Novel Gene Signature for Prediction of Response to Standard of Care for High Grade Gliomas

This technology is a new gene signature-based assay that could be used to help determine which glioma patients will not respond favorably to radiation therapy with or without temozolomide, which is standard of care. Currently, only ~25% of patients diagnosed with high grade glioma respond to the standard treatment course. The remaining patients must then be treated with alternative therapies, such as bevacizumab, etoposide, or platinum-based therapies after enduring futile treatment with standard first-line therapy. Our diagnostic signature developed using retrospective patient outcome data statistically significantly predicts survival in glioma patients treated with standard therapy.

COMMERCIAL OPPORTUNITY

- High grade gliomas (anaplastic astrocytomas and glioblastoma multiforme) are currently diagnosed using primarily traditional histopathology techniques. However, tissue staining and microscopic visualization does not differentiate tumor biology, which is important in determining prognosis of an individual patient.
- High grade gliomas account for about 30% of the nearly 23,000 primary brain tumors diagnosed in adults and are the 2nd most common cause of cancer death in children younger than 15 years old.
- Some patients will respond well to the adjuvant standard of care (radiation therapy +/- temozolomide), while others (~75%) of patients will be refractory to the standard of care and should be prescribed alternative or investigational salvage chemotherapy.
- Diagnostic assays that allow for prospective risk-stratification of patients enable more individualized and potentially effective therapy options to be considered earlier during cancer treatment.
- The market is attractive as evidenced by the two diagnostic products available from Castle Biosciences, Inc., which determine mortality risk in glioblastoma patients (DecisionDX-GBM) and distinguish between borderline low and high grade gliomas (DecisionDX-G-CIMP) based upon gene expression.

TECHNOLOGY

The inventors used 14 known senescence-associated genes, and developed a senescence-associated gene expression signature that gives an overall senescence score. Gene expression information from frozen tumor samples of 60 patients, ages 32 to 88 years, with the histologic diagnosis of high grade glioma, was integrated with age and clinical outcome using principal component analysis to produce a senescence score. This score correlates with poor prognosis ($p=0.0098$) despite having received standard therapy, with median survival being 13 vs. 28 months for high vs. low senescence score. Additionally, increased expression of two of these senescence-associated genes were each statistically significantly associated with reduced patient survival (13-14 vs. 38 months).

PUBLICATION/PATENT

- US non-provisional patent application filed 8/29/2012 for Drs. Coppola, Brem and Chen.

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