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1 **Title**

2 **Haploinsufficiency of the mouse *Tshz3* gene leads to kidney defects**

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28

29 **Abstract**

30 Renal tract defects and autism spectrum disorder (ASD) deficits represent the phenotypic
31 core of the 19q12 deletion syndrome caused by the loss of one copy of the *TSHZ3* gene.
32 While a proportion of *Tshz3* heterozygous (*Tshz3^{+/-lacZ}*) mice display ureteral defects, no
33 kidney defects have been reported in these mice. The purpose of this study was to
34 characterize the expression of *Tshz3* in adult kidney as well as the renal consequences of
35 embryonic haploinsufficiency of *Tshz3* by analyzing the morphology and function of
36 *Tshz3* heterozygous adult kidney. Here, we described *Tshz3* expression in the smooth
37 muscle and stromal cells lining the renal pelvis, the papilla and glomerular endothelial
38 cells (GENCs) of the adult kidney as well as in the proximal nephron tubules in neonatal
39 mice. Histological analysis showed that *Tshz3^{+/-lacZ}* adult kidney had an average of 29%
40 fewer glomeruli than wild type kidney. Transmission electron microscopy (TEM) of
41 *Tshz3^{+/-lacZ}* glomeruli revealed a reduced thickness of the glomerular basement membrane
42 and a larger foot process width. Compared to wild type, *Tshz3^{+/-lacZ}* mice showed lower
43 blood urea, phosphates, magnesium and potassium at 2 months of age. At the molecular
44 level, transcriptome analysis identified differentially expressed genes related to
45 inflammatory processes in *Tshz3^{+/-lacZ}* compare to wild type (WT; control) adult kidneys.
46 Lastly, analysis of the urinary peptidome revealed 33 peptides associated with *Tshz3^{+/-lacZ}*
47 adult mice. These results provide the first evidence that in the mouse *Tshz3*
48 haploinsufficiency leads to cellular, molecular and functional abnormalities in the adult
49 mouse kidney.

50 **Introduction**

51 Congenital anomalies of the kidneys and urinary tract (CAKUT) are the most common
52 cause of renal failure in children (1). Ureteropelvic junction obstruction (UPJO), the most

53 common paediatric renal obstructive disorder, has an incidence of 1 in 1000-1500 live
54 births screened by antenatal ultrasound (2). Congenital UPJO is usually caused by the
55 presence of an aperistaltic segment of the ureter, preventing the efficient transport of the
56 urine from the kidney to the bladder. UPJO can result from the decrease in the number of
57 smooth muscle cells, interstitial Cajal-like cells and nerve fibers in the ureteropelvic
58 junction. Therefore, impaired transport of urine can lead to an increase in back-pressure
59 on the kidney, hydronephrosis, and progressive damage to the kidney function (3).

60 The *TSHZ3* gene (Teashirt zinc-finger homeobox family member 3; also known as
61 *ZNF537*), which encodes a zinc-finger transcription factor, was recently identified as the
62 critical region for a 19q12 deletion syndrome (19q12DS): patients with *TSHZ3*
63 heterozygous deletion show lower (i.e. vesicoureteral reflux grade 2) and upper (i.e.
64 UPJO) urinary tract defects as well as kidney (i.e. hydronephrosis and nephrolithiasis)
65 defects(4).

66 *Tshz3* homozygous mutant mice (*Tshz3^{lacZ/lacZ}*) have been used to explore the
67 pathogenesis of *Tshz3* in UPJO (5, 6). Studies have shown that from embryonic day (E)
68 12.5 onwards TSHZ3 positive cells are detected in the mouse ureter and the kidney (5).
69 In the embryo, *Tshz3* plays a key role in smooth muscle differentiation by regulating
70 *Myocardin* (*myocd*) expression and MYOCD activity (5, 6). *Tshz3^{lacZ/lacZ}* mutant mice die
71 perinatally because of their inability to breathe and display bilateral UPJO and
72 hydronephrosis (5, 7). In comparison, one-fourth of *Tshz3^{+ / lacZ}* heterozygous embryos
73 display a unilateral UPJO and hydronephrosis and about 50% die at birth (5-7). However,
74 the impact of *Tshz3* haploinsufficiency on the postnatal kidneys has never been
75 investigated so far.

76 Therefore, the main aim of this study was to determine whether *Tshz3* heterozygote mice
77 exhibit kidney defects in order to gain insights on whether haploinsufficiency may help
78 explaining kidney diseases reported in patients with heterozygous deletion of *TSHZ3*.

79

80 **Results**

81 **TSHZ3 expression in adult kidneys.**

82 Previous analyses performed during development indicate that the temporal and spatial
83 distribution of β -galactosidase (β -gal) protein in *Tshz3^{+lacZ}* mice faithfully reproduces the
84 expression of *Tshz3*/TSHZ3 (5, 6). Here we used the same approach to characterize the
85 expression of *Tshz3*/TSHZ3 in sections of *Tshz3^{+lacZ}* adult kidneys. X-Gal staining
86 performed on *Tshz3^{+lacZ}* adult kidney revealed that *Tshz3* is expressed in the pelvic region
87 and ureter, the papilla, perivascular region and the glomeruli (**Fig. 1A-F**). To further
88 characterize the expression of TSHZ3 in the glomeruli, we performed immunostaining,
89 using glomerular cells markers. These analyses showed that β -gal positive cells were
90 endothelial cell (CD31-positive) but not podocytes (Dachshund 1 positive) or mesangial
91 cells (NG2 positive) (**Fig. 1G-I**). In one-week old postnatal *Tshz3^{+lacZ}* mouse kidneys,
92 TSHZ3 was detected in the tufts of maturing glomeruli and in nuclei of thin tubule-like
93 structures in the kidney cortex (**Fig. 2A**). Subsets of tubule-like profiles also
94 immunostained for TSHZ3 in the outer medulla and the inner medulla (**Fig. 2A-C**).
95 Comparison with immunostaining patterns for aquaporin-1, uromodulin and calbindin-
96 28 (**Fig. 2D-L**), suggest that thin descending limbs of loops of Henle express TSHZ3
97 because patterns for this protein and aquaporin-1 are similar in the thin tubules within the
98 inner medulla. In this location, calbinin-28 positive collecting ducts are wider diameter
99 and uromodulin is not detected. The TSHZ3 positive tubules in the cortex and outer
100 medulla may also include the pars recta, or straight section, of the aquaporin-1 positive

101 proximal tubules. The tubule signals for TSHZ3 appeared attenuated in adult kidneys into
102 which we did not observe any major morphological changes (data not shown).
103 Double immunostaining for β -gal and Smooth muscle alpha-actin (SMAA) confirmed the
104 expression of TSHZ3 in smooth muscle cells in the pelvic region and in SMA-negative
105 Dachshund 1-positive stromal cells lining the urothelium (**Fig. 3**).

106

107 ***Tshz3*^{+/*lacZ*} mice showed glomerular defects.**

108 Comparison of 8-week-old adult kidney histology revealed a decrease of 28.8% in
109 glomerular density in *Tshz3*^{+/*lacZ*} compared to WT (**Fig. 4A, B and supplementary Fig.**
110 **4**). The same analysis performed with 40-week-old adult kidneys revealed a 44.2%
111 reduction of glomerular density in *Tshz3*^{+/*lacZ*} vs. WT. In order to identify glomerular
112 morphological changes in *Tshz3*^{+/*lacZ*} mice, we conducted an ultrastructural analysis using
113 transmission electron microscopy (TEM). While this analysis did not identify a
114 significant variation of the proportion of the size of the fenestration and endothelial layer
115 (**Fig. 4C, D**), it revealed a significant reduction of the thickness of the glomerular
116 basement membrane (GBM) in glomeruli of *Tshz3*^{+/*lacZ*} mutants (144.2 ± 4.2 nm)
117 compared to WT (155.1 ± 3.32 nm) (**Fig. 4E, F**). TEM analysis also showed that in the
118 *Tshz3*^{+/*lacZ*} kidneys the foot processes were effaced, reflected by a foot process width
119 (FPW) of 351.7 ± 5.03 nm, $\approx 14\%$ larger ($P < 0.0001$) than in the WT kidneys ($303.4 \pm$
120 6.57 nm) (**Fig. 4G, H**).

121 **Blood electrolytes are modified in *Tshz3*^{+/*lacZ*} mice.**

122 To characterize the effects of *Tshz3* haploinsufficiency on kidney filtration, we performed
123 biochemical measurements on blood samples and generated biochemical profiles for
124 *Tshz3*^{+/*lacZ*} and WT adult mice tested at 58-64 days-of-age. Blood analysis demonstrated
125 that *Tshz3*^{+/*lacZ*} mice have significant reduction of the urea ($P < 0.013$), phosphates

126 (P<0.011), magnesium (P<0.014), potassium (P<0.0034) as well as an increased
127 concentration of sodium (P <0.012) (**Fig. 5; Table 1a**). We found no significant variation
128 in creatinine concentration in *Tshz3^{+lacZ}* compared to WT (15.91 ± 1.51 vs. 12.36 ± 2.07
129 μM/l; P<0.09).

130
131 **The *Tshz3^{+lacZ}* adult kidney showed differential expression of genes involved in**
132 **inflammatory processes.**

133 To identify *Tshz3*-regulated genes in the adult kidney, RNA sequencing analysis was
134 performed with samples extracted from *Tshz3^{+lacZ}* (n=6) and wild type (WT; controls,
135 n=6) adult mouse kidneys. 97 differentially expressed genes (DEGs) were identified,
136 among which 55 were up-regulated and 42 were down-regulated (adjusted p-value <
137 0.01) (**Table 1b**). Thereafter, we sought to take advantage of the single-cell
138 transcriptome of mouse glomeruli (8) and adult kidney(9) to identify the cell types in
139 wild type kidneys that expressed the genes differentially expressed in *Tshz3^{+lacZ}*
140 kidney. This analysis identified 58 genes expressed in podocytes, 31 in mesangial cells,
141 27 in immune cells, 40 in tubules and 43 in GECs, which might be direct targets of
142 TSHZ3 (**Table 1c**). We also found that some DEGs were shown to be markers of
143 proximal tubules (*Aspdh*, *Snhg11* and *D630029K05Rik*, a long non-coding RNA) or
144 myeloid lineage (*Cd74*, *Gusb*, *H2-Aa*, *H2-Ab1*, *Lyz2*, *Mpeg1* and *Vcam1*), including
145 macrophages and dendritic cells (10).

146 To characterize the differential expression data and to identify biological changes that
147 occur in *Tshz3^{+lacZ}* kidneys, we performed different enrichment analyses. As only a few
148 genes showed very strong differential expression, we applied gene set enrichment
149 analysis (GSEA (11, 12)) using a ranked gene list. We chose the updated public genesets
150 available on MSigDB (12) and identified positive enrichment in the kidneys of *Tshz3^{+lacZ}*
151 adult mice for gene sets related to “interferon-gamma response”, “epithelial to

152 mesenchymal transition”, “inflammatory response” and negative enrichment for genes
153 related to “Oxidative Phosphorylation” and “Xenobiotic Metabolism” (**Table 1d**;
154 **Supplementary Fig. 1**). Furthermore, ingenuity pathway analysis (IPA) of the DEGs
155 revealed enrichment of cellular processes centered on inflammatory and kidney diseases
156 (**Supplementary Fig. 2A, B**). This analysis showed that the relevant toxicity phenotypes
157 and pathology endpoints associated with the DEGs in *Tshz3^{+lacZ}* mice were centered on
158 the kidney and identified interferon-gamma (IFNG) as an upstream regulator
159 (**Supplementary Fig. 2B, C**). Moreover, enrichment analysis of pathways and
160 transcription factor using enrichR (13) also identified the “*interferon gamma*” pathway
161 but also “*collagen formation*” and “*extracellular matrix organization*” as significantly
162 enriched in *Tshz3^{+lacZ}* adult kidneys (**Table 1e**). Interestingly, the ChIP enrichment
163 analysis (ChEA) and a database search revealed that 22 DEGs (21.68%) are direct targets
164 of the transcription factor interferon regulatory factor 8 (IRF8) (**Table 1f**).
165 Using RT-qPCR we confirmed the DEG status observed by RNA-seq analysis for *Ciita*,
166 *Pld4* (two targets of IRF8), *Tlr7* (IRF8 target that promotes IFNG production (14)) and
167 the proinflammatory *Npy* (**Supplementary Fig. 3**).

168

169 **Genes differentially expressed in *Tshz3^{+lacZ}* adult kidney are associated with ASD**

170 To gain insights into *TSHZ3* function, we studied the disease association of the 80 non-
171 ambiguous human orthologs of the mouse DEGs (**Table 1g**). This analysis identified
172 35/80 genes (43.75%), which were established or putative causes for kidney disorders.
173 Interestingly, 8 of these genes have been also associated with ASD (**Table 1h**).

174

175 **Identification of *Tshz3^{+LacZ}*-related urinary peptides**

176 Since *Tshz3^{+lacZ}* mice exhibit dysregulated kidney expression of several genes and altered
177 hematological parameters, we sought to analyze their urinary peptidome. Urine samples

178 derived from *Tshz3^{+LacZ}* (n=15) and WT (n=12) were analyzed by capillary
179 electrophoresis coupled to mass spectrometry (CE-MS). Comparison of urinary
180 peptidome profiles led to the identification of 33 peptides that were significantly (adjusted
181 p-value < 0.05) associated with *Tshz3^{+lacZ}* (**Fig. 6**). Protein fragments from clusterin
182 (CLUS), complement factor D (CFAD), histone H2B type 1-F/J/L (H2B1F), major
183 urinary protein 17 (MUP17), tripeptidyl-peptidase 1 (TPP1) and uromodulin (UMOD),
184 as well as a large number (27) of collagen fragments, were identified (**Table 1i**).
185 *Tshz3^{+lacZ}* mice showed a decreased concentration of uromodulin and an increased
186 concentration of peptides from CLUS, CFAD, H2B1F, MUP17 as well as TPP1
187 fragments. Twelve collagen peptides were in higher abundance and fifteen in lower
188 abundance. As UPJO can lead to significant kidney damage, we compared the identified
189 33 urinary peptides from mice with those of the CKD273 classifier, a predictive marker
190 of chronic kidney disease (CKD) progression in humans(15). This analysis identified 14
191 similar (orthologs) human peptides in the CKD273 classifier, most of which were
192 collagen fragments (10 from collagen type I alpha-1 chain and 3 from type III alpha-1
193 chain). One peptide fragment was from uromodulin.

194

195

196 **Discussion**

197 Previously, we reported that in mice and humans, haploinsufficiency of *Tshz3/TSHZ3*
198 results in hydroureter (5, 16) and that individuals with *TSHZ3* heterozygous deletion are
199 at risk to develop kidney diseases (16). However, the expression of *Tshz3* in adult kidney
200 and the morphology of *Tshz3* heterozygous adult kidney have not been investigated
201 before. Herein, we characterized TSHZ3 expression in the adult mouse kidney, in
202 particular in glomeruli where TSHZ3 is specifically expressed in endothelial cells
203 (GEnCs), which is supported by single-cell RNA sequencing analysis (8). Using
204 *Tshz3^{+lacZ}* heterozygous mice, we have also uncovered a key role for the TSHZ3

205 transcription factor in controlling the glomerular density and morphology. Notably, we
206 showed that *Tshz3^{+/-lacZ}* mice have abnormal blood electrolytes and identified *Tshz3^{+/-lacZ}*-
207 related urinary peptides. In addition, by coupling transcriptomics with *in silico* analysis,
208 we showed that in kidneys from *Tshz3^{+/-lacZ}* mice, the expression of genes associated with
209 inflammatory processes and of renal- and ASD-associated was different from that in WT
210 mice. Combined with our previous reports, our data suggest that the *Tshz3* heterozygous
211 mice constitute a model that replicates many of the corresponding human disease
212 phenotypes.

213 The GEnCs, together with the glomerular basement membrane (GBM) and the podocytes,
214 constitute the glomerular filtration barrier (GFB), which selectively filtrates the plasma.
215 The GBM derives from the fusion of the basement membranes of both GEnCs and
216 podocytes, and in adult kidney, the GEnCs may contribute to the renewed biosynthesis
217 of the GBM. Because abnormalities in each of the three constituents of the GFB can lead
218 to proteinuria and kidney disease, TEM was used to assess fine structures of the GFB.
219 While TEM analysis revealed no obvious structural phenotype in TSHZ3-expressing
220 GEnCs, it provided evidence that *Tshz3* haploinsufficiency leads to GBM thinning and
221 change in podocyte morphology evidenced by effaced foot process. Interestingly,
222 hematuria has been reported in individuals with a thin GBM (17) but we did not observe
223 blood staining (macrohematuria) in the urine samples from *Tshz3* heterozygous mice. In
224 the future, it would be interesting to investigate whether these mice have microhematuria.
225 At present, the primary cause of the structural defects observed in the GBM and the
226 podocytes remains unknown. However, since communication between intraglomerular
227 cells is required for proper development and maintenance of the GFB (18), GBM thinning
228 and larger FPW might be the direct or indirect consequences of an abnormal cross-talk
229 between the TSHZ3-positive GEnCs and other glomerular cells. Furthermore, *Tshz3* may

230 be transiently expressed in glomerular cell lineages. Nevertheless, the comparison of the
231 urinary peptidome of *Tshz3^{+lacZ}* and WT adult led to the identification of 27 collagen and
232 6 non-collagen peptides associated with *Tshz3^{+lacZ}* mice. Among the collagen fragments
233 displaying a deregulation (e.g. 12 increased or 15 decreased), we identified thirteen
234 collagen fragments that overlap the CKD273 classifier that might be indicative of the
235 development of fibrosis (19, 20). As previously suggested (21), the fragments
236 overlapping the human CKD273 classifier could be used as biomarkers to assess renal
237 function in patients with *TSHZ3* heterozygous deletion. Interestingly, our analysis of
238 urinary peptides also revealed an under-representation of a MUP17 peptide in *Tshz3^{+lacZ}*
239 mice. The MUP17 protein is predominantly expressed in males and dominant males
240 significantly increased the secretion of MUP17 in social conditions (22, 23). In the future,
241 it would be interesting to study the relationship between variations in the level of MUP17
242 and the severity of the social behavior deficit observed in *Tshz3^{+lacZ}* mice. To further
243 evaluate renal function, we performed biochemical measurements on blood samples and
244 generated biochemistry profiles. This analysis identified a significantly reduced
245 concentration for urea, phosphates, magnesium and potassium in *Tshz3^{+lacZ}* mice.
246 Reduced serum urea is less frequent and usually of less clinical significance than
247 increased serum urea (24, 25). The lower plasma magnesium (hypomagnesaemia),
248 phosphate (hypophosphatemia) and potassium (hypokalemia) serum concentration are
249 associated with defective reabsorption/excretion process in the distal nephron (26-28).
250 However, the decrease in potassium concentration in *Tshz3^{+lacZ}* mice should be viewed
251 with caution since the method of euthanasia had an effect on potassium level (29). In line
252 with this, single-cell transcriptional profiling of the healthy kidney of 4-8 weeks old mice
253 showed expression of *Tshz3* in the proximal tubule, distal convoluted tubule as well as in
254 collecting duct principal and intercalated cells (9) and our immunostaining studies

255 suggest that *Tshz3* is indeed not only expressed in glomeruli but also, at least in the early
256 post-natal period, in subsets of tubules, most likely the straight section of the proximal
257 tubule and the thin descending limb of the loop of Henle. This segments are respectively
258 implicated in reclaiming substances, including magnesium, from the glomerular
259 ultrafiltrate, and in the mechanism required for urinary concentration in the medulla (30-
260 32). Altogether, our data suggest that *Tshz3* haploinsufficiency might impact different
261 components of the nephron.

262 To identify pathways that might be altered, we performed RNA-seq analysis and detected
263 97 statistically significant changes in gene expression in adult kidneys of *Tshz3^{+lacZ}* as
264 compared to WT. Based on the results of enrichment analyses, we detected the
265 involvement of inflammation-related pathways such as interferon-gamma. Of note, seven
266 DEGs (*Crym*, *Ctss*, *Fasn*, *Fcgrt*, *Gabrb3*, *Lyz2*, and *Vcam1*) were found to be
267 associated with kidney diseases, including renal inflammation, crescentic
268 glomerulonephritis or end-stage renal failure. Interestingly, population-based studies
269 support that autism spectrum disorder (ASD) and kidney disease coexist in several genetic
270 disorders (for review see Table 2 in (33)), suggesting that the same genetic modification
271 can affect neurodevelopment and nephrogenesis. However, because the genetic
272 alterations (deletion or duplication) associated with these disorders often encompass
273 several genes, it is still unclear how these genes contribute to the underlying molecular
274 mechanisms. In this context, the *TSHZ3* gene which associates ASD with a congenital
275 kidney condition is quite unique (4) and our findings that heterozygous deletion of *Tshz3*
276 leads to kidneys defects might be relevant for patients with *TSHZ3* heterozygous deletion.
277 For example, we found a decreased glomerular density that potentially might lead to a
278 reduced glomerular filtration rate (GFR), a defect that was reported in a patient with
279 heterozygous deletion of the *TSHZ3* gene (Table1 in (4)) who required renal transplant

280 (Table 2 in (34)). However, we did not find that creatinine level was significantly altered
281 in *Tshz3* heterozygous mice but this measurement is not very accurate to estimate the
282 GFR. Therefore, we must be cautious about whether *Tshz3* heterozygous mice have an
283 altered GFR. It is possible to measure GFR in adult mice, although the technology to do
284 so is technically challenging (35). In future, this could be applied to our mouse model.
285 The reduced number of glomeruli also questions about the mechanism leading to this
286 defect. The reduction of the glomerular density could be a secondary defect in a subtle
287 branching defect but it would require a new study to formally validate this hypothesis.
288 We actually do not observe *Tshz3* expression in the ureteric bud-collecting duct epithelial
289 lineage ((5) and this study). On the other hand, we do see *Tshz3* in the interstitial stroma
290 around this epithelial lineage ((5) and this study) and we cannot exclude that there is a
291 defect in the crosstalk between these two compartments (36) in *Tshz3* heterozygous mice.
292 Our results might also provide to be of interest for cognitive defects link to TSHZ3
293 haploinsufficiency. For now, the role of low plasma concentration of magnesium in ASD
294 is still a matter of debate. While two studies did not find a statistically significant
295 difference in levels of magnesium in children diagnosed ASD (37, 38), two other studies
296 (39, 40) demonstrated lower levels of magnesium in children diagnosed with ASD. So
297 far, *Tshz3* mouse models have been shown to be quite analogous to the clinical problems
298 (i.e. ASD-associated deficits, hydroureter and hydronephrosis) reported in patients with
299 *TSHZ3* heterozygous conditions (4, 5). Our results generate new hypotheses that might
300 lead to further understanding of the clinical problems and to a better diagnosis
301 management of *TSHZ3* patients.

302

303

304 **Materials and methods**

305

306 **Mouse strain and genotype**

307 The *Tshz3^{+/-LacZ}* mouse line has been described previously (5).

308

309 **Samples collection and RNAseq**

310 For RNA sequencing, *Tshz3^{+/-LacZ}* and wild-type mice kidneys were collected at 60 days-
311 of-age. The mean values for body weight of the *Tshz3^{+/-LacZ}* and wild-type were 34.7 ± 3.9
312 g (n=6) and 34.6 ± 6.5 g (n=6), respectively. Dissected kidneys were stored in RNAlater
313 solution (Qiagen) and kept frozen at -80 °C until RNA extraction.

314 Total individual kidney RNA was extracted using anRNeasy Maxi kit75162
315 Lot.260018727/ Lot.160012031 from Qiagen according to manufacturer's instructions.

316 The integrity of RNA was assessed using a chip-based capillary electrophoresis machine
317 and RNA concentration determined using a full spectrum (220-750nm)
318 spectrophotometer. The quality control of the RNA was additionally checked with RNA
319 6000 Pico de Agilent Technologies, according to the manufacturer's instructions. To
320 obtain two independent total RNA preparations from the two different conditions (wild
321 type: WT1 & WT2; *Tshz3^{+/-LacZ}*: HET1 & HET2) we pooled RNA from 3 kidneys per
322 group in the same proportion. The starting material (1µg Total mRNA, dissolved in
323 RNase-, DNase- and protease-free molecular grade water) was sent to GATC (Eurofins)
324 for sequencing (Genome Sequencer Illumina HiSeq).

325 Sequences (fastq format) were mapped to the mm10 version of the mouse genome to
326 generate Sequence Alignment/Map (SAM/BAM) format. After normalization, analysis
327 of differentially expressed genes (DEGs) was performed using both the Bioconductor
328 (<http://www.bioconductor.org>) package DESeq/DESeq2 and the package edgeR.

329 This analysis generated differential expression lists with False Discovery Rates (FDRs),
330 which are derived from p-values corrected for multiple testing using the Benjamini-
331 Hochberg method. 6 files in total were generated: FDR 1%, 10% for both UCSC
332 (transcripts) and ENSEMBL (genes).

333 EnrichR tool (13) was used to performed enrichment analysis with “pathways”, gene
 334 ontology biological processes (GOBP) and transcription factor (ChIP Enrichment
 335 Analysis, ChEA). Gene set enrichment analysis (GSEA) was performed using the
 336 software provided by the Broad Institute (41, 42) with default parameters and a pre-
 337 ranked gene list calculated based on the $10 \log_{10}$ of the *P*-value from DESeq2
 338 analysis multiplied by the sign of differential expression.

339

340 **mRNA extraction, cDNA synthesis and quantitative real-time PCR (RT-qPCR)**

341 Total RNA from adult kidneys of WT and *Tshz3^{+/-lacZ}* mice was prepared using a RNeasy
 342 Maxi Kit (ref 75162 Qiagen™), and first-strand cDNA was synthesized using a Maxima
 343 First Strand cDNA Synthesis Kit with dsDNase (ThermoFisher Scientific™ ref K1671
 344 50). All samples from each experiment were reverse-transcribed at the same time, and
 345 real-time PCR was performed on a StepOne+ qPCR detection system (Applied
 346 Biosystems™) using Luminaris Color HiGreen High ROX qPCR Master Mix (Thermo
 347 Fisher Scientific™ ref K0362). RT-qPCR conditions were as follows: 40 cycles of 95 °C
 348 for 15 s and 60 °C for 60 s. Reactions were run in triplicate in three independent
 349 experiments. The geometric mean of the housekeeping gene GAPDH was used as an
 350 internal control to normalize variability in expression levels, and samples were also
 351 normalized to their respective control group. Specificity of reactions was verified by melt
 352 curve analysis. Primer sequences used for Sybr qPCR are as follows:

353

	gene	Primer FW	Primer Rev
1	<i>Gbp4</i>	CAGGCTCTACATGGACATGAGG	TGCCTGCAAGATGGAACCTCTCG
2	<i>Ciita</i>	ACCTTCGTCAGACTGGCGTTGA	GCCATTGTATCACTCAAGGAGGC
3	<i>Tlr7</i>	GTGATGCTGTGTGTTTGTCTGG	CCTTTGTGTGCTCCTGGACCTA
4	<i>Npy</i>	TACTCCGCTCTGCGACTACTACA	GGCGTTTTCTGTGCTTTCCTCA
5	<i>Gapdh</i>	GTCTCCTGCGACTTCAACAGCA	ACCACCCTGTTGCTGTAGCCGT

354

355 Expression data were normalized to controls and the variability in expression levels was
356 analyzed using the $2^{-\Delta\Delta CT}$ method described Livak and Schmittgen (43).
357 Variables which showed a p-value less than 0.05 in the resulting model were considered
358 to have a significant effect. These statistical analyses were performed by unpaired t-tests
359 with the qbase+ software version 2 (Biogazelle).

360

361 **Immunological and in situ hybridization analysis**

362 Adult mice were transcardially perfused with phosphate-buffered saline (PBS, 10 mM,
363 pH 7.4), followed by 4% paraformaldehyde (PFA) in PBS under ketamine (150 mg/kg)
364 and xylazine (20 mg/kg) anesthesia. Kidneys were post-fixed in 4% paraformaldehyde
365 (PFA; EMS Lot.160401) for 2 h at 4 °C, cryoprotected with 30% sucrose solution in PBS
366 and frozen (Iso-Pentane RPE524391 Carlo Erba at dry ice temperature). Immunostaining
367 was performed on 12- μ m cryosections from tissues embedded in OCT compound.
368 Cryosections were washed with 0.2% Tween/PBS for 15 min and then blocked in 10%
369 goat serum 0.1%/0.1% Tween/PBS for 1 h. Sections were incubated with primary
370 antibodies overnight at 4 °C. Secondary antibodies were incubated 2 h at room
371 temperature, and after several washes, sections were counterstained with DAPI for 10
372 minutes.

373 The following primary antibodies were used: anti- β -galactosidase (chicken, 1/1000,
374 ab9361, Abcam; rabbit, 1/1000, Cappel), mouse anti-NG2 (1/100, MAB5384 Millipore),
375 rabbit anti-CD31/Pecam (1/100 MEC13.3, BD Pharmingen) and rabbit anti-DACH11
376 (1/100, Proteintech 10914-1-AP). Secondary antibodies: Alexa-Fluor-546 goat anti-
377 mouse; Alexa-Fluor-546 donkey anti-rabbit, Alexa-Fluor 488 donkey anti-mouse, Alexa-
378 Fluor-488 donkey anti-chicken. Slides were mounted with Fluoromount-G, Southern
379 Biotech Lot: B0216-N156. Images were acquired using a laser scanning confocal
380 microscope (LSM780; Carl Zeiss) and processed using Adobe Photoshop.

381 For X-gal staining, kidneys/ureters were dissected from non-perfused animals, kidneys
382 were cut in two according to the sagittal plane, and tissues were fixed for 1 h in 1% PFA.
383 Detection of β -galactosidase activity was done on tissues or on 14- μ m cryostat sections
384 incubated in the dark in staining solution at 37 °C. X-gal staining was performed as
385 described (44). Samples were paraffinized after washing in increasing alcohol
386 concentrations (70%, 80%, 90%, 97% and 100%) VWR chemicals for one day and finally
387 with Xylene 33817 (Sigma-Aldrich) for 2 h, and immersed in paraffin Paraplast X-TRA
388 from Sigma at 65 °C. Staining was performed with Hematoxylin (HHS32-1L Lot.
389 064K4354 Sigma-Aldrich), Eosin (Ht110230-1L Sigma-Aldrich), Trichrome Masson
390 (Lot.17301-V04 Ral Diagnostics).

391 To characterize the expression of TSHZ3 in the tubules, immunostaining was performed
392 on kidneys of *Tshz3^{+lacZ}* mice, using renal tracts of normal external appearance (e.g. no
393 hydronephrosis). Paraformaldehyde-fixed kidneys were embedded in paraffin and 4 μ m
394 sections were cut, dewaxed and rehydrated. These sections were incubated overnight at
395 4°C with antibodies raised in rabbits to define nephron segments and collecting ducts, as
396 described (30-32, 45, 46): aquaporin-1 (1:500, Abcam, ab15080), a marker of proximal
397 tubules and the thin descending limb of the loop of Henle; uromodulin (1:200, Santa Cruz,
398 sc-20631), a marker of the thick ascending limb of the loop of Henle; and calbindin-28,
399 a marker of distal tubules of the nephron and also of collecting ducts (1:500, Abcam,
400 ab25085). For immunostaining of TSHZ3, we used an antibody (1:1000) raised in guinea
401 pig, as described (5). Our preliminary experiments showed that this antibody did not work
402 well on paraffin section but was effective on optimal cutting temperature compound
403 (OCT)-embedded frozen sections; thus the latter technique was used for TSHZ3. OCT-
404 embedded frozen tissue sections were fixed in pre-cooled acetone for 15 min, then washed
405 twice in PBS. Primary antibodies were detected using appropriate Biotin-conjugated

406 secondary antibodies: 1:500, goat anti-guinea pig IgG (Abcam ab6970) and 1:200, goat
407 polyclonal anti-rabbit IgG (Abcam ab6720) and a peroxidase-based system, generating a
408 brown colour followed by haematoxylin counterstain (46). Negative controls omitted
409 primary antibodies and these experiments showed no significant signal (data not shown).

410

411 **Quantitation of glomeruli**

412 The number of glomeruli was determined using kidney images acquire from multiple
413 mid-sagittal longitudinal sections (12 μ m; *Tshz3^{+lacZ}*, n=58; WT, n=52) of whole P60
414 adult kidneys (*Tshz3^{+lacZ}*, n=4; WT, n=4) stained by hematoxylin/eosin. We used
415 ImageJ(47) to measure the renal cortex area into which the number of glomeruli was
416 counted. The results are reported as the number of glomeruli per area (glomeruli/cm²).

417 **Transmission electronic microscopy and quantification**

418 Kidneys were perfused as described above, rapidly dissected and postfixed in 2% PFA,
419 2.5% glutaraldehyde in cacodylate buffer (pH 7.2) overnight at 4 °C. The kidneys were
420 put in 1% OsO₄ solution in cacodylate buffer for 1 h on ice, then dehydrated on ice and
421 embedded in resin (EPON 912). Sample were polymerized 48 h at 60 °C. Ultrathin
422 sections (80-nm) performed on Leica UCT were poststained with 2% uranyl acetate,
423 followed by Reynolds' lead citrate. Section were examined with a high-resolution
424 transmission electron microscope (Tecnai G2 (FEI), Netherland) at 200 kV and images
425 were acquired with a Veleta camera (Olympus). EM images were opened and analyzed
426 with ImageJ software (48); the straight-line tool was used to measure GBM thickness and
427 endothelial cell fenestration on randomly selected electron micrographs. The same
428 approach was used for morphometric analysis of foot process width, as described
429 previously (49, 50).

430

431 **Blood samples**

432 Blood samples were collected from *Tshz3^{+/-LacZ}* (n= 11; 5 females and 6 males) and WT
433 mice (n=11; 6 females and 5 males) at 60 days-of-age. The mean values for body weight
434 of *Tshz3^{+/-LacZ}* and wild-type were 38.27 ± 7.8 (n=11) and 33.01 ± 4.9 (n=11). Mice were
435 anaesthetized by an intraperitoneal injection of ketamine/xylazine (0.1 ml/10 g body
436 weight) prior to manipulation. Anesthesia was maintained by using 1.7% to 2.5%
437 isoflurane delivered in 600 ml/min oxygen and a closely fitting facemask. Blood was
438 collected by cardiocentesis puncture in heparinized tubes with EDTA and also in tubes
439 without anticoagulant, centrifuging at 4 °C immediately after extraction. The total blood
440 volume in 30-40 g mice is approximately 2 to 3 ml. The maximum volume that could be
441 collected safely at a single survival time point was approximately 800-1000 μ l. Blood
442 tests were outsourced to Laboklin G.m.b.H. and performed using a Siemens' high-volume
443 hematology analyzer (ADVIA 2120i) and a Roche' chemistry analyzer (Cobas 8000
444 c701).

445

446 **Urine samples**

447 Urine samples were collected from *Tshz3^{+/-LacZ}* (n= 7; 4 females and 3 males) and WT
448 mice (n=7; 6 females and 1 males) at 60 days-of-age.

449 Animals were placed in a clean, dry, empty, and transparent individual cage. A non-
450 absorbable plastic, fully sanitizable material was laid on the floor of the cage. During
451 urine collection, water bottles were provided but no food was given to limit contamination
452 with faeces or animal feed. The mouse was monitored all time and removed as soon as it
453 urinated. The voided urine was aspirated with a Gilson Pipetman and transferred to a 1.5
454 mL sterile microcentrifuge tube (kept on ice). Collected urine was stored at -80C prior to
455 analysis. Due to the small amount of urine collected, the procedure was repeated during
456 three consecutive days to obtain 300ul of urine for each mouse.

457

458 **Urinary Proteomics**

459 *Sample Preparation:* Urine samples were collected and frozen at -80°C as described
460 above. Immediately before preparation, mice urine samples were thawed on ice. 150 µl
461 of urine was mixed with a similar volume of a solution containing 2 M urea, 10 mM
462 NH₄OH, and 0.02% sodium dodecyl sulfate (SDS). To remove high molecular weight
463 molecules, samples were ultrafiltrated (3,400 × g for 45 min at 4°C) using a Centriscart
464 20kDa cut-off centrifugal filter device (Satorius, Göttingen, Germany) until 200 µl of
465 filtrate was obtained. Afterwards, the filtrate was desalted by a NAP5 gel filtration
466 column (GE Healthcare BioSciences, Uppsala, Sweden) to eliminate electrolytes and
467 urea, hence decreasing matrix effects. The samples were lyophilized in a Savant
468 SpeedVac SVC100H connected to a Virtis 3L Sentry freeze dryer (Fischer Scientific,
469 Illkirch, France), consequently stored at 4°C. Shortly before CE-MS analysis, the samples
470 were resuspended in 10 µl high-performance liquid chromatography grade water (HPLC-
471 H₂O).

472 *CE-MS analysis and data processing:* CE-MS experiments were conducted as previously
473 reported (51). Briefly, a Beckman Coulter Proteome Lab PA800 capillary electrophoresis
474 system (Fullerton, CA) online coupled to a micrOTOF II MS (Bruker Daltonic, Bremen,
475 Germany) was used. The electro-ionization (ESI) sprayer (Agilent Technologies, Palo
476 Alto, CA) was grounded, and the ion spray interface potential was established to -4.5 kV.
477 Subsequently, data acquisition and MS acquisition methods were automatically measured
478 through the CE by contact-close-relays. Spectra were accrued every 3 seconds, over a
479 range of m/z 350 to 3000.

480 Mass spectral ion peaks signifying identical molecules at different charges were
481 deconvoluted into singles masses using MosaiquesVisu (52). The subsequent peak lists
482 categorized each peptide according to its molecular mass (kDa), CE-migration time (min)
483 and signal intensity (amplitude). Due to the analytical variances of urine samples,

484 migration time and ion signal intensity (amplitude) were normalized using endogenous
485 “housekeeping” peptides, normally displaying a small difference between at least 90% of
486 all urine samples, as reported elsewhere (51). Lastly, all detected peptides were deposited,
487 matched and annotated in a Microsoft SQL database (51). Thus, further comparisons and
488 statistical analysis among both groups were performed.

489 *Sequencing of peptides:* Tandem mass spectrometry (MS/MS) analysis were conducted
490 to retrieve the sequence information of the peptides, as previously described (51). Briefly,
491 MS/MS experiments were performed on a Dionex Ultimate 3000 RSLC nanoflow system
492 (Dionex, Camberly, UK) coupled to an Orbitrap Velos MS instrument (Thermo Fisher
493 Scientific). Thereafter, all resulting data files were evaluated by the use of SEQUEST
494 (using Thermo Proteome Discoverer 1.2) without any enzyme specificity and searched
495 beside the Swiss-Prot *Mus Musculus* database, as previously described(53).

496 *Statistical analysis:* For the identification of potential significant different urinary
497 peptides, urine samples from both groups (wild type and *Tshz3^{+lacZ}*) were compared. *P*-
498 values were calculated according to the Wilcoxon Rank-Sum test. For multiple testing
499 correction, the reported *p*-values were further adjusted via false discovery rate method
500 described by Benjamini and Hochberg (54). Only peptides with *p*-values less than 0.05
501 and detected in a frequency threshold of $\geq 70\%$ in at least one of both groups were further
502 considered as statistically significant. Statistical analysis was performed using Prism 7.05
503 (GraphPad Software, USA) and results considered significant at $P < 0.05$.

504

505 **Data availability**

506 The data that support the findings of this study are available from the corresponding
507 author upon reasonable request. Raw data (FastQ files) from the sequencing experiment
508 (triplicates from wild-type and *Tshz3^{+lacZ}* adult kidney) and raw abundance
509 measurements for genes (read counts) for each sample are available from Gene

510 Expression Omnibus (GEO) under accession GSE182010, which should be quoted in any
511 manuscript discussing the data.

512

513 **Ethics Statement**

514 The Experiments were ethically approved by the 1) “*Comité National de Réflexion*
515 *Ethique sur l’Expérimentation Animale 14*” (ID numbers 57-07112012) and were in
516 agreement with the European Communities Council Directive (2010/63/EU);
517 2) Registered Medical and Scientific Departments of the University of Manchester. Mice
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520

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535

536 **Conflict of Interest Statement**

537 The authors declare no conflicts of interest and no competing financial interests.

538

539

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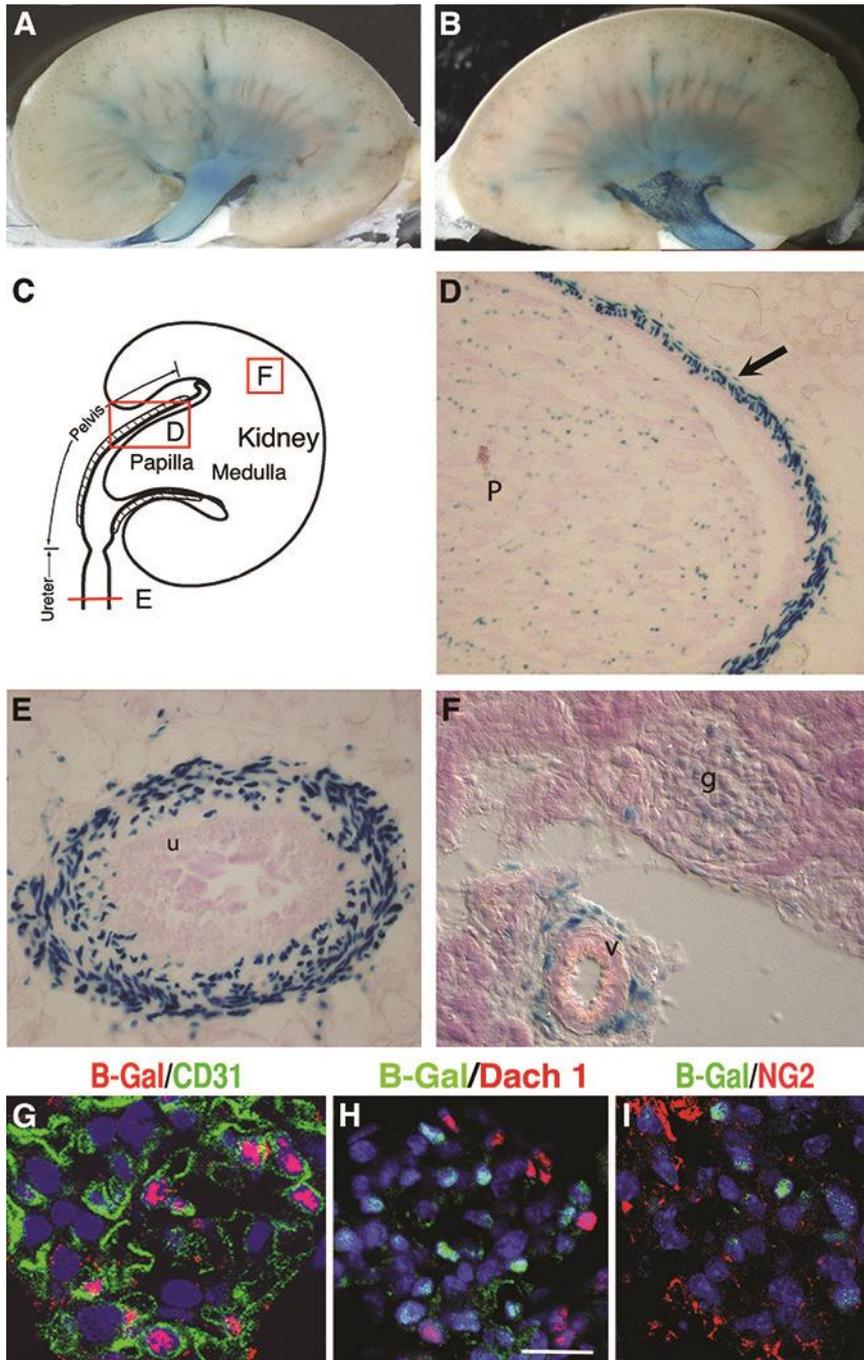
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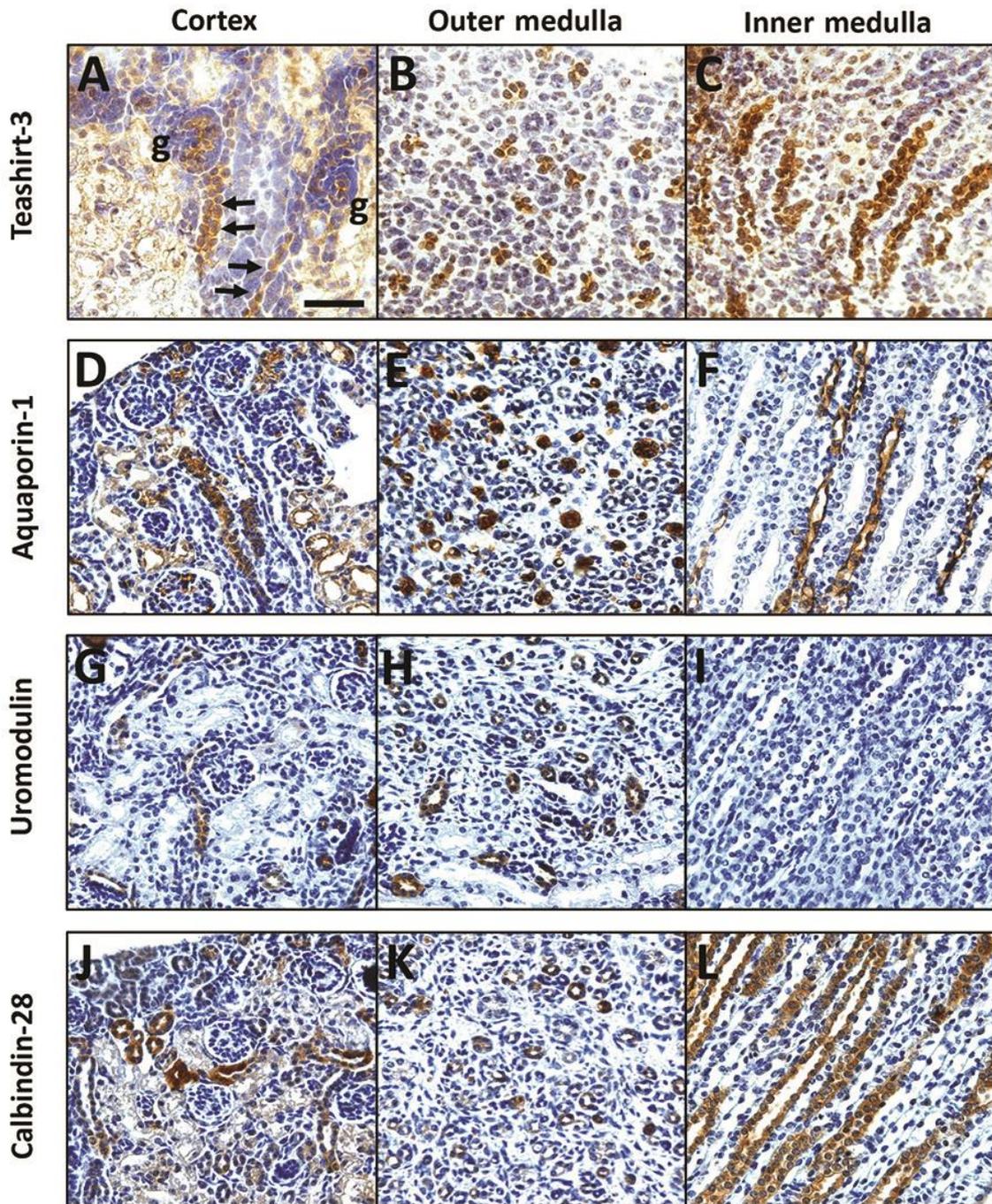
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Figure 1. Distribution of Xgal-positive cells in *Tshz3^{+lacZ}* adult renal tract. (A, B) The two halves of the same adult kidney stained with X-Gal. (C) Cartoon showing the section sites and planes for D, E and F. (D-F) Xgal-Positive cells were found in papilla (p) and smooth muscle present in the pelvic region (arrow) (D), in the mesenchymal part of the ureter (E), in the glomeruli (g) and in close proximity to blood vessel (v) (F). (G-I) In glomeruli, TSHZ3 (β-Gal) is detected in CD31+ glomerular endothelial cells (G) but not

729 in DACH1+ podocytes (H) or in NG2+ mesangial cells (I); scale bar, in G-I, 20 μ m. B-
 730 Gal, Beta-Galactosidase; u: urothelium.
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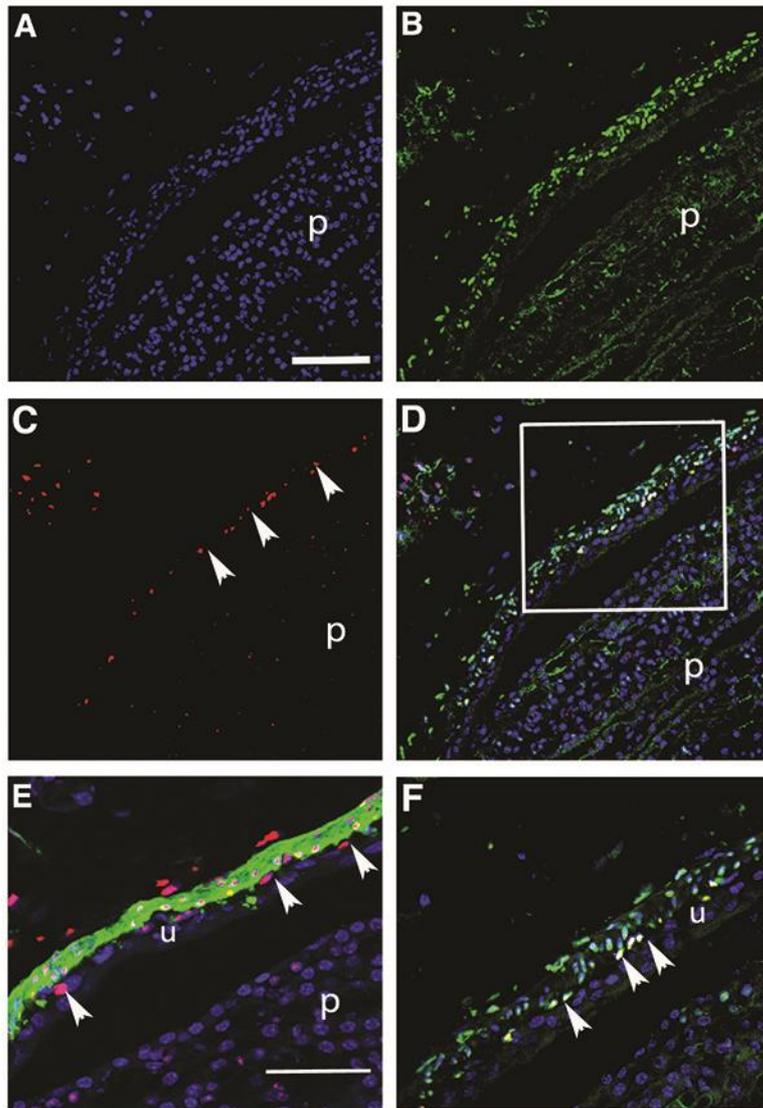
734 **Figure 2. Immunohistochemistry for TSHZ3 and kidney segment markers.**

735 Immunohistochemistry (brown positive signal) of one week postnatal *Tshz3^{+lacZ}* mouse

736 kidneys for: A-C. Teashirt-3 (TSHZ3); D-F. Aquaporin-1 (marker of proximal tubules

737 and thin descending limb of loop of Henle; G-I. Uromodulin (marker of the thick

738 ascending limb of loop of Henle); and J-L. Calbindin-28 (marker of distal nephron tubules
739 and collecting ducts). A-C are from frozen sections, and D-L are from paraffin-embedded
740 sections; the latter processing tends to make the tissue appear more compact. All sections
741 counterstained with haemotoxylin (blue nuclei). A, D, G and J show the cortex, with the
742 outside of the organ uppermost; B, E, H and K are transverse sections through the outer
743 medulla; and C, F, I and L are longitudinal sections through the inner medulla. In the
744 cortex (A), TSHZ3 was immunodetected in nuclei within tufts of maturing glomeruli (g)
745 and in nuclei of thin tubule-like structures (arrowed). Subsets of tubule-like profiles also
746 immunostained for TSHZ3 in the outer medulla (B) and the inner medulla (C).
747 Comparison with immunostaining patterns for aquaporin-1, uromodulin and calbindin-
748 28, suggest that thin descending limbs of loops of Henle express TSHZ3 because patterns
749 for this protein and aquaporin-1 are similar in the thin tubules within the inner medulla.
750 In this location, calbinin-28 positive collecting ducts are wider diameter and uromodulin
751 is not detected. The TSHZ3 positive tubules in the cortex and outer medulla may also
752 include the pars recta, or straight section, of the aquaporin-1 positive proximal tubule.
753 Bars are 50 μ m.
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757 **Figure 3. Characterization of β -galactosidase-positive cells in the pelvic region of**

758 ***Tshz3^{+lacZ}* adult kidney. (A-D) Comparative expression of β -galactosidase (green) and**

759 **Dachshund 1 (red) in the pelvic region. (F) Close up of the region boxed in D. Merge**

760 **image (D, F) shows that a subset of β gal+ cells expresses DACH1 (arrowheads in C and**

761 **F). These cells represent a cell layer in a sub urothelial position. (E) Double**

762 **immunostaining for β galactosidase (red) and smooth muscle actin (green) indicates that**

763 **β gal expression is found in SMA expressing cells. Some β gal+ cells adjacent to the**

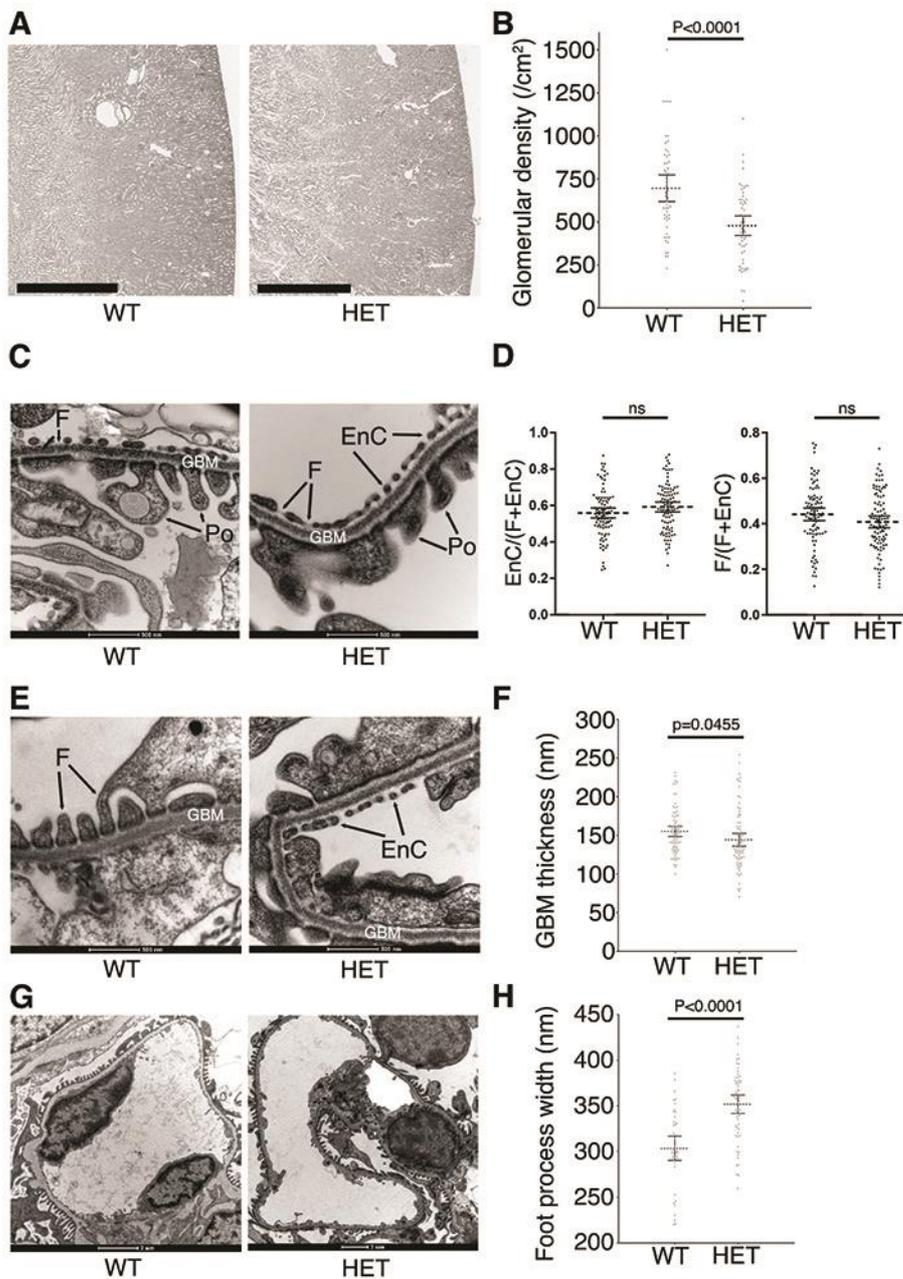
764 **urothelium do not express SMA (arrowheads in E). P: papilla, u: urothelium. Scale bars,**

765 **in A, 100 μ m; in E, 50 μ m.**

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771 **Figure 4: Reduced glomerular density, glomerular basement membrane thinning**

772 **and larger foot process width in heterozygous *Tshz3^{lacZ/+}* mice.** (A) Representative

773 images of haematoxylin and eosin-stained sections of WT and *Tshz3^{lacZ/+}* adult kidneys

774 at post-natal day 60. Scale bar 1mm. (B) The graph shows the significant (P<0.0001)

775 reduction of the glomerular density in heterozygous *Tshz3^{lacZ/+}* (471 ± 0.29 /cm², 48

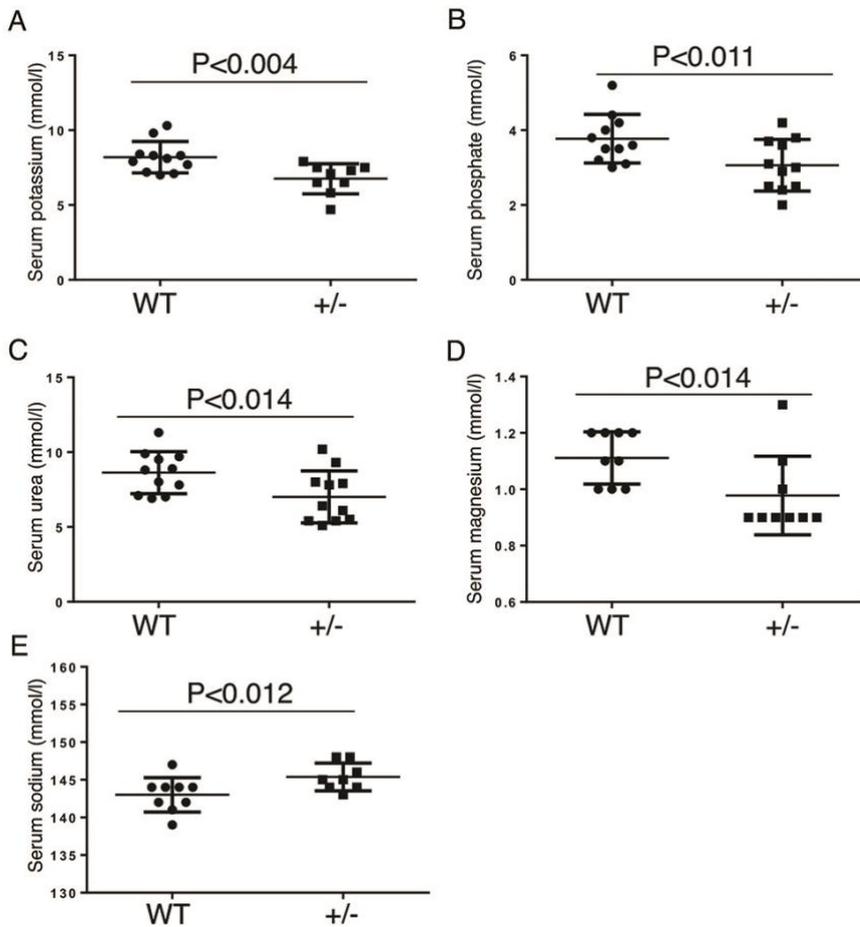
776 sections from 3 kidneys) compare to wild-type kidney (695 ± 0.38 /cm², 41 sections from

777 3 kidneys). (C, E, G) Representative TEM images of wild type and *Tshz3^{lacZ/+}* adult

778 kidneys. (D, F, H) TEM morphometric analysis. (C) TEM: No abnormalities in

779 endothelial cell fenestration are observe in *Tshz3^{lacZ/+}* mice. Scale bar, 500nm. (D)

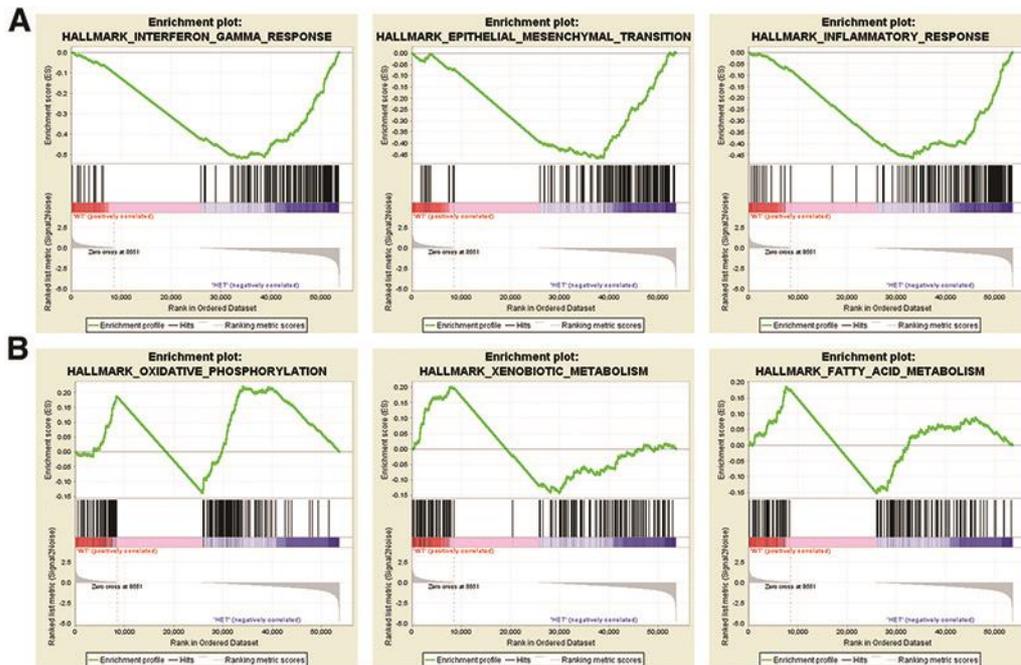
780 Morphometric analysis of the fenestration reveals no significant difference between WT
 781 and *Tshz3^{+/-lacZ}* mice. (E) TEM: *Tshz3^{+/-lacZ}* kidney shows a reduction of the thickness of
 782 the GBM in *Tshz3^{lacZ/+}* compared to WT. Scale bar, 500nm. (F) Morphometric analysis
 783 reveals a significant reduction ($P < 0.0455$) of the thickness of the GBM in *Tshz3^{lacZ/+}*
 784 (144.2 ± 4.2 nm, 84 sections from 3 kidneys) compare to wild-type (155.1 ± 3.32 nm, 78
 785 sections from 3 kidneys). (G) TEM: illustrating foot processes in *Tshz3^{lacZ/+}* and WT
 786 mice. Scale bar, $2\mu\text{m}$. (H) Foot process width in *Tshz3^{lacZ/+}* (351.7 ± 5.03 nm, 61 sections
 787 from 9 kidneys) is significantly larger ($P < 0.0001$) compared to WT (303.4 ± 6.57 nm, 42
 788 sections from 7 kidneys) mice. Data are shown as mean and its 95% CI. EnC, endothelial
 789 cell cytoplasm; F, endothelial fenestration; GBM, glomerular basement membrane; HET,
 790 hererozygous; Po, podocyte foot process; SD, standard deviation; WT, wild type.
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 793 **Figure 5. Differences in serum biochemical parameters between control and**
 794 ***Tshz3^{lacZ/+}* mice.** Plasma concentration of potassium (A), phosphates (B), urea (C),
 795 magnesium (D) and sodium (E). Data are represented as means \pm SEM. Statistically
 796 significant difference from control at * $p < 0.02$; ** $p < 0.004$. WT, wild type; +/-, *Tshz3^{+/-lacZ}*

805 **Supplementary Figures**

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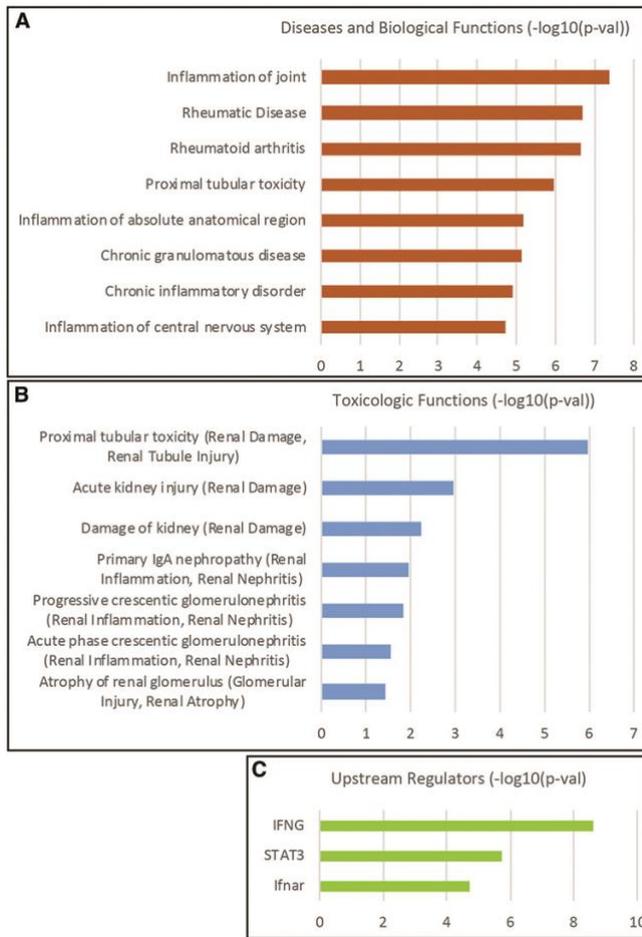
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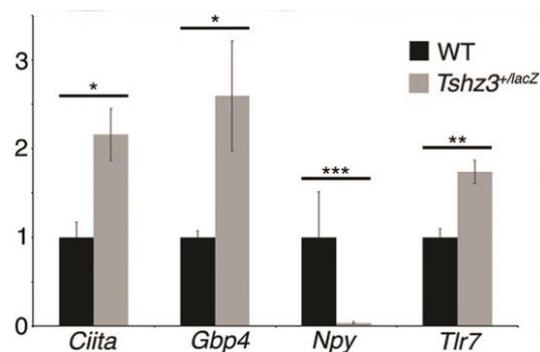
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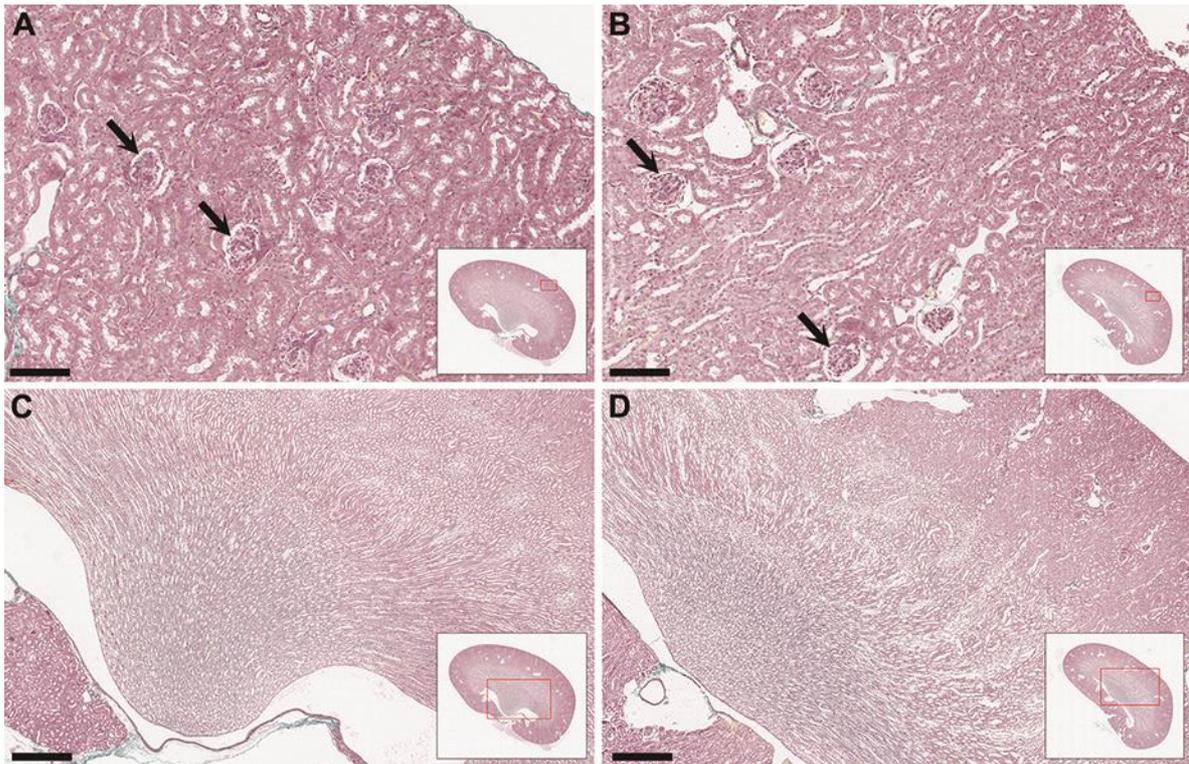
Supplementary figure 1: Enrichment plots from gene enrichment analysis (GSEA). GSEA results showing positive (A) and negative (B) enrichment in the kidneys of *Tshz3^{+/lacZ}* adult mice for gene sets related to “interferon gamma response”, “epithelial to mesenchymal transition”, “inflammatory response” (A) and to “Oxydative Phosphorylation”, “Xenobiotic Metabolism” and Fatty Acid Metabolism (B).



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 815 **Supplementary Figure 2: Functional characterization of differentially expressed**
 816 **genes (DEGs) in *Tshz3*^{+/*lacZ*} adult kidneys, using Ingenuity Pathway Analysis (IPA).**
 817 (A) Significant enrichments observed in the Diseases and Biological Functions
 818 annotations. (B) Relevant toxicity phenotypes and clinical pathology endpoints
 819 associated with the DEGs. (C) Major upstream regulators of the DEGs. Minus Log of the
 820 p-values calculated from Fisher's exact test are shown on the x-axis.
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 823 **Supplementary figure 3: Quantitative real-time PCR validation of four**
 824 **differentially expressed genes in *Tshz3*^{+/*lacZ*} kidney as identified by RNAseq.** Bar
 825 graph showing significant variation in mRNA levels as determined by qRT-PCR in
 826 *Tshz3*^{+/*lacZ*} versus WT mice for *Ciita*, *Gbp4*, *Npy* and *Tlr7*. Data are shown as means ±
 827 s.e.m. Unpaired two-tailed t test. *, *P* < 0.03; **, *P* < 0.006; ***, *P* < 0.002.
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Supplementary Figure 4. Histological analysis of WT and *Tshz3*^{+/-lacZ} kidney.
Representative images of haematoxylin and eosin-stained sections of WT (A, C) and *Tshz3*^{+/-lacZ} (B, D) adult kidneys at post-natal day 60. Sections of the cortical region (A, B) and the papilla (C, D). Arrows indicate glomeruli. In the box showing the whole section, the red rectangle indicates which part of the section is shown as A, B, C or D. Scale bars, in A and B, 125µm; in C and D, 500µm.

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Table 1a. Blood serum biochemical measurements for control and *Tshz3^{+/lacZ}* mice.

Parameters (mmol/l)	Control (n=11)	<i>Tshz3^{+/lacZ}</i> (n=11)	p-Value (t-test)
Potassium	8.31 ± 1.05	6.83 ± 0.97	P<0.004
Phosphates	3.77 ± 0.65	3.06 ± 0.61	P<0.011
Magnesium	1.11 ± 0.09	0.98 ± 0.074	P<0.014
Urea	8.6 ± 1.4	7.01 ± 1.8	P<0.014
Sodium	143 ± 2.1	145.36 ± 1.85	P<0.012

Blood serum biochemical measurements for control and *Tshz3^{+/lacZ}* mice.

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Table 1b. Significantly differentially expressed genes (DEGs) between WT and HET. FDR cutoff chosen was $FDR \leq 0.01$

Ensembl ID	Gene symbol	Gene Name	baseMean	log2 Fold Change	lfcSE	stat	pvalue	padj
ENSMUSG00000054676	1600014C10Rik	RIKEN cDNA 1600014C10 gene(1600014C10Rik)	7360,92	-0,63	0,14	4,41	1,0E-05	6,1E-03
ENSMUSG00000086474	9130204K15Rik	RIKEN cDNA 9130204K15 gene	181,94	-0,78	0,21	3,68	2,3E-04	6,9E-02
ENSMUSG00000004668	Abca13	ATP-binding cassette, sub-family A (ABC1), member 13	5366,75	0,63	0,18	3,52	4,4E-04	9,6E-02
ENSMUSG00000031659	Adcy7	Adenylate cyclase 7	474,95	0,73	0,20	3,62	2,9E-04	7,7E-02
ENSMUSG00000004730	Adgre1	Adhesion G protein-coupled receptor E1	387,86	0,69	0,20	3,49	4,8E-04	9,6E-02
ENSMUSG00000060470	Adgrg3	Adhesion G protein-coupled receptor G3	347,56	0,65	0,19	3,53	4,2E-04	9,6E-02
ENSMUSG00000085180	Ai838599	Expressed sequence AI838599	473,16	0,71	0,17	4,06	4,8E-05	2,2E-02
ENSMUSG00000033715	Akr1c14	aldo-keto reductase family 1, member C14(Akr1c14)	30143,69	-0,68	0,19	3,53	4,2E-04	9,6E-02
ENSMUSG00000028356	Ambp	Alpha 1 microglobulin/bikunin precursor	105,82	0,89	0,22	4,08	4,4E-05	2,1E-02

ENSMUSG0000 0020609	Apob	Apolipoprotein B	6556,7 9	-0,58	0, 17	3,4 7	5,1E -04	9,97E -02
ENSMUSG0000 0040694	Apobec2	apolipoprotein B mRNA editing enzyme, catalytic polypeptide 2	175,14	1,27	0, 21	5,9 4	2,8E -09	1,1E- 05
ENSMUSG0000 0020604	Arsg	Arylsulfatase G	2625,2 3	-0,77	0, 17	4,5 9	4,5E -06	3,2E- 03
ENSMUSG0000 0038704	Aspdh	aspartate dehydrogenase domain containing(Aspdh)	5008,2 6	-0,59	0, 17	3,5 1	4,4E -04	9,6E- 02
ENSMUSG0000 0017929	B4galt5	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 5(B4galt5)	18312, 69	-0,65	0, 18	3,6 2	2,9E -04	7,7E- 02
ENSMUSG0000 0090486	BC035947	CDNA sequence BC035947	4151,5 7	-0,60	0, 17	3,4 8	5,0E -04	9,96E -02
ENSMUSG0000 0030268	Bcat1	branched chain aminotransferase 1	6109,7 5	-0,92	0, 14	6,5 1	7,7E -11	3,6E- 07
ENSMUSG0000 0058914	C1qtnf3	C1q and tumor necrosis factor related protein 3(C1qtnf3)	9805,3 8	-0,72	0, 20	3,5 9	3,3E -04	8,3E- 02
ENSMUSG0000 0022416	Cacna1i	calcium channel, voltage-dependent, alpha 1I subunit	126,26	0,91	0, 21	4,2 4	2,2E -05	1,1E- 02
ENSMUSG0000 0038128	Camk4	Calcium/calmodulin-dependent protein kinase IV	274,72	0,84	0, 21	4,0 5	5,2E -05	2,2E- 02

ENSMUSG0000 0024610	Cd74	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)(Cd74)	12439, 99	0,62	0, 18	3,4 7	5,2E -04	9,97E -02
ENSMUSG0000 0022504	Ciita	class II transactivator	431,87	1,10	0, 19	5,8 6	4,6E -09	1,4E- 05
ENSMUSG0000 0056025	Clca3a1	Chloride channel accessory 3A1	875,04	0,74	0, 16	4,5 6	5,2E -06	3,6E- 03
ENSMUSG0000 0040663	Clcf1	Cardiotrophin-like cytokine factor 1	246,91	0,74	0, 20	3,6 5	2,6E -04	7,2E- 02
ENSMUSG0000 0024330	Col11a2	Collagen, type XI, alpha 2	191,72	1,00	0, 21	4,8 3	1,4E -06	1,4E- 03
ENSMUSG0000 0030905	Crym	Crystallin, mu	2030,9 9	-0,87	0, 20	4,4 2	9,7E -06	6,1E- 03
ENSMUSG0000 0038642	Ctss	Cathepsin S [Source:MGI Symbol;Acc:MGI:107341]	1091,2 7	0,74	0, 16	4,7 3	2,3E -06	1,9E- 03
ENSMUSG0000 0027014	Cwc22	CWC22 spliceosome-associated protein(Cwc22)	3557,8 8	1,18	0, 16	7,2 6	3,8E -13	2,4E- 09
ENSMUSG0000 0015340	Cybb	Cytochrome b-245, beta polypeptide	747,51	0,62	0, 17	3,6 7	2,4E -04	6,9E- 02
ENSMUSG0000 0074254	Cyp2a4	cytochrome P450, family 2, subfamily a, polypeptide 4(Cyp2a4)	9870,2 5	-0,53	0, 14	3,8 5	1,2E -04	4,2E- 02
ENSMUSG0000 0108332	D530033 B14Rik	RIKEN cDNA D530033B14 gen	751,19	-0,83	0, 18	4,6 6	3,1E -06	2,4E- 03
ENSMUSG0000 0031294	D630029K 05Rik	RIKEN cDNA D630029K05 gene(D630029K05Rik)	7305,0 9	-0,65	0, 17	3,7 5	1,8E -04	5,8E- 02

ENSMUSG0000 0025279	Dnase1l3	Deoxyribonuclease 1-like 3	124,40	0,77	0,22	3,51	4,4E-04	9,6E-02
ENSMUSG0000 0040658	Dnph1	2,-deoxynucleoside 5,-phosphate N-hydrolase 1	926,16	-0,72	0,19	3,71	2,1E-04	6,4E-02
ENSMUSG0000 0020143	Dock2	Dedicator of cyto-kinesis 2	420,46	0,84	0,20	4,25	2,1E-05	1,1E-02
ENSMUSG0000 0025153	Fasn	fatty acid synthase(Fasn)	17210,76	0,94	0,16	5,83	5,6E-09	1,5E-05
ENSMUSG0000 0003420	Fcgrt	Fc receptor, IgG, alpha chain transporter(Fcgrt)	14127,59	-0,74	0,14	5,21	1,8E-07	3,8E-04
ENSMUSG0000 0078650	G6pc	glucose-6-phosphatase, catalytic(G6pc)	36170,90	-0,64	0,18	3,51	4,6E-04	9,6E-02
ENSMUSG0000 0033676	Gabrb3	Gamma-aminobutyric acid (GABA) A receptor, subunit beta 3	6443,23	-0,75	0,15	5,09	3,5E-07	5,5E-04
ENSMUSG0000 0040264	Gbp2b	Guanylate binding protein 2b	129,28	0,94	0,22	4,28	1,9E-05	9,6E-03
ENSMUSG0000 0079363	Gbp4	guanylate binding protein 4	1227,60	0,93	0,18	5,26	1,4E-07	3,3E-04
ENSMUSG0000 0046352	Gjb2	gap junction protein, beta 2(Gjb2)	10013,45	-0,50	0,14	3,58	3,4E-04	8,4E-02
ENSMUSG0000 0066407	Gm10263	Predicted gene 10263	1387,86	-0,64	0,17	3,88	1,0E-04	4,1E-02

ENSMUSG00000087353	Gm13727	Predicted gene 13727	121,13	1,13	0,22	5,15	2,7E-07	5,0E-04
ENSMUSG00000093006	Gm24157	Predicted gene, 24157	284,34	1,01	0,20	5,04	4,6E-07	6,2E-04
ENSMUSG00000098747	Gm27216	predicted gene 27216(Gm27216)	590,10	-0,88	0,21	4,13	3,6E-05	1,7E-02
ENSMUSG00000110631	Gm42047	Predicted gene, 42047	281,02	0,69	0,19	3,62	3,0E-04	7,7E-02
ENSMUSG00000104737	Gm42937	Predicted gene 42937	180,85	0,84	0,22	3,86	1,1E-04	4,1E-02
ENSMUSG00000115154	Gm49067	Predicted gene, 49067	315,01	-0,67	0,19	3,52	4,3E-04	9,6E-02
ENSMUSG00000111942	Gm5182	Predicted gene 5182	831,08	0,77	0,20	3,92	8,8E-05	3,6E-02
ENSMUSG00000072324	Gm8420	predicted gene 8420	98,70	2,07	0,22	9,36	7,8E-21	8,1E-17
ENSMUSG00000025534	Gusb	glucuronidase, beta(Gusb)	10329,15	-0,96	0,19	5,07	3,9E-07	5,6E-04
ENSMUSG00000036594	H2-Aa	histocompatibility 2, class II antigen A, alpha(H2-Aa)	5036,52	0,49	0,14	3,55	3,8E-04	9,1E-02
ENSMUSG00000073421	H2-Ab1	histocompatibility 2, class II antigen A, beta 1(H2-Ab1)	4559,45	0,69	0,19	3,74	1,8E-04	5,9E-02
ENSMUSG00000037649	H2-DMa	Histocompatibility 2, class II, locus DMa [Source:MGI Symbol;Acc:MGI:95921]	615,87	0,76	0,20	3,73	1,9E-04	6,0E-02

ENSMUSG0000 0067235	H2-Q10	Histocompatibility 2, Q region locus 10	395,64	0,77	0,22	3,51	4,5E-04	9,6E-02
ENSMUSG0000 0034551	Hdx	Highly divergent homeobox	63,83	0,79	0,22	3,61	3,1E-04	7,9E-02
ENSMUSG0000 0054072	ligp1	Interferon inducible GTPase 1	977,29	0,85	0,18	4,79	1,6E-06	1,5E-03
ENSMUSG0000 0000157	Itgb2l	Integrin beta 2-like	154,29	0,79	0,21	3,73	1,9E-04	6,0E-02
ENSMUSG0000 0058740	Kcnt1	Potassium channel, subfamily T, member 1	1126,40	0,64	0,16	4,04	5,4E-05	2,2E-02
ENSMUSG0000 0063177	Klk1b27	Kallikrein 1-related peptidase b27	46,56	0,72	0,20	3,50	4,7E-04	9,6E-02
ENSMUSG0000 0028581	Laptm5	Lysosomal-associated protein transmembrane 5	978,54	0,61	0,17	3,56	3,7E-04	8,9E-02
ENSMUSG0000 0022587	Ly6e	lymphocyte antigen 6 complex, locus E(Ly6e)	16502,33	-0,47	0,13	3,57	3,6E-04	8,9E-02
ENSMUSG0000 0069516	Lyz2	lysozyme 2(Lyz2)	2476,37	0,86	0,17	5,01	5,6E-07	6,9E-04
ENSMUSG0000 0012187	Mogat1	monoacylglycerol O-acyltransferase 1(Mogat1)	4309,18	-0,88	0,20	4,41	1,0E-05	6,1E-03
ENSMUSG0000 0046805	Mpeg1	Macrophage expressed gene 1	1305,66	0,74	0,16	4,76	2,0E-06	1,7E-03
ENSMUSG0000 0022679	Mpv17l	Mpv17 transgene, kidney disease mutant-like(Mpv17l)	85348,94	-0,60	0,17	3,54	4,0E-04	9,3E-02

ENSMUSG00000019992	Mtfr2	Mitochondrial fission regulator 2	47,96	0,79	0,22	3,65	2,6E-04	7,2E-02
ENSMUSG00000038670	Mybpc2	Myosin binding protein C, fast-type	151,73	0,76	0,22	3,47	5,1E-04	9,97E-02
ENSMUSG00000001056	Nhp2	NHP2 ribonucleoprotein(Nhp2)	3353,02	-0,66	0,19	3,50	4,6E-04	9,6E-02
ENSMUSG00000074151	Nlrc5	NLR family, CARD domain containing 5	375,84	0,81	0,21	3,87	1,1E-04	4,1E-02
ENSMUSG00000029819	Npy	neuropeptide Y(Npy)	221,31	-1,99	0,21	9,35	8,7E-21	8,1E-17
ENSMUSG00000032690	Oas2	2,-5, oligoadenylate synthetase 2	158,43	0,79	0,22	3,69	2,2E-04	6,8E-02
ENSMUSG00000021913	Ogdhl	Oxoglutarate dehydrogenase-like	276,39	0,86	0,21	4,04	5,3E-05	2,2E-02
ENSMUSG00000038910	Plcl2	Phospholipase C-like 2	782,25	-0,82	0,18	4,63	3,7E-06	2,8E-03
ENSMUSG00000052160	Pld4	Phospholipase D family, member 4	403,71	0,79	0,18	4,41	1,0E-05	6,1E-03
ENSMUSG00000042251	Pm20d1	Peptidase M20 domain containing 1	9189,12	-0,67	0,18	3,81	1,4E-04	4,8E-02
ENSMUSG00000030423	Pop4	Processing of precursor 4, ribonuclease P/MRP family	634,04	0,72	0,17	4,29	1,8E-05	9,6E-03
ENSMUSG00000020684	Rasl10b	RAS-like, family 10, member B	149,28	1,06	0,22	4,83	1,4E-06	1,4E-03

ENSMUSG0000 0021876	Rnase4	ribonuclease, RNase A family 4(Rnase4)	4455,7 6	-0,66	0, 15	4,3 8	1,2E -05	6,8E- 03
ENSMUSG0000 0031609	Sap30	sin3 associated polypeptide(Sap30)	3295,6 3	-0,59	0, 16	3,6 7	2,4E -04	6,9E- 02
ENSMUSG0000 0038224	Serpinf2	serine (or cysteine) peptidase inhibitor, clade F, member 2(Serpinf2)	21474, 96	-0,78	0, 20	3,8 6	1,1E -04	4,1E- 02
ENSMUSG0000 0035699	Slc51a	solute carrier family 51, alpha subunit(Slc51a)	6523,7 0	-0,65	0, 17	3,7 5	1,8E -04	5,8E- 02
ENSMUSG0000 0025790	Slco3a1	Solute carrier organic anion transporter family, member 3a1	11292, 58	-0,67	0, 19	3,5 0	4,7E -04	9,6E- 02
ENSMUSG0000 0040693	Slco4c1	Solute carrier organic anion transporter family, member 4C1	324,30	0,76	0, 20	3,8 6	1,1E -04	4,1E- 02
ENSMUSG0000 0044349	Snhg11	Small nucleolar RNA host gene 11	2094,3 2	0,99	0, 19	5,1 1	3,2E -07	5,5E- 04
ENSMUSG0000 0096054	Syne1	Spectrin repeat containing, nuclear envelope 1	1889,0 3	0,59	0, 17	3,5 2	4,3E -04	9,6E- 02
ENSMUSG0000 0056296	Synpr	Synaptoporin	1611,7 8	-0,90	0, 19	4,6 6	3,1E -06	2,4E- 03
ENSMUSG0000 0022218	Tgm1	transglutaminase 1, K polypeptide(Tgm1)	5200,8 2	-0,67	0, 16	4,3 1	1,7E -05	9,2E- 03

ENSMUSG0000 0044583	Tlr7	Toll-like receptor 7	165,79	0,86	0,21	4,05	5,1E-05	2,2E-02
ENSMUSG0000 0040883	Tmem205	Transmembrane protein 205	4488,10	-0,59	0,16	3,66	2,6E-04	7,2E-02
ENSMUSG0000 0048572	Tmem252	transmembrane protein 252(Tmem252)	6035,70	-0,70	0,20	3,49	4,8E-04	9,6E-02
ENSMUSG0000 0010307	Tmem86a	transmembrane protein 86A(Tmem86a)	5856,74	-0,74	0,19	3,84	1,2E-04	4,3E-02
ENSMUSG0000 0016942	Tmprss6	Transmembrane serine protease 6	518,88	0,74	0,20	3,63	2,8E-04	7,6E-02
ENSMUSG0000 0043621	Ubxn10	UBX domain protein 10	675,26	-0,80	0,21	3,88	1,1E-04	4,1E-02
ENSMUSG0000 0031710	Ucp1	uncoupling protein 1 (mitochondrial, proton carrier)(Ucp1)	932,71	-0,94	0,21	4,53	5,9E-06	3,9E-03
ENSMUSG0000 0027962	Vcam1	Vascular cell adhesion molecule 1	1251,88	0,77	0,16	4,81	1,5E-06	1,5E-03
ENSMUSG0000 0056592	Zfp658	Zinc finger protein 658	228,62	0,98	0,20	4,92	8,8E-07	1,0E-03

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Table 1c. Cell types in wild type kidneys that expressed the genes differentially expressed in *Tshz3^{+/lacZ}* kidney

Ensembl mouse ID	Mouse Gene symbol	Endothelium	Mesangium	Podocytes	Tubules	Immune
ENSMUSG00000054676	1600014C10Rik	X	X	X	X	
ENSMUSG00000086474	9130204K15Rik					
ENSMUSG00000004668	Abca13	X		X	X	
ENSMUSG00000031659	Adcy7			X		X
ENSMUSG00000004730	Adgre1					
ENSMUSG00000060470	Adgrg3	X		X	X	
ENSMUSG00000085180	Ai838599		X	X	X	
ENSMUSG00000033715	Akr1c14	X	X			
ENSMUSG00000028356	Ambp					
ENSMUSG00000020609	Apob					
ENSMUSG00000040694	Apobec2					
ENSMUSG00000020604	Arsg	X	X	X	X	
ENSMUSG00000038704	Aspdh					
ENSMUSG00000017929	B4galt5	X	X	X	X	X
ENSMUSG00000090486	BC035947					
ENSMUSG00000030268	Bcat1					
ENSMUSG00000058914	C1qtnf3					
ENSMUSG00000022416	Cacna1i					
ENSMUSG00000038128	Camk4			X	X	
ENSMUSG00000024610	Cd74	X		X		X
ENSMUSG00000022504	Ciita					

ENSMUSG00000056025	Clca3a1						
ENSMUSG00000040663	Clcf1	X			X		X
ENSMUSG00000024330	Col11a2				X		X
ENSMUSG00000030905	Crym				X		
ENSMUSG00000038642	Ctss				X		X
ENSMUSG00000027014	Cwc22	X	X		X		X
ENSMUSG00000015340	Cybb				X		X
ENSMUSG00000074254	Cyp2a4						
ENSMUSG00000108332	D530033B14Rik						
ENSMUSG00000031294	D630029K05Rik						
ENSMUSG00000025279	Dnase1l3						
ENSMUSG00000040658	Dnph1	X			X		X
ENSMUSG00000020143	Dock2				X		
ENSMUSG00000025153	Fasn	X	X		X		X
ENSMUSG00000003420	Fcgrt	X	X		X		X
ENSMUSG00000078650	G6pc	X	X		X		X
ENSMUSG00000033676	Gabrb3						
ENSMUSG00000040264	Gbp2b	X	X		X		
ENSMUSG00000079363	Gbp4	X			X		X
ENSMUSG00000046352	Gjb2						
ENSMUSG00000066407	Gm10263	X	X		X		X
ENSMUSG00000087353	Gm13727						
ENSMUSG00000093006	Gm24157				X		X
ENSMUSG00000098747	Gm27216						
ENSMUSG00000110631	Gm42047						

ENSMUSG00000104737	Gm42937	X			X		X	
ENSMUSG00000115154	Gm49067							
ENSMUSG00000111942	Gm5182							
ENSMUSG00000072324	Gm8420	X		X		X	X	X
ENSMUSG00000025534	Gusb	X		X		X	X	X
ENSMUSG00000036594	H2-Aa	X				X		X
ENSMUSG00000073421	H2-Ab1	X				X	X	X
ENSMUSG00000037649	H2-DMa			X		X	X	X
ENSMUSG00000067235	H2-Q10	X		X		X	X	X
ENSMUSG00000034551	Hdx	X		X		X		
ENSMUSG00000054072	ligp1	X		X		X	X	
ENSMUSG00000000157	Itgb2l			X		X		
ENSMUSG00000058740	Kcnt1							
ENSMUSG00000063177	Klk1b27						X	
ENSMUSG00000028581	Laptm5	X				X		X
ENSMUSG00000022587	Ly6e	X		X		X	X	X
ENSMUSG00000069516	Lyz2					X		X
ENSMUSG00000012187	Mogat1							
ENSMUSG00000046805	Mpeg1					X		X
ENSMUSG00000022679	Mpv17l	X		X		X	X	
ENSMUSG00000019992	Mtfr2	X				X		
ENSMUSG00000038670	Mybpc2					X		
ENSMUSG00000001056	Nhp2	X		X		X	X	
ENSMUSG00000074151	Nlrc5	X		X		X		X
ENSMUSG00000029819	Npy	X		X		X	X	

ENSMUSG00000032690	Oas2					
ENSMUSG00000021913	Ogdhl					
ENSMUSG00000038910	Plcl2	X			X	X
ENSMUSG00000052160	Pld4				X	X
ENSMUSG00000042251	Pm20d1	X			X	X
ENSMUSG00000030423	Pop4	X	X		X	X
ENSMUSG00000020684	Rasl10b					
ENSMUSG00000021876	Rnase4	X	X		X	X
ENSMUSG00000031609	Sap30	X	X		X	X
ENSMUSG00000038224	Serpinf2					
ENSMUSG00000035699	Slc51a					
ENSMUSG00000025790	Slco3a1	X	X		X	X
ENSMUSG00000040693	Slco4c1					
ENSMUSG00000044349	Snhg11					
ENSMUSG00000096054	Syne1	X	X		X	X
ENSMUSG00000056296	Synpr					
ENSMUSG00000022218	Tgm1					
ENSMUSG00000044583	Tlr7	X			X	
ENSMUSG00000040883	Tmem205	X	X		X	X
ENSMUSG00000048572	Tmem252	X			X	
ENSMUSG00000010307	Tmem86a	X	X		X	X
ENSMUSG00000016942	Tmprss6					
ENSMUSG00000043621	Ubxn10					
ENSMUSG00000031710	Ucp1					
ENSMUSG00000027962	Vcam1	X	X		X	

ENSMUSG00000056592

Zfp658

X

X

[From the interactive online database at https://shiny.mdc-berlin.de/mgsca/.](https://shiny.mdc-berlin.de/mgsca/)

Karaiskos, N. *et al.* A Single-Cell Transcriptome Atlas of the Mouse Glomerulus. *Journal of the American Society of Nephrology : JASN* **29**, 2060-2068 (2018).

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Table 1d. Gene sets enriched in kidneys from wild-type (top) and *Tshz3*^{+/*lacZ*} (bottom) adult mice.

Gene Sets enriched in WT								
NAME	SIZE	ES	NES	NO M p- val	FDR q-val	FWE R p- val	RAN K AT MAX	LEADING EDGE
HALLMARK_OXIDATIVE_PHOSPHORYLATION	192	0.21979448	3.5341222	0.0	0.0	0.0	3407 4	tags=85%, list=64%, signal=233 %
HALLMARK_XENOBIOTIC_METABOLISM	185	0.20220149	3.2691824	0.0	0.0	0.0	8038	tags=35%, list=15%, signal=41 %
HALLMARK_FATTY_ACID_METABOLISM	147	0.18565473	2.6469336	0.0	6.734007E +5	0.002	7584	tags=33%, list=14%, signal=38 %
Gene Sets enriched in <i>Tshz3</i> ^{+/<i>lacZ</i>}								
NAME	SIZE	ES	NES	NO M p- val	FDR q-val	FWE R p- val	RAN K AT MAX	LEADING EDGE
HALLMARK_MITOTIC_SPINDLE	196	-0.5266113	-8.769232	0.0	0.0	0.0	2221 6	tags=94%, list=41%, signal=160 %
HALLMARK_INTERFERON_GAMMA_RESPONSE	184	-0.51867735	-8.325257	0.0	0.0	0.0	1950 4	tags=88%, list=36%,

								signal=138%
HALLMARK_G2M_CHECKPOINT	192	0	-7.6077356	0.0	0.0	0.0	20349	tags=86%, list=38%, signal=138%
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	191	-0.4679353	-7.484958	0.0	0.0	0.0	15995	tags=76%, list=30%, signal=109%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	194	-0.4516578	-7.4689045	0.0	0.0	0.0	21210	tags=85%, list=40%, signal=139%
HALLMARK_INFLAMMATORY_RESPONSE	194	-0.4648554	-7.388191	0.0	0.0	0.0	20228	tags=84%, list=38%, signal=134%
HALLMARK_E2F_TARGETS	194	-0.44707173	-7.359824	0.0	0.0	0.0	20349	tags=82%, list=38%, signal=132%
HALLMARK_APICAL_JUNCTION	191	-0.43906716	-7.0284314	0.0	0.0	0.0	20347	tags=82%, list=38%, signal=131%
HALLMARK_ALLOGRAFT_REJECTION	183	-0.43641797	-7.023872	0.0	0.0	0.0	21228	tags=83%, list=40%, signal=137%
HALLMARK_UV_RESPONSE_DN	140	-0.4880429	-6.7432823	0.0	0.0	0.0	20254	tags=86%, list=38%, signal=138%
HALLMARK_IL2_STAT5_SIGNALING	190	-0.41261196	-6.596804	0.0	0.0	0.0	24815	tags=87%, list=46%,

								signal=162 %
HALLMARK_MYOGENESIS	197	-0.39249557	-6.3807335	0.0	0.0	0.0	2368 3	tags=83%, list=44%, signal=148 %
HALLMARK_P53_PATHWAY	193	-0.38617578	-6.2882223	0.0	0.0	0.0	2383 3	tags=83%, list=44%, signal=149 %
HALLMARK_ESTROGEN_RESPONSE_EARLY	193	-0.38673815	-6.170295	0.0	0.0	0.0	2324 7	tags=82%, list=43%, signal=144 %
HALLMARK_KRAS_SIGNALING_UP	188	-0.37593746	-5.9241505	0.0	0.0	0.0	2299 3	tags=80%, list=43%, signal=140 %
HALLMARK_HYPOXIA	190	-0.358095	-5.8049035	0.0	0.0	0.0	2349 4	tags=79%, list=44%, signal=141 %
HALLMARK_COMPLEMENT	180	-0.36794096	-5.7306614	0.0	0.0	0.0	2771 7	tags=88%, list=52%, signal=182 %
HALLMARK_KRAS_SIGNALING_DN	187	-0.35026854	-5.5609736	0.0	0.0	0.0	2545 6	tags=82%, list=47%, signal=156 %
HALLMARK_INTERFERON_ALPHA_RESPONSE	88	-0.5092165	-5.549178	0.0	0.0	0.0	2027 9	tags=89%, list=38%, signal=142 %
HALLMARK_ESTROGEN_RESPONSE_LATE	190	-0.32073304	-5.2083893	0.0	0.0	0.0	2210 3	tags=73%, list=41%,

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Table 1e. ChIP enrichment analysis

Term	Overlap	Z-score	Combined Score	Genes
Interferon gamma signaling_Homo sapiens_R-HSA-877300	3/93	-1.79	11.67	CIITA;VCAM1;GBP4
Assembly of collagen fibrils and other multimeric structures_Homo sapiens_R-HSA-2022090	2/54	-2.03	9.92	COL11A2;CTSS
Interferon Signaling_Homo sapiens_R-HSA-913531	3/196	-2.08	9.26	CIITA;VCAM1;GBP4
Triglyceride Biosynthesis_Homo sapiens_R-HSA-75109	2/66	-1.98	8.93	MOGAT1;FASN
Collagen formation_Homo sapiens_R-HSA-1474290	2/85	-1.95	7.88	COL11A2;CTSS
Extracellular matrix organization_Homo sapiens_R-HSA-1474244	3/283	-1.99	6.94	VCAM1;COL11A2;CTSS
MHC class II antigen presentation_Homo sapiens_R-HSA-2132295	2/103	-1.85	6.80	CD74;CTSS
Lysine catabolism_Homo sapiens_R-HSA-71064	1/12	-1.66	5.92	CRYM
Endosomal/Vacuolar pathway_Homo sapiens_R-HSA-1236977	1/12	-1.51	5.39	CTSS
GABA A receptor activation_Homo sapiens_R-HSA-977441	1/13	-1.52	5.28	GABRB3

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Table 1f. DEGs that are known direct targets of IRF8

Ensembl mouse ID	Mouse Gene symbol
ENSMUSG00000028356	Ambp
ENSMUSG00000020604	Arsg
ENSMUSG00000024610	Cd74
ENSMUSG00000022504	Ciita
ENSMUSG00000038642	Ctss
ENSMUSG00000015340	Cybb
ENSMUSG00000079363	Gbp4
ENSMUSG00000036594	H2-Aa
ENSMUSG00000073421	H2-Ab1
ENSMUSG00000037649	H2-DMa
ENSMUSG00000054072	ligp1
ENSMUSG00000022587	Ly6e
ENSMUSG00000069516	Lyz2
ENSMUSG00000046805	Mpeg1
ENSMUSG00000032690	Oas2
ENSMUSG00000038910	Plcl2
ENSMUSG00000052160	Pld4
ENSMUSG00000030423	Pop4
ENSMUSG00000021876	Rnase4
ENSMUSG00000044583	Tlr7
ENSMUSG00000010307	Tmem86a
ENSMUSG00000056592	Zfp658

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Table 1g. Human orthologs for differentially expressed genes

Human Gene symbol	Ensembl mouse ID	Mouse Gene symbol
C19orf12	ENSMUSG00000054676	1600014C10Rik
ABCA13	ENSMUSG00000004668	Abca13
ADCY7	ENSMUSG000000031659	Adcy7
ADGRE1	ENSMUSG00000004730	Adgre1
ADGRG3	ENSMUSG000000060470	Adgrg3
AMBP	ENSMUSG000000028356	Ambp
APOB	ENSMUSG000000020609	Apob
APOBEC2	ENSMUSG000000040694	Apobec2
ARSG	ENSMUSG000000020604	Arsg
ASPDH	ENSMUSG000000038704	Aspdh
B4GALT5	ENSMUSG000000017929	B4galt5
ERVW-1	ENSMUSG000000090486	BC035947
BCAT1	ENSMUSG000000030268	Bcat1
C1QTNF3	ENSMUSG000000058914	C1qtnf3
CACNA1I	ENSMUSG000000022416	Cacna1i
CAMK4	ENSMUSG000000038128	Camk4
CD74	ENSMUSG000000024610	Cd74
CIITA	ENSMUSG000000022504	Ciita
CLCF1	ENSMUSG000000040663	Clcf1
COL11A2	ENSMUSG000000024330	Col11a2
CRYM	ENSMUSG000000030905	Crym
CTSS	ENSMUSG000000038642	Ctss
CWC22	ENSMUSG000000027014	Cwc22
CYBB	ENSMUSG000000015340	Cybb
CYP2A13	ENSMUSG000000074254	Cyp2a4
DNASE1L3	ENSMUSG000000025279	Dnase1l3
DNPB1	ENSMUSG000000040658	Dnph1
DOCK2	ENSMUSG000000020143	Dock2
FASN	ENSMUSG000000025153	Fasn
FCGRT	ENSMUSG000000003420	Fcgrt
G6PC1	ENSMUSG000000078650	G6pc
GABRB3	ENSMUSG000000033676	Gabrb3
GBP3	ENSMUSG000000040264	Gbp2b
GBP6	ENSMUSG000000079363	Gbp4
GJB2	ENSMUSG000000046352	Gjb2
GUSB	ENSMUSG000000025534	Gusb
HLA-DQA1	ENSMUSG000000036594	H2-Aa
HLA-DQB1	ENSMUSG000000073421	H2-Ab1
HLA-DMA	ENSMUSG000000037649	H2-DMa

HLA-A	ENSMUSG00000067235	H2-Q10
HDX	ENSMUSG00000034551	Hdx
ITGB2	ENSMUSG00000000157	Itgb2l
KCNT1	ENSMUSG000000058740	Kcnt1
KLK3	ENSMUSG00000063177	Klk1b27
LAPTM5	ENSMUSG00000028581	Laptm5
LY6E	ENSMUSG00000022587	Ly6e
LYZ	ENSMUSG00000069516	Lyz2
MOGAT1	ENSMUSG00000012187	Mogat1
MPEG1	ENSMUSG00000046805	Mpeg1
MPV17L	ENSMUSG00000022679	Mpv17l
MTFR2	ENSMUSG00000019992	Mtfr2
MYBPC2	ENSMUSG00000038670	Mybpc2
NHP2	ENSMUSG00000001056	Nhp2
NLRC5	ENSMUSG00000074151	Nlrc5
NPY	ENSMUSG00000029819	Npy
OAS2	ENSMUSG00000032690	Oas2
OGDHL	ENSMUSG00000021913	Ogdhl
PLCL2	ENSMUSG00000038910	Plcl2
PLD4	ENSMUSG000000052160	Pld4
PM20D1	ENSMUSG00000042251	Pm20d1
POP4	ENSMUSG00000030423	Pop4
RASL10B	ENSMUSG00000020684	Rasl10b
RNASE4	ENSMUSG00000021876	Rnase4
SAP30	ENSMUSG00000031609	Sap30
SERPINF2	ENSMUSG00000038224	Serpinf2
SLC51A	ENSMUSG00000035699	Slc51a
SLCO3A1	ENSMUSG00000025790	Slco3a1
SLCO4C1	ENSMUSG00000040693	Slco4c1
SNHG11	ENSMUSG00000044349	Snhg11
SYNE1	ENSMUSG00000096054	Syne1
SYNPR	ENSMUSG00000056296	Synpr
TGM1	ENSMUSG00000022218	Tgm1
TLR7	ENSMUSG00000044583	Tlr7
TMEM205	ENSMUSG00000040883	Tmem205
TMEM252	ENSMUSG00000048572	Tmem252
TMEM86A	ENSMUSG00000010307	Tmem86a
TMPRSS6	ENSMUSG00000016942	Tmprss6
UBXN10	ENSMUSG00000043621	Ubxn10
UCP1	ENSMUSG00000031710	Ucp1
VCAM1	ENSMUSG00000027962	Vcam1

Table 1h. Human orthologues of DEGs that are associated with renal disease and/or autism spectrum disorder

Human Gene symbol	Kidney disease	reference	ASD	reference	Genetic syndromes that associate kidney conditions and ASD	reference
C19orf12						
ABCA13			YES	MalaCards, SFARI, AutDB		
ADCY7						
ADGRE1						
ADGRG3						
AMBP	Pyelonephritis, Urolithiasis, Hydronephrosis, VUR 1, Hypertensive Nephropathy	MalaCards, DisGenet, AGR				
APOB	CKD, Nephrotic syndrome, Uremia,	MalaCards, AGR	YES	SFARI		
APOBEC2						
ARSG						
ASPDH						
B4GALT5						
ERVW-1						

BCAT1	Crescentic Glomerulonephritis	MalaCards				
C1QTNF3						
CACNA1I			YE S	SFARI, AutDB		
CAMK4	Systemic Lupus Erythematosus, Kidney disease, Glomerulonephritis, Focal Segmental Glomerulosclerosis	MalaCards	YE S	SFARI, AutDB		
CD74	Renal Cell Carcinoma (nonpapillary), Kidney disease, Systemic Lupus Erythematosus, Polycystic Kidney Disease	MalaCards				
CIITA	Systemic Lupus Erythematosus, Tuberos Sclerosis 1	MalaCards, AGR	YE S	MalaCards	Tuberos Sclerosis 1	Malacards
CLCF1						
COL11A2						
CRYM						
CTSS	Renal Cell Carcinoma	MalaCards				
CWC22						

CYBB	Renal Hypertension, Kidney Disease, ESRD, Renal fibrosis	MalaCards, DisGenet, AGR				
CYP2A13						
DNASE1L3	Systemic Lupus Erythematosus, Glomerulonephritis	MalaCards				
DNP1						
DOCK2	Systemic Lupus Erythematosus,	MalaCards				
FASN	Kidney Cancer, ESRD, Renal Fibrosis	MalaCards, DisGenet				
FCGRT	Systemic Lupus Erythematosus	MalaCards				
G6PC1						
GABRB3	RETT Syndrome	MalaCards	YES	MalaCards, SFARI, DisGenet, AGR, AutDB	RETT Syndrome	MalaCards
GBP3						
GBP6						
GJB2	Horseshoe Kidney, Branchiootorenal Syndrome	MalaCards				

GUSB						
HLA-DQA1	Lupus Erythematosus, Nephrotic Syndrome, Tubulointerstitial Nephritis with Uveitis,	MalaCards, AGR				
HLA-DQB1	Systemic Lupus Erythematosus, Nephrotic Syndrome, PKD, Tubulointerstitial Nephritis with Uveitis	MalaCards				
HLA-DMA	Systemic Lupus Erythematosus, Membranous Nephropathy	MalaCards				

HLA-A	Systemic Lupus Erythematosus, CKD, Behcet Syndrome, Chronic Pyelonephritis, Wilms Tumor 5, Wilms Tumor 1, Renal Cell Carcinoma (nonpapillary), Membranous Nephropathy, Down Syndrome, Turner Syndrome, Nephrotic Syndrome, Kidney Cancer, ESRD, Uremia, Iga Glomerulonephritis,	MalaCards	YES	MalaCards, SFARI, DisGene t, AutDB	Down Syndrome	MalaCards
HDX	CKD, Kidney Disease, ESRD,	MalaCards				
ITGB2	Autoimmune Glomerulonephritis,	MalaCards				
KCNT1	Fragile X Syndrome	MalaCards	YES	AutDB	Fragile X Syndrome	MalaCards
KLK3	Urinary Tract Obstruction, Nephrogenic Adenoma, Hydronephrosis, Lower Urinary Tract Calculus, Chromophobe Renal Cell Carcinoma	MalaCards				

LAPTM5	Systemic Lupus Erythematosus	MalaCards				
LY6E						
LYZ						
MOGAT1						
MPEG1	Tafro Syndrome	MalaCards				
MPV17L	Chromosome 16p13.3 Deletion Syndrome Proximal	MalaCards	YES	AutDB, AGR	Rubinstein-Taybi Syndrome	MalaCards, ClinVar
MTFR2						
MYBPC2						
NHP2						
NLRC5	Systemic Lupus Erythematosus, Renal Cell Carcinoma (nonpapillary), Renal fibrosis	MalaCards				
NPY	Turner Syndrome, Kidney Disease	MalaCards	YES	MalaCards		
OAS2						
OGDHL	PKD	MalaCards				
PLCL2						
PLD4	Nephrotic Syndrome (Type 7), Kidney Disease, CKD,	MalaCards				
PM20D1						
POP4						
RASL10B						

RNASE4					
SAP30	Renal Cell Carcinoma (Nonpapillary), Clear Cell Renal Celle Carcinoma	MalaCards			
SERPINF2					
SLC51A					
SLCO3A1					
SLCO4C1	CKD, Kidney Disease, PKD, Renal Oncocytoma	MalaCards, AGR			
SNHG11					
SYNE1			YE S	SFARI, AutDB	
SYNPR					
TGM1					
TLR7	Systemic Lupus Erythematosus, Behcet Syndrome, Glomerulonephritis, Turner Syndrome, Immune-Complex Glomerulonephritis	MalaCards			
TMEM205					
TMEM252					
TMEM86A					
TMPRSS6	Kidney Disease, CKD, ESRD	MalaCards			
UBXN10					

UCP1	Renal Cell Carcinoma (Nonpapillary),					
VCAM1	Systemic Lupus Erythematosus, Kidney Disease, Glomerulonephritis,	MalaCards, AGR				

Abbreviations: ASD, Autism Spectrum Disorder; CKD, Chronic Kidney Disease; ESRD, End Stage Renal Disease; PKD, Polycystic Kidney Disease.

Data bases: MALACARDS (<https://www.malacards.org>); SFARI (<https://gene.sfari.org>); ClinVar (<https://www.ncbi.nlm.nih.gov/clinvar/>); DisGenet (<https://www.disgenet.org>); AutDB (<http://autism.mindspec.org/autdb/Welcome.do>); AGR (Alliance of Genome Resources) (<https://www.alliancegenome.org>).

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Table 1i. Detailed of proteins origin of the 33 differentially excreted urinary peptides obtained by the comparison between *Tshz3^{+/lacZ}* heterozygous and WT control mice

Peptidel D	p_value BH	Mass	CE_t	Sequence	Prot_Name	Prot_Symbol	Prot_Accession	StartA	StopA	Peptidel D	Mean LacZ	Mean WT	Mean LacZ/Mea nWT	Fold-change
22340	0.012926897	1793,902	34,17476	EEASSTGRNF NVEKIN	Major urinary protein 17 (MUP 17)	MUP17	B5X0G2	19	34	22340	196,2796667	2,16625	90,608	90,608
13942	0.016090788	1379,653	48,00482	EPGVTGLQGQ AGPpG	Collagen alpha-1(VII) chain (Long-chain collagen) (LC collagen)	CO7A1	Q63870	1259	1273	13942	79,68906667	4,6420833	17,167	17,167
15681	0.025678503	1452,784	32,37929	ILGGQEAAAHA RPY	Complement factor D (EC 3.4.21.46) (28 kDa adipocyte protein) (Adipsin) (C3 convertase activator) (Properdin factor D)	CFAD	P03953	26	39	15681	484,8706667	30,8465	15,719	15,719
16620	0.029089955	1494,777	32,11926	SPGRHEAQEP FLQ	Tripeptidyl-peptidase 1 (TPP-1) (EC 3.4.14.9) (Lysosomal pepstatin-insensitive protease) (LPIC) (Tripeptidyl aminopeptidase) (Tripeptidyl-peptidase I) (TPP-I)	TPP1	O89023	293	305	16620	134,8598667	16,183833	8,333	8,333
4260	0.041691443	1002,542	28,20322	KGEpGDTGVK	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A1	P11087	815	824	4260	118,3426667	16,583833	7,136	7,136
7480	0.033417318	1130,597	29,37694	ERIASEASRL	Histone H2B type 1-F/J/L (H2B 291A)	H2B1F	P10853	72	81	7480	387,188	55,476	6,979	6,979
19556	0.027812250	1646,898	28,02357	GEAGKPGRpG ERGPpGP	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A1	P11087	222	238	19556	77,3836	16,189583	4,780	4,780

1232 5	0.0457 81039	131 5,63 8	38,8 357 5	DGTpGGpGIR GMpG	Collagen alpha-1(III) chain	CO3A 1	P08121	526	539	123 25	410,4 316	97,73	4,200	4,200
1971 1	0.0417 23205	165 5,83 7	33,5 862	GQPGAKGpG DTGVKGDA	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	810	827	197 11	1149, 64313	322,7 4108 3	3,562	3,562
972	0.0278 12250	859, 435 6	34,1 979 8	GTAGEpGKAG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	576	585	972	193,0 38266 7	56,17 025	3,437	3,437
1193 6	0.0129 26897	130 2,66	31,7 936 9	GAKGpGDTG VKGD	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	813	826	119 36	175,4 74066 7	64,55 4666 7	2,718	2,718
2167 3	0.0201 69148	175 9,90 3	34,0 971	GRpGEVGPpG PpGPAGEKG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	906	924	216 73	318,8 58933 3	119,3 34	2,672	2,672
931	0.0335 45397	857, 445 6	34,8 108 6	INKEIQN	Clusterin (Apolipoprotein J) (Apo-J) (Clustrin) (Sulfated glycoprotein 2) (SGP-2) [Cleaved into: Clusterin beta chain; Clusterin alpha chain]	CLUS	Q06890	41	47	931	477,9 65533 3	200,0 8875	2,389	2,389
7252	0.0417 23205	112 2,56 7	36,7 175 8	GPpGPpGAAG KEG	Collagen alpha-2(I) chain (Alpha-2 type I collagen)	CO1A 2	Q01149	811	823	725 2	1519, 35813 3	679,1 6475	2,237	2,237
7194	0.0365 46003	111 9,53 7	47,6 387 6	GEVGPpGPpG PAG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	909	921	719 4	4585, 02026 7	2344, 5474 2	1,956	1,956
7629	0.0278 12250	113 6,51	47,7 381 9	GQpGPpGPpG TAG	Collagen alpha-1(III) chain	CO3A 1	P08121	329	341	762 9	646,1 97533 3	429,8 4916 7	1,503	1,503

8738	0.0406 02421	118 0,58 3	37,8 385 4	ApGEKGEAGP pGP	Collagen alpha-1(III) chain	CO3A 1	P08121	828	840	873 8	3789, 51666 7	2618, 5458 3	1,447	1,447
9385	0.0182 50194	120 8,60 3	38,3 618 3	ApGDRGEAGP pGP	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	787	799	938 5	11265 ,728	1668 6,741 8	0,675	0,675
1101 8	0.0365 46003	127 1,61 6	47,9 784 2	GPpGPpGPpG PPSGG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	117 0	118 4	110 18	1161, 6598	2201, 4412 5	0,528	0,528
1934 5	0.0423 16711	163 6,82 8	40,7 328 5	GSpGSpGPDG KTGPpGPAG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	531	549	193 45	664,5 52733 3	1316, 2705	0,505	0,505
9525	0.0297 58618	121 4,59 1	47,9 075 1	GPpGPpGpPG PSGP	Collagen alpha-1(XIII) chain	CODA 1	Q9R1N 9	277	290	952 5	917,3 95866 7	1902, 3558 3	0,482	0,482
8447	0.0129 26897	116 8,60 9	37,4 637	KpGEQGVPGD LG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	646	657	844 7	2531, 80493 3	5723, 6408 3	0,442	0,442
1522 1	0.0268 16915	143 3,72 5	38,8 085 3	GEVGPpGPpG PAGEKG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	909	924	152 21	784,5 99666 7	2096, 3034 2	0,374	0,374
1544 7	0.0457 81039	144 1,68 9	48,1 270 4	GPPGPEGPpG PpGLQG	Collagen alpha-1(XIII) chain	CODA 1	Q9R1N 9	602	617	154 47	658,7 40133 3	1763, 6471 7	0,374	0,374
1498 7	0.0301 31027	142 1,71 9	39,3 592 1	RGETGpAGpQ GPpGP	Collagen alpha-1(XIV) chain	COEA 1	Q80X19	149 2	150 6	149 87	2405, 85386 7	6710, 7721 7	0,359	0,359

1928 5	0.0110 84765	163 3,82	41,1 177 4	EVGPpGPPGp AGEKGSpG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	910	927	192 85	893,8 02866 7	4596, 7776 7	0,194	0,194
1960 6	0.0026 81798	164 9,81 5	41,2 899 7	EVGPpGPPGp AGEKGSpG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	910	927	196 06	1646, 13146 7	9486, 7959 2	0,174	0,174
1339 9	0.0129 26897	135 7,64 9	31,5 735 8	NGDDGEAGKp GRpG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	218	231	133 99	583,4 16666 7	3496, 7980 8	0,167	0,167
1999 5	0.0288 18934	167 1,65	48,0 321 4	TGDSGPAGpP GPpGppGPP	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	116 0	117 8	199 95	881,2 18	6896, 0216 7	0,128	0,128
7284	0.0129 26897	112 3,55 3	36,2 466 4	GGKGEQGPA GPpG	Collagen alpha-2(I) chain (Alpha-2 type I collagen)	CO1A 2	Q01149	547	559	728 4	85,35 27333 3	893,7 9541 7	0,095	0,095
1502 932	0.0278 12250	152 0,76 3	40,0 275 7	VGPpGPpGpA GEKGSpG	Collagen alpha-1(I) chain (Alpha-1 type I collagen)	CO1A 1	P11087	911	927	150 293 2	113,7 734	1341, 7740 8	0,085	0,085
8166	0.0129 26897	115 7,54 3	47,7 683 2	GPpGPpGPpG PpA	Collagen alpha-1(XV) chain [Cleaved into: Restin (Endostatin- XV)]	COFA 1	O35206	107 5	108 7	816 6	392,0 53333 3	4803, 2158 3	0,082	0,082
2133 3	0.0417 23205	174 1,98 4	34,2 490 8	FIDQTRVLNLG PITR	Uromodulin (Tamm-Horsfall urinary glycoprotein) (THP) [Cleaved into: Uromodulin; secreted form]	URO M	Q91X17	593	607	213 33	58,21 54666 7	989,7 535	0,059	0,059

p =
hydroxylated
proline

865 **Abbreviations**

866 B-Gal, Beta-Galactosidase

867 EnC, endothelial cell cytoplasm

868 F, endothelial fenestration

869 GBM, glomerular basement membrane

870 GEC, glomerular endothelial cells

871 HET, hererozygous

872 P: papilla

873 Po, podocyte foot process

874 SD, standard deviation

875 SEM, Standard Errors of the Mean

876 u: urothelium

877 WT, wild type