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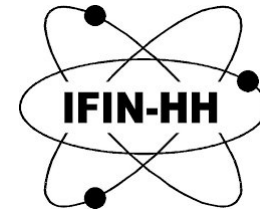
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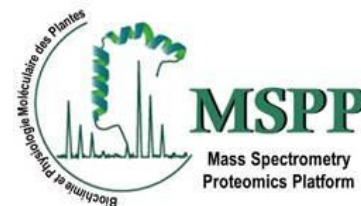
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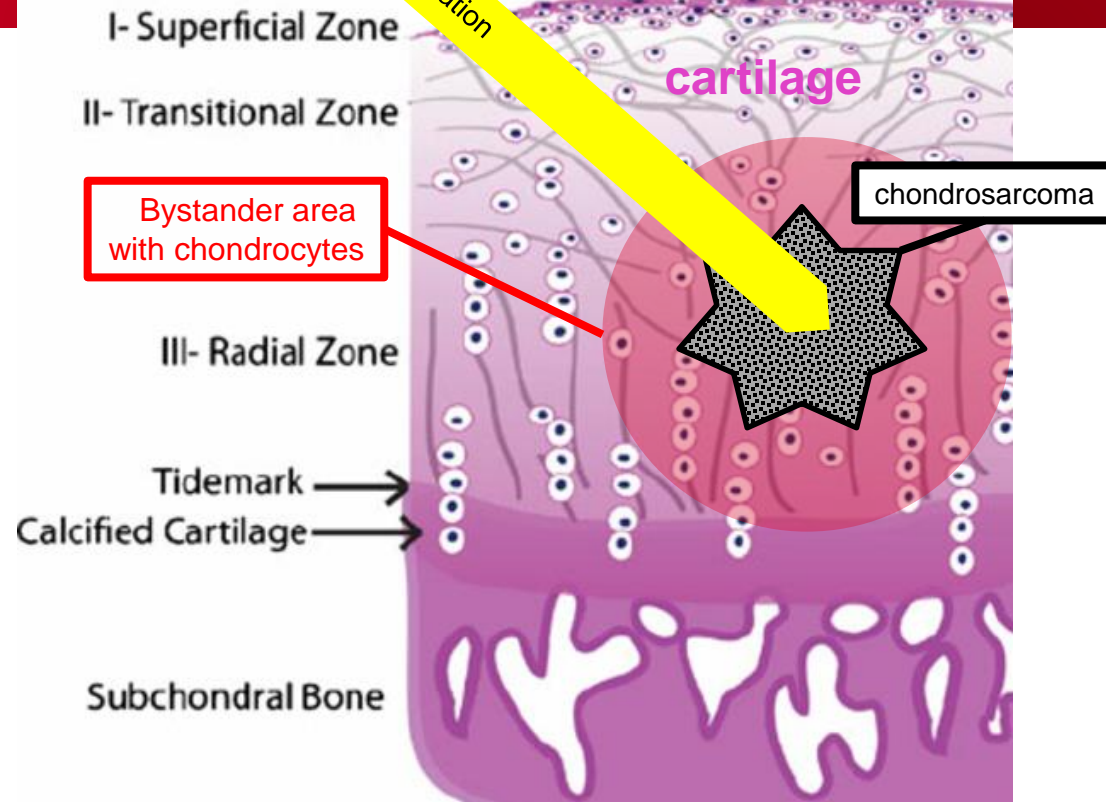
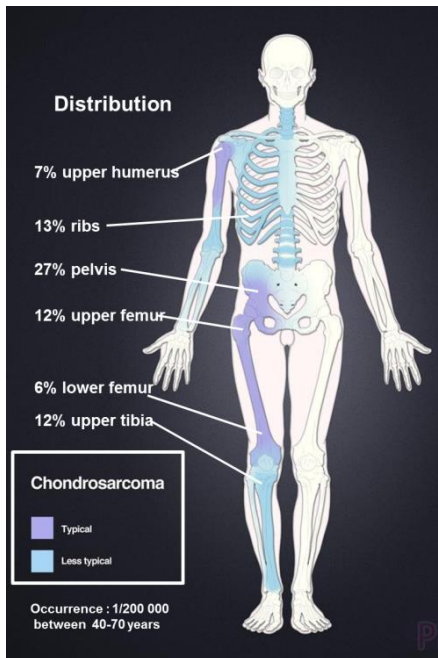
Proteomic analysis of bystander effects in chondrosarcoma cells

Gilbert Antoine¹, Tudor Mihaela^{2,3}, Lepleux Charlotte¹, Rofidal Valérie⁴, Hem Sonia⁴, Almunia Christine⁵, Armengaud Jean⁵, Brotin Emilie⁶, Haghdoust Siamak¹, Savu Diana², Francois Chevalier¹

- 1 UMR6252 CIMAP, CEA - CNRS - ENSICAEN - Université de Caen Normandie, Team LARIA, Caen, France
- 2 Department of Life and Environmental Physics, Horia Hulubei National Institute of Physics and Nuclear Engineering, Magurele, Romania
- 3 University of Bucharest, Faculty of Biology, Splaiul Independentei 91-95, Bucharest R-050095, Romania
- 4 BPMP, Mass Spectrometry Proteomics Platform, Montpellier, France
- 5 Innovative technologies for Detection and Diagnostics, CEA-DRF-Li2D, Marcoule, France
- 6 ImpedanCELL Platform, Federative Structure 4206 ICORE, Normandie Univ, UNICAEN, Inserm U1086 ANTICIPE, Biology and Innovative Therapeutics for Ovarian Cancers group (BioTICLA), Comprehensive Cancer Center F. Baclesse, 14000, Caen, France.



- **Chondrosarcoma** is a malignant tumor arising from cartilaginous tissues
- described as radiation- and chemo-resistant to conventional treatments.
- The primary treatment consists in wide surgical resection, which may lead to severe disabilities
- We previously showed the presence of a bystander effect following low dose irradiation of chondrosarcoma cells (1)



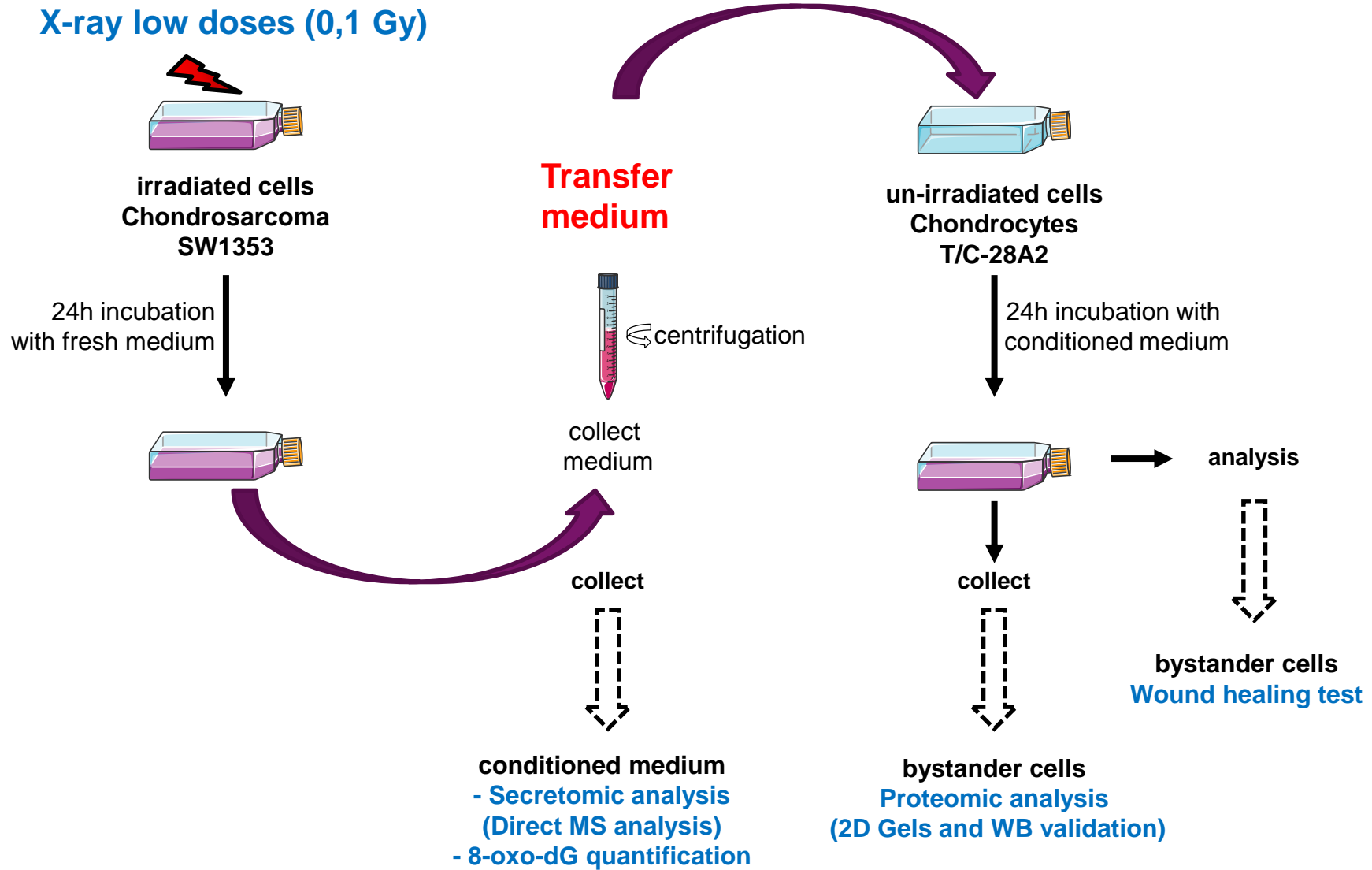
Objectives of the study:

after irradiation of chondrosarcoma (low dose X-rays), and using **proteomic tools**:

- 1) analyze **bystander response** in chondrocyte
- 2) analyse conditioned medium : **bystander factors**

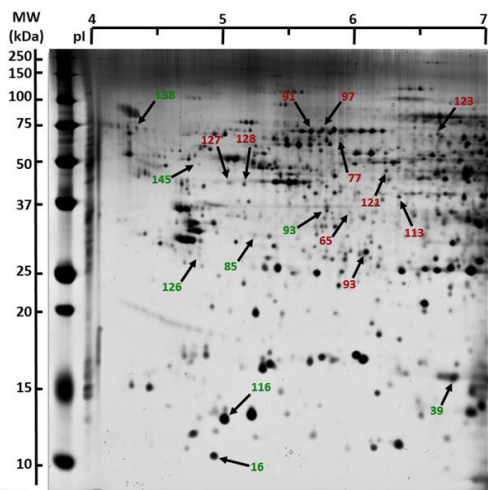


identification of **new protein factors** involved in the bystander effect



RESULTS: LIST OF MODULATED PROTEINS (0 GY vs 0,1 GY)

Proteomic analysis of bystander cells 20 proteins modulated, 9 were increased

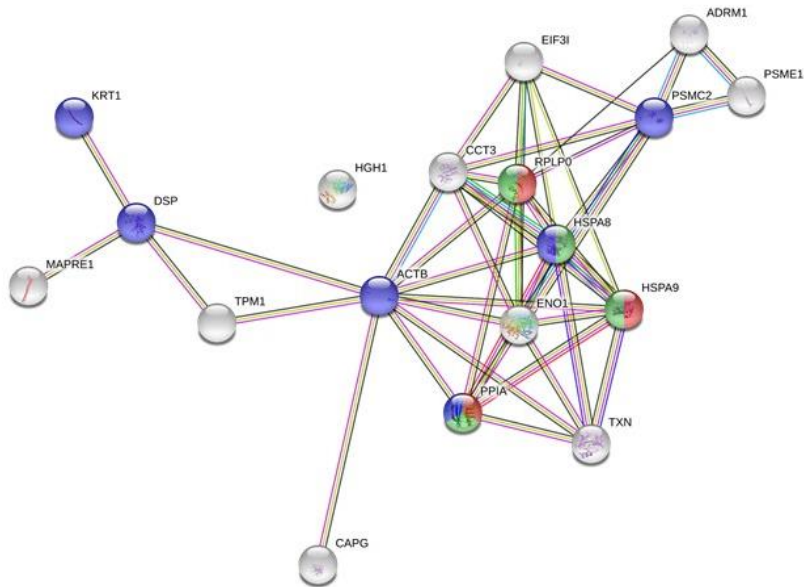


Spot number	Fold	pI	MW	Accession	Names
16	1,31	4,79	20	P60709	Actin
39	1,62	6,69	26	P62937	Cyclophilin A
85	1,38	5,11	63	Q15691	Microtubule-associated protein RP
93	1,31	5,99	57	Q06323	PSME1
116	1,27	4,87	23	P15924	Desmoplakin
116				P10599	Thioredoxin
126	1,63	4,67	56	P09493	Tropomyosin alpha-1 chain
138	1,98	4,18	145	P04264	Keratin, type II
145	1,47	4,67	98	Q9BTY7	Protein HGH1 homolog
65	1,81	5,86	72	P06733	Alpha-enolase
65				P05388	60S acidic ribosomal protein P0
77	1,56	5,79	130	P01876	IGHA1 protein
77	1,29	5,63	140	P11142	HSC 70 protein
91	1,32	5,64	141	P38646	Hspa9
97	1,27	6,25	79	P40121	CAP-G protein
113	1,47	6,15	94	P35998	26S proteasome regulatory subunit 7
121	1,31	6,56	136	P49368	T-complex protein 1 subunit gamma
123	1,31	4,91	87	P60709	Actin
128	1,36	5,03	87	Q16186	Proteasomal ubiquitin receptor ADRM1
134	1,26	5,68	73	Q13347	Eukaryotic translation initiation factor 3 subunit I

Secretomic analysis of conditioned medium from chondrosarcoma cells 40 proteins were modulated, 24 were increased

Accession	Name	pI	mass	Tfold	p value
P11940	Polyadenylate-binding protein 1	9,85	106299	23,83	2,64E-02
P24752	Acetyl-CoA acetyltransferase, mitochondrial	8,39	58871	4,00	5,13E-03
A5PLL7	Transmembrane protein 189	9,07	107703	3,33	2,78E-02
P08243	Asparagine synthetase [glutamine-hydrolyzing]	6,86	67256	3,17	1,55E-02
P35080	Profilin-2	8,87	77777	2,86	4,23E-02
P49207	60S ribosomal protein L34	10,64	21824	2,50	1,11E-03
Q9HC38	Glyoxalase domain-containing protein 4	7,94	68961	2,11	1,91E-02
P62424	60S ribosomal protein L7a	10,54	33547	2,00	1,50E-02
P62753	40S ribosomal protein S6	10,74	31799	2,00	6,42E-03
Q16181	Septin-7	8,97	244012	2,00	7,61E-03
P27361	Mitogen-activated protein kinase 3	9,14	69163	2,00	2,50E-02
O60763	General vesicular transport factor p115	5,88	159184	1,91	1,91E-02
P62979	Ubiquitin-40S ribosomal protein S27a	9,64	19523	1,84	3,56E-02
Q53SE2	Uncharacterized protein HSPD1	8,32	70924	1,83	1,86E-02
P62917	60S ribosomal protein L8	11,15	32789	1,79	1,66E-03
Q9NQR4	Omega-amidase NIT2	6,73	47093	1,75	3,35E-02
P15880	40S ribosomal protein S2	10,37	34399	1,67	1,56E-02
O75367	Core histone macro-H2A.1	9,75	68531	1,67	3,79E-02
Q13126	S-methyl-5'-thioadenosine phosphorylase	9,17	186699	1,64	3,10E-03
Q96D15	Reticulocalbin-3	5,05	46220	1,64	4,66E-03
Q7Z6E9	E3 ubiquitin-protein ligase RBBP6	9,65	98855	1,58	3,85E-02
O00370	LINE-1 retrotransposable element ORF2 protein	9,51	5633488	1,57	1,79E-02
Q9NZ08	Endoplasmic reticulum aminopeptidase 1	9,00	202092	1,50	2,19E-02
P22087	rRNA 2'-O-methyltransferase fibrillar	10,19	41124	1,50	2,19E-02
O15145	Actin-related protein 2/3 complex subunit 3	9,60	28754	-1,67	3,79E-02
Q13257	Mitotic spindle assembly checkpoint protein MAD2A	6,30	55269	-1,67	2,50E-02
O15498	Synaptobrevin homolog YKT6	8,79	96462	-1,90	1,71E-02
Q9UJS0	Calcium-binding mitochondrial carrier protein Aralar2	9,33	119145	-2,00	1,11E-03
Q00325	Phosphate carrier protein, mitochondrial	9,34	63151	-2,00	4,09E-02
Q8WXF1	Paraspeckle component 1	8,96	74454	-2,08	3,34E-04
P10155	60 kDa SS-A/Ro ribonucleoprotein	9,63	350653	-2,10	1,60E-02
Q5JXB2	Putative ubiquitin-conjugating enzyme E2 N-like	9,15	95474	-2,11	2,95E-03
P53004	Biliverdin reductase A	6,47	41158	-2,18	4,05E-02
Q9Y230	RuvB-like 2	5,40	54097	-2,24	1,69E-02
O75153	Clustered mitochondria protein homolog	6,34	190902	-2,29	4,27E-02
Q9HD20	Manganese-transporting ATPase 13A1	9,48	70012	-2,50	2,87E-03
P18754	Regulator of chromosome condensation	5,79	42947	-2,67	1,08E-02
Q09328	Alpha-1,6-mannosylglycoprotein 6-beta-N-acetylglucosaminyltransferase A	9,09	255616	-2,75	2,88E-04
Q14195	Dihydropyrimidinase-related protein 3	8,69	171819	-2,85	2,45E-02
P13645	Keratin, type I cytoskeletal 10	6,00	75115	-2,87	1,38E-02

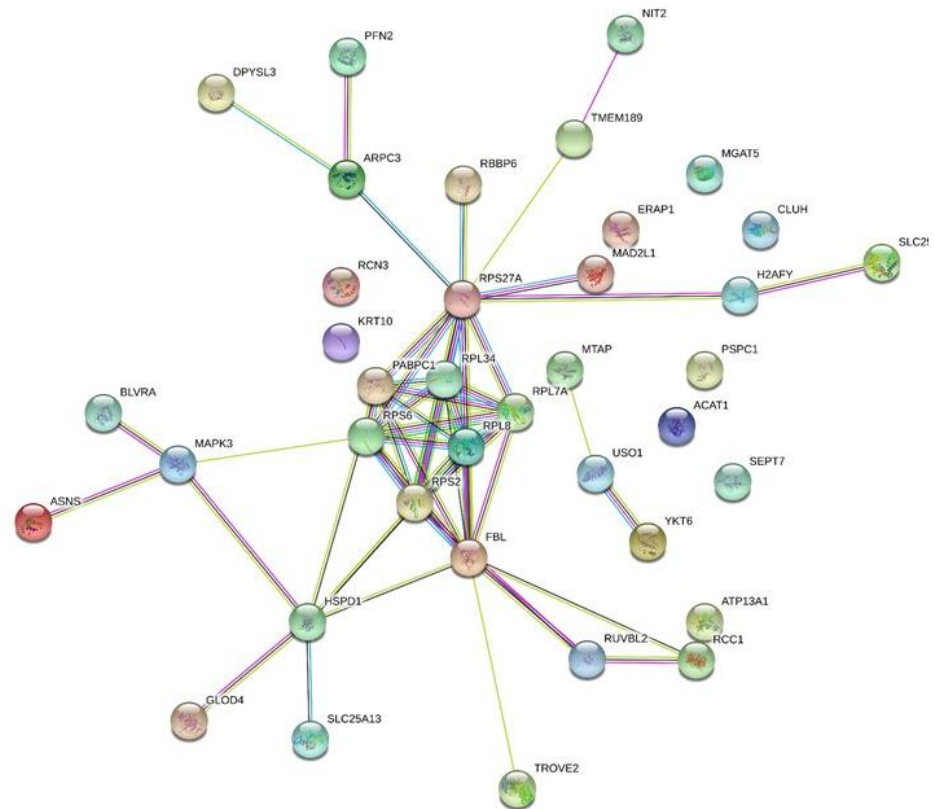
Proteomic analysis of bystander cells



Clusters in bystander cells:

- 3 proteins from **IL-12 signaling pathway**
- Heat shock cognate 71 kDa protein (middle)
- Peptidyl-prolyl cis-trans isomerase A
- Modulation of **oxidative stress-related proteins**
- Modification of **cellular motility and migration**
- Several protein involved in **exosomes**

Proteomic analysis of conditioned medium



Clusters in conditioned medium :

- 8 proteins from the 24 increased belong to **stress granules**
- **Polyadenylate-binding protein 1** is increased 24X
- Mitogen-activated protein kinase 3 increased 2X
- cellular response to DNA damage stimulus

According to the proteomic analysis of bystander cells:

- Several proteins involved in cytokine responses and pathways were modulated, in agreement with our previous results (1),
- we observed a modulation of oxidative stress-related proteins, and a modification of cellular motility and migration (in agreement with complementary experiments: 8-oxo-dG quantification and wound-healing tests)
- Extracellular exosomes are still involved, possibly in the propagation of the bystander effect

According to the secretomic analysis of irradiated cells conditioned medium:

- A significant and major enrichment in stress granules proteins is observed in the proteins increased in the secretome of 0,1Gy irradiated cells as compared with the secretome of 0Gy control cells
- Polyadenylate-binding protein 1 (involved in stress granules) appears as a good candidate in the bystander signaling (increased 20X)
- Other proteins involved in extracellular exosomes and interleukin pathways are observed

The results obtained confirm our previous results concerning the factors involved in the radiation-induced bystander effect (**interleukin, TNF, low doses**)

These results open new possibilities of researches (**stress granules, cell motility and several others modulated proteins**). It confirms the complexity of the mechanisms involved in the radiation-induced bystander effect

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