MedicalXpress

Autism speaks through gene expression

February 1 2013

Autism spectrum disorders affect nearly 1 in 88 children, with symptoms ranging from mild personality traits to severe intellectual disability and seizures. Understanding the altered genetic pathways is critical for diagnosis and treatment. New work to examine which genes are responsible for autism disorders will be presented at the 57th Annual Meeting of the Biophysical Society (BPS), held Feb. 2-6, 2013, in Philadelphia, Pa.

"Autism is the most inheritable of neurodevelopmental disorders," explains Rajini Rao of Johns Hopkins University in Baltimore, Md., "but identifying the underlying genes is difficult since no single gene contributes more than a tiny fraction of autism cases." Rather, she continues, "mutations in many different genes variably affect a few common pathways."

A team of scientists at Johns Hopkins and Tel Aviv University in Israel looked at genetic variations in DNA sequence in the ion transporter NHE9 and found that autism-associated variants in NHE9 result in a profound loss of transporter function. "Altering levels of this transporter at the synapse may modulate critical proteins on the cell surface that bring in nutrients or neurotransmitters such as glutamate," says Rao. "Elevated glutamate levels are known to trigger seizures, possibly explaining why autistic patients with mutations in these ion transporters also have seizures."

A unique aspect of the team's approach was that they exploited decades of basic research done in bacteria and yeast to study a complex human

neurological disorder. First, the group at Tel Aviv University, led by Nir Ben-Tal, built structural models of NHE9 using a bacterial relative as a template, allowing the Rao laboratory at Johns Hopkins to use the simple baker's yeast for screening the mutations. In the future, as genomic information becomes readily available for everyone, such easy, inexpensive, and rapid screening methods will be essential to evaluate rare genetic variants in autism and other disorders.

Rao and her team are optimistic about the potential benefits of their latest findings. "Although the research is still at an early stage, drugs that target the cellular pathways regulated by NHE9 could compensate for its loss of function and lead to potential therapy in the future," Rao says. "These findings add a new candidate for genetic screening of at-risk patients that may lead to better diagnosis or treatment of autism."

More information: Presentation #118-Plat, "Functional evaluation of autism associated mutations in SLC9A9 (NHE9)," will take place at 9:15 a.m. on Sunday, Feb. 3, 2013, in the Pennsylvania Convention Center, Room 113C. ABSTRACT: tinyurl.com/apjmm7a

Provided by American Institute of Physics