# **Epigenetic biomarkers of radiation-induced** cardiovascular disease and secondary cancers

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### Radiation... the good, the bad and the epigenetics



Aims

Results

### Computed Tomography (CT)



Finding DNA methylation biomarkers to estimate the risk of early and late radiation-induced cardiovascular events after breast cancer radiotherapy.

Finding microRNA (miRNA)/long non coding RNA (lncRNA) biomarkers for glioblastoma risk assessment. 2.





Validation of biomarkers in remaining breast cancer patients blood pellets



Identification of differentially expressed miRNA in glioblastoma tissue samples



#### **Preclinical investigation of DNA methylation biomarkers of RICVD**



Identification of genes  $\geq$  25% differential methylation relative to sham-irradiated rats by SureSelect Methylseq



#### Meta analysis of LncRNA biomarkers of glioblastoma:

After meta-data filtration, 4 studies were selected for further analysis



Identification of differentially expressed miRNA in human glioblastoma tissue 2. samples

> Figure 2: Relative fold change of sequencingidentified candidate glioblastoma miRNA biomarkers in in remaining glioblastoma tissue samples (\*  $\rightarrow p < 0.05$ )

#### Mir-96-5p expression was found to be significantly

*Figure 1: mRNA expression levels of SLMAP, ITPR2 and E2F6 in the blood of rats* undergoing either sham irradiation (0 Gy) or fractionated irradiation of 0.92, 6.9 and 27.6 Gy and sampled at 1.5, 3, 7 and 12 months after irradiation.

(\*=p<0.05 and \*\*=p<0.01 between different doses within the same time point, #=P<0.05 and



increased in human glioblastoma tissue samples

### Conclusions

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Fold Change 201 Change 201 Change

- Rat irradiation with 1.2 Gy induced **DNA methylation alterations** that were detectable in blood samples until 7 months after irradiation relative to sham irradiated rats.
- 3 promising differentially methylated genes were identified in irradiated rat (SLMAP, ITPR2 and E2F6), which have been associated previously with cardiac function in literature.
- **DNA methylation alterations** were observed in breast cancer patients after radiotherapy and a number of differentially methylated genes were identified (validation is ongoing)
- Meta analysis of publicly available glioblastoma RNAseq data identified 88 IncRNAs that were found to be differentially expressed in all included studies.
- miR-96-5p was found to be differentially expressed in glioblastoma tissue samples relative to normal brain tissue.

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