mRNA Expression Analysis of 97 Low Grade Gliomas Shows Unique Oligodendroglial Signature

David D. Gonda MD; Zachary J Taich BA, BS; Jiang Tao; Bob Carter; Clark C. Chen MD PhD
University of California, San Diego

Introduction

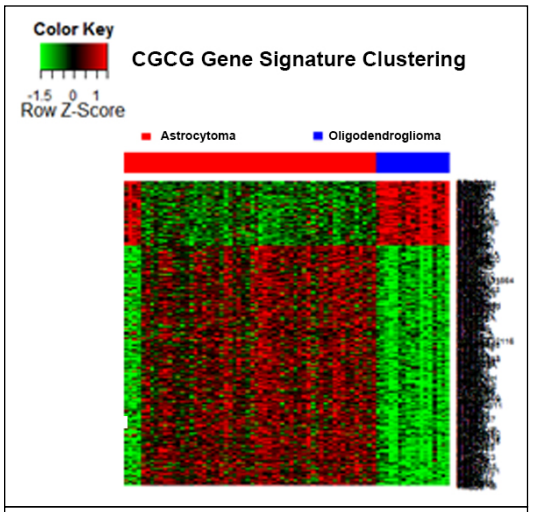
Differentiating between low grade gliomas (LGG) of astrocytic and oligodendroglial origin remains a major challenge in neuro-oncology. We analyzed the mRNA profiles of 97 grade II LGGs from the Chinese Glioma Cooperative Group (CGCG) with the goal of identifying distinct molecular characteristics that would afford accurate and reliable discrimination of astrocytic and oligodendroglial tumors.

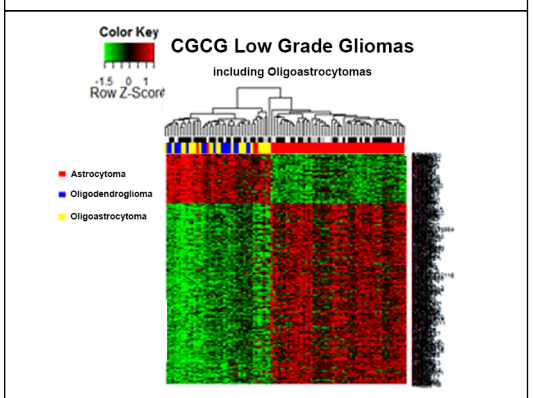
Methods

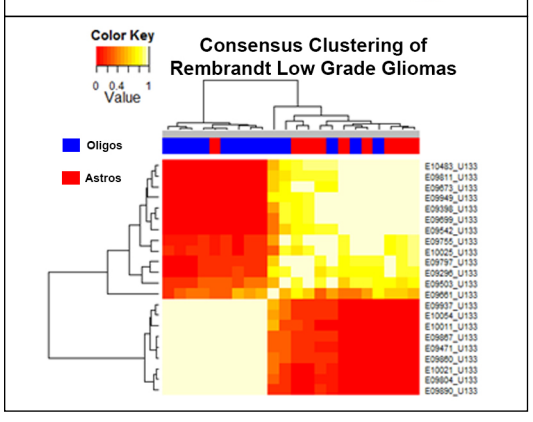
Differential gene expression of the mRNA profiles between 58 astrocytomas and 17 oligodendrogliomas was performed to identify a genetic signature (gene threshold mean fold change > 1.5, corrected P-value <0.01) characteristic of oligodendrogliomas. The signature was reapplied to the same samples with the addition of the 22 mixed oligoastrocytomas to assess its predictive power. The signature was then applied to an independent set of 22 grade II LGGS (9 astrocytomas, 13 oligodendrogliomas) from Rembrandt to validate the signature's ability to differentiate between oligodendroglial and astrocytic tumors.

Results

Gene expression analysis revealed 352 genes that were differentially expressed between oligodendrogliomas and astrocytomas from the CGCG LGGs. Two of the 58 tumors originally diagnosed as astrocytomas exhibited gene expression profiles mirroring that of the 17 oligodendrogliomas suggesting a possible error in histologic assessment of the specimens. Twenty-one of the 22 oligoastrocytomas shared the same signature pattern as the oligodendrogliomas. DAVID gene ontology analysis of the signature demonstrated enrichment of genes related to nucleotide binding in the oligodendroglial tumors. Consensus clustering of the Rembrandt grade II LGGs with the signature showed two robust clusters (scores 0.88 and 93) with a positive predictive value for oligodendrogliomas of (8/9) 88.9%.







Learning Objectives

By the conclusion of this session, participants should be able to 1) Recognize differences in mRNA expression profiles among low grade gliomas

Conclusions

Low grade gliomas harbor distinct genetic profiles that along with other known molecular markers such as IDH1 mutation, TP53 mutation, and 1p19q status may facilitate accurate and reliable pathologic diagnosis.

References

Madhavan, S., J. C. Zenklusen, et al. (2009). "Rembrandt: helping personalized medicine become a reality through integrative translational research." Molecular cancer research : MCR 7(2): 157-167.

Yan, W., W. Zhang, et al. (2012). "Molecular classification of gliomas based on whole genome gene expression: a systematic report of 225 samples from the Chinese Glioma Cooperative Group." Neuro-oncology 14(12): 1432-1440.