGNC Symbol;Acc:HGNC:13208]	5	630.049461	0.69014405	5.55E-07	367.82	429.54	659.17	710	499.09	613.08	846.6	915.1
ENSG000001	ALPP	alkaline phosphatase, placental [Source:HGNC Symbol;Acc:HGNC:439]	2	11.6092343	0.69062838	0.03209243	0	1.89	3.04	0.99	1.92	2.86	5.49	76.67
ENSG000001	DHRS3	dehydrogenase/reductase (SDR family) member 3 [Source:HGNC Symbol;Acc:HGNC:17693]	1	123.467858	0.69067197	0.00950162	87.22	100.29	109.52	178.73	57.7	110.77	149.33	194.17
ENSG000001	CSF2RB	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage) [Source:HGNC Symbol;Acc:HGNC:2436]	22	431.842531	0.69086493	0.039823	178.22	194.9	396.51	978.6	376	396.3	354.67	579.53
ENSG000001	UBA7	ubiquitin-like modifier activating enzyme 7 [Source:HGNC Symbol;Acc:HGNC:12471]	3	54.1179696	0.69178084	0.03825095	30.34	23.65	37.52	34.56	58.66	27.69	143.84	76.67
ENSG000001	AMT	aminomethyltransferase [Source:HGNC Symbol;Acc:HGNC:473]	3	210.156938	0.69223476	0.00047518	115.66	88.94	169.36	176.76	208.67	210.09	329.41	382.37
ENSG000002	SNORD3C	small nucleolar RNA, C/D box 3C [Source:HGNC Symbol;Acc:HGNC:33191]	17	47.0288385	0.69257768	0.04080568	45.5	15.14	63.89	20.74	32.7	30.56	90.04	77.67
ENSG000001	TNNT1	troponin T type 1 (skeletal, slow) [Source:HGNC Symbol;Acc:HGNC:11948]	19	293.354941	0.69260599	0.0007544	90.06	198.69	155.16	254.77	190.4	365.75	349.18	742.84
ENSG000001	DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9 [Source:HGNC Symbol;Acc:HGNC:6968]	7	1606.85078	0.69318249	0.00116994	1165.09	1467.45	1433.94	2086.55	952.01	1136.39	2223.55	2389.82
ENSG000001	CREBRF	CREB3 regulatory factor [Source:HGNC Symbol;Acc:HGNC:24050]	5	454.398006	0.69320149	1.53E-06	346.02	341.55	565.87	540.15	306.76	373.38	560	601.44
ENSG000001	C1orf106	chromosome 1 open reading frame 106 [Source:HGNC Symbol;Acc:HGNC:25599]	1	922.952654	0.69324926	1.12E-05	468.31	803.26	681.48	1326.19	490.43	1016.06	1025.58	1572.3
ENSG000001	FADS2	fatty acid desaturase 2 [Source:HGNC Symbol;Acc:HGNC:3575]	11	630.588726	0.6934407	0.00260119	466.42	554.43	674.38	760.36	353.88	470.79	993.73	770.72
ENSG000001	CCDC88B	coiled-coil domain containing 88B [Source:HGNC Symbol;Acc:HGNC:26757]	11	592.139962	0.69425836	0.04217564	237.95	380.34	198.76	405.86	281.76	518.54	1116.72	1597.2
ENSG000002	FTH1P10	ferritin, heavy polypeptide 1 pseudogene 10 [Source:HGNC Symbol;Acc:HGNC:3980]	5	260.21241	0.69485962	0.0185612	357.4	262.08	404.63	401.91	75.01	94.54	248.16	237.99
ENSG000001	SCN3B	sodium channel, voltage gated, type III beta subunit [Source:HGNC Symbol;Acc:HGNC:20665]	11	227.403708	0.69858189	0.03699404	200.98	68.12	606.43	266.62	222.14	102.18	227.3	125.47
ENSG000001	HSF4	heat shock transcription factor 4 [Source:HGNC Symbol;Acc:HGNC:5227]	16	837.769162	0.69920696	0.00014225	424.7	500.5	648.01	670.5	628.91	876.64	1394.52	1558.36
ENSG000001	PDE1B	phosphodiesterase 1B, calmodulin- dependent [Source:HGNC Symbol;Acc:HGNC:8775]	12	90.3441679	0.6995048	0.02019978	38.87	12.3	104.45	22.71	154.82	59.21	200.94	129.45
ENSG000001	IL16	interleukin 16 [Source:HGNC Symbol;Acc:HGNC:5980]	15	181.202576	0.70032441	0.01932534	94.8	131.51	148.06	133.31	139.44	121.28	332.71	348.52
ENSG000001	KLF11	Kruppel-like factor 11 [Source:HGNC Symbol;Acc:HGNC:11811]	2	1401.70515	0.70086585	0.00835394	627.58	1405	941.09	1449.63	695.26	1244.3	2035.78	2815.01
ENSG000001	ZIC1	Zic family member 1 [Source:HGNC Symbol;Acc:HGNC:12872]	3	75.4685915	0.70106535	0.02880779	36.02	55.82	90.26	63.2	60.58	51.57	99.92	146.38
ENSG000001	ST5	suppression of tumorigenicity 5 [Source:HGNC Symbol;Acc:HGNC:11350]	11	46.1392109	0.7013998	0.0377434	15.17	42.58	38.54	55.3	30.77	34.38	53.8	98.58
ENSG000001	CARD14	caspase recruitment domain family, member 14 [Source:HGNC Symbol;Acc:HGNC:16446]	17	127.334566	0.70140686	0.01198447	99.54	68.12	115.61	116.52	85.59	102.18	224	207.12

ENSG000001	S100Z	S100 calcium binding protein Z [Source:HGNC Symbol;Acc:HGNC:30367]	5	200.580144	0.70282041	0.01879518	0.95	263.02	7.1	451.28	9.62	299.85	24.16	548.66
ENSG000001	ZNF862	zinc finger protein 862 [Source:HGNC Symbol;Acc:HGNC:34519]	7	879.356045	0.7030599	1.00E-05	375.41	679.32	767.68	1219.54	618.33	976.91	875.14	1522.52
ENSG000001	TRPC1	transient receptor potential cation channel, subfamily C, member 1 [Source:HGNC Symbol;Acc:HGNC:12333]	3	124.550661	0.70441935	0.0016954	97.64	67.18	168.34	123.44	105.78	93.58	159.22	181.23
ENSG000001	TMEM200A	transmembrane protein 200A [Source:HGNC Symbol;Acc:HGNC:21075]	6	834.839483	0.70487618	0.00158309	392.47	829.75	926.89	1817.96	474.08	689.47	595.14	952.94
ENSG000000	SEMA3B	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3B [Source:HGNC Symbol;Acc:HGNC:10724]	3	39.078483	0.70572722	0.04102479	17.06	13.25	25.35	20.74	37.5	30.56	73.57	94.6
ENSG000001	TOB1	transducer of ERBB2, 1 [Source:HGNC Symbol;Acc:HGNC:11979]	17	1217.16109	0.70636364	1.50E-10	1134.76	1068.18	1877.11	1819.93	726.99	728.63	1184.79	1196.9
ENSG000002	MT-RNR2	mitochondrially encoded 16S RNA [Source:HGNC Symbol;Acc:HGNC:7471]	MT	262516.016	0.70670136	7.69E-05	212695.01	134596.25	272632.67	203589.61	247653.5	170792.41	488746.91	369421.76
ENSG000001	ERN1	endoplasmic reticulum to nucleus signaling 1 [Source:HGNC Symbol;Acc:HGNC:3449]	17	3943.46536	0.70702414	2.42E-06	3145.46	2542.25	4374.84	4018.07	3377.25	2586	6989.08	4514.77
ENSG000001	MBOAT1	membrane bound O-acyltransferase domain containing 1 [Source:HGNC Symbol;Acc:HGNC:21579]	6	1616.21354	0.70722417	1.03E-07	1220.08	1073.86	2199.59	2017.43	1193.38	1356.03	1783.23	2086.12
ENSG000001	ZDHHC14	zinc finger, DHHC-type containing 14 [Source:HGNC Symbol;Acc:HGNC:20341]	6	409.534198	0.70783985	0.00563524	341.28	383.18	423.9	516.45	203.87	256.88	530.36	620.36
ENSG000001	TP53INP1	tumor protein p53 inducible nuclear protein 1 [Source:HGNC Symbol;Acc:HGNC:18022]	8	8738.72398	0.70813657	0.01126009	6372.45	1764.53	12185.47	7080.26	12469.46	6058.19	14607.34	9372.09
ENSG000001	SOST	sclerostin [Source:HGNC Symbol;Acc:HGNC:13771]	17	9.82944586	0.70816702	0.04389184	4.74	0.95	9.13	0.99	3.85	2.86	25.26	30.87
ENSG000001	ADAMTS7	ADAM metalloproteinase with thrombospondin type 1 motif, 7 [Source:HGNC Symbol;Acc:HGNC:223]	15	71.5835585	0.70848604	0.03178329	21.8	41.63	37.52	42.46	54.81	63.03	136.16	175.25
ENSG000000	CAPG	capping protein (actin filament), gelsolin- like [Source:HGNC Symbol;Acc:HGNC:1474]	2	265.346115	0.71074817	0.03241604	141.25	220.45	183.55	208.36	142.32	171.89	539.14	515.8
ENSG000000	CECR1	cat eye syndrome chromosome region, candidate 1 [Source:HGNC Symbol;Acc:HGNC:1839]	22	32.2666279	0.71086166	0.04996386	7.58	17.03	30.42	52.34	18.27	40.11	29.65	62.73
ENSG000001	SORL1	sortilin-related receptor, L(DLR class) A repeats containing [Source:HGNC Symbol;Acc:HGNC:11185]	11	132.89059	0.71136109	0.02178647	113.76	28.38	364.06	38.51	171.17	42.02	208.63	96.59
ENSG000000	ALDH3B1	aldehyde dehydrogenase 3 family, member B1 [Source:HGNC Symbol;Acc:HGNC:410]	11	47.7277676	0.71462183	0.02186025	35.08	41.63	58.82	67.15	26.93	27.69	64.78	59.75
ENSG000001	HHLA3	HERV-H LTR-associating 3 [Source:HGNC Symbol;Acc:HGNC:4906]	1	256.373228	0.7165416	0.00768035	128.93	138.13	378.26	304.15	190.4	276.93	233.88	400.3
ENSG000001	PDCD4	programmed cell death 4 (neoplastic transformation inhibitor) [Source:HGNC Symbol;Acc:HGNC:8763]	10	709.0009	0.71709496	0.0152608	418.07	493.88	469.53	570.77	390.42	547.19	1090.36	1691.8
ENSG000000	DAPK2	death-associated protein kinase 2 [Source:HGNC Symbol;Acc:HGNC:2675]	15	198.252493	0.71751554	0.00110475	147.89	143.81	210.93	216.26	115.4	164.25	234.98	352.5
ENSG000001	AGBL3	ATP/GTP binding protein-like 3 [Source:HGNC Symbol;Acc:HGNC:27981]	7	102.114997	0.71866433	0.00349451	69.2	70.96	110.54	114.55	69.24	82.13	155.92	144.39
ENSG000001	ADAM8	ADAM metalloproteinase domain 8 [Source:HGNC Symbol;Acc:HGNC:215]	10	125.614345	0.71873495	0.04727316	29.39	67.18	90.26	135.29	75.97	122.23	392	92.61
ENSG000001	RGL4	ral guanine nucleotide dissociation stimulator-like 4 [Source:HGNC Symbol;Acc:HGNC:31911]	22	84.0044864	0.71932719	0.01664487	28.44	57.71	41.58	75.05	50	84.99	114.2	220.06

ENSG000001	KANK3		KN motif and ankyrin repeat domains 3 [Source:HGNC Symbol;Acc:HGNC:24796] chromosome 19 open reading frame 57	19	72.6074722	0.71941861	0.03652206	15.17	61.5	63.89	175.77	28.85	86.9	47.22	101.57
ENSG000001	C19orf57		[Source:HGNC Symbol;Acc:HGNC:28153] RAP2B, member of RAS oncogene family	19	191.072694	0.71949398	0.02539648	109.97	122.05	119.66	152.07	120.2	130.83	439.22	334.58
ENSG000001	RAP2B		[Source:HGNC Symbol;Acc:HGNC:9862] long intergenic non-protein coding RNA 877 [Source:HGNC	3	2300.15863	0.72003903	1.37E-05	2535.9	2344.51	3697.42	3573.71	976.05	1122.06	2215.86	1935.76
ENSG000002	LINC00877		Symbol;Acc:HGNC:27706] DEAD (Asp-Glu-Ala-Asp) box polypeptide 4	3	41.9952185	0.72080571	0.02715271	17.06	21.76	35.49	30.61	40.39	31.51	83.45	75.68
ENSG000001	DDX4		[Source:HGNC Symbol;Acc:HGNC:18700] KIAA1107 [Source:HGNC	5	18.2974353	0.720919	0.04976586	7.58	3.78	35.49	54.31	6.73	11.46	12.08	14.94
ENSG000000	KIAA1107		Symbol;Acc:HGNC:29192] myosin light chain kinase family, member 4	1	62.624181	0.72341505	0.01117229	30.34	17.03	54.76	37.52	69.24	59.21	116.39	116.5
ENSG000001	MYLK4		[Source:HGNC Symbol;Acc:HGNC:27972] solute carrier family 22, member 18	6	41.0003593	0.72424823	0.0244046	30.34	38.79	58.82	62.21	18.27	23.87	43.92	51.78
ENSG000001	SLC22A18		[Source:HGNC Symbol;Acc:HGNC:10964] argonaute RISC catalytic component 4	11	292.518745	0.72464376	0.00025733	150.73	135.3	203.83	222.18	272.14	272.16	570.99	512.82
ENSG000001	AGO4		[Source:HGNC Symbol;Acc:HGNC:18424] brevican [Source:HGNC	1	432.353963	0.72506425	0.00044165	254.06	311.28	449.25	404.87	306.76	360.97	518.28	853.37
ENSG000001	BCAN		Symbol;Acc:HGNC:23059] long intergenic non-protein coding RNA 1534 [Source:HGNC	1	335.425724	0.72679534	0.00317088	129.88	352.91	387.39	638.9	138.47	350.47	206.43	478.96
ENSG000002	LINC01534		Symbol;Acc:HGNC:51281] teashirt zinc finger homeobox 3	19	97.8171185	0.72694651	0.00562774	72.05	61.5	98.37	116.52	79.82	62.07	143.84	148.37
ENSG000001	TSHZ3		[Source:HGNC Symbol;Acc:HGNC:30700] gap junction protein, alpha 3, 46kDa	19	213.019621	0.72726112	5.78E-05	126.08	147.6	234.26	232.06	164.44	186.21	289.88	323.62
ENSG000001	GJA3		[Source:HGNC Symbol;Acc:HGNC:4277] KIAA1456 [Source:HGNC	13	130.42468	0.7274399	0.01717261	250.27	4.73	375.22	10.86	110.59	2.86	278.9	9.96
ENSG000002	KIAA1456		Symbol;Acc:HGNC:26725] phosphodiesterase 4C, cAMP-specific	8	115.151155	0.72744636	0.02933618	110.92	86.1	155.16	96.77	57.7	49.66	186.67	178.24
ENSG000001	PDE4C		[Source:HGNC Symbol;Acc:HGNC:8782] TSC22 domain family, member 3	19	79.033306	0.72801804	0.02792142	40.76	25.55	118.65	92.82	64.43	84.99	95.53	109.53
ENSG000001	TSC22D3	X	[Source:HGNC Symbol;Acc:HGNC:3051] branched chain amino-acid transaminase 1, cytosolic [Source:HGNC		4522.36941	0.72811342	0.00216553	3456.41	2208.26	4206.5	3090.83	3517.64	3166.61	10241.5	6291.21
ENSG000000	BCAT1		Symbol;Acc:HGNC:976] Leber congenital amaurosis 5	12	31.2212934	0.72815831	0.0428329	23.7	0	177.47	12.84	16.35	0.95	16.47	1.99
ENSG000001	LCA5		[Source:HGNC Symbol;Acc:HGNC:31923] phospholipase A2, group IVC (cytosolic, calcium-independent) [Source:HGNC	6	93.7994954	0.7285381	0.00704797	60.67	60.55	89.24	158.98	58.66	81.17	97.73	143.39
ENSG000001	PLA2G4C		Symbol;Acc:HGNC:9037] SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1 [Source:HGNC	19	31.5478502	0.72969386	0.04080483	18.96	9.46	35.49	34.56	38.47	14.32	59.29	41.82
ENSG000001	SMARCA1	X	Symbol;Acc:HGNC:11097] zinc finger and SCAN domain containing 1		42.415525	0.73084697	0.04969411	12.32	5.68	94.31	80.97	28.85	32.47	32.94	51.78
ENSG000001	ZSCAN1		[Source:HGNC Symbol;Acc:HGNC:23712] dynein, axonemal, heavy chain 6	19	10.3479418	0.73109423	0.04489517	1.9	2.84	19.27	15.8	7.69	4.77	17.57	12.94
ENSG000001	DNAH6		[Source:HGNC Symbol;Acc:HGNC:2951] interferon, alpha-inducible protein 27	2	64.3666982	0.73135169	0.0159742	40.76	39.74	84.17	58.26	40.39	50.61	62.59	138.41
ENSG000001	IFI27		[Source:HGNC Symbol;Acc:HGNC:5397] chemokine (C-C motif) receptor 1	14	56.2310223	0.73135944	0.04030943	33.18	17.03	156.17	40.49	50.97	31.51	85.65	34.85
ENSG000001	CCR1		[Source:HGNC Symbol;Acc:HGNC:1602] coagulation factor II (thrombin) receptor- like 1 [Source:HGNC	3	2094.09693	0.73176419	0.04467106	670.24	391.7	6872.58	3430.52	1344.36	830.8	2119.23	1093.34
ENSG000001	F2RL1		Symbol;Acc:HGNC:3538] family with sequence similarity 71, member F2 [Source:HGNC Symbol;Acc:HGNC:27998]	5	14.8581197	0.73214955	0.03352524	0	1.89	19.27	25.67	2.88	14.32	21.96	32.86
ENSG000002	FAM71F2			7	54.5335349	0.73247132	0.02913204	31.28	39.74	47.66	69.12	19.23	53.48	80.16	95.59

ENSG000000	FAS	Fas cell surface death receptor [Source:HGNC Symbol;Acc:HGNC:11920]	10	2952.79988	0.73252999	0.00202374	2501.77	1988.76	5407.2	5494.36	1877.1	1715.09	2243.31	2394.8
ENSG000002	RUNDC3A-AS	RUNDC3A antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:51344]	17	22.5085797	0.73332205	0.04924703	9.48	0.95	31.44	27.65	28.85	6.68	57.1	17.92
ENSG000002	EFCAB2	EF-hand calcium binding domain 2 [Source:HGNC Symbol;Acc:HGNC:28166]	1	394.027122	0.73389175	2.12E-06	389.63	316.95	635.84	498.68	242.33	217.73	434.83	416.23
ENSG000001	NABP1	nucleic acid binding protein 1 [Source:HGNC Symbol;Acc:HGNC:26232]	2	3199.71732	0.73420034	4.14E-12	3098.06	2195.96	5339.26	3520.38	2360.8	1830.63	4281.29	2971.35
ENSG000001	GRM8	glutamate receptor, metabotropic 8 [Source:HGNC Symbol;Acc:HGNC:4600]	7	50.4498472	0.73465357	0.02525578	17.06	28.38	37.52	37.52	45.2	39.15	81.26	117.5
ENSG000002	VIT	vitrin [Source:HGNC Symbol;Acc:HGNC:12697]	2	10.4214167	0.73469853	0.03996332	9.48	2.84	38.54	19.75	2.88	0	9.88	0
ENSG000001	DDB2	damage-specific DNA binding protein 2, 48kDa [Source:HGNC Symbol;Acc:HGNC:2718]	11	3888.70779	0.73517785	1.07E-08	3117.02	2650.11	5169.9	4683.64	3324.36	2464.72	4887.41	4812.51
ENSG000001	TRPM8	transient receptor potential cation channel, subfamily M, member 8 [Source:HGNC Symbol;Acc:HGNC:17961]	2	133.609449	0.73520684	0.00446173	58.78	29.33	149.07	46.41	197.13	84.04	387.61	116.5
ENSG000001	C5AR1	complement component 5a receptor 1 [Source:HGNC Symbol;Acc:HGNC:1338]	19	27.9037412	0.73559888	0.04692565	13.27	16.08	72	32.59	15.39	17.19	20.86	35.85
ENSG000002	CDKN2B-AS1	CDKN2B antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:34341]	9	118.147227	0.73664869	0.01068489	137.46	82.31	174.43	143.19	54.81	59.21	171.3	122.48
ENSG000001	PLXNB2	plexin B2 [Source:HGNC Symbol;Acc:HGNC:9104]	22	13673.8659	0.73683903	1.71E-11	9468.62	9660.92	15961.99	18383.99	11038.56	10438.53	17882.82	16555.5
ENSG000001	ST20	suppressor of tumorigenicity 20 [Source:HGNC Symbol;Acc:HGNC:33520]	15	35.5210301	0.7369065	0.03183665	32.23	25.55	63.89	54.31	16.35	16.23	52.71	22.9
ENSG000000	ITGAL	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide) [Source:HGNC Symbol;Acc:HGNC:6148]	16	12176.9681	0.73815159	1.66E-09	9278.07	8360.94	15812.92	12234.93	10057.69	8135.2	19227.93	14308.07
ENSG000002	PRAMEF11	PRAME family member 11 [Source:HGNC Symbol;Acc:HGNC:14086]	1	20.5271462	0.73896367	0.02997856	1.9	3.78	1.01	3.95	2.88	6.68	6.59	137.41
ENSG000001	FRMD6	FERM domain containing 6 [Source:HGNC Symbol;Acc:HGNC:19839]	14	434.309743	0.73923212	0.01141729	274.92	259.24	613.53	951.93	305.8	305.58	371.14	392.33
ENSG000002	ASB16-AS1	ASB16 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:25442]	17	850.262364	0.74006945	1.09E-06	607.67	511.86	1093.2	1061.55	632.75	756.32	992.64	1146.12
ENSG000001	SNX32	sorting nexin 32 [Source:HGNC Symbol;Acc:HGNC:26423]	11	155.889393	0.74009723	0.00051118	115.66	95.56	178.48	154.05	101.93	132.74	199.84	268.86
ENSG000001	ARHGEF40	Rho guanine nucleotide exchange factor (GEF) 40 [Source:HGNC Symbol;Acc:HGNC:25516]	14	419.604042	0.74016962	0.0021298	190.55	263.02	238.31	369.32	290.41	390.57	732.4	882.24
ENSG000002	DGCR9	DiGeorge syndrome critical region gene 9 (non-protein coding) [Source:HGNC Symbol;Acc:HGNC:17227]	22	96.1277285	0.74069785	0.00360337	54.04	82.31	120.68	152.07	38.47	99.31	75.77	146.38
ENSG000001	LGALS9	lectin, galactoside-binding, soluble, 9 [Source:HGNC Symbol;Acc:HGNC:6570]	17	158.28913	0.74078489	0.00042518	155.47	81.37	309.3	142.2	118.28	95.49	221.81	142.39
ENSG000002	C1orf132	chromosome 1 open reading frame 132 [Source:HGNC Symbol;Acc:HGNC:32018]	1	361.57059	0.74090149	5.81E-05	386.78	235.59	664.24	335.74	250.02	172.85	544.63	302.71
ENSG000001	LAMB3	laminin, beta 3 [Source:HGNC Symbol;Acc:HGNC:6490]	1	116.827605	0.74126831	0.03383232	44.56	78.53	80.11	61.22	68.28	82.13	245.96	273.83
ENSG000000	CD44	CD44 molecule (Indian blood group) [Source:HGNC Symbol;Acc:HGNC:1681]	11	20606.7214	0.74131892	0.00035246	16744.51	15071.83	45410.55	26334.23	14409.07	10961.85	18542.75	17378.99
ENSG000001	MICAL1	microtubule associated monooxygenase, calponin and LIM domain containing 1 [Source:HGNC Symbol;Acc:HGNC:20619]	6	3081.78668	0.74140464	3.80E-11	1620.13	1400.27	2961.18	2184.32	2890.66	3192.39	5180.59	5224.75
ENSG000002	IGFL2	IGF-like family member 2 [Source:HGNC Symbol;Acc:HGNC:32929]	19	11.373329	0.74178132	0.02483025	4.74	3.78	28.39	6.91	0.96	0	36.24	9.96
ENSG000001	HERC5	HECT and RLD domain containing E3 ubiquitin protein ligase 5 [Source:HGNC Symbol;Acc:HGNC:24368]	4	1241.37623	0.74196374	1.62E-09	897.76	966	1493.77	1492.09	789.5	1014.15	1450.52	1827.22

ENSG000001	SCN2A	sodium channel, voltage gated, type II alpha subunit [Source:HGNC Symbol;Acc:HGNC:10588]	2	31.6155563	0.74263519	0.04425886	9.48	3.78	21.3	33.57	36.54	25.78	74.67	47.8
ENSG000002	FAM90A28P	family with sequence similarity 90, member A28, pseudogene [Source:HGNC Symbol;Acc:HGNC:43747]	19	15.2532986	0.74355042	0.03847183	0	3.78	1.01	4.94	1.92	13.37	4.39	92.61
ENSG000001	LATS2	large tumor suppressor kinase 2 [Source:HGNC Symbol;Acc:HGNC:6515]	13	434.50772	0.74564116	1.94E-07	263.54	280.05	446.21	471.03	325.99	401.08	541.34	746.82
ENSG000002	GTF2IRD2P1	GTF2I repeat domain containing 2 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:33127]	7	365.085811	0.74574288	9.33E-05	269.23	288.57	616.58	519.42	244.25	242.56	376.63	363.45
ENSG000002	CSPG4P11	chondroitin sulfate proteoglycan 4 pseudogene 11 [Source:HGNC Symbol;Acc:HGNC:48363]	15	59.8411152	0.74578764	0.02335203	36.02	33.11	89.24	112.57	39.43	45.84	53.8	68.71
ENSG000001	SLC2A13	solute carrier family 2 (facilitated glucose transporter), member 13 [Source:HGNC Symbol;Acc:HGNC:15956]	12	82.868035	0.74631368	0.01237323	87.22	59.61	130.82	84.92	47.12	34.38	126.28	92.61
ENSG000001	RHPN1	rhopilin, Rho GTPase binding protein 1 [Source:HGNC Symbol;Acc:HGNC:19973]	8	332.763236	0.7469387	1.43E-05	80.58	180.71	157.19	338.71	254.83	475.56	454.59	719.93
ENSG000002	ITPRIPL2	inositol 1,4,5-trisphosphate receptor interacting protein-like 2 [Source:HGNC Symbol;Acc:HGNC:27257]	16	1288.54987	0.74757197	0.00113255	1319.61	672.7	2968.28	1750.81	861.62	686.61	1084.87	963.9
ENSG000001	TMEM198B	transmembrane protein 198B, pseudogene [Source:HGNC Symbol;Acc:HGNC:43629]	12	776.369375	0.74768286	2.06E-07	397.21	374.67	588.18	636.93	730.84	738.17	1428.56	1316.39
ENSG000002	INTS6-AS1	INTS6 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:42691]	13	27.7491543	0.74838731	0.04055097	14.22	10.41	51.72	42.46	23.08	17.19	34.04	28.88
ENSG000001	PHF11	PHD finger protein 11 [Source:HGNC Symbol;Acc:HGNC:17024]	13	146.320405	0.74945844	0.00923532	93.85	159.9	200.79	189.6	43.27	117.46	141.65	224.05
ENSG000001	YPEL5	yippee-like 5 [Source:HGNC Symbol;Acc:HGNC:18329]	2	953.17836	0.75000968	0.00043226	412.38	386.97	1012.08	835.41	1027.98	1007.47	1279.23	1663.91
ENSG000001	GPR171	G protein-coupled receptor 171 [Source:HGNC Symbol;Acc:HGNC:30057]	3	12.6756115	0.75048525	0.04376797	8.53	10.41	31.44	28.64	1.92	3.82	7.69	8.96
ENSG000001	SLC37A2	solute carrier family 37 (glucose-6-phosphate transporter), member 2 [Source:HGNC Symbol;Acc:HGNC:20644]	11	64.0392778	0.75105726	0.01879414	30.34	49.2	50.71	66.16	27.89	60.16	94.43	133.43
ENSG000001	DQX1	DEAQ box RNA-dependent ATPase 1 [Source:HGNC Symbol;Acc:HGNC:20410]	2	32.2818577	0.75190766	0.0401466	14.22	21.76	22.31	48.39	5.77	34.38	41.73	69.7
ENSG000001	GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1) [Source:HGNC Symbol;Acc:HGNC:4709]	14	889.356734	0.75232548	0.02490383	227.52	79.47	3766.38	1813.02	259.64	196.72	356.87	415.23
ENSG000001	USP18	ubiquitin specific peptidase 18 [Source:HGNC Symbol;Acc:HGNC:12616]	22	27.1148257	0.75450382	0.03894717	8.53	8.52	45.63	21.72	25.96	21.01	41.73	43.81
ENSG000001	CEP295NL	CEP295 N-terminal like [Source:HGNC Symbol;Acc:HGNC:44659]	17	17.5133657	0.75506996	0.04243736	4.74	5.68	23.32	25.67	14.42	12.41	32.94	20.91
ENSG000001	GUCY1A2	guanylate cyclase 1, soluble, alpha 2 [Source:HGNC Symbol;Acc:HGNC:4684]	11	491.610929	0.75569147	0.00069264	460.73	351.96	937.03	908.49	283.68	248.29	394.2	348.52
ENSG000001	ZMAT1	zinc finger, matrin-type 1 [Source:HGNC Symbol;Acc:HGNC:29377]	X	143.443911	0.75677429	0.00104683	95.75	59.61	145.02	121.46	117.32	129.87	187.77	290.76
ENSG000000	GPR137B	G protein-coupled receptor 137B [Source:HGNC Symbol;Acc:HGNC:11862]	1	466.980064	0.75722748	0.00023396	341.28	273.43	804.18	348.58	401	296.03	702.75	568.58
ENSG000001	CCDC38	coiled-coil domain containing 38 [Source:HGNC Symbol;Acc:HGNC:26843]	12	28.5464401	0.75770107	0.02844643	21.8	17.03	36.51	44.44	19.23	13.37	46.12	29.87
ENSG000002	LINC00638	long intergenic non-protein coding RNA 638 [Source:HGNC Symbol;Acc:HGNC:28325]	14	45.8809945	0.76027626	0.02393179	25.6	35.01	77.07	70.11	27.89	26.74	32.94	71.69
ENSG000001	DEK	DEK proto-oncogene [Source:HGNC Symbol;Acc:HGNC:2768]	6	1569.93039	0.76095928	0.00030924	725.22	1801.43	2034.29	2649.42	577.94	1509.77	1071.7	2189.67
ENSG000001	TTYH1	tweety family member 1 [Source:HGNC Symbol;Acc:HGNC:13476]	19	26.2233373	0.76148802	0.03371739	15.17	12.3	37.52	31.6	12.5	22.92	43.92	33.86

ENSG000001:ZNF117	zinc finger protein 117 [Source:HGNC Symbol;Acc:HGNC:12897]		7	580.375224	0.76224608	1.15E-08	455.99	421.97	845.76	757.4	344.26	469.83	572.08	775.7
ENSG000001:IRF7	interferon regulatory factor 7 [Source:HGNC Symbol;Acc:HGNC:6122]		11	192.621656	0.76245558	9.15E-05	83.42	87.99	157.19	182.68	196.17	191.94	323.92	317.65
ENSG000001:ZNF763	zinc finger protein 763 [Source:HGNC Symbol;Acc:HGNC:27614]		19	36.7114669	0.7631387	0.03237779	15.17	30.28	47.66	32.59	21.16	21.01	68.08	57.75
ENSG000001:LGALS3	lectin, galactoside-binding, soluble, 3 [Source:HGNC Symbol;Acc:HGNC:6563]		14	2465.66772	0.76341398	5.88E-11	1956.67	1636.8	3591.96	2952.58	1866.52	1745.64	3309.52	2665.65
ENSG000001:PLK2	polo-like kinase 2 [Source:HGNC Symbol;Acc:HGNC:19699]		5	483.655171	0.76350688	1.37E-08	433.24	253.56	743.34	444.37	422.16	303.67	730.2	538.71
ENSG000001:ACOXL	acyl-CoA oxidase-like [Source:HGNC Symbol;Acc:HGNC:25621]		2	170.182529	0.76457777	0.01875938	189.6	12.3	760.58	21.72	149.05	16.23	191.06	20.91
ENSG000002:MALAT1	metastasis associated lung adenocarcinoma transcript 1 (non-protein coding) [Source:HGNC Symbol;Acc:HGNC:29665]		11	27055.4866	0.76459524	8.34E-07	21396.34	13972.43	38359.49	31973.75	22311.75	21449.08	33770.48	33210.57
ENSG000001:CCNE2	cyclin E2 [Source:HGNC Symbol;Acc:HGNC:1590]		8	1350.3569	0.76574922	0.00404377	1124.33	1021.82	1393.38	1318.29	826.04	714.3	2238.92	2165.78
ENSG000001:ZNF700	zinc finger protein 700 [Source:HGNC Symbol;Acc:HGNC:25292]		19	800.376862	0.76629469	0.00088829	585.86	624.44	883.28	778.14	502.93	517.58	1234.21	1276.56
ENSG000001:CATSPER1	cation channel, sperm associated 1 [Source:HGNC Symbol;Acc:HGNC:17116]		11	24.3117561	0.76663542	0.03875078	4.74	3.78	50.71	20.74	20.19	20.05	38.43	35.85
ENSG000002:PTCHD4	patched domain containing 4 [Source:HGNC Symbol;Acc:HGNC:21345]		6	12.4896963	0.76711195	0.01461208	1.9	0	48.68	27.65	3.85	0	9.88	7.97
ENSG000002:TRIM53CP	tripartite motif containing 53C, pseudogene [Source:HGNC Symbol;Acc:HGNC:43979]		11	124.038084	0.76774578	0.03829296	2.84	35.95	3.04	26.66	22.12	107.91	23.06	770.72
ENSG000001:IL18RAP	interleukin 18 receptor accessory protein [Source:HGNC Symbol;Acc:HGNC:5989]		2	16.1531922	0.76804212	0.03093789	6.64	1.89	78.09	14.81	10.58	0.95	14.27	1.99
ENSG000001:AHNAK2	AHNAK nucleoprotein 2 [Source:HGNC Symbol;Acc:HGNC:20125]		14	15.3745837	0.76830197	0.03836069	3.79	3.78	7.1	12.84	9.62	11.46	50.51	23.9
ENSG000001:SEPN1	selenoprotein N, 1 [Source:HGNC Symbol;Acc:HGNC:15999]		1	73.8441371	0.76847791	0.00703333	33.18	53.93	74.03	73.07	51.93	59.21	101.02	144.39
ENSG000001:ARHGFE6	Rac/Cdc42 guanine nucleotide exchange factor (GEF) 6 [Source:HGNC Symbol;Acc:HGNC:685]	X		135.076797	0.7688846	0.00616109	54.98	89.88	84.17	119.49	69.24	129.87	141.65	391.33
ENSG000001:KCNC3	potassium channel, voltage gated Shaw related subfamily C, member 3 [Source:HGNC Symbol;Acc:HGNC:6235]		19	188.169575	0.76884901	0.01357759	68.26	177.87	288.01	406.84	75.97	169.98	115.3	203.13
ENSG000002:COL11A2	collagen, type XI, alpha 2 [Source:HGNC Symbol;Acc:HGNC:2187]		6	233.136039	0.7689389	0.00377545	132.72	123	410.71	272.55	169.25	216.77	239.37	300.72
ENSG000001:CRACR2B	calcium release activated channel regulator 2B [Source:HGNC Symbol;Acc:HGNC:28703]		11	1417.09154	0.7695175	4.18E-05	801.06	1193.07	1226.05	1660.95	927.97	1096.28	2225.74	2205.61
ENSG000002:TRIM51GP	tripartite motif-containing 51G, pseudogene [Source:HGNC Symbol;Acc:HGNC:43972]		11	41.8671378	0.76974725	0.0376905	0	10.41	2.03	8.89	7.69	42.02	10.98	252.92
ENSG000001:GDPD2	glycerophosphodiester phosphodiesterase domain containing 2 [Source:HGNC Symbol;Acc:HGNC:25974]	X		53.8752151	0.77135683	0.029809	40.76	19.87	114.59	96.77	42.31	23.87	45.02	47.8
ENSG000001:IGFBP3	insulin-like growth factor binding protein 3 [Source:HGNC Symbol;Acc:HGNC:5472]		7	132.099099	0.77141718	0.02791828	65.41	52.04	304.23	206.38	98.09	95.49	140.55	94.6
ENSG000001:ZNF442	zinc finger protein 442 [Source:HGNC Symbol;Acc:HGNC:20877]		19	40.283321	0.77145682	0.03673338	12.32	35.95	73.02	31.6	23.08	15.28	70.28	60.74
ENSG000001:CXCL12	chemokine (C-X-C motif) ligand 12 [Source:HGNC Symbol;Acc:HGNC:10672]		10	9.53600339	0.77200756	0.02626712	2.84	1.89	15.21	0.99	4.81	0.95	40.63	8.96
ENSG000001:KIAA1644	KIAA1644 [Source:HGNC Symbol;Acc:HGNC:29335]		22	1696.04837	0.7720272	0.03564344	547.94	372.77	4386	3242.9	1462.64	556.73	2043.47	955.93
ENSG000001:LMNTD2	lamin tail domain containing 2 [Source:HGNC Symbol;Acc:HGNC:28561]		11	102.497315	0.77258531	0.00467608	38.87	58.66	72	74.06	74.05	99.31	178.98	224.05

ENSG000001:SSU72P4	SSU72 pseudogene 4 [Source:HGNC Symbol;Acc:HGNC:43623]		11	68.2379135	0.77331468	0.03344687	1.9	26.49	3.04	24.69	8.65	83.08	18.67	379.38
ENSG000001:HIST1H2AC	histone cluster 1, H2ac [Source:HGNC Symbol;Acc:HGNC:4733]		6	343.924509	0.77499565	0.00466426	139.36	136.24	433.02	325.87	356.76	329.46	674.2	356.48
ENSG000001:XIRP1	xin actin binding repeat containing 1 [Source:HGNC Symbol;Acc:HGNC:14301]		3	19.1175995	0.77571958	0.02880988	1.9	0.95	52.73	9.87	16.35	7.64	29.65	33.86
ENSG000001:ANK3	ankyrin 3, node of Ranvier (ankyrin G) [Source:HGNC Symbol;Acc:HGNC:494]		10	36.1904058	0.77644774	0.03190946	17.06	3.78	142.99	58.26	26.93	4.77	30.75	4.98
ENSG000001:WFDC11	WAP four-disulfide core domain 11 [Source:HGNC Symbol;Acc:HGNC:20478]		20	16.163583	0.77689106	0.03515318	14.22	7.57	39.55	19.75	4.81	7.64	9.88	25.89
ENSG000001:ENO3	enolase 3 (beta, muscle) [Source:HGNC Symbol;Acc:HGNC:3354]		17	2021.19796	0.77734302	2.65E-07	1071.24	1178.88	2199.59	2357.12	1704.01	1963.37	2871.4	2823.97
ENSG000002:GATS	GATS, stromal antigen 3 opposite strand [Source:HGNC Symbol;Acc:HGNC:29954]		7	664.498506	0.77742133	0.01786011	245.53	322.63	931.96	1387.42	442.35	673.24	464.47	848.39
ENSG000001:SESN3	sestrin 3 [Source:HGNC Symbol;Acc:HGNC:23060]		11	647.251354	0.77935369	0.00376146	380.15	352.91	964.41	868.99	563.52	458.37	539.14	1050.53
ENSG000001:TMEM198	transmembrane protein 198 [Source:HGNC Symbol;Acc:HGNC:33704]		2	404.257736	0.78010541	1.57E-06	246.48	280.05	521.25	510.53	305.8	332.32	502.91	534.72
ENSG000001:CHIT1	chitinase 1 (chitotriosidase) [Source:HGNC Symbol;Acc:HGNC:1936]		1	10.5790068	0.78019171	0.03000971	6.64	2.84	19.27	15.8	0.96	5.73	16.47	16.93
ENSG000000:TSPAN32	tetraspanin 32 [Source:HGNC Symbol;Acc:HGNC:13410]		11	15.3895101	0.78066289	0.0217354	5.69	0	8.11	3.95	8.65	0.95	65.88	29.87
ENSG000002:MT-TF	mitochondrially encoded tRNA phenylalanine [Source:HGNC Symbol;Acc:HGNC:7481]	MT		385.100449	0.78111143	4.36E-05	133.67	251.67	250.48	533.24	298.11	402.99	404.08	806.57
ENSG000001:APOC1	apolipoprotein C-1 [Source:HGNC Symbol;Acc:HGNC:607]		19	87.1440474	0.781138	0.00706569	32.23	94.61	63.89	130.35	25	86.9	77.96	186.21
ENSG000001:CDKL2	cyclin-dependent kinase-like 2 (CDC2-related kinase) [Source:HGNC Symbol;Acc:HGNC:1782]		4	56.6514268	0.78185525	0.03403683	36.02	5.68	274.82	29.62	35.58	10.5	56	4.98
ENSG000001:LG14	leucine-rich repeat LG1 family, member 4 [Source:HGNC Symbol;Acc:HGNC:18712]		19	69.1269326	0.78219641	0.01987068	45.5	21.76	48.68	40.49	52.89	43.93	139.45	160.32
ENSG000001:KIR3DX1	killer cell immunoglobulin-like receptor, three domains, X1 [Source:HGNC Symbol;Acc:HGNC:25043]		19	17.1143652	0.78331381	0.03321849	8.53	7.57	14.2	26.66	10.58	9.55	32.94	26.89
ENSG000001:ASAP2	ArfGAP with SH3 domain, ankyrin repeat and PH domain 2 [Source:HGNC Symbol;Acc:HGNC:2721]		2	338.897786	0.78358439	0.01670584	184.86	270.59	202.82	324.88	165.4	197.67	670.91	694.04
ENSG000001:CAV1	caveolin 1, caveolae protein, 22kDa [Source:HGNC Symbol;Acc:HGNC:1527]		7	201.531489	0.78408151	0.00173124	187.7	157.06	433.02	325.87	114.43	81.17	131.77	181.23
ENSG000001:ZNF827	zinc finger protein 827 [Source:HGNC Symbol;Acc:HGNC:27193]		4	13.7516066	0.78409432	0.03220958	4.74	2.84	35.49	13.82	12.5	3.82	20.86	15.93
ENSG000001:PLEKHN1	pleckstrin homology domain containing, family N member 1 [Source:HGNC Symbol;Acc:HGNC:25284]		1	156.32614	0.78440156	0.00095357	66.36	75.69	135.89	99.74	146.17	134.65	338.2	253.92
ENSG000001:ZNF441	zinc finger protein 441 [Source:HGNC Symbol;Acc:HGNC:20875]		19	474.538328	0.78442289	0.00071955	421.86	389.8	596.29	552.99	281.76	240.65	743.38	569.57
ENSG000000:ABCA7	ATP-binding cassette, sub-family A (ABC1), member 7 [Source:HGNC Symbol;Acc:HGNC:37]		19	2372.34619	0.78443144	2.74E-09	1099.68	1040.74	1701.67	2156.67	2420.42	2304.29	4376.82	3878.48
ENSG000002:PRR7-AS1	PRR7 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:27961]		5	131.422703	0.78581061	0.00093693	135.56	94.61	205.86	161.95	74.05	65.89	158.12	155.34
ENSG000001:BACH2	BTB and CNC homology 1, basic leucine zipper transcription factor 2 [Source:HGNC Symbol;Acc:HGNC:14078]		6	1082.28565	0.78621419	4.79E-10	806.75	1155.22	1370.05	2036.19	417.35	771.6	834.52	1266.61
ENSG000001:MAML2	mastermind-like 2 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:16259]		11	10.3454954	0.78740705	0.0261583	3.79	0.95	9.13	3.95	4.81	2.86	48.31	8.96
ENSG000001:USP11	ubiquitin specific peptidase 11 [Source:HGNC Symbol;Acc:HGNC:12609]	X		1182.23763	0.78813053	0.00053604	712.9	767.31	1966.35	1754.76	821.23	958.77	1102.44	1374.15

ENSG000001	PTPRR	protein tyrosine phosphatase, receptor type, R [Source:HGNC Symbol;Acc:HGNC:9680]	12	73.1683994	0.79112986	0.01236683	27.49	35.01	90.26	106.65	65.39	64.94	101.02	94.6
ENSG000002	TEX22	testis expressed 22 [Source:HGNC Symbol;Acc:HGNC:40026]	14	163.760911	0.79116512	0.00256337	93.85	163.68	179.5	203.42	72.12	117.46	161.41	318.64
ENSG000002	BDNF-AS	BDNF antisense RNA [Source:HGNC Symbol;Acc:HGNC:20608]	11	38.8021355	0.79138778	0.02028349	26.54	24.6	56.79	67.15	28.85	15.28	38.43	52.78
ENSG000001	SPATA31C2	SPATA31 subfamily C, member 2 [Source:HGNC Symbol;Acc:HGNC:24508]	9	10.4337244	0.79143641	0.02999156	6.64	2.84	20.28	15.8	5.77	1.91	25.26	4.98
ENSG000001	TRIM49B	tripartite motif containing 49B [Source:HGNC Symbol;Acc:HGNC:42955]	11	460.770655	0.79150442	0.02896294	12.32	170.3	7.1	123.44	61.54	428.77	106.51	2776.18
ENSG000001	CAPN13	calpain 13 [Source:HGNC Symbol;Acc:HGNC:16663]	2	48.4445613	0.79224164	0.02581085	36.02	25.55	48.68	43.45	22.12	24.83	125.18	61.74
ENSG000001	CASP4	caspase 4, apoptosis-related cysteine peptidase [Source:HGNC Symbol;Acc:HGNC:1505]	11	205.904903	0.79321905	0.00046279	122.29	57.71	301.19	113.56	241.37	162.34	337.1	311.67
ENSG000001	MSLNL	mesothelin-like [Source:HGNC Symbol;Acc:HGNC:14170]	16	17.3208112	0.79354692	0.01453671	2.84	3.78	55.78	69.12	3.85	0	2.2	1
ENSG000001	SHC4	SHC (Src homology 2 domain containing) family, member 4 [Source:HGNC Symbol;Acc:HGNC:16743]	15	42.1872015	0.79412614	0.0313617	18.01	11.35	126.76	53.32	21.16	23.87	68.08	14.94
ENSG000001	KLF7	Kruppel-like factor 7 (ubiquitous) [Source:HGNC Symbol;Acc:HGNC:6350]	2	286.952922	0.79462555	0.00029493	384.89	60.55	750.44	103.69	292.34	75.44	427.14	201.14
ENSG000001	TAS1R3	taste receptor, type 1, member 3 [Source:HGNC Symbol;Acc:HGNC:15661]	1	112.379262	0.79546625	0.02431868	55.93	61.5	136.9	108.62	49.04	79.26	326.12	81.65
ENSG000001	FAM117A	family with sequence similarity 117, member A [Source:HGNC Symbol;Acc:HGNC:24179]	17	1049.64859	0.79552436	0.01457021	344.12	491.99	1385.27	2183.33	720.26	1116.33	834.52	1321.37
ENSG000001	TTC9	tetratricopeptide repeat domain 9 [Source:HGNC Symbol;Acc:HGNC:20267]	14	106.020579	0.79596199	0.00114669	55.93	70.96	95.33	122.45	69.24	93.58	172.39	168.28
ENSG000001	CD53	CD53 molecule [Source:HGNC Symbol;Acc:HGNC:1686]	1	53.5146182	0.79650855	0.02489606	15.17	4.73	200.79	110.6	32.7	13.37	31.84	18.92
ENSG000001	MUC16	mucin 16, cell surface associated [Source:HGNC Symbol;Acc:HGNC:15582]	19	9.87901511	0.79659289	0.02398782	2.84	0	11.16	7.9	7.69	2.86	29.65	16.93
ENSG000001	DMC1	DNA meiotic recombinase 1 [Source:HGNC Symbol;Acc:HGNC:2927]	22	259.931673	0.79673405	2.12E-06	150.73	216.66	296.12	370.31	150.98	220.59	255.85	418.22
ENSG000001	RECK	reversion-inducing-cysteine-rich protein with kazal motifs [Source:HGNC Symbol;Acc:HGNC:11345]	9	735.621243	0.79730998	0.00122511	560.27	696.35	785.93	932.19	310.61	469.83	832.32	1297.47
ENSG000001	CMTM3	CKLF-like MARVEL transmembrane domain containing 3 [Source:HGNC Symbol;Acc:HGNC:19174]	16	36.0843513	0.79754097	0.01864879	19.91	15.14	52.73	19.75	36.54	14.32	94.43	35.85
ENSG000001	ZMAT3	zinc finger, matrin-type 3 [Source:HGNC Symbol;Acc:HGNC:29983]	3	1584.10716	0.79836478	0.00411911	1097.78	694.46	3627.45	2044.09	1386.67	934.89	1654.76	1232.75
ENSG000000	FAM214A	family with sequence similarity 214, member A [Source:HGNC Symbol;Acc:HGNC:25609]	15	3279.58237	0.79843865	3.09E-05	2424.03	1860.09	5060.38	4535.51	2553.13	2376.87	3295.24	4131.41
ENSG000001	HID1	HID1 domain containing [Source:HGNC Symbol;Acc:HGNC:15736]	17	940.258555	0.79881597	1.61E-07	562.16	702.03	1225.04	1330.14	568.32	851.81	879.54	1403.03
ENSG000000	TYMP	thymidine phosphorylase [Source:HGNC Symbol;Acc:HGNC:3148]	22	3504.72638	0.79889662	1.91E-06	3636.53	1806.16	5508.61	2848.89	2823.35	1591.9	6854.02	2968.36
ENSG000001	KCTD1	potassium channel tetramerization domain containing 1 [Source:HGNC Symbol;Acc:HGNC:18249]	18	809.14239	0.80035186	3.44E-08	588.71	670.81	1040.47	1422.96	475.05	554.82	744.48	975.84
ENSG000001	LCOR	ligand dependent nuclear receptor corepressor [Source:HGNC Symbol;Acc:HGNC:29503]	10	525.827508	0.80140005	3.49E-08	345.07	430.49	637.87	692.23	346.19	381.02	605.02	768.73
ENSG000002	ATP10A	ATPase, class V, type 10A [Source:HGNC Symbol;Acc:HGNC:13542]	15	207.100351	0.80147347	1.53E-05	152.63	122.05	294.09	208.36	183.67	120.32	375.53	200.15

ENSG000001	SLC34A2	solute carrier family 34 (type II sodium/phosphate cotransporter), member 2 [Source:HGNC Symbol;Acc:HGNC:11020]	4	77.6706824	0.80158456	0.02257419	2.84	24.6	1.01	10.86	3.85	37.24	24.16	516.8
ENSG000001	DNHD1	dynein heavy chain domain 1 [Source:HGNC Symbol;Acc:HGNC:26532]	11	1094.74842	0.80202255	2.80E-10	742.28	652.83	1335.57	1024.02	949.13	780.19	1773.35	1500.61
ENSG000001	MIB2	mindbomb E3 ubiquitin protein ligase 2 [Source:HGNC Symbol;Acc:HGNC:30577]	1	1042.59785	0.80244292	0.00149953	410.48	733.25	1155.06	2065.82	664.49	1026.57	864.16	1420.95
ENSG000001	IQSEC2	IQ motif and Sec7 domain 2 [Source:HGNC Symbol;Acc:HGNC:29059]	X	16.1220701	0.80249643	0.02892737	5.69	4.73	11.16	6.91	6.73	9.55	27.45	56.76
ENSG000002	SNORD3B-2	small nucleolar RNA, C/D box 3B-2 [Source:HGNC Symbol;Acc:HGNC:33190]	17	57.975575	0.80265886	0.01587686	42.66	22.71	79.1	24.69	38.47	33.42	125.18	97.58
ENSG000002	NBEAP1	neurobeachin pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:1007]	15	11.2627622	0.80550642	0.02710602	2.84	1.89	14.2	14.81	7.69	6.68	23.06	18.92
ENSG000001	CDC20B	cell division cycle 20B [Source:HGNC Symbol;Acc:HGNC:24222]	5	28.1447916	0.80563487	0.02842505	2.84	21.76	33.47	85.91	5.77	21.96	28.55	24.89
ENSG000001	JAK3	Janus kinase 3 [Source:HGNC Symbol;Acc:HGNC:6193]	19	1595.74712	0.80669191	5.23E-11	953.69	1058.72	1642.85	2046.07	1134.72	1407.59	1812.88	2709.46
ENSG000001	FOS	FBJ murine osteosarcoma viral oncogene homolog [Source:HGNC Symbol;Acc:HGNC:3796]	14	2253.8423	0.80679628	0.00288763	99.54	124.89	406.66	381.17	2563.71	4275.3	4605.22	5574.26
ENSG000001	PHLDA3	pleckstrin homology-like domain, family A, member 3 [Source:HGNC Symbol;Acc:HGNC:8934]	1	2186.10164	0.80938066	4.74E-05	1889.36	1718.17	2405.45	3019.73	1372.25	1163.13	3280.97	2639.76
ENSG000000	SCML1	sex comb on midleg-like 1 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:10580]	X	62.0580389	0.80973471	0.0185612	23.7	28.38	103.44	102.7	39.43	58.25	65.88	74.68
ENSG000001	FAM57B	family with sequence similarity 57, member B [Source:HGNC Symbol;Acc:HGNC:25295]	16	78.8109452	0.81031208	0.00499196	15.17	50.14	29.41	80.97	36.54	106	113.1	199.15
ENSG000002	RN7SL4P	RNA, 7SL, cytoplasmic 4, pseudogene [Source:HGNC Symbol;Acc:HGNC:10039]	3	80.672669	0.81100229	0.00754135	70.15	27.44	118.65	35.55	56.74	45.84	184.47	106.55
ENSG000001	CFAP54	cilia and flagella associated 54 [Source:HGNC Symbol;Acc:HGNC:26456]	12	148.76368	0.81164653	0.02028165	80.58	50.14	412.74	213.3	137.51	63.98	137.26	94.6
ENSG000002	MIR186	microRNA 186 [Source:HGNC Symbol;Acc:HGNC:31557]	1	43.1962173	0.81164805	0.00878573	24.65	24.6	66.93	53.32	28.85	32.47	56	58.75
ENSG000001	DUSP5	dual specificity phosphatase 5 [Source:HGNC Symbol;Acc:HGNC:3071]	10	12479.7568	0.81313287	4.76E-07	8404.96	5262.37	12731.06	8407.44	10574.09	10039.37	25322.1	19096.67
ENSG000001	DHX58	DEXH (Asp-Glu-X-His) box polypeptide 58 [Source:HGNC Symbol;Acc:HGNC:29517]	17	60.4106102	0.81367768	0.01876326	17.06	27.44	25.35	30.61	31.73	54.43	127.37	169.28
ENSG000002	H2BFS	H2B histone family, member 5 (pseudogene) [Source:HGNC Symbol;Acc:HGNC:4762]	21	49.0665532	0.81387974	0.0104752	26.54	14.19	54.76	52.34	55.77	30.56	96.63	61.74
ENSG000001	RAB15	RAB15, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:20150]	14	180.332553	0.81498298	0.00157379	137.46	71.91	219.05	110.6	161.55	85.95	501.81	154.34
ENSG000001	TRIM53BP	tripartite motif containing 53B, pseudogene [Source:HGNC Symbol;Acc:HGNC:37144]	11	211.632625	0.81708003	0.02452445	7.58	79.47	9.13	52.34	16.35	183.35	27.45	1317.39
ENSG000001	TSKU	tsukushi, small leucine rich proteoglycan [Source:HGNC Symbol;Acc:HGNC:28850]	11	142.481925	0.8173401	0.00303915	43.61	128.67	146.03	166.88	98.09	115.55	202.04	238.98
ENSG000001	E2F7	E2F transcription factor 7 [Source:HGNC Symbol;Acc:HGNC:23820]	12	970.165724	0.81744793	0.00425773	524.24	153.27	1802.06	545.09	1515.53	534.77	1932.57	753.79
ENSG000002	CHIC1	cysteine-rich hydrophobic domain 1 [Source:HGNC Symbol;Acc:HGNC:1934]	X	988.145497	0.81839934	1.74E-10	576.38	614.98	1049.6	1038.83	812.58	799.29	1382.44	1631.05
ENSG000001	CCDC136	coiled-coil domain containing 136 [Source:HGNC Symbol;Acc:HGNC:22225]	7	585.352673	0.82178379	0.00019003	156.42	271.54	205.86	428.57	335.61	702.84	715.93	1866.05
ENSG000000	STX1B	syntaxin 1B [Source:HGNC Symbol;Acc:HGNC:18539]	16	107.770984	0.8220285	0.001074	44.56	46.36	105.47	72.09	86.55	111.73	204.24	191.19
ENSG000001	FZD6	frizzled class receptor 6 [Source:HGNC Symbol;Acc:HGNC:4044]	8	1456.6961	0.82215442	1.53E-07	1103.47	1405.95	2082.97	2005.58	662.56	987.42	1380.25	2025.37

ENSG000001	IL1R1	interleukin 1 receptor, type I [Source:HGNC Symbol;Acc:HGNC:5993]	2	164.525518	0.82318281	0.0239134	111.86	13.25	817.37	70.11	125.01	24.83	132.86	20.91
ENSG000001	RASD1	RAS, dexamethasone-induced 1 [Source:HGNC Symbol;Acc:HGNC:15828]	17	20.5500306	0.82408482	0.02431868	5.69	9.46	8.11	24.69	4.81	20.05	31.84	59.75
ENSG000001	S100A1	S100 calcium binding protein A1 [Source:HGNC Symbol;Acc:HGNC:10486]	1	125.011878	0.82484577	0.00146523	132.72	66.23	237.3	196.51	73.08	62.07	108.71	123.47
ENSG000001	ZC3H6	zinc finger CCCH-type containing 6 [Source:HGNC Symbol;Acc:HGNC:24762]	2	285.234625	0.8261951	0.00020394	170.64	216.66	421.87	483.87	172.13	209.13	226.2	381.38
ENSG000001	TRIM73	tripartite motif containing 73 [Source:HGNC Symbol;Acc:HGNC:18162]	7	155.63771	0.82630755	0.00124119	83.42	77.58	211.95	211.32	122.13	139.42	192.16	207.12
ENSG000001	ADCY6	adenylate cyclase 6 [Source:HGNC Symbol;Acc:HGNC:237]	12	1584.43483	0.82878381	9.55E-12	744.18	1053.99	1476.54	2004.59	1166.46	1576.62	2104.96	2548.15
ENSG000001	PDE4B	phosphodiesterase 4B, cAMP-specific [Source:HGNC Symbol;Acc:HGNC:8781]	1	29.8025281	0.83051867	0.02274889	19.91	5.68	83.16	43.45	16.35	16.23	30.75	22.9
ENSG000001	MST1P2	macrophage stimulating 1 (hepatocyte growth factor-like) pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:7383]	1	230.21608	0.83087183	2.82E-05	117.55	125.84	263.67	186.63	231.75	153.75	478.75	283.79
ENSG000002	TRIM51FP	tripartite motif-containing 51F, pseudogene [Source:HGNC Symbol;Acc:HGNC:43966]	11	53.2156654	0.83138173	0.02279052	0.95	9.46	6.08	11.85	8.65	49.66	5.49	333.58
ENSG000001	APOBEC3F	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F [Source:HGNC Symbol;Acc:HGNC:17356]	22	231.389236	0.83148135	3.59E-05	99.54	163.68	242.37	254.77	138.47	243.51	275.61	433.16
ENSG000001	CECR2	cat eye syndrome chromosome region, candidate 2 [Source:HGNC Symbol;Acc:HGNC:1840]	22	156.006	0.83179115	0.01156423	36.97	127.73	55.78	134.3	55.77	131.78	210.83	494.89
ENSG000001	AFAP1L2	actin filament associated protein 1-like 2 [Source:HGNC Symbol;Acc:HGNC:25901]	10	409.273324	0.83198452	0.01957478	132.72	63.39	1522.17	99.74	376	222.5	452.4	405.27
ENSG000001	EPHA2	EPH receptor A2 [Source:HGNC Symbol;Acc:HGNC:3386]	1	297.320489	0.83238133	0.00228511	266.39	71.91	333.64	134.3	375.04	80.22	821.34	295.74
ENSG000001	C11orf21	chromosome 11 open reading frame 21 [Source:HGNC Symbol;Acc:HGNC:13231]	11	16.6701583	0.83279458	0.02195695	8.53	0.95	13.18	8.89	13.46	4.77	52.71	30.87
ENSG000001	ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3 [Source:HGNC Symbol;Acc:HGNC:683]	3	739.589274	0.83283243	0.00066239	308.1	678.37	1050.61	1301.5	407.73	589.2	533.65	1047.54
ENSG000001	CUEDC1	CUE domain containing 1 [Source:HGNC Symbol;Acc:HGNC:31350]	17	20.0204245	0.83368949	0.02030571	7.58	14.19	27.38	18.76	1.92	5.73	20.86	63.73
ENSG000002	UBE2QL1	ubiquitin-conjugating enzyme E2Q family-like 1 [Source:HGNC Symbol;Acc:HGNC:37269]	5	2090.88225	0.83601953	3.92E-09	2164.28	807.99	4273.43	1742.91	1754.98	1134.48	3117.36	1731.63
ENSG000001	HAVCR2	hepatitis A virus cellular receptor 2 [Source:HGNC Symbol;Acc:HGNC:18437]	5	108.78343	0.83614651	0.02201781	61.62	20.81	477.64	131.34	70.2	21.96	64.78	21.91
ENSG000001	KLK2	kallikrein-related peptidase 2 [Source:HGNC Symbol;Acc:HGNC:6363]	19	21.476183	0.83644113	0.02134155	5.69	8.52	27.38	42.46	17.31	12.41	35.14	22.9
ENSG000001	NTN5	netrin 5 [Source:HGNC Symbol;Acc:HGNC:25208]	19	18.7078981	0.83678715	0.02086874	5.69	4.73	14.2	11.85	9.62	18.14	40.63	44.81
ENSG000002	LINC00504	long intergenic non-protein coding RNA 504 [Source:HGNC Symbol;Acc:HGNC:43555]	4	15.4443776	0.83694446	0.02179981	9.48	3.78	29.41	8.89	13.46	2.86	41.73	13.94
ENSG000002	LINC01435	long intergenic non-protein coding RNA 1435 [Source:HGNC Symbol;Acc:HGNC:50753]	10	10.1027541	0.83722401	0.01475091	7.58	3.78	31.44	27.65	0	0	4.39	5.97
ENSG000001	RAB5B	RAB5B, member RAS oncogene family [Source:HGNC Symbol;Acc:HGNC:9784]	12	508.677145	0.83747564	1.58E-06	452.2	401.16	666.27	737.65	262.53	310.36	540.24	699.02
ENSG000001	IL9R	interleukin 9 receptor [Source:HGNC Symbol;Acc:HGNC:6030]	X	190.290703	0.83749932	0.00142109	81.53	108.8	98.37	325.87	94.24	202.45	188.86	422.2
ENSG000001	TCIRG1	T-cell, immune regulator 1, ATPase, H+ transporting, lysosomal V0 subunit A3 [Source:HGNC Symbol;Acc:HGNC:11647]	11	7278.29077	0.83933625	1.35E-06	3963.58	3407.96	5409.23	6159.93	6310.22	5848.1	15005.93	12121.38

ENSG000001	ARSI	arylsulfatase family, member 1 [Source:HGNC Symbol;Acc:HGNC:32521]	5	57.2279291	0.83967508	0.01198447	20.86	38.79	32.45	57.27	21.16	51.57	93.33	142.39
ENSG000001	AHSA2	AHA1, activator of heat shock 90kDa protein ATPase homolog 2 (yeast) [Source:HGNC Symbol;Acc:HGNC:20437]	2	3749.90785	0.83978107	1.11E-10	2438.25	1942.4	3709.59	3700.1	3094.53	3010	6060.13	6044.26
ENSG000000	BZRAP1	benzodiazepine receptor (peripheral) associated protein 1 [Source:HGNC Symbol;Acc:HGNC:16831]	17	247.634678	0.83992438	0.00600287	104.28	142.87	402.6	471.03	131.74	239.69	181.18	307.69
ENSG000000	PDZD4	PDZ domain containing 4 [Source:HGNC Symbol;Acc:HGNC:21167]	X	46.9082428	0.84022781	0.01282971	2.84	40.68	14.2	61.22	18.27	47.75	43.92	146.38
ENSG000001	XAF1	XIAP associated factor 1 [Source:HGNC Symbol;Acc:HGNC:30932]	17	9.91582496	0.84146989	0.01662146	0.95	0	5.07	1.97	6.73	4.77	32.94	26.89
ENSG000002	LINC00996	long intergenic non-protein coding RNA 996 [Source:HGNC Symbol;Acc:HGNC:27800]	7	189.589479	0.84351931	0.00010859	36.97	86.1	56.79	155.04	105.78	277.89	262.43	535.72
ENSG000001	CCDC122	coiled-coil domain containing 122 [Source:HGNC Symbol;Acc:HGNC:26478]	13	65.5379796	0.8444767	0.01027811	35.08	30.28	166.31	66.16	39.43	46.79	62.59	77.67
ENSG000001	IFIT1	interferon-induced protein with tetraatricopeptide repeats 1 [Source:HGNC Symbol;Acc:HGNC:5407]	10	22.3333901	0.84537787	0.00817446	3.79	5.68	80.11	5.92	0	1.91	38.43	42.82
ENSG000001	SLC12A7	solute carrier family 12 (potassium/chloride transporter), member 7 [Source:HGNC Symbol;Acc:HGNC:10915]	5	1738.27711	0.84806417	6.38E-08	936.62	1042.63	1814.23	1766.61	1353.01	1467.75	3216.18	2309.17
ENSG000001	NBPF6	neuroblastoma breakpoint family, member 6 [Source:HGNC Symbol;Acc:HGNC:31988]	1	275.587891	0.84829203	0.0025114	166.85	173.14	253.53	214.28	158.67	183.35	474.36	580.53
ENSG000002	MBD3L2	methyl-CpG binding domain protein 3-like 2 [Source:HGNC Symbol;Acc:HGNC:18532]	19	13.8090204	0.84868707	0.01277248	0.95	0.95	0	0.99	0.96	7.64	4.39	94.6
ENSG000001	EGR2	early growth response 2 [Source:HGNC Symbol;Acc:HGNC:3239]	10	65.3152741	0.85048549	0.01795595	6.64	3.78	62.87	10.86	48.08	84.99	198.75	106.55
ENSG000001	LACC1	laccase (multicopper oxidoreductase) domain containing 1 [Source:HGNC Symbol;Acc:HGNC:26789]	13	311.815145	0.85112582	0.00748536	165.9	83.26	819.4	262.67	301.95	198.63	337.1	325.61
ENSG000002	PATL2	protein associated with topoisomerase II homolog 2 (yeast) [Source:HGNC Symbol;Acc:HGNC:33630]	15	58.6538603	0.85226539	0.00260929	33.18	21.76	86.2	41.47	54.81	41.06	102.12	88.62
ENSG000002	DNM1P51	dynamain 1 pseudogene 51 [Source:HGNC Symbol;Acc:HGNC:48500]	15	16.0863642	0.85227285	0.01883226	8.53	6.62	42.59	28.64	3.85	7.64	20.86	9.96
ENSG000002	MYO15B	myosin XVb [Source:HGNC Symbol;Acc:HGNC:14083]	17	71.9522498	0.85298386	0.0045842	18.01	29.33	59.83	85.91	72.12	68.76	114.2	127.46
ENSG000002	LPAL2	lipoprotein, Lp(a)-like 2, pseudogene [Source:HGNC Symbol;Acc:HGNC:21210]	6	89.7496511	0.8534022	0.0073143	58.78	43.52	72	79.99	60.58	47.75	159.22	196.16
ENSG000001	RND3	Rho family GTPase 3 [Source:HGNC Symbol;Acc:HGNC:671]	2	1514.80923	0.85581607	0.00444266	1240.93	237.48	3980.36	966.75	1734.78	483.2	3011.95	463.03
ENSG000001	C15orf53	chromosome 15 open reading frame 53 [Source:HGNC Symbol;Acc:HGNC:33796]	15	10.0911322	0.85725985	0.01297767	4.74	0	16.23	10.86	4.81	1.91	25.26	16.93
ENSG000001	PDGFB	platelet-derived growth factor beta polypeptide [Source:HGNC Symbol;Acc:HGNC:8800]	22	18.6687569	0.85929354	0.01770677	12.32	6.62	53.75	12.84	3.85	11.46	7.69	40.83
ENSG000000	TRAF1	TNF receptor-associated factor 1 [Source:HGNC Symbol;Acc:HGNC:12031]	9	3133.9862	0.85944893	1.22E-06	1783.19	1648.16	4418.45	3563.83	2444.46	2841.92	4324.12	4047.76
ENSG000001	MEIS3	Meis homeobox 3 [Source:HGNC Symbol;Acc:HGNC:29537]	19	20.2206307	0.8597784	0.0176726	4.74	3.78	19.27	27.65	10.58	21.01	21.96	52.78
ENSG000001	PPP1R16B	protein phosphatase 1, regulatory subunit 16B [Source:HGNC Symbol;Acc:HGNC:15850]	20	554.302653	0.85994616	1.29E-06	288.19	321.68	694.66	682.35	413.5	518.54	704.95	810.55
ENSG000001	ACER2	alkaline ceramidase 2 [Source:HGNC Symbol;Acc:HGNC:23675]	9	150.211813	0.86026552	0.0065852	91.96	79.47	309.3	313.03	111.55	64.94	132.86	98.58

ENSG000001	SCNN1D	sodium channel, non voltage gated 1 delta subunit [Source:HGNC Symbol;Acc:HGNC:10601]	1	85.1673168	0.86082489	0.00218857	60.67	35.01	85.18	105.66	66.35	56.34	152.63	119.49
ENSG000002	SRRM2-AS1	SRRM2 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44162]	16	55.2701338	0.86217086	0.00616444	25.6	14.19	44.62	56.29	44.24	52.52	113.1	91.61
ENSG000001	TRIM74	tripartite motif containing 74 [Source:HGNC Symbol;Acc:HGNC:17453]	7	68.038078	0.86250092	0.00238958	39.82	28.38	78.09	89.86	47.12	60.16	93.33	107.54
ENSG000002	UBE2CP2	ubiquitin-conjugating enzyme E2C pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:43551]	18	12.2182714	0.86457956	0.01568733	1.9	7.57	15.21	15.8	4.81	3.82	19.76	28.88
ENSG000000	BIRC3	baculoviral IAP repeat containing 3 [Source:HGNC Symbol;Acc:HGNC:591]	11	288.494355	0.86541913	0.01371472	92.9	58.66	152.12	33.57	241.37	85.95	1404.4	238.98
ENSG000001	PCYOX1L	preylcysteine oxidase 1 like [Source:HGNC Symbol;Acc:HGNC:28477]	5	1230.65203	0.86635035	8.08E-10	863.63	652.83	1769.61	1006.25	1046.25	816.48	2008.33	1681.84
ENSG000000	CAMK2A	calcium/calmodulin-dependent protein kinase II alpha [Source:HGNC Symbol;Acc:HGNC:1460]	5	22.1370587	0.86664151	0.01610189	4.74	16.08	19.27	19.75	3.85	8.59	24.16	80.66
ENSG000001	MAEL	maelstrom spermatogenic transposon silencer [Source:HGNC Symbol;Acc:HGNC:25929]	1	15.6972379	0.86676915	0.01676071	6.64	6.62	20.28	15.8	8.65	6.68	23.06	37.84
ENSG000001	DPEP2	dipeptidase 2 [Source:HGNC Symbol;Acc:HGNC:23028]	16	12.354547	0.86707294	0.00801494	3.79	1.89	8.11	10.86	0.96	0.95	27.45	44.81
ENSG000001	ITGB7	integrin, beta 7 [Source:HGNC Symbol;Acc:HGNC:6162]	12	66729.0217	0.86721607	6.72E-05	32717.35	20512.07	99235.12	48527.94	75480.3	56493.76	123418.46	77447.18
ENSG000001	ENC1	ectodermal-neural cortex 1 (with BTB domain) [Source:HGNC Symbol;Acc:HGNC:3345]	5	810.360348	0.86734549	0.00245066	543.2	319.79	1748.31	1202.76	706.8	443.1	923.46	595.46
ENSG000001	FBN1	fibrillin 1 [Source:HGNC Symbol;Acc:HGNC:3603]	15	2308.83406	0.86758845	2.12E-05	2240.12	1867.66	2988.56	3320.91	1152.03	1131.61	2879.08	2890.69
ENSG000001	LRRC63	leucine rich repeat containing 63 [Source:HGNC Symbol;Acc:HGNC:34296]	13	32.7862574	0.86856085	0.00792756	19.91	9.46	39.55	21.72	27.89	19.1	76.86	47.8
ENSG000001	SRGAP3	SLIT-ROBO Rho GTPase activating protein 3 [Source:HGNC Symbol;Acc:HGNC:19744]	3	110.540873	0.86876268	0.00182503	142.2	67.18	241.36	122.45	58.66	26.74	125.18	100.57
ENSG000001	CALHM3	calcium homeostasis modulator 3 [Source:HGNC Symbol;Acc:HGNC:23458]	10	24.4188445	0.86916718	0.0150998	16.12	7.57	29.41	13.82	4.81	5.73	79.06	38.83
ENSG000001	ADGRB2	adhesion G protein-coupled receptor B2 [Source:HGNC Symbol;Acc:HGNC:944]	1	574.081907	0.87008547	0.0100663	58.78	409.67	53.75	510.53	169.25	586.34	1082.68	1721.67
ENSG000001	FSD2	fibronectin type III and SPRY domain containing 2 [Source:HGNC Symbol;Acc:HGNC:18024]	15	15.336445	0.87110534	0.01594255	6.64	3.78	28.39	17.77	14.42	1.91	31.84	17.92
ENSG000001	BVES	blood vessel epicardial substance [Source:HGNC Symbol;Acc:HGNC:1152]	6	185.717468	0.87142918	2.31E-05	127.03	83.26	239.33	133.31	170.21	114.59	338.2	279.81
ENSG000002	TRIM53AP	tripartite motif containing 53A, pseudogene [Source:HGNC Symbol;Acc:HGNC:19025]	11	238.753023	0.87322444	0.01454347	6.64	88.94	11.16	58.26	19.23	196.72	38.43	1490.65
ENSG000001	EDA2R	ectodysplasin A2 receptor [Source:HGNC Symbol;Acc:HGNC:17756]	X	2259.61397	0.87346264	4.43E-09	1773.71	1457.98	3797.82	3154.02	1616.5	1340.75	2438.77	2497.36
ENSG000001	PRAMEF2	PRAME family member 2 [Source:HGNC Symbol;Acc:HGNC:28841]	1	153.353717	0.87377066	0.01420368	5.69	48.25	16.23	31.6	40.39	130.83	84.55	869.3
ENSG000001	SLC2A8	solute carrier family 2 (facilitated glucose transporter), member 8 [Source:HGNC Symbol;Acc:HGNC:13812]	9	2904.04928	0.87400991	2.07E-07	1808.78	1599.9	3406.37	4003.26	2481.01	2038.81	4904.98	2989.27
ENSG000000	TP73	tumor protein p73 [Source:HGNC Symbol;Acc:HGNC:12003]	1	1480.41347	0.87428793	0.00082351	74.89	1985.92	189.64	2787.67	218.29	2025.44	917.97	3643.48
ENSG000001	TPST2	tyrosylprotein sulfotransferase 2 [Source:HGNC Symbol;Acc:HGNC:12021]	22	2530.00209	0.87552617	9.91E-10	1551.87	1579.09	3518.94	3230.06	1839.6	2034.04	3239.24	3247.17
ENSG000002	RN7SK	RNA, 7SK small nuclear [Source:HGNC Symbol;Acc:HGNC:10037]	6	177.315814	0.87706143	0.00187289	157.37	116.37	309.3	138.25	75.01	97.4	225.1	299.72
ENSG000001	ARRDC3	arrestin domain containing 3 [Source:HGNC Symbol;Acc:HGNC:29263]	5	4302.82626	0.87720924	3.99E-14	2767.21	2420.2	5468.05	5042.09	3629.19	3202.89	6174.33	5718.65

ENSG000001	TRIM38	tripartite motif containing 38 [Source:HGNC Symbol;Acc:HGNC:10059]	6	1041.47251	0.87792509	0.00012363	619.99	539.29	1649.95	1503.94	771.23	824.12	1000.32	1422.94
ENSG000001	LRRC66	leucine rich repeat containing 66 [Source:HGNC Symbol;Acc:HGNC:34299]	4	29.2184356	0.87976856	0.00808176	17.06	11.35	40.56	36.54	20.19	19.1	46.12	42.82
ENSG000001	TCN2	transcobalamin II [Source:HGNC Symbol;Acc:HGNC:11653]	22	870.599436	0.8805372	1.70E-11	696.78	210.99	1195.63	414.74	916.43	593.02	1696.49	1240.72
ENSG000001	TMOD1	tropomodulin 1 [Source:HGNC Symbol;Acc:HGNC:11871]	9	96.1633627	0.88234659	0.00234432	52.14	70.01	147.05	85.91	62.51	53.48	154.82	143.39
ENSG000001	RNF122	ring finger protein 122 [Source:HGNC Symbol;Acc:HGNC:21147]	8	1952.98138	0.88277244	7.22E-06	1069.34	1228.07	1946.07	1746.86	1269.35	1570.89	3625.76	3167.51
ENSG000002	HIST2H3C	histone cluster 2, H3c [Source:HGNC Symbol;Acc:HGNC:20503]	1	144.2398	0.88278625	0.01353877	38.87	27.44	290.03	248.85	108.66	118.41	171.3	150.36
ENSG000001	CRYBB1	crystallin, beta B1 [Source:HGNC Symbol;Acc:HGNC:2397]	22	237.710013	0.88332685	0.00741267	50.24	7.57	712.91	205.4	41.35	70.67	726.91	86.63
ENSG000001	CES4A	carboxylesterase 4A [Source:HGNC Symbol;Acc:HGNC:26741]	16	631.458438	0.88473009	2.67E-09	326.11	315.06	519.22	611.25	456.77	611.17	967.38	1244.7
ENSG000002	HIST2H3A	histone cluster 2, H3a [Source:HGNC Symbol;Acc:HGNC:20505]	1	144.244067	0.88874499	0.012743	38.87	27.44	290.03	248.85	107.7	118.41	171.3	151.36
ENSG000002	DOC2GP	double C2-like domains, gamma, pseudogene [Source:HGNC Symbol;Acc:HGNC:37962]	11	100.407745	0.89007229	0.00109827	52.14	66.23	175.44	139.24	52.89	83.08	98.82	135.42
ENSG000001	SEMA6D	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D [Source:HGNC Symbol;Acc:HGNC:16770]	15	27.8948814	0.89167329	0.01313971	35.08	0	98.37	2.96	14.42	0.95	71.37	0
ENSG000000	ARHGAP31	Rho GTPase activating protein 31 [Source:HGNC Symbol;Acc:HGNC:29216]	3	78.9279597	0.89248597	0.00273862	66.36	38.79	115.61	58.26	55.77	30.56	162.51	103.56
ENSG000001	GRHL3	grainyhead-like 3 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:25839]	1	16.0408808	0.89300579	0.0130846	5.69	6.62	37.52	18.76	8.65	5.73	16.47	28.88
ENSG000001	RIN1	Ras and Rab interactor 1 [Source:HGNC Symbol;Acc:HGNC:18749]	11	41.7091154	0.89404916	0.00725583	25.6	28.38	45.63	51.35	19.23	20.05	53.8	89.62
ENSG000001	PLYLRP2	peptidoglycan recognition protein 2 [Source:HGNC Symbol;Acc:HGNC:30013]	19	50.4048465	0.89880818	0.01152147	21.8	2.84	33.47	7.9	43.27	8.59	273.41	11.95
ENSG000001	JAZF1	JAZF zinc finger 1 [Source:HGNC Symbol;Acc:HGNC:28917]	7	174.391659	0.90108364	0.00269027	149.78	58.66	664.24	112.57	112.51	49.66	147.14	100.57
ENSG000001	IL10RA	interleukin 10 receptor, alpha [Source:HGNC Symbol;Acc:HGNC:5964]	11	1165.39894	0.90278211	1.36E-07	753.66	576.19	1576.93	932.19	845.27	911.02	2178.53	1549.4
ENSG000002	C16orf96	chromosome 16 open reading frame 96 [Source:HGNC Symbol;Acc:HGNC:40031]	16	21.4665446	0.90506001	0.01079232	9.48	9.46	22.31	17.77	6.73	15.28	32.94	57.75
ENSG000000	STAG3	stromal antigen 3 [Source:HGNC Symbol;Acc:HGNC:11356]	7	453.351429	0.90515673	6.87E-05	219.94	259.24	526.32	797.89	269.26	436.41	411.77	705.99
ENSG000001	ZNF396	zinc finger protein 396 [Source:HGNC Symbol;Acc:HGNC:18824]	18	65.5690314	0.90539705	0.00089103	37.92	21.76	101.41	41.47	60.58	43.93	121.88	95.59
ENSG000001	CARN1	carnosine synthase 1 [Source:HGNC Symbol;Acc:HGNC:29268]	11	59.9419759	0.90569507	0.00372268	42.66	35.01	82.14	122.45	25.96	36.29	81.26	53.77
ENSG000002	FOXO6	forkhead box O6 [Source:HGNC Symbol;Acc:HGNC:24814]	1	93.3795533	0.90662892	0.00168683	53.09	42.58	81.13	71.1	54.81	70.67	184.47	189.19
ENSG000001	KRCC1	lysine-rich coiled-coil 1 [Source:HGNC Symbol;Acc:HGNC:28039]	2	607.321063	0.90770719	1.51E-06	492.96	478.74	1089.15	671.49	320.22	328.5	724.71	752.79
ENSG000001	MXD4	MAX dimerization protein 4 [Source:HGNC Symbol;Acc:HGNC:13906]	4	1609.51412	0.90895796	6.03E-06	865.52	844.89	1921.73	2467.72	1306.86	1276.77	1886.45	2306.18
ENSG000001	PRRT2	proline-rich transmembrane protein 2 [Source:HGNC Symbol;Acc:HGNC:30500]	16	33.8669868	0.91056447	0.01043255	7.58	5.68	37.52	51.35	23.08	31.51	39.53	74.68
ENSG000002	PTPRVP	protein tyrosine phosphatase, receptor type, V, pseudogene [Source:HGNC Symbol;Acc:HGNC:13421]	1	405.247073	0.91063512	4.04E-08	136.51	130.57	216	284.4	401.96	402.99	830.12	839.43
ENSG000001	NFKBIZ	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta [Source:HGNC Symbol;Acc:HGNC:29805]	3	950.008095	0.91286919	4.97E-05	428.5	111.64	1022.22	378.21	1482.83	590.16	2734.14	852.37

ENSG000001	MDM2	MDM2 proto-oncogene, E3 ubiquitin protein ligase [Source:HGNC Symbol;Acc:HGNC:6973]	12	54618.1792	0.91309812	0.00014392	35026.68	32208.11	104342.15	98873.83	31987.68	36167.69	43399.27	54940.03
ENSG000001	APOBEC3H	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3H [Source:HGNC Symbol;Acc:HGNC:24100]	22	644.959092	0.91375616	2.34E-06	382.99	202.47	845.76	518.43	783.73	413.49	1115.62	897.18
ENSG000001	PARM1	prostate androgen-regulated mucin-like protein 1 [Source:HGNC Symbol;Acc:HGNC:24536]	4	1200.43675	0.91618123	0.00013814	941.36	770.15	2934.82	1996.69	571.21	604.48	1040.95	743.83
ENSG000001	ZNF701	zinc finger protein 701 [Source:HGNC Symbol;Acc:HGNC:25597]	19	24.2495222	0.91628681	0.00706569	9.48	9.46	30.42	27.65	16.35	17.19	40.63	42.82
ENSG000001	NT5E	5'-nucleotidase, ecto (CD73) [Source:HGNC Symbol;Acc:HGNC:8021]	6	283.331823	0.9179978	3.76E-05	181.07	296.14	321.47	470.04	100.01	179.53	304.16	414.24
ENSG000001	CDC42BPG	CDC42 binding protein kinase gamma (DMPK-like) [Source:HGNC Symbol;Acc:HGNC:29829]	11	75.4767528	0.91866714	0.00491299	54.04	16.08	93.3	22.71	75.97	20.05	214.12	107.54
ENSG000000	ARVCF	armadillo repeat gene deleted in velocardiofacial syndrome [Source:HGNC Symbol;Acc:HGNC:728]	22	682.253052	0.918931	4.62E-10	375.41	356.69	816.35	687.29	651.99	441.19	1402.21	726.9
ENSG000001	RELB	v-rel avian reticuloendotheliosis viral oncogene homolog B [Source:HGNC Symbol;Acc:HGNC:9956]	19	826.95767	0.91993737	8.11E-07	430.39	563.89	908.64	807.76	608.71	558.64	1563.62	1174
ENSG000001	PIP5K1L	phosphatidylinositol-4-phosphate 5-kinase-like 1 [Source:HGNC Symbol;Acc:HGNC:28711]	9	31.1540292	0.9200294	0.00852019	10.43	12.3	39.55	72.09	19.23	20.05	41.73	33.86
ENSG000001	MOV10	Mov10 RISC complex RNA helicase [Source:HGNC Symbol;Acc:HGNC:7200]	1	1422.63776	0.92089656	3.31E-06	547.94	800.42	1528.25	1945.34	1074.14	1442.93	1927.08	2114.99
ENSG000001	RNF38	ring finger protein 38 [Source:HGNC Symbol;Acc:HGNC:18052]	9	2628.86027	0.92127482	2.07E-05	2135.84	2302.88	2784.73	4441.7	1156.84	1354.12	3088.81	3765.96
ENSG000001	LPAR1	lysophosphatidic acid receptor 1 [Source:HGNC Symbol;Acc:HGNC:3166]	9	101.981855	0.92136123	0.00041499	63.52	63.39	118.65	187.62	57.7	69.71	142.75	112.52
ENSG000001	CTDSPL	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase-like [Source:HGNC Symbol;Acc:HGNC:16890]	3	232.19053	0.92178467	0.00531107	110.92	141.92	145.02	175.77	100.97	121.28	472.16	589.49
ENSG000002	DDR1	discoidin domain receptor tyrosine kinase 1 [Source:HGNC Symbol;Acc:HGNC:2730]	6	726.073478	0.92186956	2.33E-07	415.22	429.54	710.89	689.26	498.12	548.14	1219.93	1297.47
ENSG000001	TMTCT1	transmembrane and tetratricopeptide repeat containing 1 [Source:HGNC Symbol;Acc:HGNC:24099]	12	21.686248	0.92209494	0.00984751	14.22	2.84	24.34	9.87	10.58	4.77	88.94	17.92
ENSG000001	SCNN1A	sodium channel, non voltage gated 1 alpha subunit [Source:HGNC Symbol;Acc:HGNC:10599]	12	28.1761859	0.92268895	0.00621773	9.48	15.14	27.38	29.62	16.35	19.1	40.63	67.71
ENSG000001	SPPL2A	signal peptide peptidase like 2A [Source:HGNC Symbol;Acc:HGNC:30227]	15	1467.84521	0.92360447	4.49E-08	1136.65	919.64	2737.07	2190.24	973.17	819.35	1606.45	1360.21
ENSG000002	SNORD3A	small nucleolar RNA, C/D box 3A [Source:HGNC Symbol;Acc:HGNC:33189]	17	103.786523	0.92417521	0.00195089	80.58	27.44	153.13	39.5	55.77	74.49	236.08	163.3
ENSG000001	KALRN	kalirin, RhoGEF kinase [Source:HGNC Symbol;Acc:HGNC:4814]	3	144.547715	0.92515029	0.00142309	55.93	73.8	249.47	162.93	114.43	108.86	166.9	224.05
ENSG000002	COL6A4P2	collagen, type VI, alpha 4 pseudogene 2 [Source:HGNC Symbol;Acc:HGNC:38501]	3	96.9293667	0.9272675	0.00909047	27.49	20.81	265.7	158	76.93	46.79	112	67.71
ENSG000001	IP6K3	inositol hexakisphosphate kinase 3 [Source:HGNC Symbol;Acc:HGNC:17269]	6	12.5482691	0.9314441	0.00303915	0.95	0.95	0	8.89	0	0.95	10.98	77.67
ENSG000001	CA10	carbonic anhydrase X [Source:HGNC Symbol;Acc:HGNC:1369]	17	45.5598833	0.9317016	0.00425773	71.1	16.08	124.73	52.34	16.35	6.68	48.31	28.88
ENSG000001	POU2F3	POU class 2 homeobox 3 [Source:HGNC Symbol;Acc:HGNC:19864]	11	17.4132283	0.93174036	0.00887503	7.58	2.84	63.89	10.86	9.62	5.73	20.86	17.92
ENSG000001	DGKQ	diacylglycerol kinase, theta 110kDa [Source:HGNC Symbol;Acc:HGNC:2856]	4	64.5932205	0.93219819	0.00079665	26.54	36.9	56.79	84.92	31.73	64.94	94.43	120.49

ENSG000001	APC2	adenomatosis polyposis coli 2 [Source:HGNC Symbol;Acc:HGNC:24036]	19	38.6022803	0.93233259	0.00869073	4.74	24.6	66.93	88.87	12.5	28.65	30.75	51.78
ENSG000001	GAL3ST4	galactose-3-O-sulfotransferase 4 [Source:HGNC Symbol;Acc:HGNC:24145]	7	33.2470226	0.93279357	0.00457286	10.43	16.08	30.42	57.27	19.23	27.69	35.14	69.7
ENSG000001	GPR55	G protein-coupled receptor 55 [Source:HGNC Symbol;Acc:HGNC:4511]	2	1919.21322	0.93422541	0.00040728	770.72	1133.46	2832.39	3602.34	1211.65	1637.74	1626.21	2539.19
ENSG000001	CPA4	carboxypeptidase A4 [Source:HGNC Symbol;Acc:HGNC:15740]	7	23.3299368	0.93472579	0.00857519	12.32	0	25.35	2.96	20.19	6.68	92.24	26.89
ENSG000001	PRR5L	proline rich 5 like [Source:HGNC Symbol;Acc:HGNC:25878]	11	10.1628658	0.93551496	0.0075296	2.84	1.89	14.2	5.92	4.81	2.86	31.84	16.93
ENSG000001	P2RX4	purinergic receptor P2X, ligand gated ion channel, 4 [Source:HGNC Symbol;Acc:HGNC:8535]	12	803.497528	0.93662641	3.25E-07	499.6	482.53	987.74	710.99	507.74	592.07	1289.11	1358.22
ENSG000001	PLXNB1	plexin B1 [Source:HGNC Symbol;Acc:HGNC:9103]	3	894.547885	0.9378645	1.64E-05	336.54	472.12	442.15	943.05	676.99	689.47	1564.72	2031.35
ENSG000001	LINC01164	long intergenic non-protein coding RNA 1164 [Source:HGNC Symbol;Acc:HGNC:49533]	10	10.316138	0.93798275	0.00301254	0.95	0.95	58.82	9.87	0.96	0	10.98	0
ENSG000001	ARHGAP27	Rho GTPase activating protein 27 [Source:HGNC Symbol;Acc:HGNC:31813]	17	1604.81371	0.93815837	1.04E-05	930.94	856.25	1319.35	1478.26	1009.71	1200.37	2890.06	3153.57
ENSG000002	HLA-DPA1	major histocompatibility complex, class II, DP alpha 1 [Source:HGNC Symbol;Acc:HGNC:4938]	6	88.143986	0.93930134	0.00234663	32.23	48.25	96.34	60.24	56.74	59.21	220.71	131.44
ENSG000001	WNT5B	wingless-type MMTV integration site family, member 5B [Source:HGNC Symbol;Acc:HGNC:16265]	12	100.541585	0.94158045	0.00052198	24.65	80.42	95.33	173.8	60.58	86.9	105.41	177.25
ENSG000001	NBPF4	neuroblastoma breakpoint family, member 4 [Source:HGNC Symbol;Acc:HGNC:26550]	1	237.534565	0.94331008	0.00044517	134.62	140.97	212.96	206.38	128.86	157.57	415.06	503.85
ENSG000001	CYSRT1	cysteine-rich tail protein 1 [Source:HGNC Symbol;Acc:HGNC:30529]	9	69.119761	0.94331102	0.00201761	28.44	35.95	73.02	129.36	39.43	57.3	109.8	79.66
ENSG000001	ORAI3	ORAI calcium release-activated calcium modulator 3 [Source:HGNC Symbol;Acc:HGNC:28185]	16	263.480512	0.9441582	3.44E-08	123.24	162.73	274.82	330.81	145.21	272.16	312.94	485.93
ENSG000001	NEK11	NIMA-related kinase 11 [Source:HGNC Symbol;Acc:HGNC:18593]	3	95.4154901	0.94485892	0.00015567	65.41	46.36	158.2	74.06	79.82	44.88	180.08	114.51
ENSG000001	ARMC12	armadillo repeat containing 12 [Source:HGNC Symbol;Acc:HGNC:21099]	6	26.147174	0.94558162	0.00616109	10.43	9.46	36.51	18.76	22.12	10.5	51.61	49.79
ENSG000001	IL23A	interleukin 23, alpha subunit p19 [Source:HGNC Symbol;Acc:HGNC:15488]	12	54.6683272	0.94817967	0.00165918	23.7	17.03	39.55	39.5	42.31	40.11	140.55	94.6
ENSG000002	PLEKHA3P1	pleckstrin homology domain containing, family A member 3 pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:19648]	19	51.6425796	0.94940567	0.00165918	38.87	38.79	110.54	72.09	16.35	26.74	56	53.77
ENSG000001	CYP4V2	cytochrome P450, family 4, subfamily V, polypeptide 2 [Source:HGNC Symbol;Acc:HGNC:23198]	4	1275.60422	0.95066244	4.03E-09	975.49	755.01	1822.34	1216.58	953.94	666.55	2160.96	1653.96
ENSG000001	WDR5B	WD repeat domain 5B [Source:HGNC Symbol;Acc:HGNC:17826]	3	210.507394	0.95122355	0.00186927	131.77	90.83	463.45	408.82	136.55	105.04	193.26	154.34
ENSG000002	RNVU1-7	RNA, variant U1 small nuclear 7 [Source:HGNC Symbol;Acc:HGNC:37500]	1	31.9475386	0.95147159	0.00731292	31.28	5.68	63.89	8.89	12.5	4.77	86.75	41.82
ENSG000002	TRIM51BP	tripartite motif-containing 51B, pseudogene [Source:HGNC Symbol;Acc:HGNC:37145]	11	388.779197	0.95308185	0.00634616	10.43	101.24	5.07	106.65	40.39	326.59	81.26	2438.61
ENSG000001	DFNA5	deafness, autosomal dominant 5 [Source:HGNC Symbol;Acc:HGNC:2810]	7	60.9099058	0.95314579	0.00296167	25.6	25.55	75.04	86.9	61.54	26.74	82.35	103.56
ENSG000001	PAPPA2	pappalysin 2 [Source:HGNC Symbol;Acc:HGNC:14615]	1	23.0863381	0.95360254	0.00648204	4.74	3.78	65.92	46.41	13.46	6.68	30.75	12.94
ENSG000001	AKAP5	A kinase (PRKA) anchor protein 5 [Source:HGNC Symbol;Acc:HGNC:375]	14	222.653218	0.95848368	0.0023951	106.18	85.15	147.05	108.62	141.36	115.55	608.32	469

ENSG000001	MDK	midkine (neurite growth-promoting factor 2) [Source:HGNC Symbol;Acc:HGNC:6972]	11	178.067202	0.9595606	3.51E-07	111.86	97.45	228.17	207.37	101.93	152.79	237.18	287.77
ENSG000001	APOD	apolipoprotein D [Source:HGNC Symbol;Acc:HGNC:612]	3	17.5037824	0.9620429	0.00653818	2.84	9.46	20.28	44.44	8.65	8.59	20.86	24.89
ENSG000001	S100A13	S100 calcium binding protein A13 [Source:HGNC Symbol;Acc:HGNC:10490]	1	149.637353	0.96207768	4.93E-06	136.51	110.7	341.75	197.5	56.74	74.49	124.08	155.34
ENSG000001	CSDC2	cold shock domain containing C2, RNA binding [Source:HGNC Symbol;Acc:HGNC:30359]	22	19.2957601	0.96254319	0.00573629	2.84	6.62	8.11	9.87	5.77	5.73	41.73	73.69
ENSG000001	PTPRO	protein tyrosine phosphatase, receptor type, O [Source:HGNC Symbol;Acc:HGNC:9678]	12	79.1917349	0.96640265	0.00633434	28.44	12.3	228.17	164.91	57.7	22.92	81.26	37.84
ENSG000001	ALPK3	alpha-kinase 3 [Source:HGNC Symbol;Acc:HGNC:17574]	15	94.114661	0.96808478	0.00015131	71.1	52.04	127.78	100.72	53.85	53.48	162.51	131.44
ENSG000001	CASQ1	calsequestrin 1 (fast-twitch, skeletal muscle) [Source:HGNC Symbol;Acc:HGNC:1512]	1	13.1357117	0.96851918	0.0054257	1.9	0	8.11	2.96	6.73	6.68	53.8	24.89
ENSG000002	LINC01136	long intergenic non-protein coding RNA 1136 [Source:HGNC Symbol;Acc:HGNC:49452]	1	33.3752515	0.9692516	0.00274258	9.48	6.62	22.31	23.7	27.89	28.65	74.67	73.69
ENSG000001	ADPRH	ADP-ribosylarginine hydrolase [Source:HGNC Symbol;Acc:HGNC:269]	3	333.684464	0.9704549	5.29E-05	202.87	137.19	583.11	441.41	273.1	223.46	435.93	372.41
ENSG000001	WISP1	WNT1 inducible signaling pathway protein 1 [Source:HGNC Symbol;Acc:HGNC:12769]	8	259.717052	0.97204216	0.00445133	8.53	170.3	12.17	205.4	10.58	272.16	102.12	1296.48
ENSG000001	VWF	von Willebrand factor [Source:HGNC Symbol;Acc:HGNC:12726]	12	52.2157265	0.97291563	0.00231821	11.38	17.03	17.24	34.56	31.73	44.88	85.65	175.25
ENSG000002	C4A-AS1	C4A antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:39753]	6	129.976405	0.97323944	0.00128131	107.12	27.44	355.95	122.45	121.17	36.29	219.61	49.79
ENSG000001	KLF10	Kruppel-like factor 10 [Source:HGNC Symbol;Acc:HGNC:11810]	8	4339.08329	0.97351722	7.69E-16	1831.53	3310.5	4268.36	6291.26	2130.01	4418.54	4441.61	8020.84
ENSG000001	PPL	periplakin [Source:HGNC Symbol;Acc:HGNC:9273]	16	31.5535876	0.97486517	0.00503709	16.12	13.25	46.65	93.81	18.27	8.59	31.84	23.9
ENSG000002	C4B-AS1	C4B antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:39752]	6	130.61245	0.97593306	0.00121955	108.07	27.44	358.99	122.45	121.17	36.29	220.71	49.79
ENSG000001	IGIP	IgA-inducing protein [Source:HGNC Symbol;Acc:HGNC:33847]	5	213.895815	0.97719973	7.98E-07	148.84	183.55	377.25	432.52	86.55	115.55	154.82	212.1
ENSG000001	CHN2	chimerin 2 [Source:HGNC Symbol;Acc:HGNC:1944]	7	409.536758	0.97770539	0.00165134	346.97	76.64	1298.05	421.66	356.76	121.28	413.96	240.97
ENSG000002	PVRIG	poliovirus receptor related immunoglobulin domain containing [Source:HGNC Symbol;Acc:HGNC:32190]	7	75.8072406	0.97796394	0.00184791	21.8	31.22	90.26	116.52	44.24	78.31	107.61	116.5
ENSG000001	PIK3IP1	phosphoinositide-3-kinase interacting protein 1 [Source:HGNC Symbol;Acc:HGNC:24942]	22	117.941667	0.97931073	0.00042725	47.4	43.52	79.1	68.14	94.24	76.4	288.79	245.95
ENSG000002	RNU1-28P	RNA, U1 small nuclear 28, pseudogene [Source:HGNC Symbol;Acc:HGNC:37498]	14	37.6507345	0.98138158	0.00537629	36.02	6.62	80.11	8.89	13.46	4.77	106.51	44.81
ENSG000002	RNU1-27P	RNA, U1 small nuclear 27, pseudogene [Source:HGNC Symbol;Acc:HGNC:37497]	14	37.7879906	0.98265222	0.00530886	36.02	6.62	80.11	8.89	13.46	4.77	107.61	44.81
ENSG000001	CYP2C9	cytochrome P450, family 2, subfamily C, polypeptide 9 [Source:HGNC Symbol;Acc:HGNC:2623]	10	20.020796	0.98353984	0.00523665	13.27	1.89	32.45	16.79	10.58	7.64	30.75	46.8
ENSG000001	ITGAV	integrin, alpha V [Source:HGNC Symbol;Acc:HGNC:6150]	2	1437.65557	0.98588712	2.48E-09	801.06	849.62	2180.32	1899.92	1049.14	1031.34	1833.74	1856.1
ENSG000001	HIST1H2BJ	histone cluster 1, H2bj [Source:HGNC Symbol;Acc:HGNC:4761]	6	137.898729	0.98601653	4.11E-05	58.78	50.14	192.68	115.54	144.24	92.63	278.9	170.27
ENSG000002	LINC01229	long intergenic non-protein coding RNA 1229 [Source:HGNC Symbol;Acc:HGNC:49682]	16	625.242699	0.98642718	0.00346372	306.2	43.52	1682.4	374.26	689.49	213.91	1479.07	213.09

ENSG000001	KLF4	Kruppel-like factor 4 (gut) [Source:HGNC Symbol;Acc:HGNC:6348]	9	158.477894	0.98812844	0.00207691	104.28	54.88	188.62	62.21	92.32	66.85	381.02	317.65
ENSG000001	GREB1	growth regulation by estrogen in breast cancer 1 [Source:HGNC Symbol;Acc:HGNC:24885]	2	91.943407	0.98874338	0.00063714	59.72	55.82	232.23	136.27	48.08	39.15	106.51	57.75
ENSG000001	LRG1	leucine-rich alpha-2-glycoprotein 1 [Source:HGNC Symbol;Acc:HGNC:29480]	19	18.3188342	0.98986293	0.00333968	0	1.89	44.62	19.75	8.65	5.73	34.04	31.86
ENSG000001	CRIP2	cysteine-rich protein 2 [Source:HGNC Symbol;Acc:HGNC:2361]	14	16.8299073	0.99027606	0.00464411	6.64	3.78	24.34	15.8	10.58	8.59	34.04	30.87
ENSG000001	RNF19B	ring finger protein 19B [Source:HGNC Symbol;Acc:HGNC:26886]	1	1329.04061	0.99057613	9.42E-09	943.26	1048.31	1723.98	1744.88	659.68	794.52	1705.27	2012.43
ENSG000002	LINC01573	long intergenic non-protein coding RNA 1573 [Source:HGNC Symbol;Acc:HGNC:51192]	9	189.28745	0.99060012	0.00019395	82.48	94.61	129.81	154.05	108.66	142.29	372.24	430.17
ENSG000000	NUCB2	nucleobindin 2 [Source:HGNC Symbol;Acc:HGNC:8044]	11	186.464358	0.99099713	4.72E-06	158.32	127.73	459.39	258.72	65.39	102.18	142.75	177.25
ENSG000001	CXCL8	chemokine (C-X-C motif) ligand 8 [Source:HGNC Symbol;Acc:HGNC:6025]	4	22.1488247	0.99242297	0.00384293	0	0	15.21	0	23.08	0.95	133.96	3.98
ENSG000001	DPYS	dihydropyrimidinase [Source:HGNC Symbol;Acc:HGNC:3013]	8	25.8258641	0.99299099	0.00373377	18.96	3.78	43.61	10.86	19.23	7.64	63.69	38.83
ENSG000001	EBI3	Epstein-Barr virus induced 3 [Source:HGNC Symbol;Acc:HGNC:3129]	19	13.688121	0.99354837	0.00356752	1.9	1.89	6.08	2.96	5.77	1.91	68.08	20.91
ENSG000001	IL17A	interleukin 17A [Source:HGNC Symbol;Acc:HGNC:5981]	6	9.58229929	0.99408982	0.00370217	2.84	1.89	15.21	13.82	1.92	2.86	24.16	13.94
ENSG000001	IFI44	interferon-induced protein 44 [Source:HGNC Symbol;Acc:HGNC:16938]	1	52.7636608	0.9950193	0.0030368	17.06	2.84	18.25	3.95	8.65	7.64	184.47	179.24
ENSG000000	GSDMB	gasdermin B [Source:HGNC Symbol;Acc:HGNC:23690]	17	1338.25481	0.99531499	1.51E-11	842.77	714.33	1460.31	1358.78	795.27	1080.05	1897.43	2557.11
ENSG000001	DCST2	DC-STAMP domain containing 2 [Source:HGNC Symbol;Acc:HGNC:26562]	1	61.376246	0.99693552	0.00252641	18.01	31.22	46.65	37.52	28.85	41.06	127.37	160.32
ENSG000001	SPOCD1	SPOC domain containing 1 [Source:HGNC Symbol;Acc:HGNC:26338]	1	44.3924719	1.00043012	0.00260119	12.32	9.46	77.07	21.72	34.62	34.38	66.98	98.58
ENSG000001	LGALS9C	lectin, galactoside-binding, soluble, 9C [Source:HGNC Symbol;Acc:HGNC:33874]	17	121.155925	1.00045436	0.00032753	128.93	42.58	186.6	141.21	70.2	52.52	199.84	147.37
ENSG000002	LINC00484	long intergenic non-protein coding RNA 484 [Source:HGNC Symbol;Acc:HGNC:27862]	9	85.1887777	1.00100425	0.00217712	13.27	36.9	81.13	169.85	30.77	108.86	61.49	179.24
ENSG000002	MBD3L5	methyl-CpG binding domain protein 3-like 5 [Source:HGNC Symbol;Acc:HGNC:37204]	19	15.4558633	1.00246313	0.00290111	0	0.95	1.01	0.99	0.96	8.59	6.59	104.55
ENSG000001	SLC45A2	solute carrier family 45, member 2 [Source:HGNC Symbol;Acc:HGNC:16472]	5	79.5715389	1.00301089	0.00247778	61.62	24.6	338.71	63.2	37.5	16.23	43.92	50.78
ENSG000001	CEND1	cell cycle exit and neuronal differentiation 1 [Source:HGNC Symbol;Acc:HGNC:24153]	11	19.7754305	1.00399067	0.00423923	13.27	3.78	44.62	37.52	6.73	4.77	39.53	7.97
ENSG000002	BZRAP1-AS1	BZRAP1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:44148]	17	233.432725	1.00405257	1.80E-07	152.63	168.41	277.86	320.93	111.55	157.57	282.2	396.31
ENSG000001	TRIM43CP	tripartite motif containing 43C, pseudogene [Source:HGNC Symbol;Acc:HGNC:43981]	2	57.8713217	1.00472086	0.00419864	0.95	13.25	2.03	11.85	4.81	40.11	17.57	372.41
ENSG000001	AREG	amphiregulin [Source:HGNC Symbol;Acc:HGNC:651]	4	54.8752209	1.0063617	0.00247591	7.58	1.89	238.31	117.51	12.5	11.46	20.86	28.88
ENSG000001	XYLT1	xylosyltransferase I [Source:HGNC Symbol;Acc:HGNC:15516]	16	664.095182	1.00670912	1.97E-09	467.36	368.04	1271.69	814.67	471.2	373.38	844.4	702.01
ENSG000001	SAT1	spermidine/spermine N1-acetyltransferase 1 [Source:HGNC Symbol;Acc:HGNC:10540]	X	1287.952	1.00703682	0.0005644	603.88	497.66	2830.36	1954.23	842.39	928.21	1070.6	1576.29
ENSG000001	C1QTNF6	C1q and tumor necrosis factor related protein 6 [Source:HGNC Symbol;Acc:HGNC:14343]	22	971.609842	1.00869523	2.21E-17	556.48	536.45	1166.22	1195.84	615.44	834.62	1261.66	1606.16

ENSG000000	BLNK	B-cell linker [Source:HGNC Symbol;Acc:HGNC:14211]	10	142.121984	1.00882326	0.00135243	43.61	25.55	173.41	146.15	156.75	106.95	252.55	232.01
ENSG000001	NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha [Source:HGNC Symbol;Acc:HGNC:7797]	14	1025.73953	1.00953196	6.74E-17	559.32	690.67	1201.71	1352.85	788.54	622.63	1784.33	1205.86
ENSG000001	TLR1	toll-like receptor 1 [Source:HGNC Symbol;Acc:HGNC:11847]	4	46.16563	1.01004647	0.00222526	22.75	10.41	92.28	59.25	32.7	29.6	62.59	59.75
ENSG000002	LINC00475	long intergenic non-protein coding RNA 475 [Source:HGNC Symbol;Acc:HGNC:23569]	9	16.7952336	1.01104899	0.00392475	5.69	7.57	29.41	29.62	8.65	4.77	19.76	28.88
ENSG000000	YPEL3	yippee-like 3 [Source:HGNC Symbol;Acc:HGNC:18327]	16	502.327081	1.01392734	3.89E-09	247.43	171.25	539.5	466.09	478.89	409.67	823.54	882.24
ENSG000002	DFNB59	deafness, autosomal recessive 59 [Source:HGNC Symbol;Acc:HGNC:29502]	2	46.0197019	1.01573122	0.00184082	22.75	20.81	70.99	32.59	38.47	12.41	105.41	64.72
ENSG000001	ADAMTS13	ADAM metalloproteinase with thrombospondin type 1 motif, 13 [Source:HGNC Symbol;Acc:HGNC:1366]	9	240.565235	1.01615792	5.73E-08	77.74	94.61	202.82	231.07	196.17	253.06	382.12	486.93
ENSG000001	PRODH	proline dehydrogenase (oxidase) 1 [Source:HGNC Symbol;Acc:HGNC:9453]	22	62.460022	1.01641848	0.00282798	19.91	18.92	25.35	34.56	37.5	25.78	236.08	101.57
ENSG000002	NPTXR	neuronal pentraxin receptor [Source:HGNC Symbol;Acc:HGNC:7954]	22	1691.53319	1.01847682	0.00084308	338.44	1469.34	547.62	1834.75	401.96	1354.12	2280.65	5305.41
ENSG000001	CNR1	cannabinoid receptor 1 (brain) [Source:HGNC Symbol;Acc:HGNC:2159]	6	33.9713777	1.01863687	0.00267067	28.44	4.73	111.55	7.9	25	4.77	61.49	27.88
ENSG000001	TCHH	trichohyalin [Source:HGNC Symbol;Acc:HGNC:11791]	1	569.580903	1.01945129	1.57E-06	309.05	322.63	509.08	581.63	361.57	370.52	1177.11	925.06
ENSG000002	RNU1-1	RNA, U1 small nuclear 1 [Source:HGNC Symbol;Acc:HGNC:10120]	1	37.6802176	1.0198773	0.00355088	36.02	5.68	79.1	8.89	13.46	4.77	108.71	44.81
ENSG000001	GNG4	guanine nucleotide binding protein (G protein), gamma 4 [Source:HGNC Symbol;Acc:HGNC:4407]	1	302.807178	1.02017633	1.11E-06	167.8	273.43	302.2	486.83	118.28	197.67	352.47	523.77
ENSG000001	TNFAIP2	tumor necrosis factor, alpha-induced protein 2 [Source:HGNC Symbol;Acc:HGNC:11895]	14	42.1055136	1.02185612	0.00350757	11.38	10.41	27.38	11.85	18.27	10.5	204.24	42.82
ENSG000001	MFGE8	milk fat globule-EGF factor 8 protein [Source:HGNC Symbol;Acc:HGNC:7036]	15	2652.60377	1.02209515	7.61E-14	784.94	1672.76	1529.27	4258.03	1610.73	2655.71	2933.99	5775.4
ENSG000001	CACNA1E	calcium channel, voltage-dependent, R type, alpha 1E subunit [Source:HGNC Symbol;Acc:HGNC:1392]	1	85.6860928	1.02246354	0.00086382	59.72	42.58	107.49	70.11	38.47	42.02	154.82	170.27
ENSG000002	C4A	complement component 4A (Rodgers blood group) [Source:HGNC Symbol;Acc:HGNC:1323]	6	6823.82505	1.0244572	1.34E-06	6445.45	1425.82	14106.18	5446.96	8090.2	1802.94	13827.73	3445.33
ENSG000001	MR1	major histocompatibility complex, class I-related [Source:HGNC Symbol;Acc:HGNC:4975]	1	2513.044	1.0300014	5.43E-17	1353.74	1427.71	3246.15	3074.04	1820.37	1894.62	3332.58	3955.16
ENSG000001	LGALS9B	lectin, galactoside-binding, soluble, 9B [Source:HGNC Symbol;Acc:HGNC:24842]	17	38.0904486	1.03280499	0.00083971	32.23	15.14	73.02	51.35	20.19	15.28	52.71	44.81
ENSG000002	MBD3L4	methyl-CpG binding domain protein 3-like 4 [Source:HGNC Symbol;Acc:HGNC:37206]	19	17.1882394	1.03362182	0.0022836	0	0.95	1.01	0.99	0.96	10.5	6.59	116.5
ENSG000001	TRIM43B	tripartite motif containing 43B [Source:HGNC Symbol;Acc:HGNC:37146]	2	241.430456	1.0336708	0.00243071	1.9	52.98	12.17	61.22	35.58	200.54	50.51	1516.54
ENSG000001	EPS8L2	EPS8-like 2 [Source:HGNC Symbol;Acc:HGNC:21296]	11	673.262228	1.03393018	0.00011597	161.16	806.1	276.85	1260.03	146.17	502.3	684.08	1549.4
ENSG000000	IL4R	interleukin 4 receptor [Source:HGNC Symbol;Acc:HGNC:6015]	16	599.408921	1.0345097	1.86E-07	447.46	163.68	1324.42	349.57	654.87	233.01	1038.75	583.52
ENSG000001	LCN12	lipocalin 12 [Source:HGNC Symbol;Acc:HGNC:28733]	9	75.1509681	1.03482498	0.00018035	19.91	32.17	34.48	68.14	37.5	75.44	117.49	216.08
ENSG000002	RPL7P50	ribosomal protein L7 pseudogene 50 [Source:HGNC Symbol;Acc:HGNC:35816]	19	47.6485239	1.03564928	0.00031103	27.49	19.87	63.89	47.4	31.73	27.69	83.45	79.66

ENSG000002	C4B	complement component 4B (Chido blood group) [Source:HGNC Symbol;Acc:HGNC:1324]	6	6231.38499	1.03640212	8.23E-07	5864.32	1330.26	12719.9	5097.39	7330.51	1640.6	12641.83	3226.26
ENSG000000	SESN1	sestrin 1 [Source:HGNC Symbol;Acc:HGNC:21595]	6	1101.97999	1.03726091	3.26E-13	741.34	704.87	1795.98	1563.19	738.53	613.08	1284.72	1374.15
ENSG000002	RNU1-3	RNA, U1 small nuclear 3 [Source:HGNC Symbol;Acc:HGNC:10130]	1	37.6884807	1.03846924	0.00290188	35.08	5.68	80.11	8.89	13.46	4.77	108.71	44.81
ENSG000002	RNU1-4	RNA, U1 small nuclear 4 [Source:HGNC Symbol;Acc:HGNC:10128]	1	37.6884807	1.03846924	0.00290188	35.08	5.68	80.11	8.89	13.46	4.77	108.71	44.81
ENSG000001	ZSCAN18	zinc finger and SCAN domain containing 18 [Source:HGNC Symbol;Acc:HGNC:21037]	19	129.527985	1.04015787	3.99E-06	85.32	53.93	202.82	159.97	95.2	81.17	174.59	183.22
ENSG000002	PRAMEF25	PRAME family member 25 [Source:HGNC Symbol;Acc:HGNC:49179]	1	20.7315668	1.04077114	0.00268998	1.9	2.84	6.08	8.89	1.92	13.37	4.39	126.46
ENSG000001	LCE1B	late cornified envelope 1B [Source:HGNC Symbol;Acc:HGNC:16611]	1	14.8872207	1.04181641	0.00209561	0	1.89	17.24	36.54	4.81	6.68	23.06	28.88
ENSG000001	TNFSF9	tumor necrosis factor (ligand) superfamily, member 9 [Source:HGNC Symbol;Acc:HGNC:11939]	19	2008.89939	1.04201253	5.37E-07	1523.43	1045.47	2392.27	1995.71	1225.12	1052.35	4093.53	2743.32
ENSG000001	PIDD1	p53-induced death domain protein 1 [Source:HGNC Symbol;Acc:HGNC:16491]	11	4030.7069	1.04915066	6.03E-09	1968.05	2468.45	3822.16	8011.46	2605.06	2798.95	5542.95	5028.59
ENSG000002	RNU1-2	RNA, U1 small nuclear 2 [Source:HGNC Symbol;Acc:HGNC:10123]	1	37.7973561	1.05373957	0.00242232	35.08	5.68	81.13	8.89	13.46	5.73	107.61	44.81
ENSG000001	N4BP2L1	NEDD4 binding protein 2-like 1 [Source:HGNC Symbol;Acc:HGNC:25037]	13	263.534285	1.05408979	1.22E-07	145.99	119.21	396.51	280.45	167.32	216.77	420.55	361.46
ENSG000001	FLG	filaggrin [Source:HGNC Symbol;Acc:HGNC:3748]	1	73.2456101	1.05546319	9.23E-05	41.71	11.35	101.41	41.47	93.28	25.78	204.24	66.72
ENSG000001	SERPINE2	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2 [Source:HGNC Symbol;Acc:HGNC:8951]	2	956.461764	1.0594052	9.53E-14	1093.04	261.13	2781.69	486.83	774.11	194.81	1633.9	426.19
ENSG000002	MUC19	mucin 19, oligomeric [Source:HGNC Symbol;Acc:HGNC:14362]	12	13.7673477	1.06013692	0.00215689	2.84	1.89	22.31	17.77	5.77	4.77	42.82	11.95
ENSG000001	ARC	activity-regulated cytoskeleton-associated protein [Source:HGNC Symbol;Acc:HGNC:648]	8	58.6372213	1.06027896	0.00178658	33.18	8.52	176.45	72.09	37.5	23.87	74.67	42.82
ENSG000001	NREP	neuronal regeneration related protein [Source:HGNC Symbol;Acc:HGNC:16834]	5	60.2459045	1.06419198	0.00051435	61.62	27.44	212.96	96.77	12.5	16.23	28.55	25.89
ENSG000001	LINC00324	long intergenic non-protein coding RNA 324 [Source:HGNC Symbol;Acc:HGNC:26628]	17	84.1402533	1.06568991	0.0020869	29.39	20.81	34.48	40.49	14.42	21.01	242.67	269.85
ENSG000001	TRIM43	tripartite motif containing 43 [Source:HGNC Symbol;Acc:HGNC:19015]	2	261.012329	1.06652549	0.00132627	2.84	48.25	6.08	69.12	32.7	228.23	43.92	1656.94
ENSG000001	EDN2	endothelin 2 [Source:HGNC Symbol;Acc:HGNC:3177]	1	64.5520729	1.06830307	9.21E-05	27.49	42.58	86.2	99.74	35.58	39.15	69.18	116.5
ENSG000002	RNVU1-18	RNA, variant U1 small nuclear 18 [Source:HGNC Symbol;Acc:HGNC:37496]	1	38.9388645	1.0687468	0.0019901	37.92	5.68	79.1	11.85	14.42	5.73	112	44.81
ENSG000001	ZNF710	zinc finger protein 710 [Source:HGNC Symbol;Acc:HGNC:25352]	15	313.242053	1.0697827	1.98E-06	179.17	200.58	450.26	300.2	158.67	198.63	510.59	507.84
ENSG000001	DDIT3	DNA-damage-inducible transcript 3 [Source:HGNC Symbol;Acc:HGNC:2726]	12	424.91831	1.07721069	6.14E-05	289.14	257.35	416.8	518.43	194.25	200.54	858.67	664.17
ENSG000001	MAP3K12	mitogen-activated protein kinase kinase kinase 12 [Source:HGNC Symbol;Acc:HGNC:6851]	12	1155.7271	1.07814879	1.08E-11	458.83	562	794.04	1200.78	849.12	904.34	2285.04	2191.67
ENSG000002	GVINP1	GTPase, very large interferon inducible pseudogene 1 [Source:HGNC Symbol;Acc:HGNC:25813]	11	577.654577	1.07951322	4.15E-06	318.53	140.03	1222	414.74	623.14	296.03	1054.13	552.65
ENSG000001	KCP	kielin/chordin-like protein [Source:HGNC Symbol;Acc:HGNC:17585]	7	231.102243	1.08135515	2.50E-05	36.02	165.57	46.65	515.47	38.47	271.21	136.16	639.28

ENSG000001: STOM	stomatin [Source:HGNC Symbol;Acc:HGNC:3383]	9	59.8755271	1.08401574	0.00151937	13.27	12.3	85.18	126.4	34.62	42.97	63.69	100.57
ENSG000001: CARD6	caspase recruitment domain family, member 6 [Source:HGNC Symbol;Acc:HGNC:16394]	5	87.8945911	1.0853176	2.07E-05	52.14	25.55	118.65	80.97	63.47	60.16	122.98	179.24
ENSG000001: APOBR	apolipoprotein B receptor [Source:HGNC Symbol;Acc:HGNC:24087]	16	68.0340748	1.08574009	0.00165188	31.28	26.49	63.89	38.51	19.23	21.96	185.57	157.33
ENSG000001: SMPD3	sphingomyelin phosphodiesterase 3, neutral membrane (neutral sphingomyelinase II) [Source:HGNC Symbol;Acc:HGNC:14240]	16	401.989528	1.08623998	3.54E-09	195.29	282.89	352.91	669.51	185.59	287.44	390.91	851.37
ENSG000001: SHOX2	short stature homeobox 2 [Source:HGNC Symbol;Acc:HGNC:10854]	3	188.305771	1.08826826	4.01E-08	62.57	128.67	156.17	360.43	84.62	177.62	177.88	358.47
ENSG000002: DUX4L4	double homeobox 4 like 4 [Source:HGNC Symbol;Acc:HGNC:38686]	4	89.1299284	1.09470352	0.00142667	7.58	15.14	3.04	40.49	18.27	28.65	90.04	509.83
ENSG000001: VWCE	von Willebrand factor C and EGF domains [Source:HGNC Symbol;Acc:HGNC:26487]	11	234.705028	1.09656405	7.58E-06	116.6	121.1	198.76	227.12	150.01	128.92	482.04	453.07
ENSG000001: C1orf228	chromosome 1 open reading frame 228 [Source:HGNC Symbol;Acc:HGNC:34345]	1	18.6132941	1.10074817	0.0014226	3.79	1.89	18.25	13.82	11.54	11.46	48.31	39.83
ENSG000001: CD3E	CD3e molecule, epsilon (CD3-TCR complex) [Source:HGNC Symbol;Acc:HGNC:1674]	11	62.6536489	1.10798676	0.00115683	29.39	22.71	60.85	34.56	22.12	21.01	170.2	140.4
ENSG000001: ASB2	ankyrin repeat and SOCS box containing 2 [Source:HGNC Symbol;Acc:HGNC:16012]	14	8809.53332	1.11101585	1.69E-08	2911.31	3630.3	10561.89	9446.27	5841.91	9506.51	11039.78	17538.31
ENSG000001: CD109	CD109 molecule [Source:HGNC Symbol;Acc:HGNC:21685]	6	70.2532609	1.11197503	0.00099915	17.06	23.65	203.83	80.97	45.2	28.65	99.92	62.73
ENSG000002: VWA7	von Willebrand factor A domain containing 7 [Source:HGNC Symbol;Acc:HGNC:13939]	6	230.107901	1.11341245	5.93E-08	125.14	92.72	240.34	183.67	146.17	163.3	409.57	479.96
ENSG000002: MIAT	myocardial infarction associated transcript (non-protein coding) [Source:HGNC Symbol;Acc:HGNC:33425]	22	77.247805	1.11568346	7.79E-05	41.71	19.87	106.48	37.52	45.2	51.57	192.16	123.47
ENSG000001: BBC3	BCL2 binding component 3 [Source:HGNC Symbol;Acc:HGNC:17868]	19	767.606593	1.12065407	1.04E-10	522.35	514.69	970.5	1266.94	372.15	433.55	1148.56	912.12
ENSG000000: TG	thyroglobulin [Source:HGNC Symbol;Acc:HGNC:11764]	8	175.105885	1.12089276	1.57E-09	84.37	77.58	187.61	206.38	144.24	111.73	336	252.92
ENSG000002: MGAM2	maltase-glucoamylase 2 (putative) [Source:HGNC Symbol;Acc:HGNC:28101]	7	22.0201675	1.12256273	0.00116145	10.43	2.84	72	32.59	6.73	6.68	32.94	11.95
ENSG000000: CHI3L2	chitinase 3-like 2 [Source:HGNC Symbol;Acc:HGNC:1933]	1	96.7276296	1.12858267	0.00074165	28.44	15.14	233.24	117.51	76.93	50.61	128.47	123.47
ENSG000001: IL21R	interleukin 21 receptor [Source:HGNC Symbol;Acc:HGNC:6006]	16	133.136371	1.12874214	0.00011792	36.97	106.91	75.04	179.72	46.16	80.22	228.39	311.67
ENSG000001: TMEM229B	transmembrane protein 229B [Source:HGNC Symbol;Acc:HGNC:20130]	14	340.022009	1.12900866	6.70E-08	145.04	236.53	533.42	472.02	162.52	249.24	334.9	586.5
ENSG000001: ISG15	ISG15 ubiquitin-like modifier [Source:HGNC Symbol;Acc:HGNC:4053]	1	80.8642321	1.13366568	0.00062963	22.75	16.08	38.54	22.71	40.39	42.97	218.51	244.96
ENSG000001: DDIT4	DNA-damage-inducible transcript 4 [Source:HGNC Symbol;Acc:HGNC:24944]	10	518.528009	1.13418995	1.09E-07	121.34	505.23	472.57	1125.73	113.47	534.77	294.28	980.82
ENSG000001: ACTA2	actin, alpha 2, smooth muscle, aorta [Source:HGNC Symbol;Acc:HGNC:130]	10	270.751896	1.13826767	1.50E-05	174.43	119.21	637.87	491.77	111.55	156.61	198.75	275.83
ENSG000001: OASL	2'-5'-oligoadenylate synthetase-like [Source:HGNC Symbol;Acc:HGNC:8090]	12	973.10067	1.13963622	0.00082236	171.59	178.82	519.22	346.61	183.67	295.08	2883.48	3206.35
ENSG000001: SSPN	sarcospan [Source:HGNC Symbol;Acc:HGNC:11322]	12	94.9276529	1.14062578	0.00012645	86.27	26.49	335.67	123.44	43.27	22.92	73.57	47.8
ENSG000001: ANKRD20A5F	ankyrin repeat domain 20 family, member A5, pseudogene [Source:HGNC Symbol;Acc:HGNC:33833]	18	196.177409	1.14085241	6.10E-08	81.53	61.5	189.64	206.38	181.75	138.47	354.67	355.49
ENSG000001: RHBDL3	rhomboid, veinlet-like 3 (Drosophila) [Source:HGNC Symbol;Acc:HGNC:16502]	17	38.3205423	1.14133299	0.00089548	7.58	13.25	14.2	30.61	7.69	9.55	135.06	88.62

ENSG000001	PARVG	parvin, gamma [Source:HGNC Symbol;Acc:HGNC:14654]	22	18.2915482	1.14295597	0.00090606	1.9	5.68	24.34	34.56	6.73	9.55	19.76	43.81
ENSG000001	PGF	placental growth factor [Source:HGNC Symbol;Acc:HGNC:8893]	14	67.675868	1.14506272	0.00035107	15.17	25.55	75.04	150.1	21.16	69.71	69.18	115.51
ENSG000001	CDCP1	CUB domain containing protein 1 [Source:HGNC Symbol;Acc:HGNC:24357]	3	19.1913396	1.14618148	0.00081265	8.53	5.68	36.51	14.81	6.73	6.68	41.73	32.86
ENSG000001	AXL	AXL receptor tyrosine kinase [Source:HGNC Symbol;Acc:HGNC:905]	19	22.3965168	1.14959821	0.00070837	16.12	7.57	47.66	49.37	4.81	6.68	23.06	23.9
ENSG000001	HTRA3	HtrA serine peptidase 3 [Source:HGNC Symbol;Acc:HGNC:30406]	4	65.5643161	1.14990386	0.00074165	12.32	47.31	55.78	64.19	14.42	24.83	149.33	156.33
ENSG000001	BMF	Bcl2 modifying factor [Source:HGNC Symbol;Acc:HGNC:24132]	15	4839.86478	1.1503161	1.74E-05	1015.31	1465.55	4366.73	7452.54	3032.98	5673.34	4985.14	10727.32
ENSG000001	HTR7	5-hydroxytryptamine (serotonin) receptor 7, adenylate cyclase-coupled [Source:HGNC Symbol;Acc:HGNC:5302]	10	19.929163	1.15111461	0.00075675	4.74	1.89	39.55	46.41	3.85	9.55	28.55	24.89
ENSG000000	AHRR	aryl-hydrocarbon receptor repressor [Source:HGNC Symbol;Acc:HGNC:346]	5	25.9383068	1.15533839	0.00077978	4.74	12.3	43.61	23.7	5.77	10.5	57.1	49.79
ENSG000001	FAM46A	family with sequence similarity 46, member A [Source:HGNC Symbol;Acc:HGNC:18345]	6	361.043284	1.15918584	2.14E-06	148.84	172.2	616.58	584.59	235.6	239.69	423.85	467.01
ENSG000001	PLEKHG3	pleckstrin homology domain containing, family G (with RhoGef domain) member 3 [Source:HGNC Symbol;Acc:HGNC:20364]	14	15.6849707	1.16038815	0.00036068	2.84	0.95	19.27	2.96	0.96	0.95	63.69	33.86
ENSG000001	JSRP1	junctional sarcoplasmic reticulum protein 1 [Source:HGNC Symbol;Acc:HGNC:24963]	19	22.4251755	1.16468636	0.00061087	6.64	7.57	16.23	45.42	4.81	14.32	29.65	54.77
ENSG000002	PRAMEF6	PRAME family member 6 [Source:HGNC Symbol;Acc:HGNC:30583]	1	52.7727619	1.16946048	0.00065237	4.74	8.52	5.07	24.69	3.85	30.56	13.18	331.59
ENSG000001	SERPINA1	serpin peptidase inhibitor, clade A (alpha-1 antitrypsin, antitrypsin), member 1 [Source:HGNC Symbol;Acc:HGNC:8941]	14	30.7411823	1.17122602	0.00031547	2.84	0.95	8.11	0.99	3.85	0.95	205.34	22.9
ENSG000001	IL2RG	interleukin 2 receptor, gamma [Source:HGNC Symbol;Acc:HGNC:6010]	X	31.1269382	1.17463541	0.00059675	14.22	1.89	36.51	3.95	10.58	2.86	147.14	31.86
ENSG000001	NCF2	neutrophil cytosolic factor 2 [Source:HGNC Symbol;Acc:HGNC:7661]	1	49.0273406	1.1846167	0.00047861	18.01	17.03	44.62	29.62	17.31	13.37	131.77	120.49
ENSG000001	CYP19A1	cytochrome P450, family 19, subfamily A, polypeptide 1 [Source:HGNC Symbol;Acc:HGNC:2594]	15	122.685997	1.18668121	0.00043172	57.83	17.03	506.04	154.05	70.2	19.1	127.37	29.87
ENSG000002	FLG-AS1	FLG antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:27913]	1	26.2456947	1.18742238	0.0005178	7.58	0.95	55.78	18.76	15.39	9.55	79.06	22.9
ENSG000001	MUC4	mucin 4, cell surface associated [Source:HGNC Symbol;Acc:HGNC:7514]	3	48.5317442	1.18830275	0.0004727	4.74	9.46	18.25	8.89	13.46	11.46	185.57	136.42
ENSG000001	CEL	carboxyl ester lipase [Source:HGNC Symbol;Acc:HGNC:1848]	9	1636.69119	1.18971521	2.23E-11	700.57	948.02	1334.56	2056.93	791.42	1183.18	2028.1	4050.75
ENSG000002	LINC01125	long intergenic non-protein coding RNA 1125 [Source:HGNC Symbol;Acc:HGNC:49272]	2	121.335754	1.19116711	5.31E-07	64.46	55.82	138.93	145.16	90.39	53.48	216.32	206.12
ENSG000001	CD80	CD80 molecule [Source:HGNC Symbol;Acc:HGNC:1700]	3	16.8241655	1.20004324	0.00041175	1.9	0.95	28.39	16.79	9.62	3.82	58.2	14.94
ENSG000001	IL22RA1	interleukin 22 receptor, alpha 1 [Source:HGNC Symbol;Acc:HGNC:13700]	1	61.2977255	1.20014502	0.00023338	2.84	35.95	37.52	107.64	10.58	63.98	62.59	169.28
ENSG000001	COL5A1	collagen, type V, alpha 1 [Source:HGNC Symbol;Acc:HGNC:2209]	9	465.917882	1.20416578	6.61E-05	19.91	400.21	29.41	712.96	26.93	372.43	168	1997.49
ENSG000001	CELP	carboxyl ester lipase pseudogene [Source:HGNC Symbol;Acc:HGNC:1849]	9	264.122435	1.20464189	6.15E-09	121.34	141.92	244.4	344.63	125.97	179.53	301.96	653.22
ENSG000001	PLEK	pleckstrin [Source:HGNC Symbol;Acc:HGNC:9070]	2	67.3212337	1.20806428	0.00018906	30.34	21.76	261.64	48.39	27.89	19.1	85.65	43.81
ENSG000000	EBF4	early B-cell factor 4 [Source:HGNC Symbol;Acc:HGNC:29278]	20	105.518758	1.20878173	1.68E-05	15.17	42.58	37.52	79.99	44.24	98.36	219.61	306.69
ENSG000002	C2orf72	chromosome 2 open reading frame 72 [Source:HGNC Symbol;Acc:HGNC:27418]	2	198.756371	1.20887293	1.01E-09	84.37	138.13	210.93	289.33	107.7	115.55	350.28	293.75

ENSG000002	TMEM179	transmembrane protein 179 [Source:HGNC Symbol;Acc:HGNC:20137]	14	82.9255204	1.20943484	0.00012157	2.84	67.18	21.3	201.45	9.62	82.13	75.77	203.13
ENSG000001	RGL1	ral guanine nucleotide dissociation stimulator-like 1 [Source:HGNC Symbol;Acc:HGNC:30281]	1	503.263787	1.21207537	7.90E-07	215.2	304.65	915.74	1128.69	215.41	293.17	409.57	543.68
ENSG000002	SPRR2A	small proline-rich protein 2A [Source:HGNC Symbol;Acc:HGNC:11261]	1	19.5140289	1.21322393	0.00034573	13.27	0	97.35	2.96	4.81	0	30.75	6.97
ENSG000001	PLEKHG1	pleckstrin homology domain containing, family G (with RhoGef domain) member 1 [Source:HGNC Symbol;Acc:HGNC:20884]	6	113.681324	1.21725355	0.0003352	18.96	16.08	444.18	80.97	50	49.66	103.22	146.38
ENSG000001	FUCA1	fucosidase, alpha-L-1, tissue [Source:HGNC Symbol;Acc:HGNC:4006]	1	6675.92787	1.21749165	1.22E-18	1191.64	5450.65	3549.36	11361.99	1815.56	7836.3	4825.92	17376
ENSG000001	SLFN5	schlafen family member 5 [Source:HGNC Symbol;Acc:HGNC:28286]	17	882.592082	1.21844524	2.13E-07	363.08	310.33	1672.26	995.38	641.41	607.35	1148.56	1322.37
ENSG000001	FBXO32	F-box protein 32 [Source:HGNC Symbol;Acc:HGNC:16731]	8	388.400244	1.22119384	1.20E-08	286.3	145.7	713.93	369.32	223.1	168.07	886.13	314.66
ENSG000001	TRANK1	tetratricopeptide repeat and ankyrin repeat containing 1 [Source:HGNC Symbol;Acc:HGNC:29011]	3	98.0634773	1.22311731	0.00032587	21.8	9.46	504.01	54.31	56.74	8.59	97.73	31.86
ENSG000001	PLXNB3	plexin B3 [Source:HGNC Symbol;Acc:HGNC:9105]	X	262.1756	1.22677487	2.41E-12	89.11	91.77	191.67	277.48	229.83	180.49	592.95	444.11
ENSG000001	FN1	fibronectin 1 [Source:HGNC Symbol;Acc:HGNC:3778]	2	853.534939	1.22712419	8.70E-07	282.5	237.48	1559.69	657.66	692.37	614.99	1223.23	1560.35
ENSG000001	HRNR	hornerin [Source:HGNC Symbol;Acc:HGNC:20846]	1	43.4570409	1.22808673	8.19E-05	6.64	8.52	32.45	49.37	37.5	27.69	109.8	75.68
ENSG000002	TTL3	tubulin tyrosine ligase-like family member 3 [Source:HGNC Symbol;Acc:HGNC:24483]	3	1010.75496	1.23146472	5.86E-26	521.4	480.63	1368.03	1087.22	650.06	699.98	1525.19	1753.53
ENSG000000	ALOX5	arachidonate 5-lipoxygenase [Source:HGNC Symbol;Acc:HGNC:435]	10	472.692845	1.23220423	8.81E-08	230.36	167.46	803.17	692.23	328.88	298.9	608.32	652.22
ENSG000001	TBC1D10C	TBC1 domain family, member 10C [Source:HGNC Symbol;Acc:HGNC:24702]	11	58.9693762	1.23921559	2.06E-05	34.13	29.33	80.11	71.1	23.08	24.83	107.61	101.57
ENSG000001	FAM212B	family with sequence similarity 212, member B [Source:HGNC Symbol;Acc:HGNC:28045]	1	969.96482	1.24047169	7.02E-24	476.84	632.96	1184.47	1743.9	565.44	560.55	1331.93	1263.62
ENSG000001	DMBT1	deleted in malignant brain tumors 1 [Source:HGNC Symbol;Acc:HGNC:2926]	10	166.024659	1.24106212	1.10E-05	70.15	33.11	150.09	53.32	108.66	79.26	461.18	372.41
ENSG000001	GIMAP8	GTPase, IMAP family member 8 [Source:HGNC Symbol;Acc:HGNC:21792]	7	76.5741328	1.24323952	1.61E-05	12.32	33.11	75.04	115.54	26.93	83.08	82.35	184.22
ENSG000001	MACC1	metastasis associated in colon cancer 1 [Source:HGNC Symbol;Acc:HGNC:30215]	7	91.0849673	1.25080242	1.09E-05	75.84	1.89	258.6	13.82	81.74	5.73	281.1	9.96
ENSG000001	MUC2	mucin 2, oligomeric mucus/gel-forming [Source:HGNC Symbol;Acc:HGNC:7512]	11	16.9992615	1.25097538	0.00010843	0.95	0	1.01	3.95	2.88	0.95	72.47	53.77
ENSG000001	RARRES3	retinoic acid receptor responder (tazarotene induced) 3 [Source:HGNC Symbol;Acc:HGNC:9869]	11	1894.57098	1.25201702	1.20E-07	856.04	516.59	3310.03	2317.63	1574.19	1184.14	2757.2	2640.75
ENSG000002	IGHE	immunoglobulin heavy constant epsilon [Source:HGNC Symbol;Acc:HGNC:5522]	14	51.5256864	1.2538107	0.00017168	11.38	26.49	42.59	46.41	9.62	21.96	94.43	159.32
ENSG000000	KITLG	KIT ligand [Source:HGNC Symbol;Acc:HGNC:6343]	12	32.3827254	1.26568176	0.00018162	18.01	0	148.06	10.86	16.35	0	64.78	1
ENSG000001	MICALL2	MICAL-like 2 [Source:HGNC Symbol;Acc:HGNC:29672]	7	262.953284	1.26578834	1.13E-13	111.86	124.89	293.08	282.42	176.94	164.25	536.95	413.24
ENSG000002	PRAMEF15	PRAME family member 15 [Source:HGNC Symbol;Acc:HGNC:26764]	1	62.7675202	1.2675494	0.00016881	0.95	12.3	9.13	20.74	5.77	36.29	18.67	398.3
ENSG000001	WNT9A	wingless-type MMTV integration site family, member 9A [Source:HGNC Symbol;Acc:HGNC:12778]	1	137.887718	1.26890751	2.20E-08	54.98	45.41	124.73	101.71	97.12	81.17	326.12	271.84
ENSG000001	PKD1L1	polycystic kidney disease 1 like 1 [Source:HGNC Symbol;Acc:HGNC:18053]	7	207.308382	1.27298338	1.11E-06	65.41	72.85	307.27	315.99	140.4	144.2	341.49	270.85

ENSG000002	HMGB3P32	high mobility group box 3 pseudogene 32 [Source:HGNC Symbol;Acc:HGNC:39335]	16	20.9719304	1.27596597	0.00015647	1.9	5.68	31.44	28.64	9.62	6.68	34.04	49.79
ENSG000001	HSPB7	heat shock 27kDa protein family, member 7 (cardiovascular) [Source:HGNC Symbol;Acc:HGNC:5249]	1	166.959447	1.27807155	2.36E-10	57.83	58.66	163.27	201.45	126.94	121.28	297.57	308.69
ENSG000001	SUSD1	sushi domain containing 1 [Source:HGNC Symbol;Acc:HGNC:25413]	9	48.6960256	1.2818652	2.72E-05	31.28	10.41	168.34	37.52	27.89	10.5	64.78	38.83
ENSG000001	PLAC8	placenta-specific 8 [Source:HGNC Symbol;Acc:HGNC:19254]	4	36.0965502	1.28209962	0.0001392	18.96	2.84	75.04	73.07	15.39	7.64	56	39.83
ENSG000001	IL18R1	interleukin 18 receptor 1 [Source:HGNC Symbol;Acc:HGNC:5988]	2	60.4874131	1.2864824	8.29E-05	35.08	11.35	314.37	37.52	19.23	4.77	51.61	9.96
ENSG000001	DDX60L	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60-like [Source:HGNC Symbol;Acc:HGNC:26429]	4	19.1451168	1.29424575	0.00012128	4.74	4.73	36.51	16.79	8.65	2.86	45.02	33.86
ENSG000002	CYP4F35P	cytochrome P450, family 4, subfamily F, polypeptide 35, pseudogene [Source:HGNC Symbol;Acc:HGNC:39954]	18	47.5003875	1.29772048	6.03E-06	18.96	10.41	68.96	42.46	30.77	26.74	112	69.7
ENSG000001	MBD3L3	methyl-CpG binding domain protein 3-like 3 [Source:HGNC Symbol;Acc:HGNC:37205]	19	23.297758	1.3006147	0.00010273	0	0.95	2.03	2.96	0.96	13.37	8.78	157.33
ENSG000000	ABCC6	ATP-binding cassette, sub-family C (CFTR/MRP), member 6 [Source:HGNC Symbol;Acc:HGNC:57]	16	109.928593	1.30734931	5.30E-05	27.49	60.55	65.92	149.11	13.46	60.16	191.06	311.67
ENSG000001	KIR2DL4	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 4 [Source:HGNC Symbol;Acc:HGNC:6332]	19	32.4596327	1.3079528	9.84E-05	10.43	0	88.23	16.79	16.35	10.5	73.57	43.81
ENSG000001	HIST1H2BK	histone cluster 1, H2bk [Source:HGNC Symbol;Acc:HGNC:13954]	6	1124.90559	1.30882174	3.15E-15	563.11	341.55	1695.58	1158.32	992.4	583.47	2462.92	1201.88
ENSG000001	PXT1	peroxisomal, testis specific 1 [Source:HGNC Symbol;Acc:HGNC:18312]	6	256.922794	1.3088408	1.21E-06	164.95	83.26	601.36	509.54	165.4	62.07	318.43	150.36
ENSG000002	CYP4F29P	cytochrome P450, family 4, subfamily F, polypeptide 29, pseudogene [Source:HGNC Symbol;Acc:HGNC:2647]	21	108.151457	1.30904205	1.66E-08	51.19	25.55	161.24	86.9	114.43	36.29	270.12	119.49
ENSG000001	ITGAX	integrin, alpha X (complement component 3 receptor 4 subunit) [Source:HGNC Symbol;Acc:HGNC:6152]	16	25.7220418	1.31029641	9.10E-05	17.06	0	97.35	7.9	11.54	0.95	66.98	3.98
ENSG000001	CD300C	CD300c molecule [Source:HGNC Symbol;Acc:HGNC:19320]	17	45.3521655	1.31783383	8.30E-05	18.96	9.46	55.78	23.7	7.69	12.41	126.28	108.54
ENSG000001	CSPG4	chondroitin sulfate proteoglycan 4 [Source:HGNC Symbol;Acc:HGNC:2466]	15	28.6509629	1.31985093	4.56E-05	0.95	3.78	2.03	24.69	1.92	1.91	61.49	132.44
ENSG000001	NID1	nidogen 1 [Source:HGNC Symbol;Acc:HGNC:7821]	1	24.2990275	1.32383108	7.97E-05	0	15.14	8.11	65.17	0.96	8.59	8.78	87.63
ENSG000001	DRAXIN	dorsal inhibitory axon guidance protein [Source:HGNC Symbol;Acc:HGNC:25054]	1	103.174885	1.3249455	7.58E-05	17.06	9.46	21.3	27.65	14.42	30.56	341.49	363.45
ENSG000002	IGHA2	immunoglobulin heavy constant alpha 2 (A2m marker) [Source:HGNC Symbol;Acc:HGNC:5479]	14	39.292397	1.33248788	1.89E-05	8.53	19.87	31.44	49.37	14.42	18.14	77.96	94.6
ENSG000001	MATN1-AS1	MATN1 antisense RNA 1 [Source:HGNC Symbol;Acc:HGNC:40364]	1	443.371346	1.35717241	4.55E-17	154.52	211.93	391.44	726.79	203.87	377.2	572.08	909.13
ENSG000001	CALML6	calmodulin-like 6 [Source:HGNC Symbol;Acc:HGNC:24193]	1	148.150682	1.36389876	2.33E-11	61.62	80.42	152.12	216.26	63.47	92.63	202.04	316.65
ENSG000001	TNFAIP3	tumor necrosis factor, alpha-induced protein 3 [Source:HGNC Symbol;Acc:HGNC:11896]	6	619.372945	1.36595437	1.59E-15	220.88	210.04	642.94	592.49	460.62	381.98	1629.5	816.52
ENSG000001	EHF	ets homologous factor [Source:HGNC Symbol;Acc:HGNC:3246]	11	170.260497	1.37044445	6.60E-08	69.2	49.2	294.09	240.95	100.97	106	286.59	215.08
ENSG000001	NCALD	neurocalcin delta [Source:HGNC Symbol;Acc:HGNC:7655]	8	230.493932	1.37225158	2.30E-14	133.67	96.51	381.3	314.02	99.05	152.79	304.16	362.46
ENSG000001	CTLA4	cytotoxic T-lymphocyte-associated protein 4 [Source:HGNC Symbol;Acc:HGNC:2505]	2	209.873059	1.37573848	2.33E-05	35.08	62.44	474.6	552.99	70.2	90.72	252.55	140.4

ENSG000001	UNC13A	unc-13 homolog A (C, elegans) [Source:HGNC Symbol;Acc:HGNC:23150]	19	60.1807516	1.38043747	2.42E-06	26.54	21.76	61.86	135.29	27.89	21.96	95.53	90.61
ENSG000001	OLFML2B	olfactomedin-like 2B [Source:HGNC Symbol;Acc:HGNC:24558]	1	62.5306866	1.38220581	3.25E-05	21.8	0.95	370.15	5.92	23.08	0	71.37	6.97
ENSG000001	ARMCX3	armadillo repeat containing, X-linked 3 [Source:HGNC Symbol;Acc:HGNC:24065]	X	367.036017	1.38276893	2.10E-07	352.66	4.73	1532.31	25.67	296.18	7.64	664.32	52.78
ENSG000001	CYP4F2	cytochrome P450, family 4, subfamily F, polypeptide 2 [Source:HGNC Symbol;Acc:HGNC:2645]	19	13.4283978	1.38416037	1.41E-05	0	0.95	37.52	32.59	0	0.95	27.45	7.97
ENSG000002	PRAMEF26	PRAME family member 26 [Source:HGNC Symbol;Acc:HGNC:49178]	1	52.2769636	1.39150583	2.21E-05	2.84	6.62	9.13	19.75	2.88	33.42	10.98	332.58
ENSG000001	SESN2	sestrin 2 [Source:HGNC Symbol;Acc:HGNC:20746]	1	3550.37357	1.39563582	5.54E-38	1986.06	1766.42	4887.98	5167.5	2195.4	1657.79	6398.33	4343.5
ENSG000001	FILIP1	filamin A interacting protein 1 [Source:HGNC Symbol;Acc:HGNC:21015]	6	52.5302425	1.4081529	3.52E-07	30.34	16.08	101.41	73.07	18.27	26.74	74.67	79.66
ENSG000001	AP3B2	adaptor-related protein complex 3, beta 2 subunit [Source:HGNC Symbol;Acc:HGNC:567]	15	97.3053667	1.4096451	2.15E-07	59.72	48.25	216	119.49	44.24	20.05	137.26	133.43
ENSG000001	PVRL4	poliovirus receptor-related 4 [Source:HGNC Symbol;Acc:HGNC:19688]	1	311.56991	1.4169356	4.27E-08	191.5	87.04	457.36	623.1	179.82	106.95	517.18	329.6
ENSG000001	SEPT5	septin 5 [Source:HGNC Symbol;Acc:HGNC:9164]	22	219.007554	1.41764413	7.74E-07	16.12	133.4	90.26	266.62	38.47	193.85	306.36	706.99
ENSG000001	C3	complement component 3 [Source:HGNC Symbol;Acc:HGNC:1318]	19	25.1100411	1.42135206	1.71E-05	3.79	1.89	24.34	5.92	9.62	0.95	128.47	25.89
ENSG000002	PRAMEF4	PRAME family member 4 [Source:HGNC Symbol;Acc:HGNC:31971]	1	36.2821628	1.42934085	1.55E-05	0.95	2.84	4.06	9.87	2.88	17.19	16.47	235.99
ENSG000001	GPR132	G protein-coupled receptor 132 [Source:HGNC Symbol;Acc:HGNC:17482]	14	30.5633265	1.4322068	1.50E-05	9.48	1.89	26.37	19.75	5.77	7.64	99.92	73.69
ENSG000001	MMP13	matrix metalloproteinase 13 [Source:HGNC Symbol;Acc:HGNC:7159]	11	185.835224	1.44571533	8.88E-06	60.67	8.52	1141.88	39.5	67.31	5.73	147.14	15.93
ENSG000001	PLP1	proteolipid protein 1 [Source:HGNC Symbol;Acc:HGNC:9086]	X	17.1209813	1.45025343	1.12E-05	4.74	0.95	30.42	17.77	5.77	1.91	50.51	24.89
ENSG000001	CLCNKA	chloride channel, voltage-sensitive Ka [Source:HGNC Symbol;Acc:HGNC:2026]	1	262.073316	1.45433933	5.46E-19	91.96	91.77	292.06	299.21	168.29	179.53	490.83	482.94
ENSG000001	TGM5	transglutaminase 5 [Source:HGNC Symbol;Acc:HGNC:11781]	15	79.164169	1.45556311	1.07E-06	33.18	16.08	162.26	149.11	36.54	33.42	113.1	89.62
ENSG000000	GRAMD1B	GRAM domain containing 1B [Source:HGNC Symbol;Acc:HGNC:29214]	11	398.904155	1.50406312	1.27E-06	84.37	77.58	1008.02	814.67	200.02	146.11	493.02	367.44
ENSG000001	RSAD2	radical S-adenosyl methionine domain containing 2 [Source:HGNC Symbol;Acc:HGNC:30908]	2	127.385868	1.50555554	3.59E-06	55.93	2.84	268.74	21.72	3.85	3.82	406.28	255.91
ENSG000001	PTPN14	protein tyrosine phosphatase, non-receptor type 14 [Source:HGNC Symbol;Acc:HGNC:9647]	1	43.8141198	1.51320248	1.21E-07	28.44	13.25	116.62	67.15	15.39	9.55	59.29	40.83
ENSG000001	F2RL3	coagulation factor II (thrombin) receptor- like 3 [Source:HGNC Symbol;Acc:HGNC:3540]	19	38.8038271	1.51511108	3.54E-06	11.38	2.84	35.49	14.81	7.69	7.64	144.94	85.64
ENSG000001	ATF3	activating transcription factor 3 [Source:HGNC Symbol;Acc:HGNC:785]	1	1192.56032	1.52125666	4.98E-15	541.31	297.08	1553.61	678.4	750.07	480.34	3580.74	1658.94
ENSG000001	PRF1	perforin 1 (pore forming protein) [Source:HGNC Symbol;Acc:HGNC:9360]	10	267.933463	1.52675771	9.00E-09	28.44	184.5	133.86	1214.61	18.27	157.57	63.69	342.54
ENSG000001	PLIN4	perilipin 4 [Source:HGNC Symbol;Acc:HGNC:29393]	19	38.8912154	1.53619703	1.32E-06	6.64	9.46	52.73	105.66	11.54	15.28	35.14	74.68
ENSG000001	CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1) [Source:HGNC Symbol;Acc:HGNC:1784]	6	22569.2327	1.53708148	2.75E-12	11682.19	8588.96	24724.86	24186.45	10676.02	8194.41	51702.71	40798.25
ENSG000001	NCF4	neutrophil cytosolic factor 4, 40kDa [Source:HGNC Symbol;Acc:HGNC:7662]	22	102.092013	1.54009317	4.19E-11	20.86	37.85	83.16	171.82	38.47	82.13	118.59	263.88
ENSG000001	LGMN	legumain [Source:HGNC Symbol;Acc:HGNC:9472]	14	857.828933	1.5407914	8.95E-13	45.5	275.32	186.6	678.4	303.88	953.99	1675.62	2743.32

ENSG000001	IFNG	interferon, gamma [Source:HGNC Symbol;Acc:HGNC:5438]	12	912.165804	1.56139791	5.52E-16	360.24	181.66	1443.07	768.26	924.13	331.37	2058.84	1229.76
ENSG000001	SPRR2D	small proline-rich protein 2D [Source:HGNC Symbol;Acc:HGNC:11264]	1	41.801127	1.5649859	1.10E-06	17.06	5.68	81.13	20.74	11.54	2.86	173.49	21.91
ENSG000001	TUSC3	tumor suppressor candidate 3 [Source:HGNC Symbol;Acc:HGNC:30242]	8	100.198102	1.58923019	2.34E-07	31.28	23.65	184.57	328.83	23.08	33.42	80.16	96.59
ENSG000001	CRYBA4	crystallin, beta A4 [Source:HGNC Symbol;Acc:HGNC:2396]	22	27.4853686	1.59677961	8.70E-07	4.74	0.95	26.37	17.77	7.69	5.73	120.79	35.85
ENSG000000	RGS1	regulator of G-protein signaling 1 [Source:HGNC Symbol;Acc:HGNC:9991]	1	134.607752	1.62054962	6.34E-09	10.43	11.35	24.34	54.31	93.28	42.02	691.77	149.36
ENSG000001	LCP1	lymphocyte cytosolic protein 1 (L-plastin) [Source:HGNC Symbol;Acc:HGNC:6528]	13	520.906809	1.62202286	4.18E-15	232.26	132.46	1248.36	551.02	338.49	182.4	1000.32	481.95
ENSG000000	HHATL	hedgehog acyltransferase-like [Source:HGNC Symbol;Acc:HGNC:13242]	3	18.6873518	1.62585362	5.37E-07	1.9	0.95	41.58	4.94	4.81	0.95	72.47	21.91
ENSG000001	FRMPD2	FERM and PDZ domain containing 2 [Source:HGNC Symbol;Acc:HGNC:28572]	10	60.7183613	1.62732461	5.06E-07	7.58	5.68	65.92	232.06	14.42	13.37	57.1	89.62
ENSG000001	ZC3H12C	zinc finger CCCH-type containing 12C [Source:HGNC Symbol;Acc:HGNC:29362]	11	163.866952	1.6471798	8.59E-15	131.77	15.14	413.75	60.24	106.74	25.78	437.02	120.49
ENSG000001	COL6A3	collagen, type VI, alpha 3 [Source:HGNC Symbol;Acc:HGNC:2213]	2	129.072425	1.64775887	1.21E-15	24.65	61.5	81.13	239.96	63.47	66.85	258.04	236.99
ENSG000001	BTG2	BTG family, member 2 [Source:HGNC Symbol;Acc:HGNC:1131]	1	11115.5287	1.66614989	1.86E-38	4070.71	3680.44	13577.84	15384.02	6798.73	6071.56	21351.55	17989.39
ENSG000002	LINC01480	long intergenic non-protein coding RNA 1480 [Source:HGNC Symbol;Acc:HGNC:51124]	19	10156.6071	1.67311743	1.17E-35	4433.79	3022.88	17578.47	11359.03	5839.98	5255.08	19426.68	14336.94
ENSG000002	ADGRG1	adhesion G protein-coupled receptor G1 [Source:HGNC Symbol;Acc:HGNC:4512]	16	142.840541	1.67763987	7.44E-08	8.53	41.63	121.69	609.28	6.73	84.04	31.84	238.98
ENSG000001	CHODL	chondrolectin [Source:HGNC Symbol;Acc:HGNC:17807]	21	69.9676769	1.67935422	1.81E-10	29.39	37.85	161.24	177.75	11.54	20.05	58.2	63.73
ENSG000001	CYP4F3	cytochrome P450, family 4, subfamily F, polypeptide 3 [Source:HGNC Symbol;Acc:HGNC:2646]	19	125.590179	1.73684503	6.51E-08	15.17	2.84	476.63	347.59	19.23	5.73	86.75	50.78
ENSG000001	LCE1E	late cornified envelope 1E [Source:HGNC Symbol;Acc:HGNC:29466]	1	82.7419002	1.73826432	3.29E-08	11.38	12.3	77.07	322.91	21.16	20.05	84.55	112.52
ENSG000001	ADAMTS14	ADAM metalloproteinase with thrombospondin type 1 motif, 14 [Source:HGNC Symbol;Acc:HGNC:14899]	10	289.282372	1.73970627	5.98E-20	33.18	129.62	108.51	606.32	77.89	236.83	360.16	761.76
ENSG000001	KCNN3	potassium channel, calcium activated intermediate/small conductance subfamily N alpha, member 3 [Source:HGNC Symbol;Acc:HGNC:6292]	1	1500.58642	1.74553686	2.59E-11	1044.7	27.44	4406.28	60.24	648.14	25.78	5716.44	75.68
ENSG000001	PADI4	peptidyl arginine deiminase, type IV [Source:HGNC Symbol;Acc:HGNC:18368]	1	34.0188639	1.75962694	4.36E-08	4.74	0.95	68.96	66.16	5.77	6.68	79.06	39.83
ENSG000001	HSPG2	heparan sulfate proteoglycan 2 [Source:HGNC Symbol;Acc:HGNC:5273]	1	123.814167	1.76559789	1.97E-08	28.44	9.46	66.93	60.24	31.73	18.14	511.69	263.88
ENSG000001	PHLDA1	pleckstrin homology-like domain, family A, member 1 [Source:HGNC Symbol;Acc:HGNC:8933]	12	550.089634	1.78765119	6.20E-17	206.66	187.33	1285.88	984.52	204.83	217.73	666.52	647.24
ENSG000001	PYHIN1	pyrin and HIN domain family, member 1 [Source:HGNC Symbol;Acc:HGNC:28894]	1	161.156137	1.8030241	1.41E-11	60.67	24.6	427.95	229.1	83.66	40.11	266.83	156.33
ENSG000001	CSF2	colony stimulating factor 2 (granulocyte-macrophage) [Source:HGNC Symbol;Acc:HGNC:2434]	5	131.675314	1.85617748	1.09E-19	40.76	59.61	195.72	227.12	44.24	51.57	216.32	218.07
ENSG000001	LPXN	leupaxin [Source:HGNC Symbol;Acc:HGNC:14061]	11	392.792413	1.85993089	2.20E-32	95.75	104.07	408.68	339.69	184.63	228.23	789.5	991.78
ENSG000001	RRAD	Ras-related associated with diabetes [Source:HGNC Symbol;Acc:HGNC:10446]	16	24.6596714	1.8619617	4.83E-09	2.84	0.95	57.8	21.72	5.77	1.91	93.33	12.94
ENSG000001	MATN1	matrilin 1, cartilage matrix protein [Source:HGNC Symbol;Acc:HGNC:6907]	1	212.860957	1.8720089	2.73E-15	33.18	99.34	198.76	703.09	41.35	107.91	186.67	332.58

ENSG000001 LIN7A	lin-7 homolog A (C, elegans) [Source:HGNC Symbol;Acc:HGNC:17787]	12	1045.29836	1.87892349	1.39E-17	378.25	136.24	1932.88	1100.06	649.1	362.88	2727.55	1075.42
ENSG000000 CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein) [Source:HGNC Symbol;Acc:HGNC:1814]	19	180.208166	1.89738546	2.74E-15	28.44	11.35	135.89	38.51	108.66	72.58	477.65	568.58
ENSG000001 TRIM22	tripartite motif containing 22 [Source:HGNC Symbol;Acc:HGNC:16379]	11	742.39749	2.06091704	1.16E-11	200.03	32.17	3099.1	1210.66	237.52	29.6	811.46	318.64
ENSG000001 CXCL10	chemokine (C-X-C motif) ligand 10 [Source:HGNC Symbol;Acc:HGNC:10637]	4	51.3251874	2.06922728	2.37E-11	3.79	0	110.54	1.97	20.19	0	270.12	3.98
ENSG000001 DDX60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 [Source:HGNC Symbol;Acc:HGNC:25942]	4	125.911109	2.13072787	5.85E-12	23.7	3.78	144	21.72	13.46	11.46	368.94	420.21
ENSG000001 LAPTM5	lysosomal protein transmembrane 5 [Source:HGNC Symbol;Acc:HGNC:29612]	1	308.409569	2.34569358	8.79E-23	13.27	132.46	95.33	1084.26	18.27	135.6	281.1	706.99
ENSG000001 CPM	carboxypeptidase M [Source:HGNC Symbol;Acc:HGNC:2311]	12	247.852711	2.45891823	3.66E-23	52.14	35.01	632.8	529.29	49.04	57.3	287.69	339.55
ENSG000001 ABCA12	ATP-binding cassette, sub-family A (ABC1), member 12 [Source:HGNC Symbol;Acc:HGNC:14637]	2	158.220224	2.47021643	2.87E-19	28.44	21.76	360.01	537.19	23.08	17.19	152.63	125.47
ENSG000001 GDF15	growth differentiation factor 15 [Source:HGNC Symbol;Acc:HGNC:30142]	19	48.2166584	2.60154308	1.22E-18	3.79	3.78	54.76	144.17	2.88	4.77	77.96	93.6
ENSG000001 VANGL2	VANGL planar cell polarity protein 2 [Source:HGNC Symbol;Acc:HGNC:15511]	1	408.143688	2.82570413	1.72E-46	35.08	119.21	214.99	1315.33	32.7	98.36	306.36	1143.13
ENSG000000 TNC	tenascin C [Source:HGNC Symbol;Acc:HGNC:5318]	9	467.108491	3.01296294	5.04E-44	68.26	73.8	912.69	1467.4	48.08	74.49	404.08	688.07
ENSG000001 LIF	leukemia inhibitory factor [Source:HGNC Symbol;Acc:HGNC:6596]	22	317.351159	3.13521663	1.53E-51	87.22	27.44	767.68	378.21	49.04	24.83	818.05	386.35

[Click here to view linked References](#)

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Targeting the methyltransferase SETD8 impairs tumor cell survival and overcomes drug resistance independently of p53 status in multiple myeloma

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34 **ABSTRACT**

1 35
2 36 **Background:** Multiple myeloma (MM) is a malignancy of plasma cells that largely remains
3
4 37 incurable. The search for new therapeutic targets is therefore essential. In addition to a
5
6 38 wide panel of genetic mutations, epigenetic alterations also appear as important players
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8 39 in the development of this cancer, thereby offering the possibility to reveal novel
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10 40 approaches and targets for effective therapeutic intervention.

11 41 **Results:** Here, we show that a higher expression of the lysine methyltransferase SETD8,
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13 42 which is responsible for the mono-methylation of histone H4 at lysine 20, is an adverse
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15 43 prognosis factor associated with a poor outcome in two cohorts of newly diagnosed
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17 44 patients. Primary malignant plasma cells are particularly addicted to the activity of this
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19 45 epigenetic enzyme. Indeed, the inhibition of SETD8 by the chemical compound UNC-
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21 46 0379 and the subsequent decrease in histone H4 methylation at lysine 20 are highly toxic
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23 47 in MM cells compared to normal cells from the bone marrow microenvironment. At the
24
25 48 molecular level, RNA sequencing and functional studies revealed that SETD8 inhibition
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27 49 induces a mature non-proliferating plasma cell signature and, as observed in other
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29 50 cancers, triggers an activation of the tumor suppressor p53, which together cause an
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31 51 impairment of myeloma cell proliferation and survival. However, a deadly level of
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33 52 replicative stress was also observed in p53-deficient myeloma cells treated with UNC-
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35 53 0379, indicating that the cytotoxicity associated with SETD8 inhibition is not necessarily
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37 54 dependent on p53 activation. **Consistent with this, UNC-0379 triggers a specific p53-
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39 55 independent nucleolar stress characterized by nucleolin delocalization and reduction of
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41 56 nucleolar RNA synthesis.** Finally, we showed that SETD8 inhibition is strongly synergistic
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43 57 with melphalan and may overcome resistance to this alkylating agent widely used in MM
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45 58 treatment.

46 59 **Conclusions:** Altogether, our data indicate that the up-regulation of the epigenetic
47
48 60 enzyme SETD8 is associated with a poor outcome and the deregulation of major signaling
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50 61 pathways in MM. Moreover, we provide evidences that myeloma cells are dependent on
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52 62 SETD8 activity and its pharmacological inhibition synergizes with melphalan, which could
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54 63 be beneficial to improve MM treatment in high-risk patients whatever their status for p53.
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INTRODUCTION

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68 Multiple Myeloma (MM) is a cancer of terminally differentiated plasma cells[1] and
69 is the second most common hematological malignancy[2]. Over the past 15 years, several
70 advances in treatments have led to a significantly higher survival of intensively treated
71 patients[3]. Unfortunately, despite the recent progress in MM treatments, most patients
72 will ultimately relapse and develop drug resistance.

73 In addition to a wide panel of genetic mutations, recent studies have pinpointed
74 that epigenetic alterations, including aberrant DNA and histone methylation, might be also
75 important players in MM development[4]. These recent findings could illuminate new
76 mechanisms central to the genesis of MM and offer the possibility to reveal novel
77 approaches and targets for effective therapeutic intervention. For example, the inhibition
78 of the histone H3K27 methyltransferase EZH2 has recently emerged as a potential
79 strategy for the treatment of myeloma[5]. Moreover, classic epigenetic modulating agents,
80 such as histone deacetylase and DNA methyltransferase inhibitors, are already tested as
81 monotherapy or in combination with conventional anti-MM agents[6, 7]. However, the
82 occurrence of important side effects and the appearance of resistance to these drugs
83 increase the need to identify novel epigenetic targets in MM and evaluate their pre-clinical
84 perspective.

85 SETD8 (also known as SET8, PR-Set7, KMT5A) has been identified as the
86 epigenetic enzyme responsible for the mono-methylation of histone H4 at lysine 20
87 (H4K20me1) [8]. SETD8 and H4K20me1 are naturally increased during mitosis and play
88 a critical role in chromatin compaction, gene regulation and cell-cycle progression[8–
89 10][10]. In addition, SETD8 could induce the methylation of non-histone proteins, such as
90 the replication factor PCNA and the tumor suppressor p53[11, 12]. While SETD8-

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91 mediated methylation of p53 inhibits apoptosis[12], PCNA methylation by SETD8 might
92 enhance the interaction with the Flap endonuclease FEN1 and promote cell
93 proliferation[11]. Consistent with this, the overexpression of SETD8 has been reported in
94 many different solid tumors[14–17] and pharmacological inhibition of SETD8 is sufficient
95 to activate the p53 pro-apoptotic program in neuroblastoma cell lines[18]. This has
96 suggested that this enzyme could be an attractive target to rescue p53 functions in
97 cancers displaying a low incidence of *TP53* genetic alterations, as it is the case at early
98 stages in MM[19]. However, the role of SETD8 and its incidence in the development of
99 MM or any hematological malignancies is not known.

100 Here, we provide evidence that malignant plasma cells are addicted to SETD8
101 expression, which is associated with a poor outcome independently of changes in the
102 steady state level of histone H4K20me1. Although inducing p53 canonical pathway, **we**
103 **show that the pharmacological inhibition of SETD8 by the chemical compound UNC-0379**
104 **causes specific nucleolar alterations and cytotoxic effects independently of p53 status.**
105 Finally, the combination of UNC-0379 with the cytotoxic agent melphalan strongly
106 enhances DNA damage and overcomes drug resistance, suggesting that targeting
107 SETD8 activity could be beneficial to improve MM treatment in high-risk patients
108 independently of their mutational status for p53.

MATERIALS AND METHODS

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112 **Primary multiple myeloma cells**

113 Patients' MMCs were purified using anti-CD138 MACS microbeads (Miltenyi Biotec,
114 Bergisch Gladbach, Germany) and their gene expression profile (GEP) obtained using
115 Affymetrix U133 plus 2.0 microarrays as described[20, 21][22]. We also used publicly
116 available Affymetrix GEP (Gene Expression Omnibus, accession number GSE2658) of a
117 cohort of 345 purified MMC from previously untreated patients from the University of
118 Arkansas for Medical Sciences (UAMS, Little Rock, AR), termed in the following UAMS-
119 TT2 cohort. These patients were treated with total therapy 2 including high-dose
120 melphalan (HDM) and autologous stem cell transplantation (ASCT)[23]. We also used
121 Affymetrix data from total therapy 3 cohort (UAMS-TT3; n=158; E-TABM-1138)[24].
122 Mouse 5T33MMvv cells originated spontaneously in aging C57BL/KaLwRij mice and have
123 since been propagated *in vivo* by intravenous transfer of diseased marrow in young
124 syngeneic mice as described[25, 26].

125 **Treatment of primary MM cells**

126 Bone marrow of patients with previously untreated MM (n = 8) at the university hospital of
127 Montpellier was obtained after patients' written informed consent in accordance with the
128 Declaration of Helsinki and agreement of the Montpellier University Hospital Centre for
129 Biological Resources (DC-2008-417). Mononuclear cells were treated with or without
130 UNC-0379 (1µM, 2.5µM or 5µM) and MMC cytotoxicity was evaluated using anti-CD138-
131 phycoerythrin monoclonal antibody (Immunotech, Marseille, France) as described[27].

132 **Apoptosis assays**

133 Cells were cultured in 24-well, flat-bottomed microtiter plates at 10⁵ cells per well in
134 RPMI1640–10% FCS or X-VIVO 20 culture media with or without IL-6 (3ng/mL) and

135 appropriate concentration of chemical drugs. After 4 days of culture, cells were washed
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2 136 twice in PBS and apoptosis was assayed with PE-conjugated Annexin V labeling (BD
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5 137 Biosciences) using a Fortessa flow cytometer (BD) following manufacturer protocols.
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7 138 **Human Myeloma Cell Lines (HMCLs)**

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10 139 XG human myeloma cell lines (HMCLs) were cultured in the presence of recombinant IL-
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12 140 6 as previously described[28]. XG7 Melphalan-resistant cell line was derived from the
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15 141 sensitive parental XG7 cells[29]. JJN3 was kindly provided by Dr Van Riet (Brussels,
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17 142 Belgium), JIM3 by Dr MacLennan (Birmingham, UK) and MM1S by Dr S. Rosen (Chicago,
18
19 143 USA). AMO-1, LP1, L363, U266, OPM2, and SKMM2 were purchased from DSMZ
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21
22 144 (Braunschweig, Germany) and RPMI8226 from ATTC (Rockville, MD, USA). HMCLs were
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24 145 authenticated according to their short tandem repeat profiling and their gene expression
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27 146 profiling using Affymetrix U133 plus 2.0 microarrays deposited in the ArrayExpress public
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29 147 database under accession numbers E-TABM-937 and E-TABM-1088[28].
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31 148 **Establishment of shRNA expressing HMCLs**

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34 149 Control and p53 shRNA sequences were cloned in the pLenti4-EZ-miR plasmid as
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36 150 previously described[30]. SETD8 and associated control shRNA sequences were cloned
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39 151 into a puromycin retroviral vector RNAi Ready pSiren as described[31]. Retroviral
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41 152 particles were produced in 293FT cells. Briefly, 293FT cell line was cultured in Dulbecco's
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44 153 modified Eagle's medium and supplemented with 10% defined fetal bovine serum,
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46 154 500µg/mL geneticin, 4mM L-glutamine, and 1mM MEM sodium pyruvate. The day before
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49 155 transfection, cells were plated into a 10cm tissue culture plate to 90%-95% confluence.
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51 156 9µg of ViraPower packaging mix (Invitrogen) and 9µg of lentiviral plasmids were co-
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54 157 transfected into 293FT cells using 36µL Lipofectamine 2000 reagent (Invitrogen). Forty-
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56 158 eight hours later, culture supernatants were collected, concentrated 100-fold by
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58 159 ultracentrifugation (20,000 g; 4 hours) and viral titers determined. Corresponding HMCLs
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160 were transduced with virus and stable transduced cells were obtained by adding zeocin
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2 161 (10 µg/mL) for pLenti4-EZ-miR and puromycin (2.5 µg/mL) for pSIREN viral particles.
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4 162 **Growth assays and cell cycle analysis**

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7 163 Cells were cultured for 4 days in 96-well flat-bottom microtiter plates in RPMI 1640
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9 164 medium, 10% FCS, and 2 ng/ml IL-6 (control medium) in the presence of UNC-0379. Cell
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11 165 growth was evaluated by quantifying intracellular ATP amount with a Cell Titer Glo
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13 166 Luminescent Assay (Promega, Madison, WI) using a Centro LB 960 luminometer
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15 167 (Berthold Technologies, Bad Wildbad, Germany). For cell cycle analysis, cells were
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17 168 cultured in 24-well flat-bottomed microtiter plates at 10⁵ cells per well in RPMI1640–10%
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19 169 FCS or X-VIVO 20 culture media with or without IL-6 (3ng/mL). The cell cycle was
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21 170 assessed using DAPI staining (Sigma-Aldrich, Saint-Louis, MO, USA) and cells in the S
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23 171 phase using incubation with bromodeoxyuridine (BrdU) for 1 h and labeling with an anti-
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25 172 BrdU antibody (APC BrdU flow kit, BD Biosciences, San Jose, CA, USA) according to the
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27 173 manufacturer's instructions. Flow cytometry analysis was done on a Fortessa flow
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29 174 cytometer (BD, Mountain View, CA, USA).
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34 175 **RNA sequencing**

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36 176 HMCLs were cultured for 16 hours with or without 5 µM of UNC-0379, or infected with
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38 177 shControl or shRNA SETD8 pSIREN vectors for 48h. RNA samples were collected as
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40 178 previously described. The RNA sequencing (RNA-seq) library preparation was done with
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42 179 150ng of input RNA using the Illumina TruSeq Stranded mRNA Library Prep Kit. Paired-
43
44 180 end RNA-seq were performed with Illumina NextSeq sequencing instrument (Helixio,
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46 181 Clermont-Ferrand, France). RNA-seq read pairs were mapped to the reference human
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48 182 GRCh37 genome using the STAR aligner[32]. All statistical analyses were performed with
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50 183 the statistics software R (version 3.2.3; available from <https://www.r-project.org>) and R
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52 184 packages developed by BioConductor project (available from
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185 <https://www.bioconductor.org/>)[33]. The expression level of each gene was summarized
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2 186 and normalized using DESeq2 R/Bioconductor package[34]. Differential expression
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5 187 analysis was performed using DESeq2 pipeline. P values were adjusted to control the
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7 188 global FDR across all comparisons with the default option of the DESeq2 package. Genes
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10 189 were considered differentially expressed if they had an adjusted p-value of 0.05 and a fold
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12 190 change of 1.5. Pathway enrichment analyses were performed using online the curated
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15 191 gene set collection on the Gene Set Enrichment Analysis software
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17 192 (<http://software.broadinstitute.org/gsea/msigdb/index.jsp>)[35, 36].

193 **Gene expression profiling and statistical analyses**

194 Gene expression data were normalized with the MAS5 algorithm and analyses processed
195 with GenomicScape (<http://www.genomicscape.com>)[37] the R.2.10.1 and bioconductor
196 version 2.5 programs[33]. Gene Set Expression Analysis (GSEA) was used to identify
197 genes and pathways differentially expressed between populations. Univariate and
198 multivariate analysis of genes prognostic for patients' survival was performed using the
199 Cox proportional hazard model. Difference in overall survival between groups of patients
200 was assayed with a log-rank test and survival curves plotted using the Kaplan-Meier
201 method (Maxstat R package)[38].

202 **53BP1 Staining-immunofluorescence microscopy**

203 After deposition on slides using a Cytospin centrifuge (600 r.p.m. for 10 minutes), cells
204 were fixed with 4% PFA, permeabilized with 0.5% Triton in PBS and saturated with 5%
205 bovine milk in PBS. The rabbit anti-53BP1 (Novus Biologicals - Littleton, CO, USA –
206 NB100304) antibody was diluted 1/300 in 5% bovine milk in PBS, and deposited on
207 cytopins for 60 minutes at room temperature. Slides were washed twice and anti-rabbit
208 alexa 488-conjugated antibody (diluted 1/500 in 5% bovine milk in PBS) was added for
209 60 minutes at room temperature. Slides were washed and mounted with Vectashield and

210 1% DAPI. Images and fluorescence were captured with a ZEISS Axio Imager Z2
211 microscope (X63 objective) (Oberkochen, Germany), analyzed with Omero
212 (omero.mri.cnrs.fr) server and ImageJ software.

213 **Nucleolar proteins staining-immunofluorescence microscopy**

214 After indicated treatments and deposition on slides as described above, cells were fixed
215 with 4% PFA for 10 minutes at RT, permeabilized with 0.1% Triton in PBS-0.5% BSA for
216 10 minutes, and saturated with PBS-1% BSA for 20 minutes. Anti-nucleolin (ab22758,
217 Abcam) and anti-fibrillarin (ab5821, Abcam) antibodies were diluted 1/200 in saturation
218 buffer, and incubated for 90 minutes in a humid chamber at room temperature. Slides
219 were washed 3 times with PBS-0.01% Tween-20 and anti-rabbit Alexa Texas Red-
220 conjugated antibody (diluted 1/500 in saturation buffer) was added for 45 minutes in a
221 humid chamber at room temperature protected from light. Slides were washed 3 times (5
222 minutes each) as previously, incubated with DAPI (20 µg/ml in water) for 5 minutes
223 protected from light, washed 3 times with water, air dried and mounted with ProLong
224 (Invitrogen). Images and fluorescence were captured with a ZEISS Axio Imager Z1
225 microscope (X40 objective) (Oberkochen, Germany), and analyzed with Omero
226 (omero.mri.cnrs.fr) server. Quantification of cells with nucleolin delocalization was visually
227 performed.

228 **5-Ethynyl Uridine (EU) staining-immunofluorescence microscopy**

229 Cells were treated with UNC-0379 3 µM or the vehicle DMSO (0.0003%) for 24h. EU (0.2
230 mM) was added during the last 5 minutes of treatment. Cells were deposited on slides as
231 described above, fixed with 4% PFA for 10 minutes at RT, permeabilized with 0.5% Triton
232 in PBS-0.5% BSA for 10 minutes, saturated with PBS-1% BSA for 20 minutes and Click-
233 it reaction was performed. Briefly, for 10 slides, a mix of 438 µl PBS 1X + 15 µl CuSO₄
234 (0.1 M) + 2.5 µl Azide AF555 + 50 µl Vitamine C (100 mM) was prepared by adding the

235 reagents in the mentioned order. Slides were incubated in a humid chamber protected
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2 236 from light for 15 minutes at RT, washed 3 times with PBS-0.01% Tween-20, and
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4 237 subsequently incubated with DAPI and mounted as described above. Image acquisition
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7 238 was performed with a ZEISS Axio Imager Z1 microscope (X40 objective) (Oberkochen,
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9 239 Germany), and analyzed with Omero (omero.mri.cnrs.fr) server. Quantification of EU
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12 240 intensity was performed with CellProfiler™ “Human Cell” pipeline.

14 241 **Immunoblot analysis.** Cells washed with phosphate-buffered saline (PBS) were lysed in
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17 242 SDS buffer and boiled at 94°C for 5 minutes. After measuring protein quantity by Bradford,
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19 243 equal amounts of protein were resolved by SDS-PAGE, transferred to a nitrocellulose
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22 244 membrane (Millipore) and probed with one of the following antibodies: mouse anti-Chk1
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24 245 (1:1000, abcam), rabbit anti-p21 (1:500, Cell signaling), rabbit anti- p53 (1:1000, Cell
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26 246 Signaling), rabbit anti-SETD8 (1:1000, Cell Signaling), mouse anti-β-actin (1:20000,
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29 247 Sigma), rabbit anti-H2A.X and anti-phospho-H2A.X-Ser139 (1:1000, Cell signaling),
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32 248 rabbit anti-H4-K20me1 (1:1000 Cell Signaling), and rabbit anti-Histone H4 (1:1000, Cell
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34 249 Signaling), rabbit anti-tubulin (1:1000, Cell signaling). Membranes were then incubated
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36 250 with the appropriate horseradish peroxidase (HRP)-conjugated secondary antibodies.
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39 251 The immunoreactive bands were detected by chemiluminescence (Pierce).

41 252 **Drug combination study**

43 253 The interaction between the drugs tested in vitro was investigated with a concentration
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46 254 matrix test, in which increasing concentration of each single drug were assessed with all
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49 255 possible combinations of the other drugs. For each combination, the percentage of
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51 256 expected growing cells in the case of effect independence was calculated according to
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53 257 the Bliss equation (Combes et al., 2019; Greco et al., 1995):

$$56 \text{ 258 } fuC = fuA.fuB$$

259 where fuC is the expected fraction of cells unaffected by the drug combination in the case
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2 260 of effect independence, and fuA and fuB are the fractions of cells unaffected by treatment
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4 261 A and B, respectively. The difference between the fraction of living cells in the cytotoxicity
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7 262 test and the fuC value was considered as an estimation of the interaction effect, with
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10 263 positive values indicating synergism and negative values antagonism.

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12 264 Synergy matrix was built with the R package “SynergyFinder”.

14 265 ***In vitro* Plasma Cell differentiation**

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17 266 Peripheral blood cells from healthy donors were purchased from the French Blood Center
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19 267 (Toulouse, France) and CD19+ CD27+ MBCs purified (>95% purity) using “MBC isolation
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22 268 kit” (Order no. 130-093-546, Miltenyi) according to manufacturer’s instructions.
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24 269 Preplasmablasts (prePB), plasmablasts (PB) and plasma cells (PC) were generated as
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27 270 reported[39, 40], by a 3-step *in vitro* protocol. At day 7 of differentiation, when PB was the
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29 271 most abundant population in the culture, UNC-0379 (at 1, 2.5 or 5 μ M) or the vehicle
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32 272 DMSO (=mock, at 0.0005%) were added, and cells were incubated for the next 3 days
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34 273 during their differentiation into PC. At the end of this treatment, all cells were collected,
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37 274 visually counted with Trypan Blue to assess viability, apoptosis was analyzed as described
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39 275 above, and PCs (CD38+ CD138+ cells) were quantified by cytometry. Data are expressed
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41
42 276 as percentage of CD38+ CD138+ cells compared to the mock sample (100%).

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RESULTS

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5 284 **SETD8 up-regulation in myeloma is associated with a poor outcome.** In order to
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7 285 identify epigenetic factors potentially involved in MM, we used public Affymetrix
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9 286 microarrays gene expression data sets to identify which genes encoding histone-
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11 287 modifying enzymes are differentially expressed between normal bone marrow plasma
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13 288 cells (BMPCs, n=22), purified primary MM cells from newly diagnosed patients (MMCs, n
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15 289 = 345) and human myeloma cell lines (HMCLs, N=42)¹⁹. As shown in Figure 1A,
16
17 290 significantly higher levels of mRNAs encoding the histone H4K20 mono-
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19 291 methyltransferase SETD8 were found in HMCLs compared to BMPCs and MMCs (**Figure**
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21 292 **1A**). Furthermore, although we did not observe a statistical difference with BMPCs,
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23 293 *SETD8* mRNA levels appeared heterogeneous in MMCs (**Figure 1A**) ranging from 65 to
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25 294 63338 in Affymetrix signal. These contrasted *SETD8* mRNA levels were not restrained to
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27 295 a particular MM molecular sub-type (**Supplementary Figure S1A**). Immunoblot analysis
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29 296 with a specific SETD8 antibody showed that HMCLs and some MMCs displayed higher
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31 297 SETD8 protein levels compared with normal plasma cells (PC) (**Figure 1B**). These higher
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33 298 SETD8 protein levels were independent of the natural cell-cycle fluctuation of the
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35 299 enzyme[9], as the levels of the mitotic marker histone H3-S10 phosphorylation were
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37 300 relatively similar in all tested samples (**Figure 1B**). SETD8 is known as the unique enzyme
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39 301 responsible for the mono-methylation of histone H4 at lysine 20 (H4K20me1)[8]. Yet,
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41 302 levels of H4K20me1 remained roughly unchanged in HMCLs and MMCs displaying higher
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43 303 SETD8 levels and similar levels of the G2/M marker histone H3-S10 phosphorylation
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45 304 (**Figure 1B**), indicating that SETD8 up-regulation is not accompanied by a significant
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47 305 increase in the steady state level of histone H4K20me1 in MM.
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306 We next investigated the prognostic value of SETD8 up-regulation in two
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2 307 independent cohorts of previously untreated MM patients (UAMS-TT2 n=256 and UAMS-
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4 308 TT3 n=158 cohorts), using Maxstat R algorithm. High *SETD8* mRNA levels were
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7 309 predictive of both shorter event free survival and overall survival in the two cohorts (**Figure**
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10 310 **1C**). Consistent with these results, *SETD8* mRNA levels were significantly increased in
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12 311 patients harboring Chr1q21 gain (**Supplementary Figure S1B**) or presenting a high gene
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14 312 expression-based proliferation index (GPI) (**Supplementary Figure S1C**), molecular
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16 313 features being associated with a poor outcome in MM patients. However, *SETD8*
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19 314 expression did not correlate with MMC plasma cell labeling index (PCLI) in a cohort of
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22 315 101 newly diagnosed patients (**Supplementary Figure S1D**), suggesting that SETD8 up-
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24 316 regulation is likely not a hallmark of MMC proliferation status. Gene set expression
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26 317 analysis (GSEA) of patients with high *SETD8* expression highlighted a significant
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29 318 enrichment of genes involved in IRF4 targets, MYC-MAX targets, MAPK pathway and
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31 319 DNA repair (**Supplementary Figure S2**, $P < 0.001$), suggesting that SETD8 up-regulation
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34 320 correlates with changes in signaling pathways involved in MM pathophysiology.
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36 321 Furthermore, SETD8 expression is significantly higher in MM cells from relapsed patients
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39 322 compared to newly diagnosed patients, underlining a potential role of SETD8 in drug
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41 323 resistance (**Supplementary Figure S3**). Altogether, these data reveal that the epigenetic
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44 324 enzyme SETD8 is overexpressed in myeloma and this up-regulation is associated with a
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46 325 poor outcome and deregulation of major signaling pathways in MM patients.
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51 327 **UNC-0379-mediated SETD8 inhibition leads to cell-cycle defects and apoptosis in**
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53 328 **MMCs.** To determine the biological significance of SETD8 up-regulation in MM
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56 329 pathophysiology, the effects of the small-molecule SETD8 inhibitor UNC-0379 were
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58 330 examined in eight different HMCLs representative of the disease. UNC-0379 is a well-
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331 characterized substrate-competitive inhibitor selective for SETD8 [15, 18, 42]. As shown
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2 332 in Figure 2A, UNC-0379 treatment was sufficient to inhibit the growth of all HMCLs in a
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5 333 dose dependent manner with an average half maximal inhibitory concentration (IC_{50})
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7 334 ranging from 1.25 to 6.3 μ M (**Figure 2A**). To determine the molecular mechanisms of this
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10 335 HMCL growth inhibition, the effects of UNC-0379 treatment on SETD8 activity, cell
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12 336 proliferation and survival were examined using immunoblot and flow cytometry assays in
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14 337 XG7 and XG25 MM cell lines, which displayed similar IC_{50} values for UNC-0379. Analysis
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17 338 of whole cell extracts after 24 hours of treatment showed a strong decrease in H4K20me1,
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19 339 thereby demonstrating the rapid and efficient inhibition of SETD8 activity
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22 340 (**Supplementary Figure S4A**). In the following hours, this SETD8 inhibition was
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24 341 associated with cell-cycle defects, as shown in both cell lines by an accumulation in G1
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26 342 phase and a decrease in DNA replication (S) phase 48 hours after treatment (**Figure 2B**
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29 343 and **Supplementary Figure S4B**). At later time points, these cell cycle defects were
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31 344 followed by the activation of apoptosis, as measured by the appearance of 33% and 26%
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34 345 of annexin-V positive cells in XG7 and XG25 cell lines respectively (**Figure 2B** and
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36 346 **Supplementary Figure S4C**).

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39 347 To demonstrate that **SETD8 is indeed** required for growth and viability of malignant
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41 348 plasma cells, **bone marrow (BM) cells isolated from two healthy donors and from eight**
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43 349 **MM patients were cultured** with recombinant interleukin 6 in presence or not of UNC-0379.
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46 350 Four days after treatment, the percentage of plasma cells was measured by flow
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49 351 cytometry after staining with anti-CD138 and anti-CD38 antibodies. **As shown in Figure**
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51 352 **2C, the viability of normal mature plasma cells remained roughly unaffected by UNC-0379**
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53 353 **treatment except at the highest dose for one donor.** In contrast, the median number of
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56 354 malignant plasma cells in MM patient samples was decreased in a dose-dependent
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58 355 manner with 50% and 63% of reduction with 2.5 μ M and 5 μ M of UNC-0379 respectively
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356 ($P = 0.001$ and $P < 0.0001$; $N=8$), whereas non-tumoral CD138-negative BM cells
357 displayed less sensitivity, like normal plasma cells (Figure 2D). **Consistent with a**
358 **cytotoxicity of UNC-0379 preferentially in malignant plasma cells, normal plasma cells**
359 **generated *in vitro* by differentiation of memory B cells remained largely unaffected by**
360 **SETD8 inhibitor, even at high doses (Supplementary figure S5).** In the perspective of
361 potential preclinical studies with SETD8 inhibitors, primary 5T33vv murine MM models
362 [25] were also treated with growing concentrations of UNC-0379 for 24h hours before cell
363 viability analysis. As observed with human primary MM cells, UNC-0379 treatment results
364 in a significant reduction of 5T33vv viability in a dose dependent manner (**Supplementary**
365 **Figure S6**). Altogether, these results indicate that malignant plasma cells are particularly
366 addicted to SETD8 activity and that UNC0379 treatment is highly toxic to these tumor
367 cells, leading rapidly to their growth inhibition and death.

SETD8 inhibition impairs MM cell proliferation together with activation of p53-target
370 **gene pathways.** SETD8 has been involved in all nuclear processes that use DNA as a
371 matrix, including a critical role in the regulation of gene expression [8]. In order to gain
372 insights into the mechanisms contributing to SETD8-mediated MM cell growth inhibition
373 and death, we performed transcriptome analysis in XG7 and XG25 HMCLs after SETD8
374 inhibition using RNA sequencing (**Figure 3A**). To identify gene expression alterations
375 caused by SETD8 inhibition in HMCLs, we isolated total RNAs 18 hours after UNC-0379
376 treatment or 48 hours after shRNA-induced SETD8 silencing, when H4K20me1 decrease
377 had not yet triggered DNA replication defects [31, 43]. A common signature of 820 up-
378 regulated genes and 360 down-regulated genes was found in UNC-0379-treated and
379 SETD8-depleted cell lines compared to the untreated and shRNA control cell lines (Fold
380 change > 2 ; $FDR \leq 0.05$) (**Supplementary Figure S7A** and **Supplementary Table 1**).

381 Gene Set Enrichment Analysis (GSEA) identified, as the most down-regulated pathways,
382 genes involved in cell-cycle, stem cells, proliferating plasmablasts and MM proliferating
383 molecular subgroup together with genes repressed upon loss of the histone H3K27
384 methyltransferase EZH2 (**Figures 3B** and **Supplementary Figure S7B**). Conversely and
385 consistent with the presence of a functional p53 in XG7 and XG25 cell lines [41], a
386 significant positive enrichment was found for p53 target genes, including *p21* and
387 *GADD45A* genes, and genes overexpressed in mature BMPCs versus plasmablasts
388 (**Figures 3B** and **Supplementary Figure S7C**). A positive enrichment for genes normally
389 down-regulated by c-MYC, EZH2, DNA methylation or histone deacetylases (HDAC) was
390 also observed (**Figure 3B**), which might suggest some impairment of chromatin silencing
391 pathways upon SETD8 inhibition in MM cells. As shown in figure 3C, immunoblot analysis
392 of UNC-0379-treated XG7 HMCLs confirmed the increased levels of p53 and p21 proteins
393 upon UNC-0379 treatment. However, we did not observe a significant phosphorylation of
394 the histone variant H2A.X (**Figure 3C**), suggesting p53 activation in XG7 MM cells treated
395 with UNC-0379 likely occurs in absence or low level of DNA damage. Altogether, these
396 data indicate that the cytotoxic effects of SETD8 inhibition in p53-proficient HMCLs are
397 associated with activation of the p53 canonical pathway and a mature non-proliferating
398 plasma cell transcriptional signature.

The cytotoxicity of UNC-0379 treatment is not dependent on p53 in malignant plasma cells. Previous studies showed that UNC-0379-induced cell death depends on the activation of p53 in neuroblastoma cancer models (NB), thereby rendering p53-deficient NB cells more resistant to SETD8 inhibition [41]. To determine whether the cytotoxic effects of the pharmacological inhibition of SEDT8 mediated by UNC-0379 were also dependent on p53 activation in MM cells, we compared the UNC-0379 response in p53

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406 wild-type HMCLs (n=7) and p53-deficient HMCLs (n=5) [28, 41] that displayed similar
407 *SETD8* expression levels (**supplementary figure S8A**). Of note, there was no significant
408 correlation between *SETD8* and *TP53* expression in HMCLs (**Supplementary Figure**
409 **S8B**). Although IC₅₀ values for p53-deficient HMCLs following UNC-0379 treatment were
410 more heterogeneous, we found no statistical difference with the group of p53 wild-type
411 HMCLs (**Figure 4A**). We also observed no statistical difference in the IC₅₀ values of UNC-
412 0379 according to the expression levels of p53 in HMCLs, whatever their mutational p53
413 status (**Supplementary Figure S9**). Altogether, these results suggested that the absence
414 of a functional p53 did not alter significantly the sensitivity of malignant plasma cells to
415 the pharmacological inhibition of SETD8 activity. To verify this hypothesis, we examined
416 by immunoblot and flow cytometry analysis the cytotoxic effects of UNC-0379 treatment
417 on p53-proficient XG7 HMCL transduced with high-titer of lentivirus encoding either a p53
418 shRNA or an irrelevant control shRNA. Both cell lines showed relatively similar IC₅₀ values
419 for UNC-0379 (3.7 μM in control shRNA and 4.8 μM in p53 shRNA expressing cells).
420 Immunoblot analysis confirmed the efficient p53 depletion in p53 shRNA XG7 HMCL
421 compared to control cells (**Figure 4B**). Consistent with results in Figure 3C, UNC-0379
422 treatment led to an up-regulation of p53 without detectable DNA damage in shRNA control
423 XG7 cells (**Figure 4B**). In contrast, higher levels of DNA damage and replicative stress
424 were observed in UNC-0379-treated XG7 cells depleted for p53, as evidenced by the
425 increased levels of both phosphorylated histone variant H2A.X and checkpoint protein
426 Chk1 (**Figure 4B**) and by an accumulation of cells in G2/M phase of the cell cycle (**Figure**
427 **4C**). Accordingly, an increase in DNA damage and replicative stress was also observed
428 in XG1 HMCL naturally harboring a mutated inactive p53 (**Supplementary Figure S10A**).
429 In XG1, as well as in XG7 inactive for p53, this was followed by changes in cell cycle
430 distribution (**Supplementary Figure S10B**) and the appearance of a high percentage of

431 apoptotic cells (**Figure 4C** and **Supplementary Figure S10C**). Thus, these results
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2 432 indicated that UNC-0379-induced cytotoxicity in MM cells is independent on p53 status
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4 433 and that a high level of SETD8 likely protects MM cells from DNA damage and excessive
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7 434 replicative stress.
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12 436 **UNC-0379 induces nucleolar stress independently of p53 activation**

14 437 Nucleolar stress can lead to cell-cycle defects and apoptosis with and without p53[44].
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16 438 Since SETD8 interacts with nucleolar proteins and has been involved in the regulation of
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19 439 nucleoli structure and function[45, 46], we asked whether the cytotoxicity of UNC-0379
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22 440 treatment might be related to nucleolar dysfunction independently of p53 activation in
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24 441 myeloma cells. To address this question, we first examined, by immunofluorescence, the
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27 442 localization of the major nucleolar proteins fibrillarin and nucleolin in control and p53-
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29 443 depleted XG7 cells untreated or treated with 3 μ M of UNC-0379 for 24 hours. Whereas
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32 444 the steady-state levels of nucleolar proteins and the localization of fibrillarin remained
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34 445 largely unaltered in all experimental conditions (**Supplementary figure S11**), a massive
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36 446 delocalization of the nucleolin pool from nucleoli to the nucleoplasm was observed in
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39 447 control and p53-depleted XG7 cells upon UNC-0379 treatment (**Figure 5A**). Nucleolin is
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41 448 required for the transcription of ribosome DNA (rDNA) and alteration of its nucleolar
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44 449 transcriptional function can lead to apoptosis in cancer cells[47]. Therefore, to determine
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46 450 whether nucleolin delocalization upon UNC-0379 is associated with defective nucleolar
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49 451 transcription, cells were pulsed labeled with 5-Ethynyl Uridine (EU) for 5 minutes and
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51 452 nascent RNAs incorporating EU were detected *in situ* by click chemistry. Consistent with
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54 453 nucleoli being the sites of the most active RNA synthesis, short EU pulse labeling resulted
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56 454 in an intense granular staining specifically in nucleoli of untreated control and p53-
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58 455 depleted XG7 cells (**Figure 5B**). Upon UNC-0379 treatment, this intense nucleolar EU
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456 staining was almost abolished in both control and p53 depleted cells, indicating a strong
457 decrease of rDNA transcription independently of p53 activation. Taken together, these
458 results show that, prior to p53 activation, treatment with UNC-0379 leads to specific
459 nucleolar alterations characterized by massive nucleolin delocalization and a strong
460 decrease in nucleolar RNA synthesis, thus providing an explanation for the cytotoxic
461 effects of this SETD8 inhibitory compound on malignant plasma cells regardless of p53
462 status.

463 **UNC-0379-mediated inhibition of SETD8 synergizes with melphalan.** The results
464 presented above indicate that the pharmacological inhibition of SETD8 by UNC-0379
465 could constitute a promising strategy to improve MM treatment by genotoxic agents. To
466 gain further insights into this possibility, we investigated whether SETD8 inhibition could
467 enhance the cytotoxicity of melphalan and overcome resistance to this alkylating agent
468 widely used in MM treatment. To this end, we first measured the viability of XG7 and XG1
469 cells continuously treated for 4 days with different concentrations of each compound alone
470 or in combination. The synergy score of each combination dose was then evaluated using
471 bliss model. As shown in Figures 6A and 6B, we observed a significant synergism of the
472 combination compared to the individual treatments in XG7 cell line and, to a lesser extent,
473 in XG1 for the highest melphalan doses (**Figures 6A and 6B**). **Importantly, the higher**
474 **sensitivity to melphalan was also observed in XG7 cells depleted for SETD8 after lentiviral**
475 **shRNA expression (Supplementary figure S12A-C) and,** consistent with results in Figure
476 4C, XG7 cells depleted for p53 displayed a similar sensitivity to the combination than the
477 shRNA-control XG7 cells (**Supplementary Figure S12D**). **These data demonstrate that**
478 **the lethal synergy between UNC-0379 and melphalan is indeed related to SETD8**
479 **inhibition and does not depend on p53 activation.** As shown in **Figure 6C**, the lethality
480 induced by the co-treatment of melphalan and UNC-0379 was preceded by high levels of

481 DNA breaks, as measured by the significant increase in the number of DNA damage-
482 induced 53BP1 foci in combined versus single agent therapy, in both XG7 and XG1 cell
483 lines. This was also observed in melphalan-resistant XG7 clones [29] (**Figure 6D**), which
484 coincided with higher levels of γ H2AX signal upon melphalan/UNC-0379 combination
485 (**Supplementary Figure S13**). At later time points, we observed a significant increase in
486 apoptotic cell death as measured by annexin V staining (**Figure 6E**). Altogether, these
487 results indicate that UNC-0379-mediated SETD8 inhibition enhances the cytotoxic effects
488 of melphalan in MM cells in a p53 independent manner. This demonstrates the potential
489 therapeutic interest to target SETD8-mediated lysine methylation in MM regardless of p53
490 status (**Figure 7**).

DISCUSSION

496 This study unveils for the first time a role of the histone H4K20 mono-
497 methyltransferase SETD8 in MM pathophysiology. We have shown that elevated levels
498 of SETD8 are associated with a poor prognosis and correlate with the deregulation of
499 regulatory nodes involved in MM, including IRF4, MYC/MAX, MAPK and DNA repair
500 pathways (**Figure 1 and Supplementary Figure S2**). Moreover, patients displaying
501 higher SETD8 expression are associated with specific molecular features, such as
502 increased copy of Chr1q21 or a high GPI index (**Supplementary Figure S1**). Consistent
503 with this, primary MM cells are particularly addicted to SETD8 activity and the recently
504 developed small-molecule inhibitor of SETD8, UNC-0379, demonstrated a higher toxicity
505 in MM cells compared to normal cells from the bone marrow microenvironment **and**

506 **normal plasma cells (Figure 2)**. From a mechanistic point of view, our RNA-seq results
1
2 507 show that genetic or pharmacological inhibition of SETD8 in MM cell lines results in the
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4 508 activation of a mature non-proliferating plasma cell signature and of the p53 canonical
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7 509 pathway (**Figure 3**). However, UNC-0379-induced cytotoxicity does not necessarily
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10 510 require p53 activation as p53 wild-type and deficient MM cells display similar sensitivity
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12 511 to SETD8 inhibition (**Figures 3 and 4**). **Indeed, we provide evidence that UNC-0379 is an**
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14 512 **inhibitor of nucleolar RNA synthesis independently of p53 activation (Figure 5)**. Finally,
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17 513 we have shown that UNC-0379 treatment leads to a significant lethal synergy with the
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19 514 DNA-damaging agent melphalan and can overcome the resistance associated with this
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22 515 cytotoxic drug in both p53 wild-type and deficient MM cells (**Figure 6**). Altogether, these
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24 516 results provide evidence for SETD8 inhibition as a potential novel therapeutic strategy in
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27 517 MM independently from the mutational p53 status of these tumors (**Figure 7**).

29 518 An up-regulation of SETD8 is not specific to MM, as it has also been observed in
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31 519 different types of solid tumors [11], such as papillary thyroid cancer [16], breast carcinoma
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34 520 [14, 48], and childhood tumors of the nervous system [15, 18]. However, the mechanisms
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36 521 that contribute to elevated levels of SETD8 in cancer still remained unclear. In
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39 522 neuroblastoma, a higher level of SETD8 could be due in part to DNA copy-number gains
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41 523 at chr12q24, the region that encompasses *SETD8* encoding gene²⁶. Another non-
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44 524 exclusive mechanism is related to the deregulation of oncogenic c-MYC pathway, since
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46 525 *SETD8* encoding gene has been found as a transcriptional target of c-MYC[49] and
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49 526 functionally required to mediate MYC-induced cell growth [15]. It is widely established that
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51 527 c-MYC is a key regulator in MM with deregulations related to translocations, gains and
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53 528 amplification, mutations in RAS genes and MYC transcription or translation activation [50].
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56 529 Interestingly, while chr12q24 gains are not present in myeloma, we identified here a
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58 530 significant enrichment of c-MYC/MAX target genes in MM patients characterized by high
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531 *SETD8* expression, thereby supporting a potential role of this oncogenic pathway in
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2 532 *SETD8* deregulation. Furthermore, *SETD8* depletion or inhibition results in up-regulation
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5 533 of genes repressed upon c-MYC expression (**Figure 3C**) suggesting that *SETD8* might
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7 534 also participate in deregulation of c-MYC functions in MM.

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10 535 A striking result of our study is that the up-regulation of *SETD8* in malignant plasma
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12 536 cells is not associated with visible changes in the global levels of the histone H4K20 mono-
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14 537 methylation (H4K20me1), the primary target of *SETD8* [8], although we cannot rule out
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17 538 that some local changes can occur at specific loci. This result is independent from cell-
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19 539 cycle progression, since changes in the levels of *SETD8* do not correlate with cell
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22 540 proliferation (**Figure 1B and Supplementary Figure S2**). One hypothesis is that the
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24 541 overexpression of the H4K20me1-specific demethylase PHF8, observed in many cancers
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26 542 including hematopoietic malignancies [51, 52], could attenuate the impact of *SETD8* up-
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29 543 regulation on histone H4K20 [53]. Nevertheless, H4K20me1 is critical in the maintenance
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31 544 of genome integrity [8] and its decrease upon UNC-0379 treatment would most likely
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34 545 contribute to the cytotoxic effects of this *SETD8* inhibitor in myeloma cells.

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36 546 Recent studies have suggested that the role of *SETD8* in cancer might also involve
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39 547 the methylation of other substrates than histone H4. Thus, Takawa et al. proposed that
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41 548 *SETD8* can methylate the proliferating cell nuclear antigen PCNA and thus favor HeLa
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44 549 cell proliferation [11]; but this result was never further confirmed in other cell types.
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46 550 Additionally, *SETD8* can induce the mono-methylation of the tumor suppressor p53 at
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49 551 lysine 382 (p53K382me1), which attenuates its pro-apoptotic and growth arrest functions
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51 552 [12, 18]. Hence, in neuroblastoma, inhibition of *SETD8* by UNC-0379 leads to cell death
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54 553 in a p53-dependent manner and p53K382me1 is important for this phenotype [18]. Our
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56 554 RNA-seq and functional studies in MM cells show that the genetic or pharmacological
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58 555 inhibition of *SETD8* leads to the activation of p53 conventional pathways, which correlates
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556 with an increased in p53 and p21 protein levels, and cell cycle arrest followed by cell
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2 557 death. However, in contrast to neuroblastoma [18], UNC-0379-induced cytotoxicity in MM
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5 558 cells is not necessarily dependent on p53 activation and, despite several attempts, we
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7 559 were unable to detect p53K382me1. Since the appearance of nucleolar stress or DNA
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10 560 damage is sufficient to activate p53 functions [54, 55] and occurs independently of p53
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12 561 upon UNC-0379 (**Figures 4 and 5**), we propose that the activation of p53 upon SETD8
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14 562 inhibition is mainly caused by these stress signals rather than the potential loss of SETD8-
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16 563 induced p53 methylation in MM cells. Since nucleolar dysfunction can lead to apoptosis
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18 564 without p53[44], the induction of these cellular stress prior to p53 activation provides an
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21 565 explanation of the cell-growth inhibition and apoptotic effects of UNC-0379 in p53-
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24 566 deficient cells. While the appearance of DNA damage might be related to SETD8
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26 567 functions in chromatin structure [50], the reasons of nucleolar alterations upon UNC-0379-
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29 568 mediated SETD8 inhibition remain unclear. Future work will be necessary to unravel the
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32 569 SETD8 nucleolar functions, which could be related to the apparent ability of SETD8 to
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34 570 interact directly with ribosomal proteins or regulate their expression[45, 46]. Altogether,
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36 571 our findings are consistent with a model in which UNC-0379-mediated cell death is
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39 572 triggered by multiple cellular stress signals followed by p53 activation in p53-proficient
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41 573 MM cells and deadly cell-cycle progression in absence of p53, thereby rendering multiple
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44 574 myeloma sensitive to SETD8 inhibition whatever the status of p53.

46 575 In spite of effective therapeutic protocols developed in MM, drug resistance
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49 576 remains a major concern. In this regard, we report here that high *SETD8* expression is
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51 577 associated with a poor prognosis in patients treated by high-dose of melphalan and
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53 578 autologous stem cell transplantation (**Figure 1**). *SETD8* expression is also significantly
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56 579 up-regulated in patients at relapse compared to newly diagnosed patients
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58 580 (**Supplementary Figure S3**). In agreement with this, UNC-0379 treatment potentiates the
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581 cytotoxicity of melphalan and overcomes melphalan drug resistance in MM cells,
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2 582 underlining the interest to target SETD8 to improve the treatment of MM patients.
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5 583 Deletion of the short arm of chromosome 17 (del 17p) is associated with a poor
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7 584 outcome in MM independently of treatment regimen [56–60]. Interestingly, MM cell toxicity
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9 585 mediated by SETD8 inhibitor is mainly p53-independent. The frequency of events
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11 586 targeting p53 (del 17p, *TP53* mutation or double hits) increases during the progression of
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13 587 MM and consecutive relapses underlining a selection of cells harboring *TP53*
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15 588 abnormalities in association with resistance to treatment. *TP53* bi-allelic events are also
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17 589 associated with a dramatic impact on MM patients' survival after relapse [61]. Therapies
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19 590 inducing significant toxicity of p53 defective-MM cells are needed. Our results
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21 591 demonstrate the therapeutic interest of SETD8 inhibitor to target p53 deficient MM cells
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23 592 by increasing replicative stress and DNA breaks. Accordingly, the use of this epigenetic
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25 593 drug in combination with cytotoxic agents, such as melphalan, could be of clinical interest,
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27 594 notably in newly diagnosed patients presenting del17p and/or *SETD8* overexpression and
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29 595 eligible to high dose melphalan and ASCT (**Figure 6**). Thus, SETD8 inhibition appears of
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31 596 therapeutic interest to overcome drug resistance and improve the treatment of MM
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33 597 patients at relapse independently of the p53 status.
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41 598 **Conclusion**

42 599
43 600 Our data reveal that the up-regulation of the histone H4K20 mono-methyltransferase
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45 601 SETD8 is associated with a poor prognosis and the deregulation of major signaling
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47 602 pathways in multiple myeloma patients. The inhibition of this enzyme leads to deadly
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49 603 cellular stress in multiple myeloma cells and a lethal synergy was identified when SETD8
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51 604 inhibition is combined with melphalan alkylating agent. Altogether, these results
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53 605 demonstrate that SETD8 is a novel epigenetic target in multiple myeloma and that its
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606 pharmacological inhibition could be beneficial in high-risk MM patients whatever their p53

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FIGURE LEGENDS

Figure 1. SETD8 expression is a prognosis value in MM. (A) SETD8 gene expression in BMPCs, patients' MMCs and HMCLs. Data are MAS5-normalized Affymetrix signals (U133 plus 2.0 microarrays). Statistical difference was assayed using a student t-test. **(B)** Immunoblot analysis of indicated proteins in total lysates from normal plasma cells, MMCs and HMCLs (XG1, XG7, XG25). β -actin and histone H4 were used as loading controls. **(C)** Overall survival and of newly diagnosed MM patients (UAMS-TT2, N=345; and UAMS-TT3, N=158) who's MMCs highly expressed *SETD8* gene. The splitting of the patients into two groups according to SETD8 expression in MMCs was done using the Maxstat algorithm.

Figure 2. SETD8 inhibitor UNC-0379 is highly toxic to malignant plasma cells. (A) Graphical representation of HMCLs viability upon exposure to various concentrations of UNC-0379. Color scale represents cell viability, from the highest (blue) to the lowest (red) values. The IC50 value of each tested HMCL is indicated. Data are mean values \pm standard deviation (SD) of five experiments determined on sextuplet culture wells. **(B)** The first bar graph results from the quantitation of cellcycle distribution of control (untreated) and UNC-0379-treated XG7 and XG25 HMCLs 48 hours after treatment. After short-pulse of BrdU incorporation, cellcycle was analyzed by FACS using DAPI and anti-BrdU antibody. Second bar graph represents the results from the quantitation of apoptosis in control and UNC-0379-treated XG7 and XG25 HMCLs by flow cytometry with AnnexinV-PE staining at 96h after UNC-0379 treatment. Data shown are mean values \pm SD of 4 separate experiments. Statistical analysis was done with a paired t-test. (*)

635 indicates a significant difference compared to control cells using a Wilcoxon test for pairs
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2 636 ($P \leq 0.05$). (C) Percentage of normal mature plasma cells (CD38+ CD138+) from two
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4 637 different donors and quantified by FACS after *in vitro* treatment with increasing
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6 638 concentrations of UNC-0379 or the vehicle DMSO at the highest concentration (MOCK)
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9 639 for 4 days. Samples were treated and analyzed in duplicates. (D) Percentage of *in vitro*
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11 640 cultivated primary MM cells (CD138+ tumor cells) and bone marrow microenvironment
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13 641 (CD138- non-malignant cells) upon increasing concentrations of UNC-0379 treatment for
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15 642 4 days. Data shown are mean values of 8 patient samples. (*) indicates a significant
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17 643 difference compared to control cells using a Wilcoxon test for pairs ($P \leq 0.05$).
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24 645 **Figure 3. Gene expression changes in HMCLs upon genetic or pharmacological**
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26 646 **inhibition of SETD8. (A)** Diagram of the experimental plan. **(B)** Molecular signatures of
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28 647 UNC-0379 and shSETD8 downregulated (blue bar plot) and up-regulated (red bar plot)
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30 648 genes compared to control were investigated using GSEA Database (all curated gene
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32 649 sets), and relevant pathways are presented (FDR q-value ≤ 0.05). **(C)** Immunoblot
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34 650 analysis of indicated proteins in total lysates from UNC-0379-treated or untreated XG7
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36 651 HMCL. β -actin and H2A.X were used as loading controls.
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43 653 **Figure 4. UNC-0379 toxicity is independent of p53. (A)** Comparison of UNC-0379 IC₅₀
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45 654 (μ M) according to HMCLs *TP53* status. **(B)** Immunoblot analysis of indicated proteins in
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47 655 total lysates from UNC-0379-treated (5 μ M) or untreated XG7-shControl and XG7-shp53
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49 656 HMCLs. β -actin and H2A.X were used as loading controls. **(C)** First bar plot represents
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51 657 cell cycle of control and 48h UNC-0379-treated (5 μ M) XG7-shp53 analyzed by flow
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53 658 cytometry using DAPI, BrdU incorporation and labelling with an anti-BrdU antibody.
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55 659 Results are representative of three independent experiments. Second bar plot represents
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660 apoptosis induction in control and UNC-0379-treated (5 μ M) XG7-shControl and XG7-
661 shp53 analyzed by AnnexinV-PE staining and flow cytometry after 96h treatment. Data
662 shown are mean values \pm SD of 4 separate experiments. Statistical analysis was done
663 with a paired t-test. * indicates a significant difference compared to control cells using a
664 Wilcoxon test for pairs ($P \leq 0.05$).

Figure 5: UNC-0379 treatment causes similar nucleolar alterations in wild-type and p53 depleted-myeloma cells. (A) immunofluorescence microscopy of nucleolin localization and DNA (DAPI staining) in XG7 cells depleted or not for p53 and treated with 3 μ M of UNC-0379 or the vehicle DMSO (mock) for 24 hours. Scale bar: 10 μ m. Visual quantification of percentage of cells with nucleolin diffusion out of the nucleolus. A minimum of 300 cells were quantified per condition. N = 3. Statistical significance between conditions was assessed using Student paired t-test (*: pvalue<0.05, ** pvalue<0.01, ns: not significant). **(B)** Analysis of RNA synthesis by 5 minutes 5-Ethynyl Uridine (EU) pulse-labeling in XG7 cells depleted or not for p53 and treated with 3 μ M of UNC-0379 or the vehicle DMSO (mock) for 24 hours. Scale bar: 10 μ m. EU intensity was quantified using CellProfiler "Human cell" pipeline. A minimum of 200 cells were quantified per condition. Graph shows the quantification of one representative experiment of 3.

Figure 6: UNC-0379 treatment sensitizes HMCLs to Melphalan-induced DNA damage. (A) Dose-response matrix inhibition and landscape representation for experimentally measured drug synergy in XG7 cells treated with increased concentration of the combination of melphalan and SETD8 inhibitor (UNC-0379). Synergy scores are displayed using a continuous pseudo-color scale ranging from dark-green=antagonistic to dark-red=synergistic **(B)** Landscape and 3-D matrix representation for experimentally

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685 measured drug synergy in XG1 cells. **(C)** Number of 53BP1 foci in XG7 and XG1 HMCLs,
686 treated with melphalan (3 μ M), UNC-0379 (3 μ M) or the combination of the two drugs for
687 6h or 24h as indicated. Number of foci per cell was quantified using ImageJ software
688 (mean number of cells counted: 300). Statistical significance between conditions was
689 assessed using Student paired t-test (*: pvalue<0.05). **(D)** Measure of 53BP1 foci in
690 melphalan-resistant XG7 cells treated with melphalan (15 μ M), UNC-0379 (3 μ M) or the
691 combination of the two drugs for 24h. Number of foci per cell was quantified using ImageJ
692 software (mean number of cells counted: 300). Statistical significance between conditions
693 was assessed using Student paired t-test (*: pvalue<0.05). **(E)** Measure of AnnexinV-
694 positive cells in the same drug concentrations as in D. AnnexinV-PE staining was
695 analyzed by flow cytometry 96h after drug treatment. Statistical significance between
696 conditions was assessed using Student paired t-test (*: pvalue<0.05).

Figure 7: SETD8 inhibition is of therapeutic interest in MM independently of p53 status and could overcome melphalan resistance. High *SETD8* expression is associated with a poor outcome in MM and represent a therapeutic target independently of p53 status. In p53 WT patients SETD8 inhibition results in MM cell cytotoxicity mediated by p53 pathway activation. In p53 deficient MM cells, SETD8 inhibition increases replicative stress in association with MM cell death. Furthermore, SETD8 inhibition overcomes melphalan resistance in MM.

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718 **Author contributions**

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721 EJ and JM designed the project, supervised the research, and wrote the paper. LH, FI,
722 EJ and SO designed, performed the research and analyzed the data. LH and SO
723 contributed to paper writing. OKC, CG, CB participated to the research. LV and GC
724 participated to clinical data analysis. AM and JJ contributed to design and production of
725 SETD8 inhibitor. ED and EDB contributed to experiments with primary murine models.

727 **Conflict of interest**

728 The authors declare that they have no competing interests.

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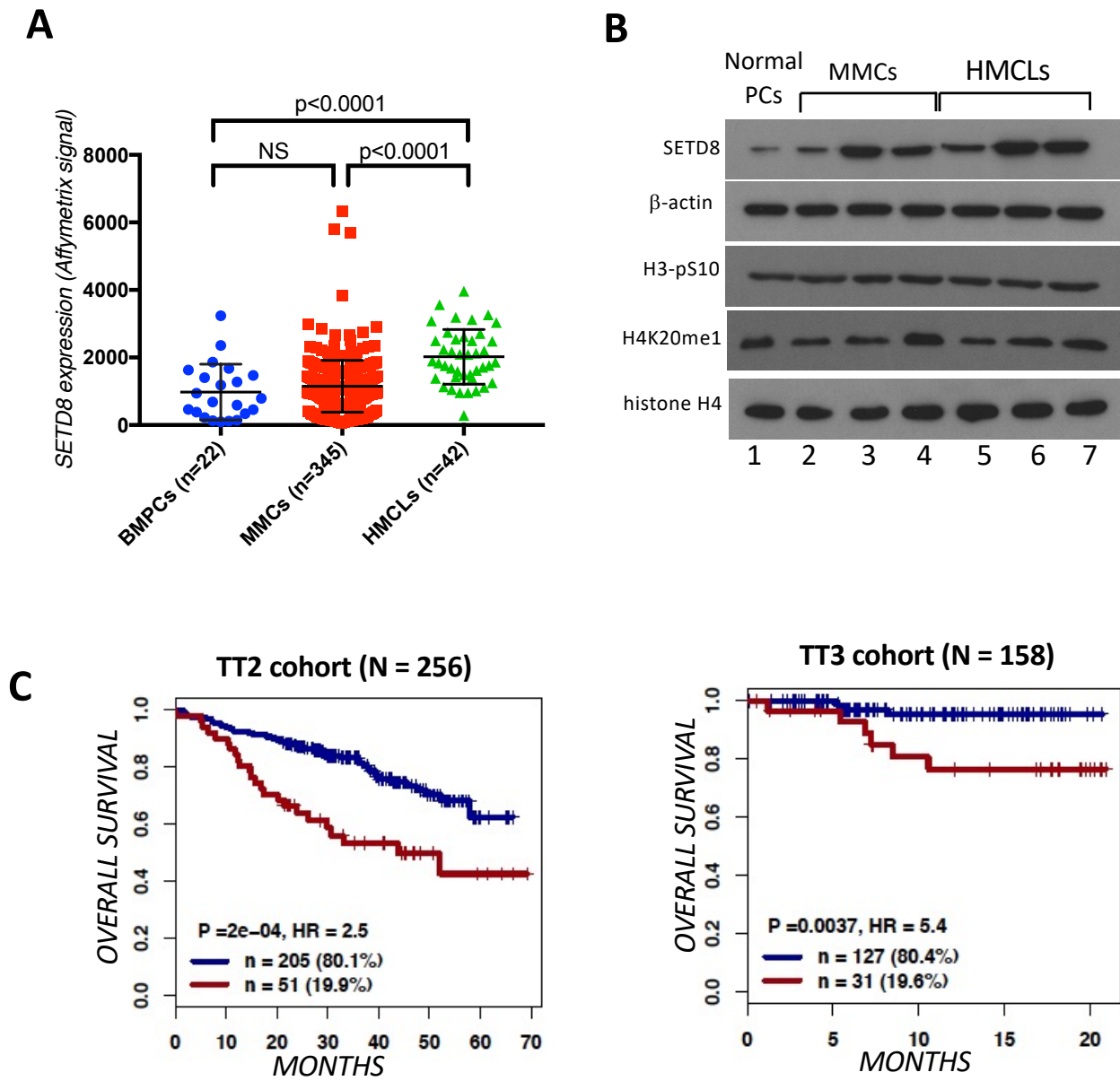


Figure 1 (Hervioui et al.)

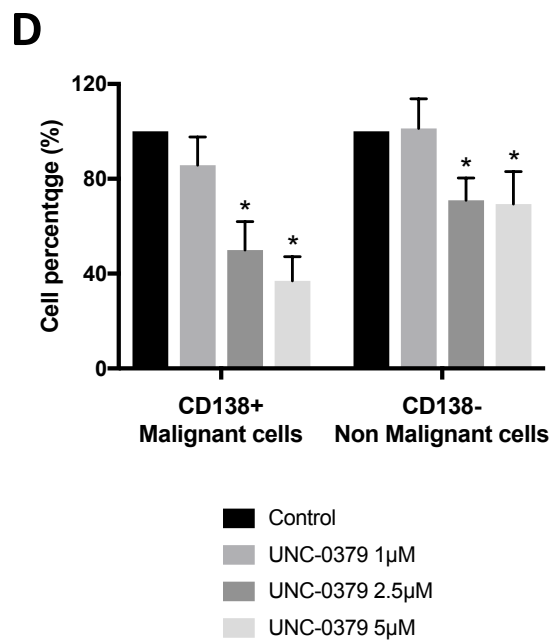
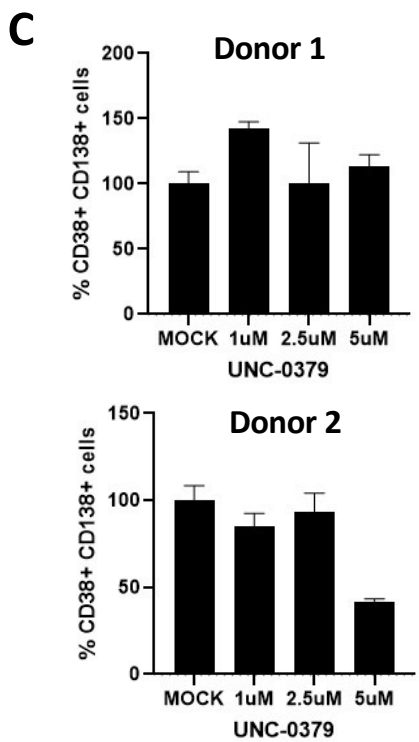
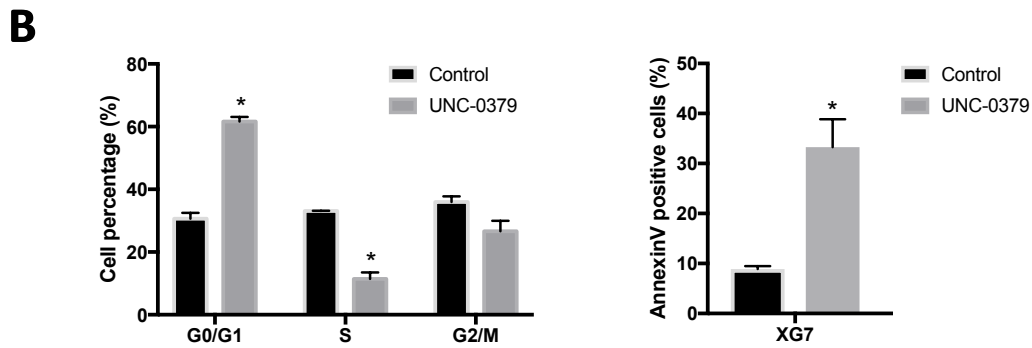
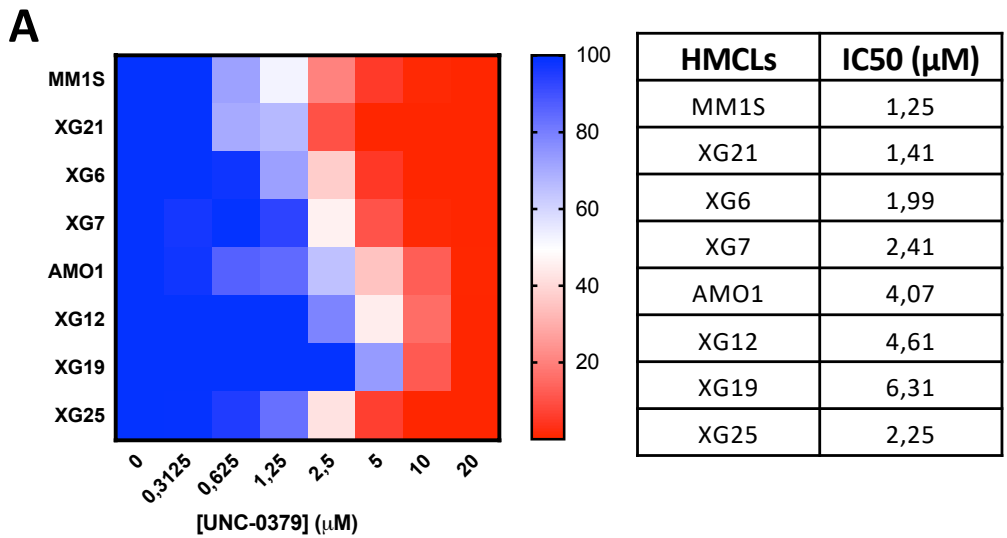


Figure 2 (Herviou et al.)

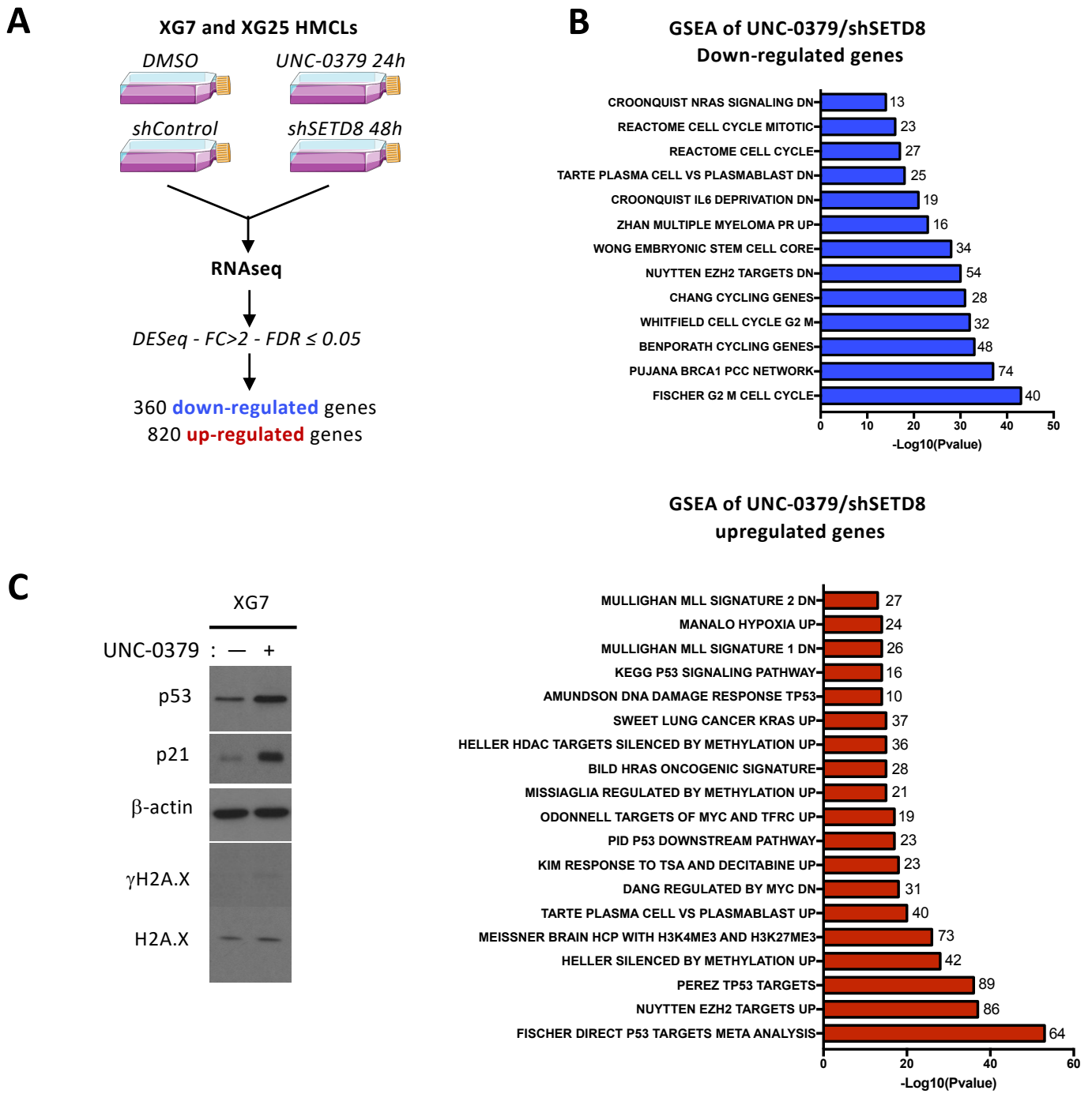


Figure 3 (Herviou et al.)

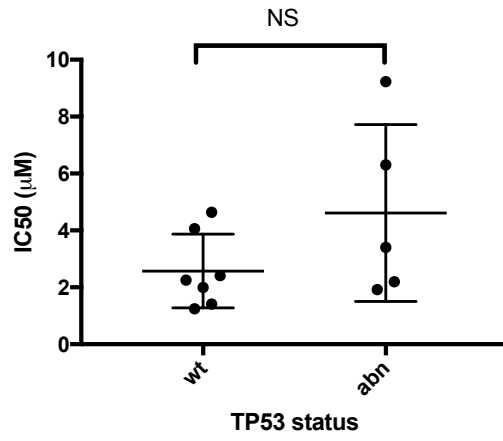
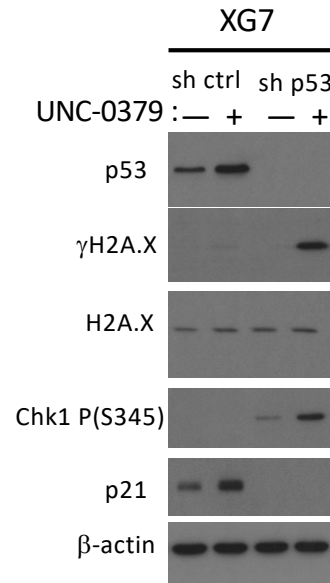
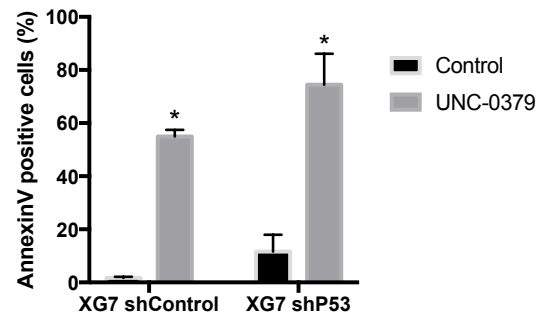
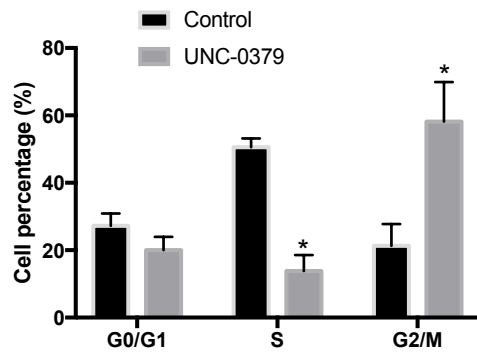
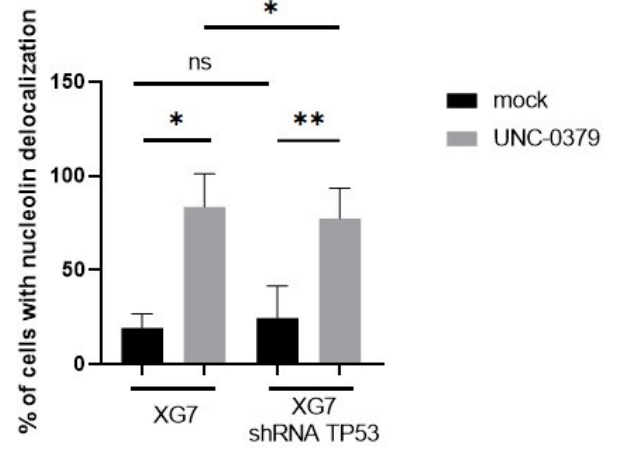
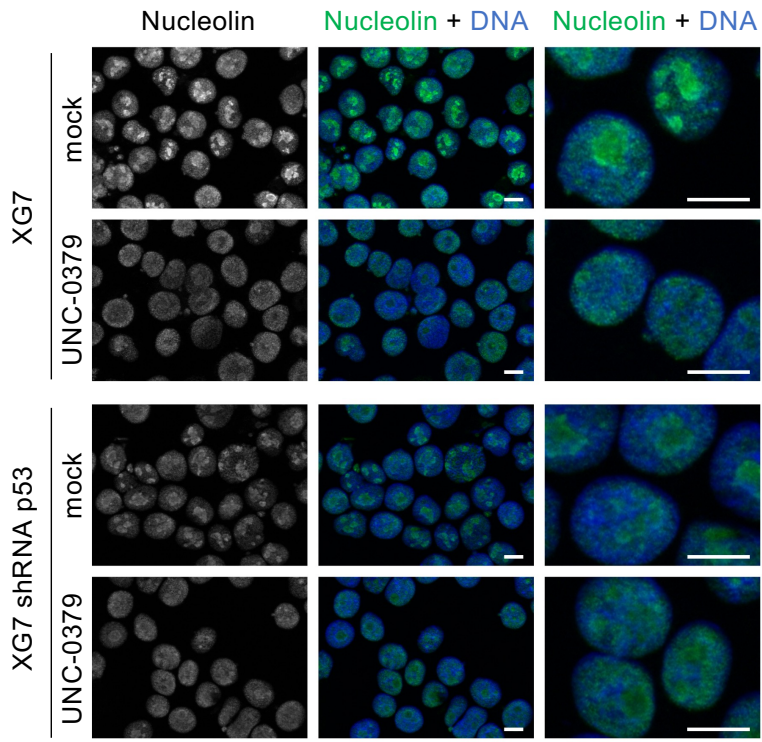
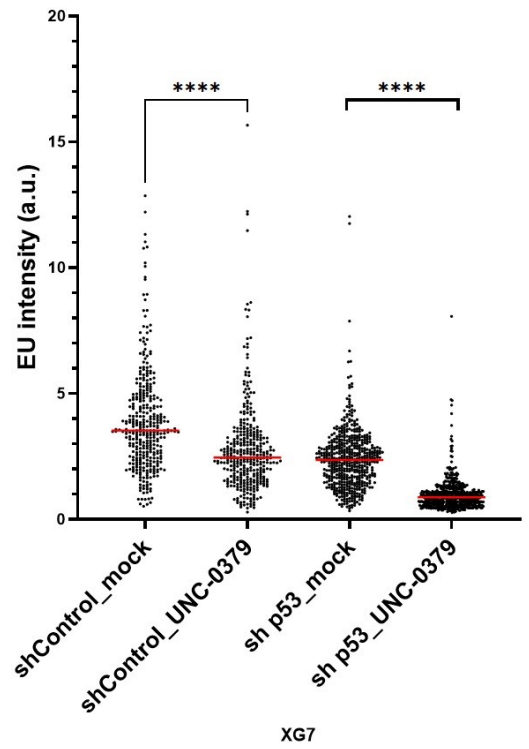
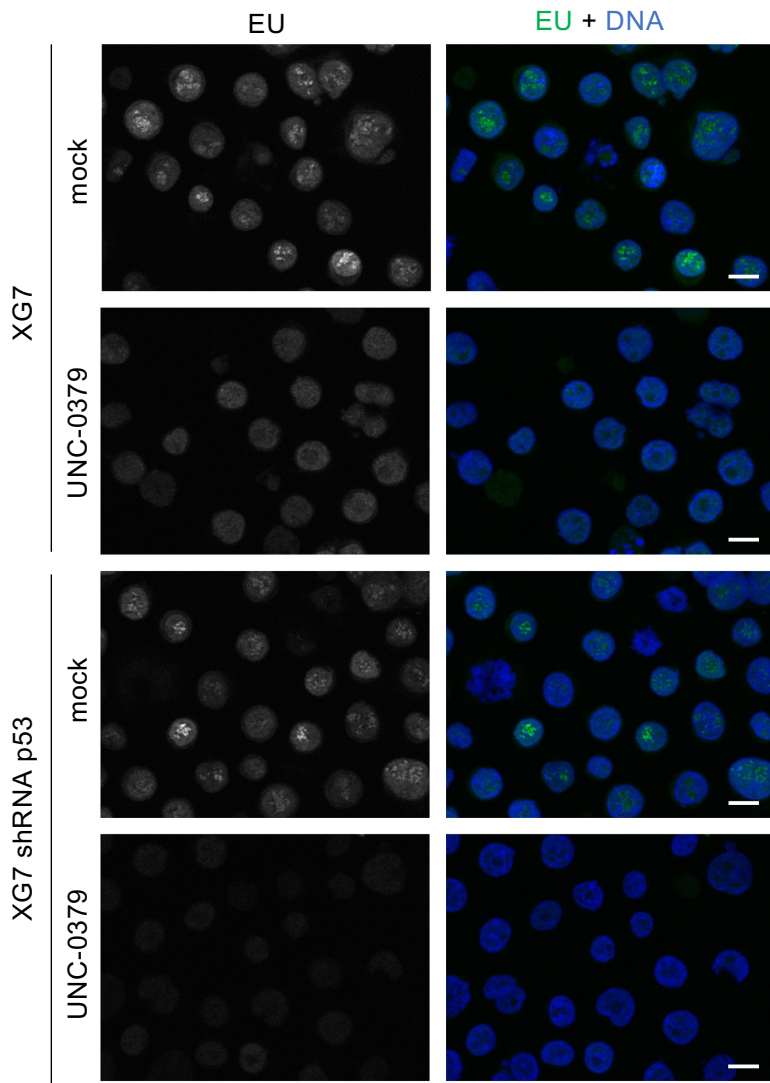
A**B****C**

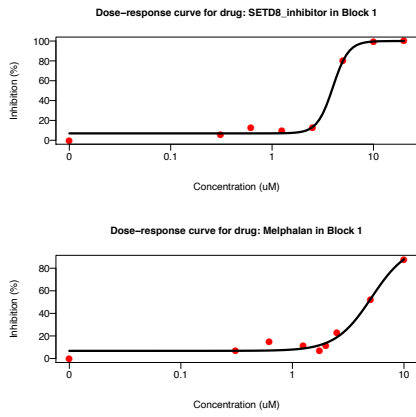
Figure 4 (Herviou et al.)

A**B**

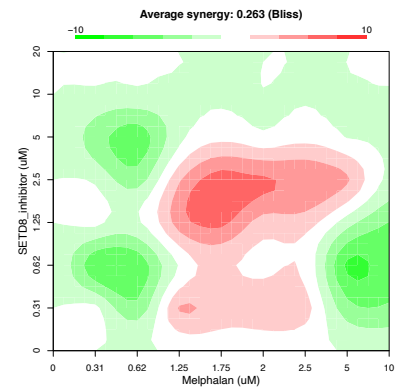
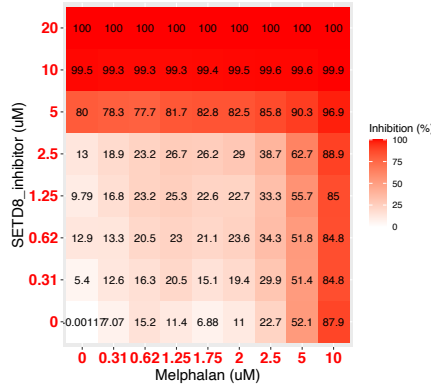
New Figure 5 (Herviou et al.)

A

XG7

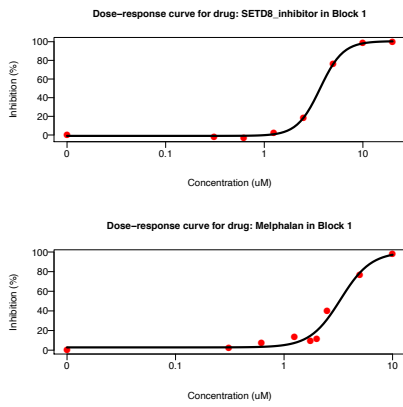


Dose-response matrix (inhibition)
BlockID: 1

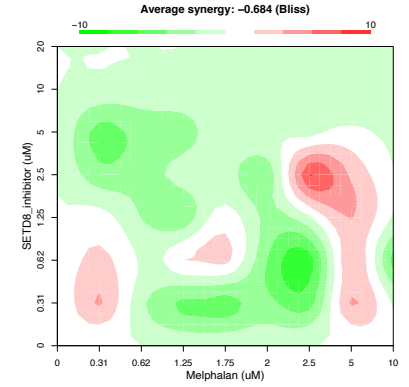
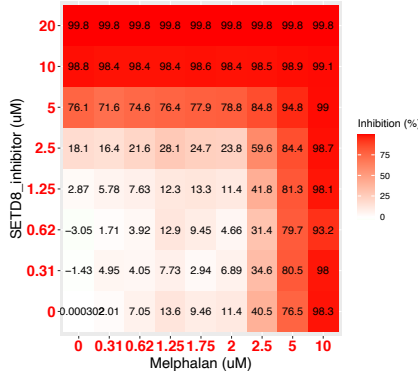


B

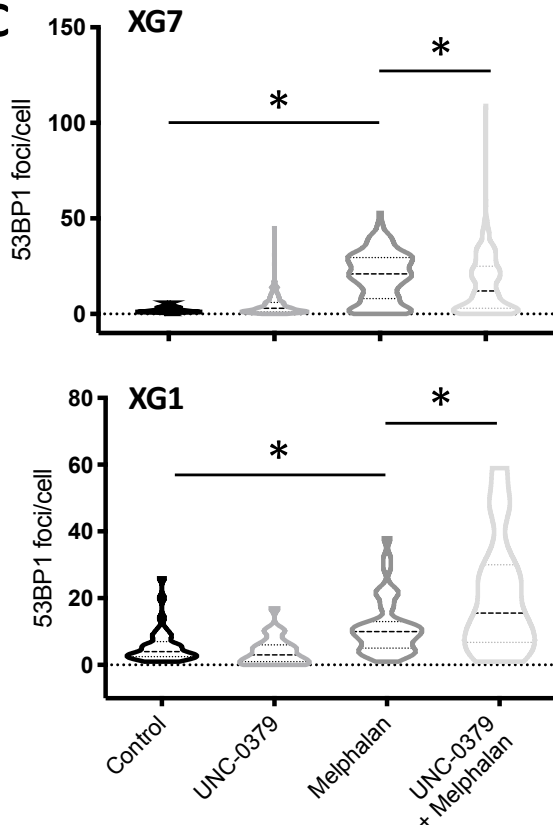
XG1



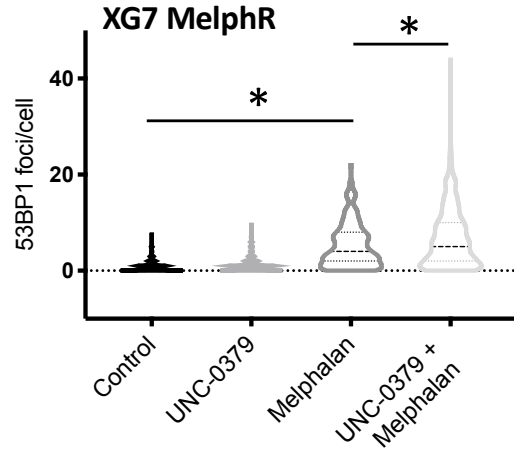
Dose-response matrix (inhibition)
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C



D



E

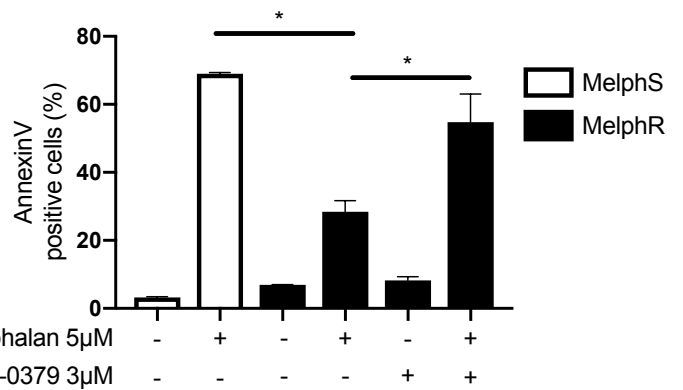


Figure 6 (Herviou et al.)

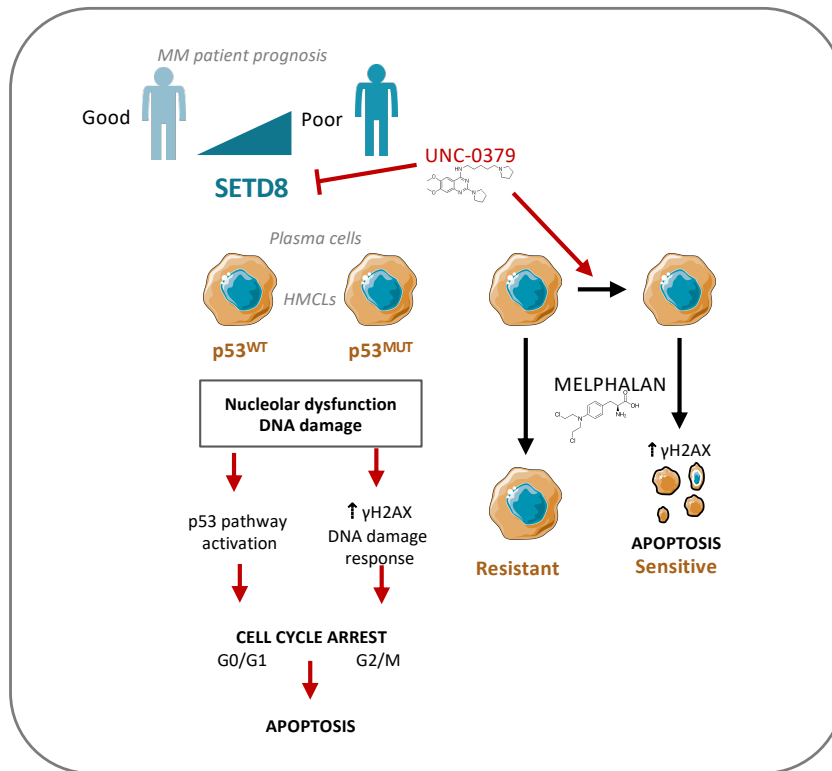


Figure 7 (Herviou et al.)



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To Clinical Epigenetics Editorial Office

Re : CLEP-D-20-00523

Montpellier 23rd April 2021

Dear Dr. LICHT,

Please find the revised version of the manuscript **CLEP-D-20-00523** entitled "Targeting the methyltransferase SETD8 impairs tumor cell survival and overcomes drug resistance independently of p53 status in multiple myeloma". We have performed several additional experiments in order to address all the issues raised by the reviewers. Notably, as requested, we provide additional mechanistic information underlining how SETD8 inhibitor is working in myeloma cells. Regardless of the status of p53 and in addition to induce DNA damage, we now reveal that the treatment of malignant myeloma cells with the SETD8 inhibitor triggers a specific nucleolar stress characterized by the delocalization of the pool of Nucleolin and a strong decrease in nucleolar RNA synthesis.

We thank the reviewers for their valuable comments. Please find our point-by-point response below:

Reviewer 1

Overall the studies are relatively clear and straightforward, however it remains unclear what the mechanism by which SETD8 inhibition results in cell death. The authors have ruled out changes in total H4K20me so its not clear how they can conclude that gene expression changes are direct effects of SETD8 inhibition. It seems equally plausible that they are changes that are associated with any event that would result in decreased proliferation. They authors also ruled out TP53. So why do the cells stop growing and die?

Regarding the concern raised by reviewer 1, we have performed additional experiments shown in a new figure 5. The obtained results indicate that, in addition to induce DNA damage, the SETD8 inhibitor leads to a nucleolar dysfunction, in myeloma cells, independently of the p53 status. This nucleolar impairment is notably

characterized by the delocalization of the nucleolin and a strong decrease in nucleolar RNA synthesis, which are known to contribute to growth inhibition and cell death regardless of the p53 status (see James A et al., 2014 Nucleus, 402-426). These data have been included in the manuscript lines 492 to 523.

SETD8 inhibition is SET8 up-regulation in multiple myeloma is not associated with global changes in H4K20me1 levels. However, we cannot exclude that some local changes can occur. Since H4K20me1 is critical for the maintenance of genome integrity, the loss of H4K20me1 upon UNC0379 treatment may also impact cell proliferation and survival. We clarify this point in the discussion section (lines 626 to 641). Regarding gene expression changes upon SETD8 inhibition and as indicated in lanes 424 to 427, RNAseq analysis after SETD8 inhibition was performed when H4K20me1 was reduced but before the appearance of cell-proliferation defects in order to minimize gene expression changes resulting indirectly from proliferation decreased.

Reviewer 2.

1- In line 318, the authors stated that malignant plasma cells are particularly addicted to SETD8 activity. The conclusion was driven by the increased toxicity of the inhibitor in CD138+ cells. The authors did not compare cytotoxicity between malignant plasma cells and normal plasma cells isolated from healthy donors. Thus, the authors cannot rule out preferential cytotoxicity towards mature plasma cells regardless of their malignant status.

As requested by reviewer 2, we now compare the cytotoxicity of the SETD8 inhibitor between malignant plasma cells and normal plasma cells from healthy donors. We also examine the cytotoxicity of the inhibitor in normal plasma cells generated *in vitro* by differentiation of memory B cells. These new results are described in lines 396 to 410 and shown in Figure 2C and supplementary Figure S5. We demonstrated that SETD8 inhibition is toxic for malignant plasma cells and not to normal ones.

2- The authors need to compare melphalan sensitivity between SETD8 knockdown and control cells to confirm that the synergistic effect of the inhibitor with melphalan is due to SETD8 inhibition.

As suggested by reviewer 2, we used a doxycycline-inducible shRNA lentiviral vector to silence SETD8 expression in XG7 cells and we measured melphalan sensitivity between SETD8 depleted and control cells. The results are shown in new

supplementary Figure 12A-C and described in lanes 534 to 540. We validated that SETD8 depletion sensitizes MM cells to melphalan toxicity.

3- In figure 5E, I think that the melphalan and UNC-0379 label colors are switched?! The cells should be resistant to melphalan not UNC-0379.

To avoid confusion, we modified the panel of Figure 6E (previously Figure 5E) and added the percentage of annexin-positive cells in the sensitive cell line treated with melphalan. Thus, we can clearly observe the therapeutic interest of SETD8 inhibition to overcome Melphalan resistance in the XG7 MeIR cell line.

4- Did the authors observe an increase in SETD8 levels in melphalan-resistant cells? Such an observation would support the evidence that SETD8 inhibition increases melphalan sensitivity.

By performing RT-qPCR and immunoblots, a significant increase in SETD8 expression was not observed in melphalan resistant cells. We did not include these results in the revised manuscript.

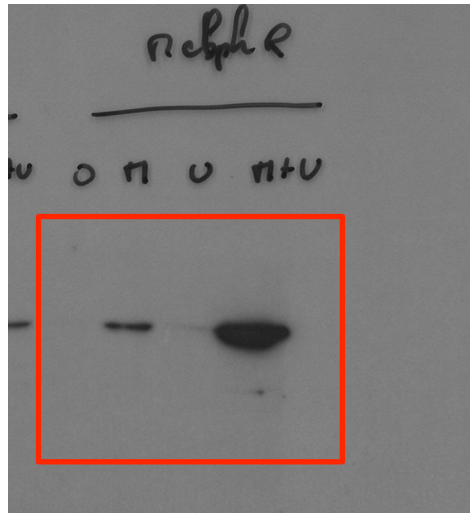
We have answered all comments and we hope that our manuscript could be published in Clinical Epigenetics.

With our best regards,

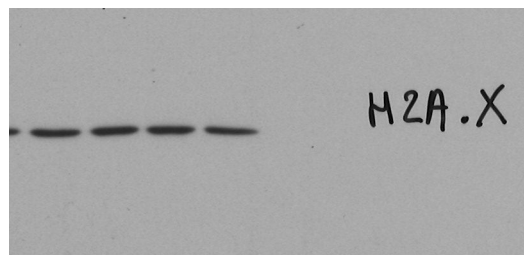
Eric JULIEN and Jérôme MOREAUX

RAW DATA FIGURE S11 (Herviou et al.)

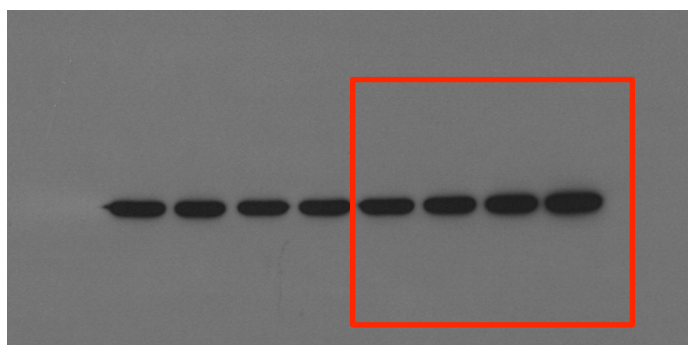
Gamma H2A.X



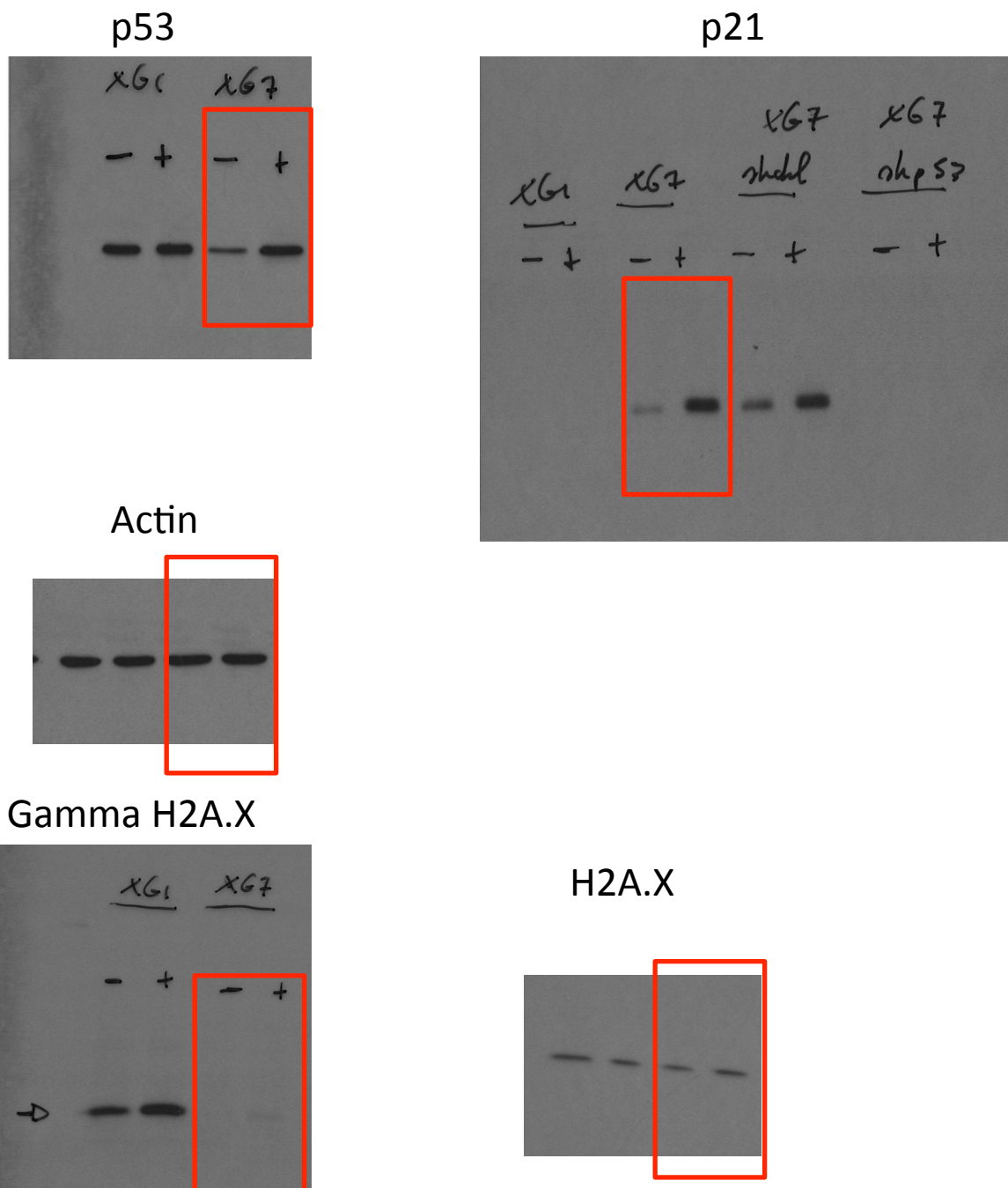
H2A.X



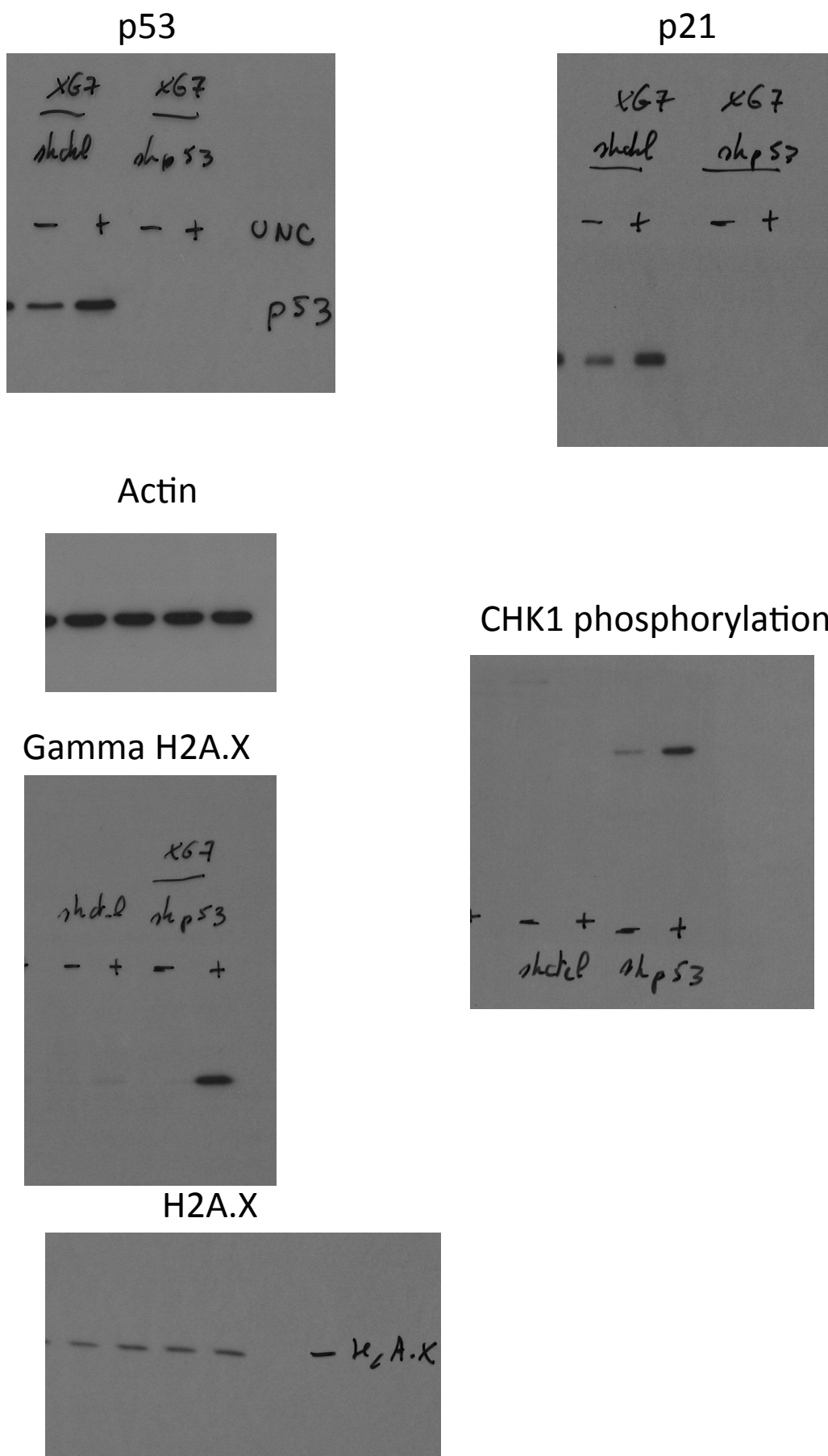
Actin



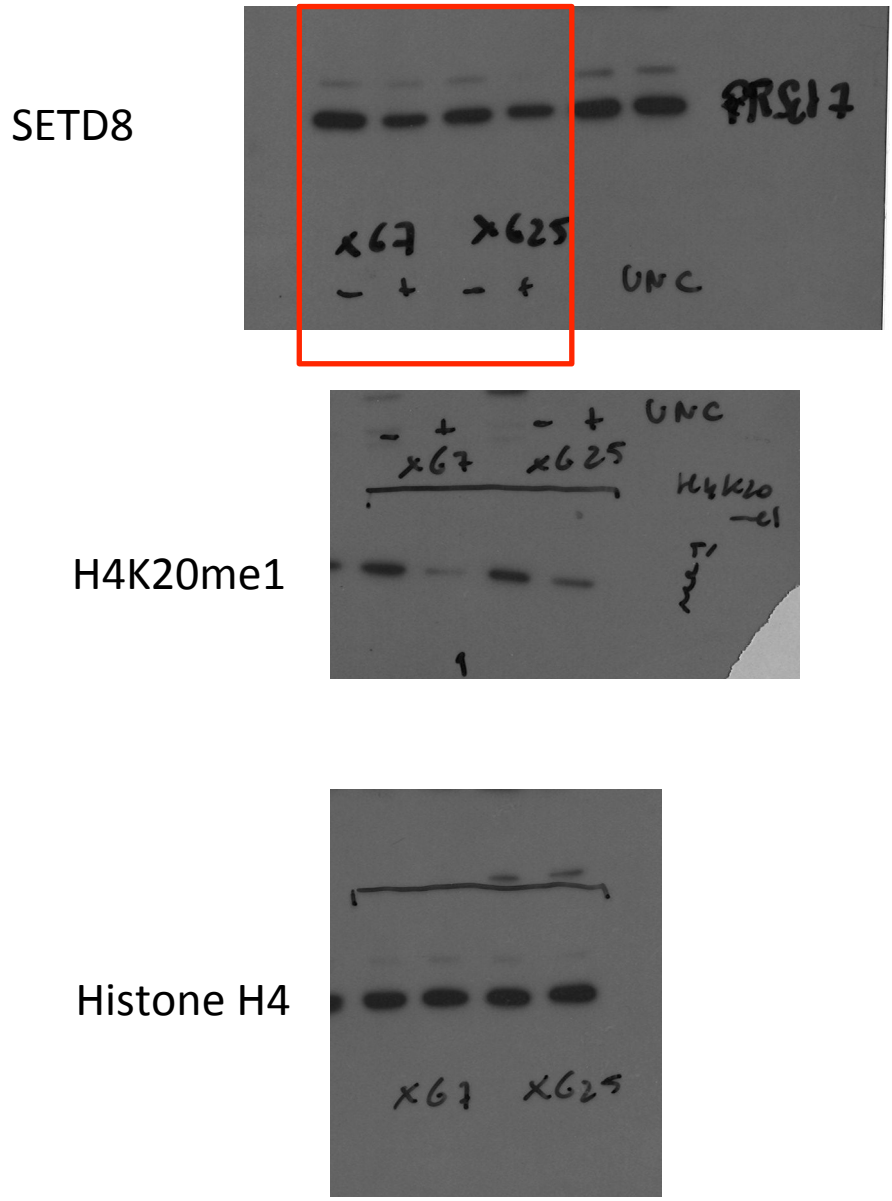
RAW DATA FIGURE 3C (Herviou et al.)



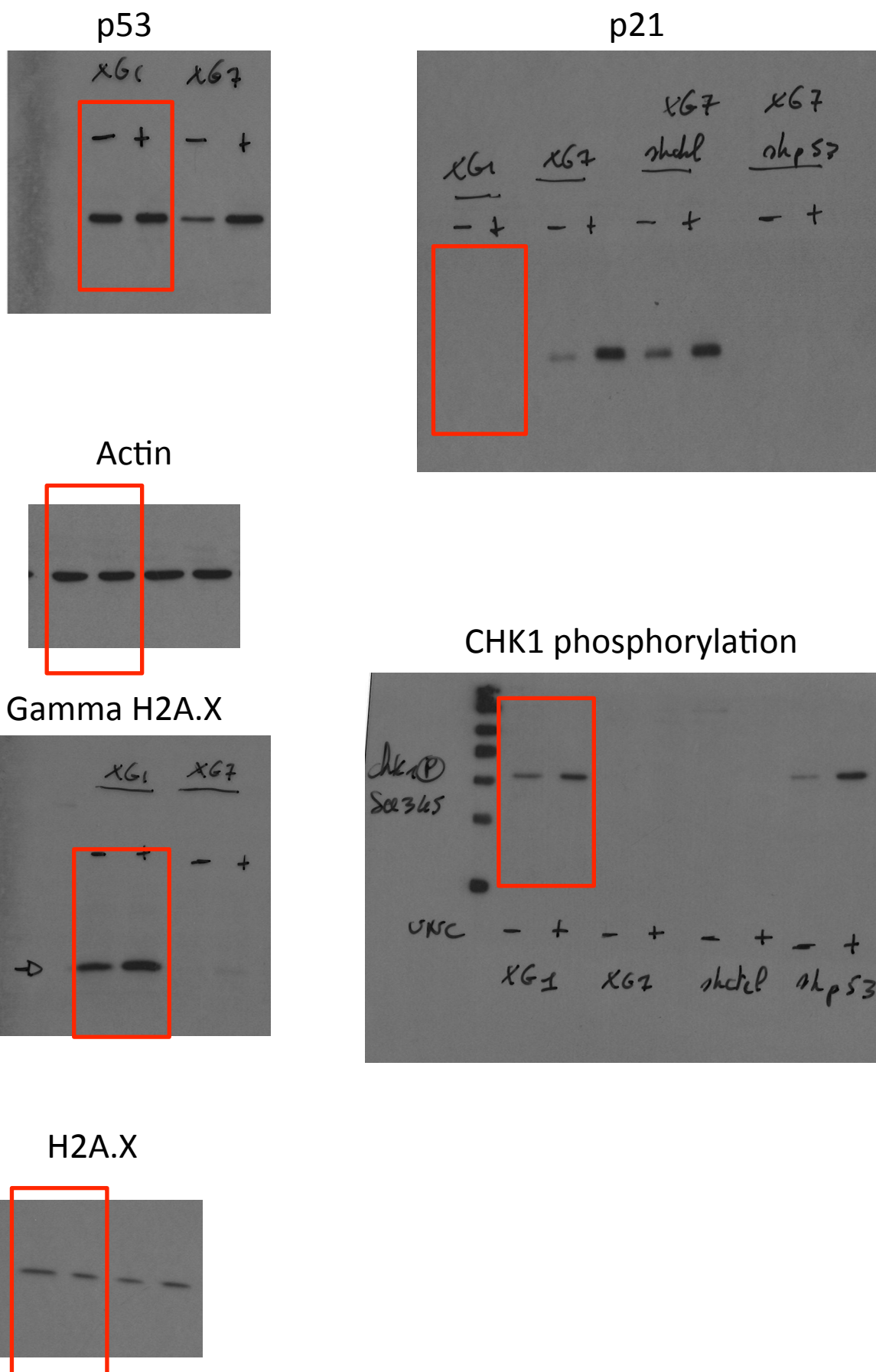
RAW DATA FIGURE 4B (Herviou et al.)



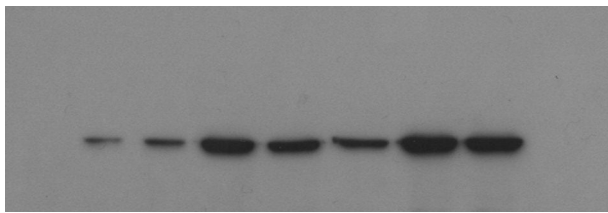
RAW DATA FIGURE S4 (Herviou et al.)



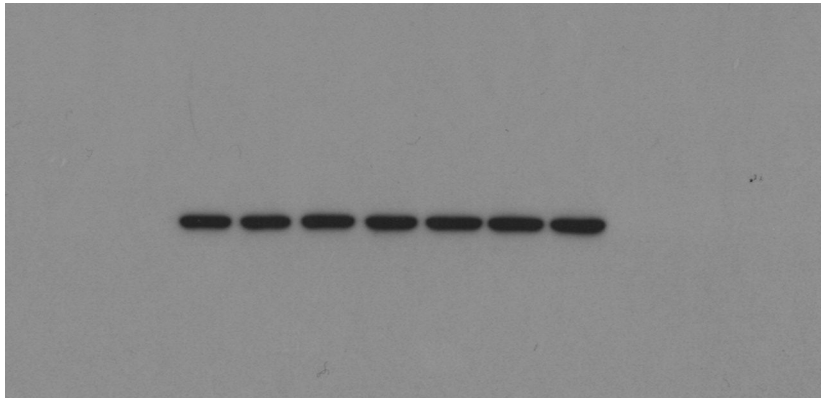
RAW DATA FIGURE S9 (Herviou et al.)



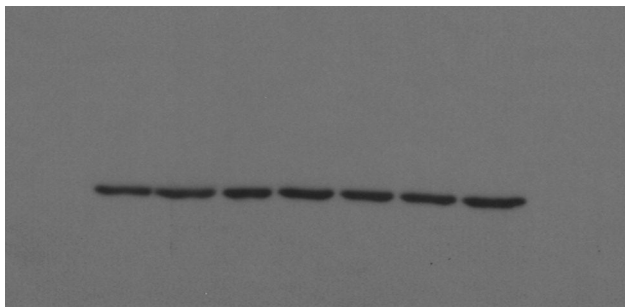
RAW DATA FIGURE 1B (Herviou et al.)



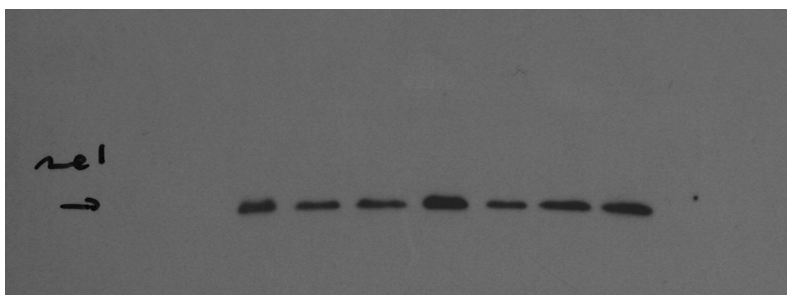
SETD8



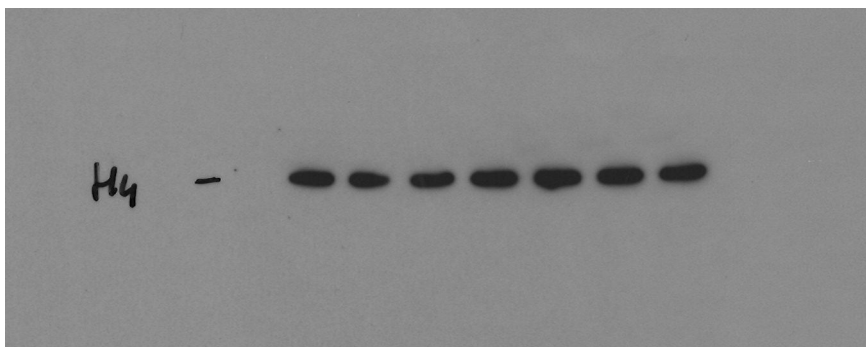
Actin



h3S10 P



H4K20me1



Histone H4