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## Modulation of GBM radiosensitivity by senescent endothelial cells

## "Impact of endothelial cell senescence in Glioblastoma multiforme resistance"

## Dr. François Paris

In summary the research interest of Dr. Paris involves working with senescent cells to understand the reason behind treatment failure and resistance in GBM patients. GBM is most common primary tumor. It is very infiltrative and angiogenic. In case of treatment failure only 10% of survival at 5years and it is known for systematic relapse. Treatment strategy for GBM patients include:

1. Telomolamide
2. Radiation therapy.

There has been 90% relapse in conditions where radiation was given. Senescent endothelial cells are found in patients treated for GBM. 30% of blood vessels cell are senescent. Beta-Galactosidase is a senescent marker. There is colocalisation of blood vessels with senescence. How can blood vessels go into senescence?

His aim for this work was to look at which molecular pathways are associated in Radiation induced senescence?

For this he used HMVEC-1 cells. He also looked at DNA damage by measuring Gamma H2AX foci 21 days after the damage. pATM levels, pDNA-pkcs, p CH2 levels were shown to be increased after IR. And p53 levels were reduced after treatment with ATM inhibitor. His key findings also show that Radiation induces mitochondrial dysfunction; and that p53 and ROS are independently involved in IR induced endothelial senescence. He also studied impact of IR induced senescent cells on Glioblastoma and key findings suggest that SASP15 enhances radioresistance. SASP15 medium also has shown an increase in genomic instability. His work also suggest not clearly though that EMT markers are expressed more in senescent cells. His ongoing work focusses on better molecular characterization and RNA sequencing with a focus to continue these studies into mice.

Pelin Kucuk and Shipra Chaudhary