

could guide the use of precision therapeutics to treat patients with such genetic alterations.” —*Janet Colwell* ■

Diagnostic Advances Made for CNS-PNET

A recently published study concludes that a majority of children diagnosed with primitive neuroectodermal tumors of the central nervous system (CNS-PNET) may have other CNS cancers instead (*Cell* 2016;164:1060–72). The findings may lead to more accurate diagnoses and better-tailored treatment plans based on the molecular profiles of their tumors.

Historically, it has been difficult to distinguish CNS-PNETs from other CNS tumors because diagnoses have been based solely upon their appearance under the microscope, says the study’s co-first author Brent Orr, MD, PhD, of St. Jude Children’s Research Hospital in Memphis, TN. As a result, patients with CNS-PNETs have often been lumped together with patients with medulloblastoma in clinical trials because of the histopathologic similarities of their tumors.

In the new study, an international team of researchers analyzed DNA methylation patterns from 323 tumors classified as CNS-PNET and from 211 other well-defined brain tumors. They determined that 61% of the CNS-PNETs could be reclassified as other types of tumors based on their molecular profiles.

They also found that the remaining fraction fell into one of four new molecular subtypes of CNS-PNETs: CNS neuroblastoma with *FOXR2* activation, CNS Ewing sarcoma family tumor with *CIC* alteration, CNS high-grade neuroepithelial tumor with *MNI* alteration, and CNS high-grade neuroepithelial tumor with *BCOR* alteration.

Subsequently, the researchers performed next-generation sequencing on tumors from each group and identified specific genetic fusions, deletions, and rearrangements underlying each of the four molecular subtypes. Some of these alterations were shared

or similar to abnormalities found in other cancers, including Ewing sarcomas and clear cell sarcomas of the kidney, and patients whose tumors have these alterations could potentially be treated with existing approved drugs.

The findings have significant therapeutic implications, says Jim Olson, MD, PhD, professor of pediatric hematology/oncology at the University of Washington School of Medicine in Seattle. CNS-PNETs, which account for about 1% of pediatric brain tumors and primarily affect young children, are treated with very high doses of craniospinal radiation and more-toxic chemotherapy than is typically used to treat other types of CNS tumors.

“Some children could receive other, less-toxic treatments if we know the correct diagnosis from the start, and these new genomic analyses allow us to do that,” says Olson, who leads an international phase III Children’s Oncology Group (COG) clinical trial for patients with high-risk medulloblastoma. “We can also now identify patients with CNS-PNETs and potentially guide them towards targeted therapies that are aligned with the genetic drivers of their disease.”

The COG clinical trial is testing the efficacy of treating patients with high-risk medulloblastoma with carboplatin radiosensitization in combination with cisplatin-based chemotherapy. Olson closed the CNS-PNET arm of the trial about 2 years ago based on the data emerging from the St. Jude study showing that some patients originally diagnosed with PNETs might have different types of tumors. Researchers are now analyzing tumor samples from patients in the discontinued arm to determine how patients with the four PNET subtypes responded to treatment. They expect to release their findings within the next year.

“The data analysis will allow us to look at patients who actually had CNS-PNETs and determine what fraction of them survived,” Olson says. “We hope that will help us to identify trends that can help us shape future clinical trials.” —*Janet Colwell* ■

NOTED

The genetic testing company **Ambry Genetics** launched **AmbryShare**, a disease-specific public database that includes anonymized, aggregated data from 10,000 patient samples. The company sequenced the exomes of deidentified patients with hereditary breast and ovarian cancers and found 10-fold more genes implicated in these conditions than previously known.

A report issued by the California Life Sciences Association and Boston Consulting Group found that **FDA review times for new drugs have steadily declined since 2009**, when a review took 21 months on average. That average was cut to 9 months by 2014, with cancer treatments receiving some of the fastest reviews.

Microsoft cofounder **Paul Allen will launch an eponymous foundation with \$100 million to advance biologic research**. His Paul G. Allen Frontiers Group announced several grants, including a \$20 million grant to fund the Allen Discovery Center at Tufts University that will help researchers understand the “biological code that determines anatomical structure and function during embryogenesis, regeneration, and tumor suppression.”

Developed by researchers at The University of Texas MD Anderson Cancer Center in Houston, **a new staging system for breast cancer considers five factors**—preclinical stage, estrogen receptor status, HER2 status, grade, and posttreatment pathologic stage. Researchers say that the new tool will refine prognostic stratification and help clinicians decide which patients would benefit from additional therapy (*JAMA Oncol* 2016 March 17 [Epub ahead of print]).

Of 2,211 doctors recently polled, 64% thought that regular colon cancer screenings should begin before age 50, the current recommendation. The poll was conducted in response to two recent studies—one found that nearly 15% of patients with colorectal cancer are diagnosed before age 50, and another concluded that younger patients are more likely to have advanced disease (*Cancer Med* 2015;4:1863–70; *Cancer* 2016;122:929–34).

For more news on cancer research, visit *Cancer Discovery* online at <http://cancerdiscovery.aacrjournals.org/content/early/by/section>.