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Team develops framework to identify genetic missense mutations linked to autism spectrum disorder

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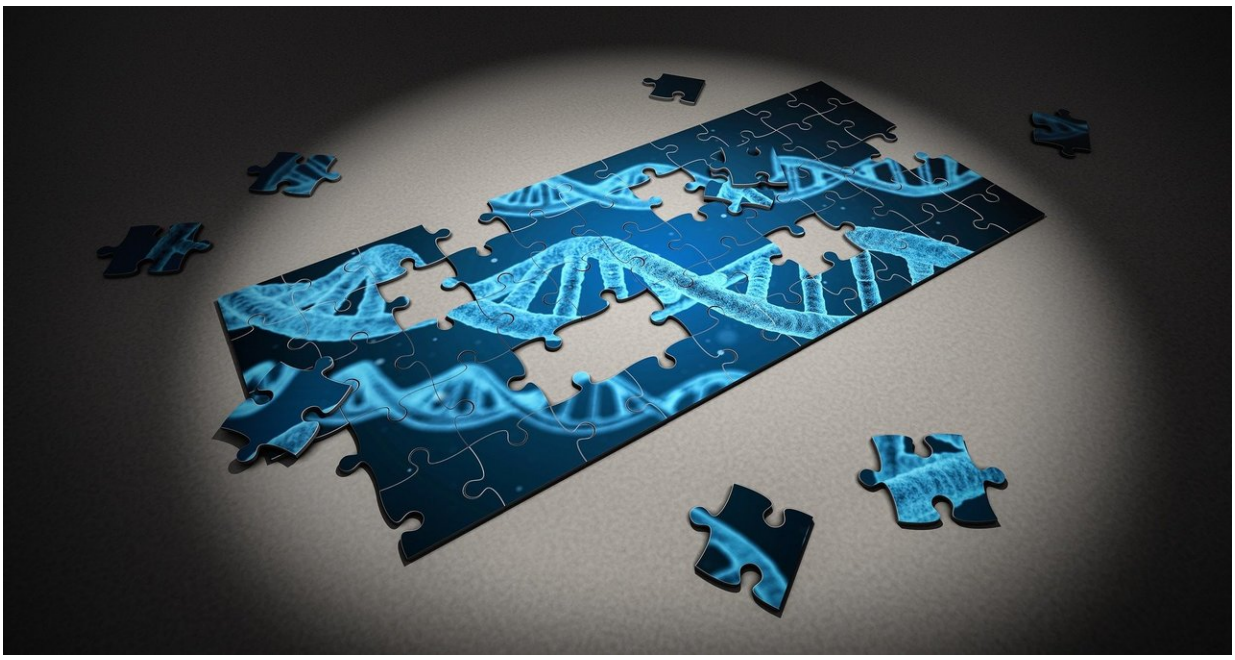

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Missense mutations occur when there is a change in one gene's DNA base pair, and the change results in the substitution of one amino acid for another in the gene's protein. Mutations that disrupt the function of proteins are widely recognized as a risk source for development disorders such as intellectual disability, congenital heart defects and

autism spectrum disorder (ASD).

A new study published in *Nature Genetics* established a computationally integrated approach to investigate the functional impact of missense mutations. The team, which includes Carnegie Mellon University's Kathyrn Roeder, tested the approach by analyzing genetic structures of individuals with ASD who also had mutations as well as their siblings who did not have the mutations. They found that the framework successfully identified and prioritized missense mutations that contribute to disease or disorder risk.

"Identifying genetic mutations that increase the likelihood of disease is a major challenge to progress for personalized medicine. Using a machine learning model that predicts which mutations are likely to perturb the human interactome network, we showed that these mutations are much more likely to occur in autistic children than their siblings," said Roeder, the UPMC Professor of Statistics and Life Sciences in the Dietrich College of Humanities and Social Sciences. "This result extends to several other mental disorders suggesting that our finding may have even broader applicability."

More information: Siwei Chen et al, An interactome perturbation framework prioritizes damaging missense mutations for developmental disorders, *Nature Genetics* (2018). DOI: 10.1038/s41588-018-0130-z

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