Title: cAMP regulation in Glioblastoma multiforme under hypoxia.

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Keywords:
Glioblastoma multiforme, hypoxia, cAMP, genetic biosensors

Abstract

Glioblastoma multiforme (GBM) is an aggressive brain tumor with poor prognosis, largely due to treatment resistance arising from hypoxia adaptations under the low-oxygen tumor microenvironment. Existing studies under ambient conditions fail to capture the altered molecular mechanisms driving this resistance. cAMP, a critical second messenger, plays a pivotal role in various cancer-related metabolic pathways, including drug resistance. Its activity is also notably altered under hypoxic conditions. This research aims to investigate the role of cAMP signaling in GBM cell lines under hypoxia using a specialized portable mini-incubator. Current methods for detecting and quantifying cAMP are inefficient due to its dynamic regulation. In this project, we plan to apply genetic biosensors to detect cAMP regulation in GBM cells. Key methods include inducing chemical and physical hypoxia in GBM cell lines (SNB19, LN229), using a chemical agent ($CoCl_2$) and the Oxygenie™ hypoxia platform respectively. To assess cAMP signaling dynamics, novel, genetically-encoded biosensors that function by utilizing bioluminescence resonance energy transfer (BRET)-based technology are applied, followed by capture of bioluminescence and fluorescence to assess cAMP signaling dynamics.

Preliminary results show that cellular ROS activity, migration rate and IC Calcium levels increase within the GBM cells under chemical and physical hypoxia environments, while the Live/dead ratio does not vary significantly. We aim to further present the observations made with BRET-based cAMP biosensors under hypoxia, and their significance in GBM cell death.

With this research, we hope to study how hypoxia can regulate cAMP signaling in GBM and understand its potential in improving therapeutic strategies.