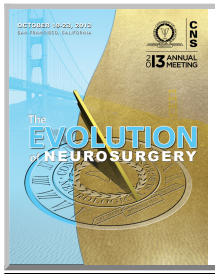

Gene Expression Analysis Revealed Distinct Physiology in G-CIMP+ and G-CIMP- Gliomas

Zachary J Taich BA, BS; Amit Goyal MD; David D. Gonda MD; Eric Marcusson; Vivek Kaimal; Tao Jiang; Bob Carter; Clark C. Chen MD PhD

UC San Diego, Division of Neurosurgery

Center for Theoretical and Applied Neuro-Oncology

Introduction

The discovery that gliomas can be categorized by their CpG Island Methylator Phenotype (G-CIMP) status has fundamentally altered our understanding of glioblastoma pathogenesis. However, the inherent physiologies associated with the G-CIMP phenotype remains unclear. Here, we utilized gene signature expression analysis to better understand these physiologies.

Methods

Published expression signatures associated with pathway activation of receptor tyrosine kinases (EGFR, PTEN), Ras (Ras, MAPK, MEK, RAF), cell-cycle progression (TGF-b, E2F3), tumor initiation (CD133, glioblastoma tumorigenicity signature), cell migration (Epithelial Mesenchymal Transformation (EMT) and glioblastoma invasion signature), inflammation (NFkb), and angiogenesis (VEGF) were applied to glioma transcriptomes published by the Chinese Glioma Cooperative Group (CGCG; n=155) and the Rembrandt group (n=288). Gliomas in these database were categorized into G-CIMP+ or G-CIMP- status using a published gene expression signatures.

Results

There was a graded increase in gene expression associated with RTK and Ras pathway activation, cell cycle progression, tumor initiation, cell migration, inflammation, as well as angiogenesis during glioma progression from stage II to stage IV. Genes associated with activation of RTK, Ras, NFkb, EMT and angiogenesis were expressed at higher levels in G-CIMP- glioblastomas relative to G-CIMP+ glioblastomas. On the other hand, genes associated with tumor invasiveness were expressed at higher levels in G-CIMP+ glioblastomas. Despite these differences, gene signatures reflecting tumor initiating capacity and cell cycle progression were comparable between G-CIMP+ and G-CIMP- glioblastomas. Similar expression patterns were observed in Grade II G-CIMP+ and G-CIMP- gliomas.

Learning Objectives

By the conclusion of this session, participants should be able to:

1) Describe the importance of gene signature expression for understanding underlying molecular events.

2) Describe the molecular activities which increase and decrease in a graded fashion in glioma samples.

3) Identify differences in the transcriptomal physiology of G-CIMP+ and G-CIMP- gliomas.

Conclusions

G-CIMP+ and G-CIMP- gliomas exhibited patterns of gene expression that suggest inherently distinct molecular physiology.