Impact of Ionizing Radiation on the Energy Metabolism of Normal and Tumor Cells in the Brain

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Abstract

Metabolic reprogramming of tumor cells is considered one of the hallmarks of cancer. Studies have shown that abnormal activation of oncogenes and cancer-related signaling pathways as well as the inactivation of tumor suppressor genes can induce metabolic reprogramming in tumor cells. These metabolic changes facilitate rapid proliferation, continuous growth, survival in harsh conditions, invasion, metastasis, and immune evasion. Following the application of radiotherapy, the activity of several metabolic pathways significantly changes, potentially leading to the development of radioresistance. However, a differential effect of ionizing radiation on tumor and normal cells is not well understood. Our goal is to collect quantitative data on the metabolic changes in normal astrocytes and glioma cells in response to irradiation to better understand the effect of ionizing radiation on the energy metabolism on a molecular level. As part of a collaborative effort between the Laboratory for Applied Radiobiology of the University Hospital Zurich and the Institute of Pharmacology and Toxicology of the University of Zurich, we are developing a novel tool that will allow measuring dynamic metabolite changes upon irradiation in vivo and in real-time. This tool combines imaging of recently developed fluorescent biosensors and millimeter-scaled irradiation. Moreover, our research aims at identifying the global metabolic signature of glioma cells and normal astrocytes before and after irradiation to identify pathway changes correlated with radiosensitivity. We perform global as well as targeted metabolomic analysis using liquid chromatography coupled to mass spectrometry in collaboration with the Functional Genomics Center Zurich. These methods are expected to provide knowledge to increase the efficiency of radiotherapy.