Improving diagnostic accuracy of brain tumors — Cores and faculty demonstrate value of new technique

When a patient is diagnosed with a brain tumor, the prognosis and treatment decisions are informed by histologic diagnosis based on the tumor's appearance under a microscope.

Not all of the roughly 100 different tumor types in the central nervous system are easily categorized when viewed under the microscope. One approach to classifying tumors is to look at DNA methylation — a form of chemical modification to the DNA molecules that doesn't change the sequence — across the entire tumor genome, and then group tumors by the distribution of the methylation marks.

DNA methylation profiling has been used to discover new brain tumor categories, and to give a more specific diagnosis for histologically ambiguous cases, including tumors in an unusual category called CNS primitive neuroectodermal tumors (CNS-PNETs). An OHSU team collaborated to generate data from a proof-of-principle cohort to support use of methylation profiling of clinical biopsies on a research basis.

> DNA methylation profiling can help categorize diagnostically challenging tumors and can be applied to tumor samples archived at OHSU to help identify rare tumor types.

Greater accuracy

A team led by Matthew Wood, M.D., Ph.D., assistant professor of pathology in the Department of Pathology, School of Medicine, demonstrated that DNA methylation profiling could improve diagnostic accuracy in CNS-PNETs diagnosed at OHSU. DNA from six patients who died with a diagnosis of CNS-PNET was extracted and analyzed. Wood used Illumina EPIC BeadChip arrays at the Gene Profiling Shared Resource to obtain genome-wide DNA methylation data. He then entered the results into a classification database maintained by the German Cancer Research Center.

The results showed that by DNA methylation profiling, half of the tumors diagnosed as CNS-PNET matched with a more specific diagnosis. Two more cases did not match with a specific diagnosis but did show chromosomal copy number changes suggesting a more specific type of tumor. Most of the tumors matched with or showed molecular features of glioblastoma, which is the most common primary tumor in the brain. One other tumor matched with pleomorphic xanthoastrocytoma, which is a less common primary brain tumor with a better prognosis than glioblastoma, and one matched with medulloblastoma, an aggressive form of childhood brain cancer that arises in the cerebellum.

Wood is using molecular testing to find ways to more accurately characterize brain tumors

Open doors for new research

This study showed that DNA methylation profiling can be successfully applied to archived tumor samples using resources at the Gene Profiling Shared Resource unit of the Integrated Genomics Laboratory. This platform could be used in the future to help pathologists and clinicians categorize diagnostically challenging cases and to help identify rare tumor types at OHSU for new scientific studies.