Novel neurodevelopmental disorder associated with mutations or deletions of PAX5 gene

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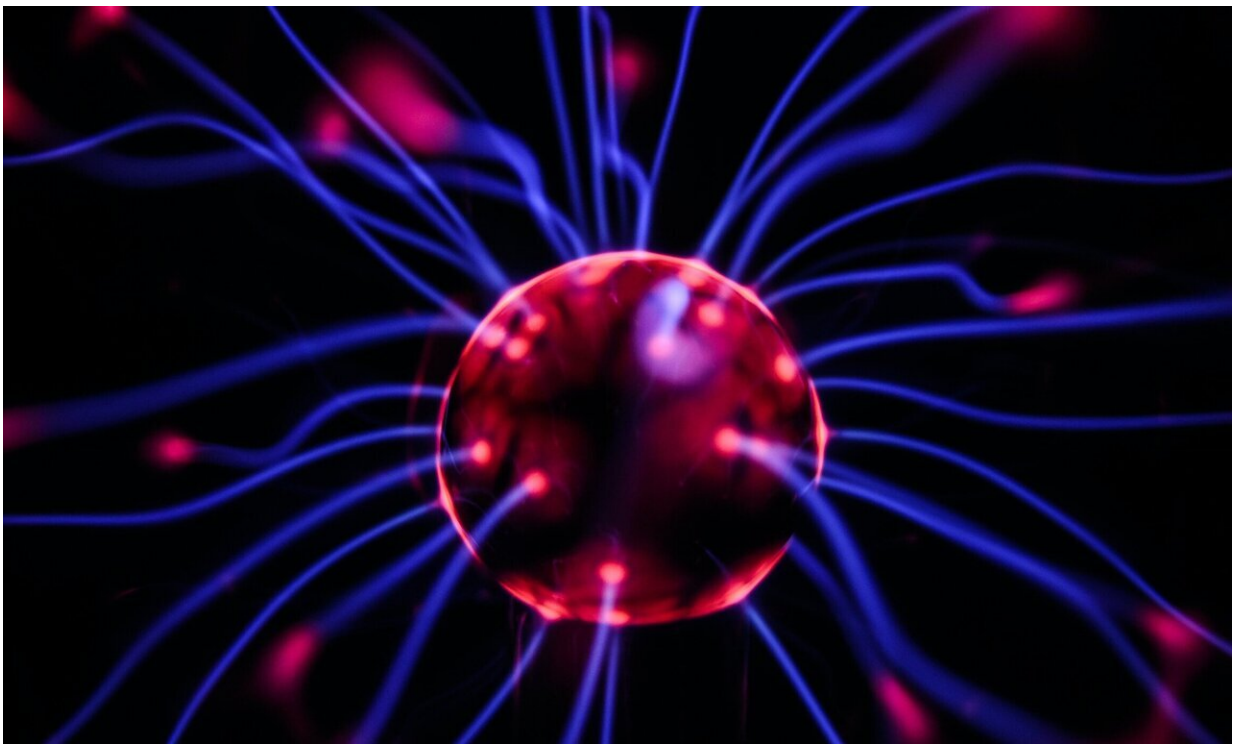

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Researchers led by a team at Baylor College of Medicine have identified a novel neurodevelopmental disorder associated with mutations or deletions affecting a gene called PAX5. Their findings are published in

the journal *Human Mutation*.

Led by corresponding author Dr. Daryl Scott, the Baylor team connected with researchers around the globe who studied PAX5 using an online site called GeneMatcher. Working together, the group described 16 patients who exhibited similar characteristics, including developmental delay, intellectual disability and autism spectrum disorder. Some patients also experienced seizures and hearing loss.

The researchers also examined data from the International Mouse Phenotyping Consortium and discovered that defects in PAX5 caused similar symptoms in mouse models.

"The data shows that PAX5 is a gene that causes medical problems even if only one copy is mutated or deleted," said Scott, associate professor in the Department of Molecular and Human Genetics at Baylor. "This gene also stood out as being really important for normal brain function in mouse models, which mirrored what we saw in our patients."

Patients in the cohort did not have a recurrent pattern of abnormal brain MRI findings, structural birth defects or dysmorphic features. Scott stresses that the lack of these findings should not deter doctors from performing genetic testing for their patients with neurodevelopmental symptoms.

"Children who don't look like they have a genetic syndrome, but have these neurodevelopmental issues, could carry changes in this gene," Scott said. "That's why we should be doing genetic testing for all children who have developmental delay and intellectual disability."

Documenting phenotypes of disease genes like PAX5 can help expedite basic science and clinical research. According to Scott, the findings in this report provided long-awaited answers to the families in the study

and will have an immediate impact for undiagnosed patients in genetics clinics.

"As we discover new genes like PAX5, our diagnostic tests get better," Scott said. "From this point forward, diagnostic labs will start to check for changes in this gene. As geneticists, we are constantly reviewing older patient data to see if we can come up with new diagnoses thanks to discoveries like this one."

Dr. Yoel Gofin, second-year medical genetics fellow in the Department of Molecular and Human Genetics at Baylor, is first author of the paper. Other authors at Baylor include Dr. Aliska M. Berry, Dr. Mahshid S. Azamian, Dr. Carlos A. Bacino, Dr. Seema R. Lalani and Jill A. Rosenfeld.

More information: Yoel Gofin et al, Delineation of a novel neurodevelopmental syndrome associated with PAX5 haploinsufficiency, *Human Mutation* (2022). DOI: 10.1002/humu.24332

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