

## New biomarker assay detects neuroblastoma with greater sensitivity

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Investigators at The Saban Research Institute of Children's Hospital Los Angeles have developed and tested a new biomarker assay for quantifying disease and detecting the presence of neuroblastoma even when standard evaluations yield negative results for the disease. In a study, led by Araz Marachelian, MD, of the Children's Center for Cancer and Blood Diseases, researchers provide the first systematic comparison of standard imaging evaluations versus the new assay that screens for five different neuroblastoma-associated genes and determine that the new assay improves disease assessment and provides prediction of disease progression. Results of the study are published in the journal *Clinical Cancer Research*.

Neuroblastoma is a cancer of the nervous system that exists outside the brain and typically is diagnosed in children 5 years or age or younger. Forty-five percent of patients have high-risk, metastatic tumors (stage 4) when diagnosed.

While children with <u>neuroblastoma</u> often respond to therapy and many are declared to be in a "remission" based on standard tests, many will still relapse. "Clearly, there is some remaining tumor in the body that we cannot detect with standard tests and physicians have a hard time predicting if a patient is likely to relapse," said Marachelian, who is medical director of the New Approaches to Neuroblastoma (NANT) consortium, headquartered at CHLA.

The new assay, which was developed in the laboratories of Robert



Seeger, MD, and Shahab Asgharzadeh, MD, at CHLA, tests for five different genes that are specific to neuroblastoma. The test evolved to address the need for a better way to quantify the disease and fully understand its impact on the patient. Previously, assays used for detecting disease screened for only one NB-associated gene at a time, which was less effective. Instead of running five different tests, the research team figured out a way to test for multiple neuroblastomaassociated genes, simultaneously, using a different technology platform. This test can quantify infinitesimal amounts of tumor, akin to finding "a needle in a haystack".

According to Marachelian, in a population of patients with relapsed or refractory neuroblastoma, it is important to understand if the therapeutics given to patients are working. But standard clinical evaluations such as scans (CT, MRI and MIBG) and bone marrow evaluation can be limited in their ability to do this because of variability and an inability to indicate severity of disease or how aggressive the treatment should be.

"With imaging scans, disease that is starting to grow versus disease that is getting better can look very similar when you first look," explained Marachelian, who is also an assistant professor of Clinical Pediatrics at the Keck School of Medicine of the University of Southern California. "This assay could have the potential to be like an advance warning system - we can see if things are getting worse and be poised to take action. Alternately, if we see things are getting better or the <u>disease</u> is no longer detectable even with this very sensitive test, we can decrease the treatment to protect the patient from unnecessary exposure to toxicity and side effects."

Now that that the team has validated the new assay for its predictive ability, they have begun running the <u>test</u> for each individual therapeutic to see how the results of the assay change in response to different kinds



of treatments. "Our hope is that it will help oncologists and <u>patients</u> make decisions about the course of therapy," added Marachelian.

The assay has been incorporated into all of NANT's national trials with patient samples being sent to CHLA for analysis. The next step will be to validate its ability to support treatment decisions with the goal of the assay becoming a standard clinical evaluation.

**More information:** Araz Marachelian et al, Expression of Five Neuroblastoma Genes in Bone Marrow or Blood of Patients with Relapsed/Refractory Neuroblastoma Provides a New Biomarker for Disease and Prognosis, *Clinical Cancer Research* (2017). <u>DOI:</u> <u>10.1158/1078-0432.CCR-16-2647</u>

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