Uncovering Therapeutic Targets FOR Glioblastoma: A Systems Biology Approach

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Even though glioblastoma, WHO grade IV (GBM) is one of the most devastating adult cancers, current treatment regimens have not led to any improvements in patient life expectancy or quality of life. The constitutively active EGFRvIII receptor is one of the most commonly mutated proteins in GBM and has been linked to radiation and chemotherapeutic resistance. To define the mechanisms by which this protein alters cell physiology, we have recently performed a phosphoproteomic analysis of EGFRvIII signaling networks in GBM cells. The results of this study provided important insights into the biology of this mutated receptor, including oncogene dose effects and differential utilization of signaling pathways. Moreover, clustering of the phosphoproteomic data set revealed a previously undescribed crosstalk between EGFRvIII and the c-Met receptor. Treatment of the cells with a combination employing both EGFR and c-Met kinase inhibitors dramatically decreased cell viability in vitro. In this perspective, we highlight the use of systems biology as a tool to better understand the molecular basis of GBM tumor biology as well as to uncover non-intuitive candidates for therapeutic target validation.

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