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## **Analysis of ionizing radiation induced effects in radioresistant tumours and bystander normal cells**

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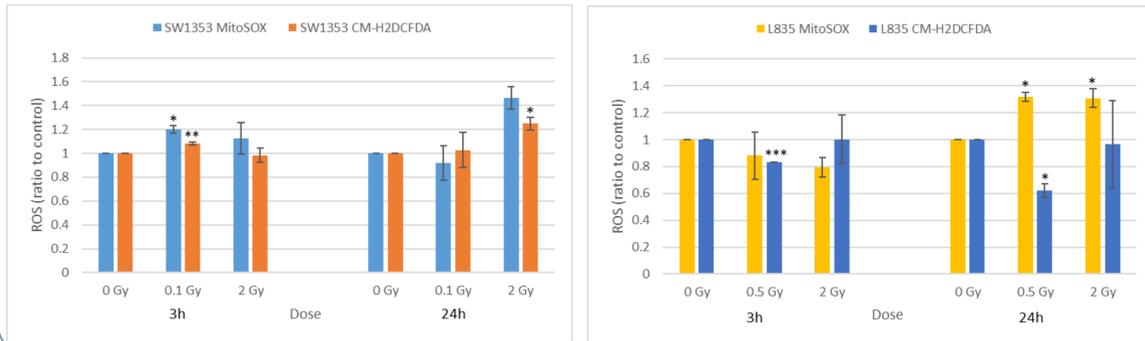
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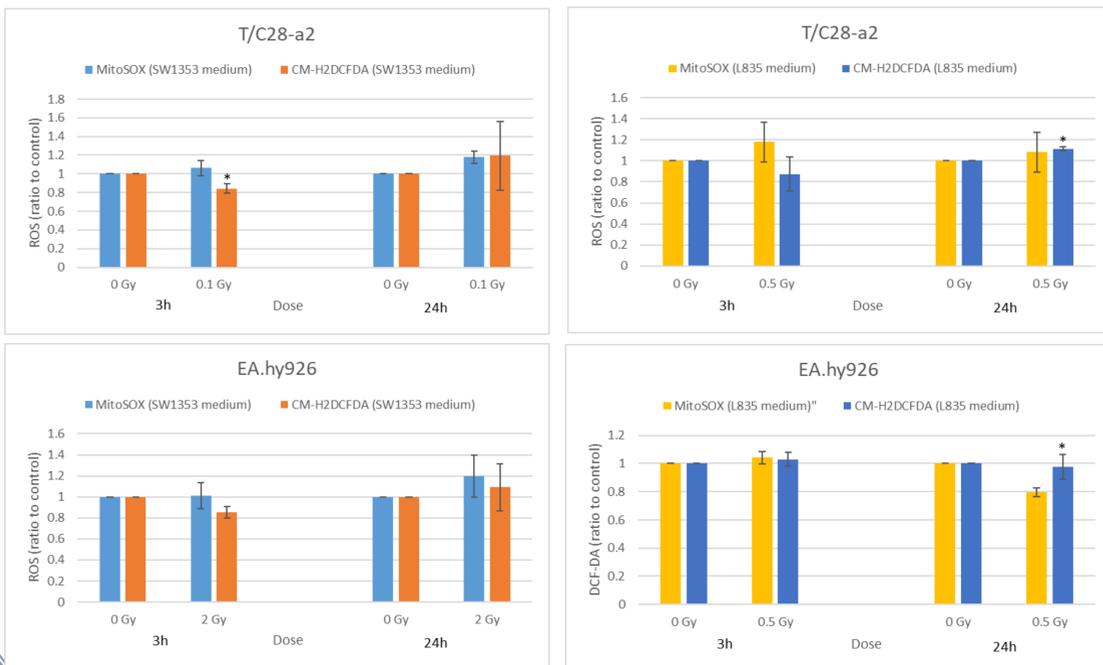
Chondrosarcoma is a chemo and radioresistant tumour for which the main treatment remains surgery. Hadron therapy has shown better specificity and lower toxicity for the surrounding normal tissue when compared to conventional photon therapy.

**Study focus:** analysing cellular mechanisms involved in stress and response to DNA damage induced by ionizing radiation in radioresistant tumour cells and bystander normal cells.

## Results X-ray – direct effect:



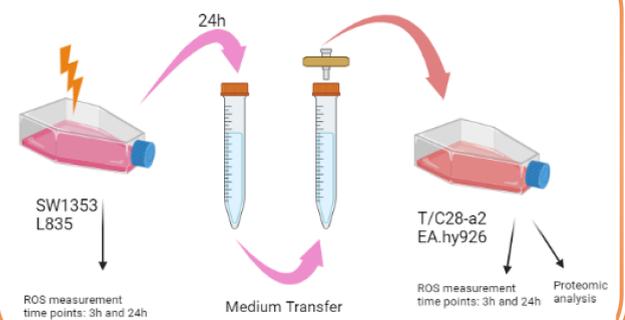
## Results X-ray – bystander effect:



## Materials and methods:

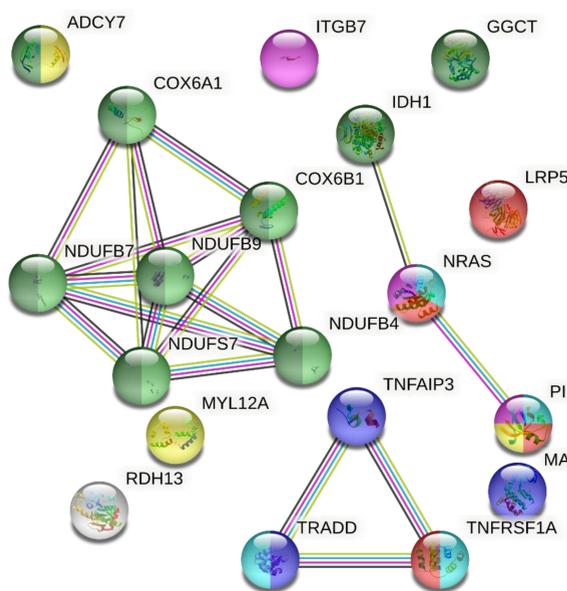
- Cell culture - human:
  - 2 chondrosarcoma cell lines: SW1353 and L835;
  - 2 bystander cell lines: chondrocytes T/C28-a2 and endothelial cells EA.hy926;
- Irradiation doses: 0.1 Gy, 0.5 Gy, 2 Gy;
- Irradiation facilities: X-ray (XSTRAHL XRC 160 machine) and low energy protons (TR-19 cyclotron) of IFIN-HH;
- Bystander induction: conditioned medium transfer 24h after cell exposure;
- Endpoints: flow cytometry - mitochondrial and cellular reactive oxygen species (ROS) generation; mass spectrometry – proteomic analysis.

## Experimental design



**Proteomic analysis of T/C28-a2 bystander cells – protons:** chondrocytes presented a number of 85 modulated proteins, some of them are implicated pathways such as apoptosis, autophagy, oxidative phosphorylation signaling, IL-17 signaling or metabolic pathway. Such proteins are: GTPase Nras, Phosphatidylinositol 3-kinase regulatory subunit beta, TNFR1-associated DEATH domain protein, NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9, Cytochrome c oxidase subunit 6B1.

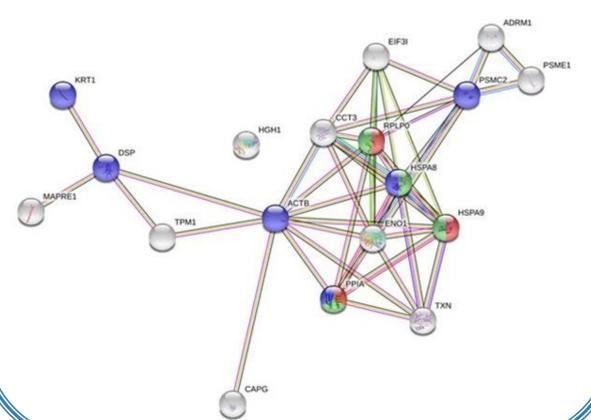
## Bystander effect – protons



## Proteomic analysis of T/C28-a2 bystander cells – X-ray:

- Proteins from IL-12 pathway: Cyclophilin A, 60S acidic ribosomal protein P0, Hspa9;
- Modulation of oxidative stress proteins: thioredoxin;
- Cell motility and growth and exosome related proteins: alpha-enolase, T-complex protein 1 (Tudor et al, 2021).

## Bystander effect – X-ray



**In conclusion,** X-ray irradiation induces variations of oxidative stress levels in chondrosarcoma cells and in bystander chondrocyte and endothelial cells. Our results showed the potential for proteins identified in X-ray and protons bystander chondrocyte cells to be good biomarker candidates involved in cellular response.

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