SFB 1389 UNITEGLIOBLASTOMA

FOCUS A – TUMOR INTRINSIC MECHANISMS | FOCUS B – TUMOR MICRO-ENVIRONMENT | FOCUS C – TECHNOLOGICAL INNOVATION | FOCUS D – UNITE CORES

C05 – OVERCOMING GLIOBLASTOMA RADIORESISTANCE WITH PARTICLE THERAPY

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SUMMARY

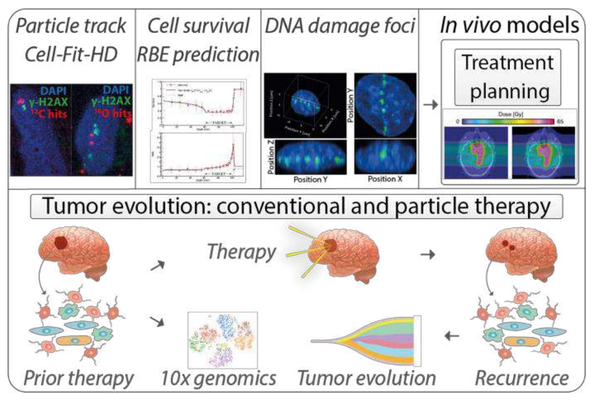
This project aims to explore the potential of particle radiotherapy to eradicate radioresistant glioblastoma subpopulations and overcome glioblastoma therapy refractoriness by resensitizing tumors to antiangiogenic, immune modulating and tumor targeting agents via modulation of the tumor-stroma communication.

TASK

Task 1 –

Multi-scale radiobiological characterization of Unite glioma models after conventional photon radiotherapy versus clinical quality proton, helium, carbon and oxygen ion beams

VISUAL ABSTRACT



WORKFLOW

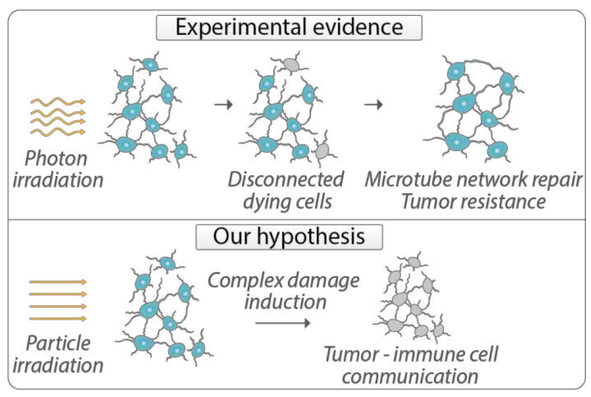
Biophysical characterization of radiation response:

- Cell-fluorescence ion track hybrid detector (Cell-Fit-HD)
- DNA damage quantification
- Gene expression analysis
- Biophysical models: predicting glioma response to radiotherapy

Radioresistant models will be further investigated in-vivo

Task 2 –

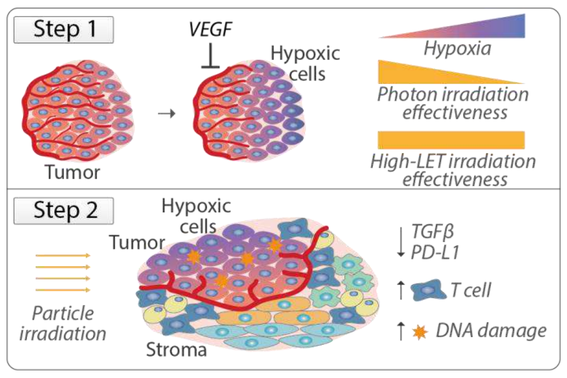
Characterization of the impact of intercellular communication in development of radioresistance



- Investigate patterns of microtube induction as a function of radiation quality
- Characterize particle beam effect on formation of complex damage
- Analyze differential pathways triggered by DNA damage and their impact on cell survival signals throughout the microtube network

Task 3 –

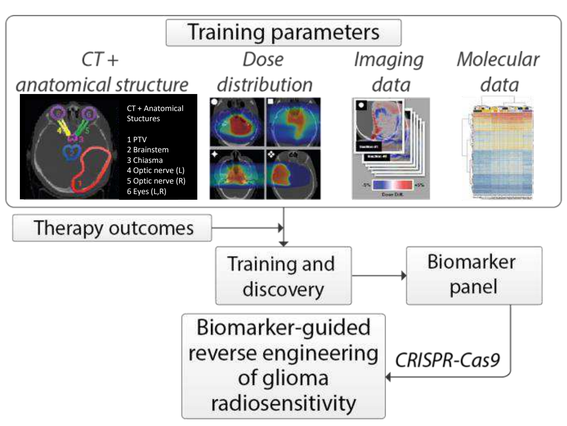
Investigation of mechanisms of glioma resistance at the tumor-stroma interface



- Step 1: Evaluate impact of high-LET irradiation to eradicate hypoxic glioma subpopulation generated after VEGF inhibitors
- Step 2: Elaborate stroma modulation towards an immunologically enhanced radiotherapy

Task 4 –

Development of biomarker of glioma response to radiotherapy



Integrative analysis of UNITE functional genomic approaches to define a panel of prediction and surveillance biomarkers:

- Tumor tissue specific epigenetic, genetic and proteomic patterns
- Tumor radio-modality and dose distribution specific alterations
- Development of candidate biological targets using CRISPRCas9 based gene editing

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