



Development of new strategies of DNA repair inhibitors induced radiosensitization of glioblastoma exposed to low and high linear transfer energy radiotherapy

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The DORADIOS project will develop novel approaches for treating glioblastoma, the most frequent and deadliest form of brain cancer that represents a major health problem affecting young children. Radiotherapy plays a crucial role in glioma treatment, however, glioma cells survive the treatment, one reason being the presence of cancer stem cells with high DNA repair capacity. We aim at identifying radiation-drug combinations inhibiting DNA repair and exploring how such treatment combinations work in cells irradiated with high-LET versus low-LET radiotherapy (X-ray, protons and carbon-ions). We also aim at identifying new promising biomarkers signatures that may support the development of the personalized treatment.

An original approach will be employed by using a new DNA repair high-throughput drug screening, unique in the world, available at Norwegian partner, to identify drugs that could be used as glioma radiosensitizers in association with radiotherapy. The ideal glioma cancer stem cells model will be used. Moreover, after identifying the best candidate combination, we will perform a complex "omic" analysis of the responsive tumor cells to the selected combination. The generated information will shed light on the drug-specific resistance mechanisms employed by tumoral cells. Thus, predictive biomarker libraries could be generated to match glioma specific molecular signature with a paramount importance for subsequent clinical trial design.

The expertise of the Romanian team will be highly enhanced in the topic of mechanisms driven the DNA repair following the radiotherapy and the Norwegian researchers will be prepared for exploiting a new proton radiotherapy centre (to be opened in 2024). The outcome of the project will allow a good chance to develop new long-term collaborations with hospitals that could be end-users. The society will benefit through the development of new and better strategies to treat cancer.