

The Oligo Brain Tumor Fund
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Molecular profile-based development of accurate immunohistochemical markers
for human oligodendrogliomas
Lay Summary Report

Pathologists classify brain tumors based on their appearance under the microscope. Among high-grade gliomas, glioblastomas and anaplastic oligodendrogliomas follow very different clinical courses; oligodendrogliomas generally have a more favorable prognosis and remain the only subtype of glioma that commonly responds to chemotherapy. Unfortunately, these tumors can be difficult to classify, creating clinical uncertainty. The advent of gene expression microarray technology has allowed us to monitor simultaneously the expression of thousands of genes in tumors. In previous studies, we identified many genes that are differentially expressed in anaplastic oligodendrogliomas relative to glioblastomas. The aim of this project was to use these genetic markers to develop key immunohistochemical markers for oligodendrogliomas. Immunohistochemical markers detect the presence of molecules in tumor cells and allow the molecules to be seen under the microscope. The identification of an immunohistochemical marker will provide an objective way to identify “true” oligodendrogliomas. Identifying these tumors in a uniform and reproducible manner will allow better clinical management of individual patients. If successful, accurate immunohistochemical markers for human oligodendrogliomas would be directly and immediately applicable to clinical practice and could affect diagnostic and therapeutic decisions, as well as prognostic estimation. We have completed an in depth characterization of one marker, YKL-40. YKL-40 immunohistochemistry was able to distinguish anaplastic oligodendrogliomas from glioblastomas in a highly significant manner. Moreover, YKL-40 staining appeared to provide a better class distinction of glioblastoma versus anaplastic oligodendroglioma than GFAP, the current standard immunohistochemical marker used clinically to distinguish diagnostically challenging gliomas. Interestingly, a combination of YKL-40 and GFAP immunohistochemistry afforded even greater diagnostic accuracy. We continued to investigate this marker in more detail in order to determine whether it could aid prognostic estimation for patients with anaplastic oligodendrogliomas. To this end, we have completed a study with a large number of cases for which clinical data was available and the statistical analysis of this data is currently pending. In addition, we have participated in collaborative studies looking at additional potential markers as well as the development of novel statistical methods for studying such markers.