

ORAL PRESENTATION O1

A quantitative phosphoproteomic analysis of EGFRvIII cellular signaling networks in glioblastoma

Paul Huang¹, Zachary Brewer¹, Daniel Handal¹, Frank B. Furnari², Webster K. Cavenee² and Forest M. White¹

¹*Department of Biological Engineering and Center for Cancer Research, Massachusetts Institute of Technology, Cambridge, MA 02139, USA*

²*Ludwig Institute for Cancer Research, University of California-San Diego, La Jolla, CA 92093, USA*

EGFRvIII is a truncated mutant of the epidermal growth factor receptor (EGFR) which is implicated in the progression of many cancers. While much work has been done to elucidate the pathways initiated by EGFRvIII, the global map of its signaling network is still incomplete, making it difficult to assess downstream components involved in tumor progression. As a model system, we have used the U87MG glioblastoma cell line retrovirally transfected to express three different levels of EGFRvIII. Employing a mass spectrometric strategy previously developed in our laboratory, we have quantitatively measured global tyrosine phosphorylation events in these cell lines. This has allowed us to obtain a systems view of signaling networks initiated by the EGFRvIII receptor. We have identified many critical signaling proteins which are differentially tyrosine phosphorylated as a function of increasing EGFRvIII levels, in particular, components of the PI3K and migratory pathways. In addition, pathways normally activated by the wildtype EGFR receptor, such as the MAPK cascades are not responsive to EGFRvIII. Such quantitative signal transduction data, when used in conjunction with phenotypic measurements and computational tools will allow us to predict how tumor-associated phenotypes such as cell invasion are governed by signaling pathways downstream of the EGFRvIII receptor.