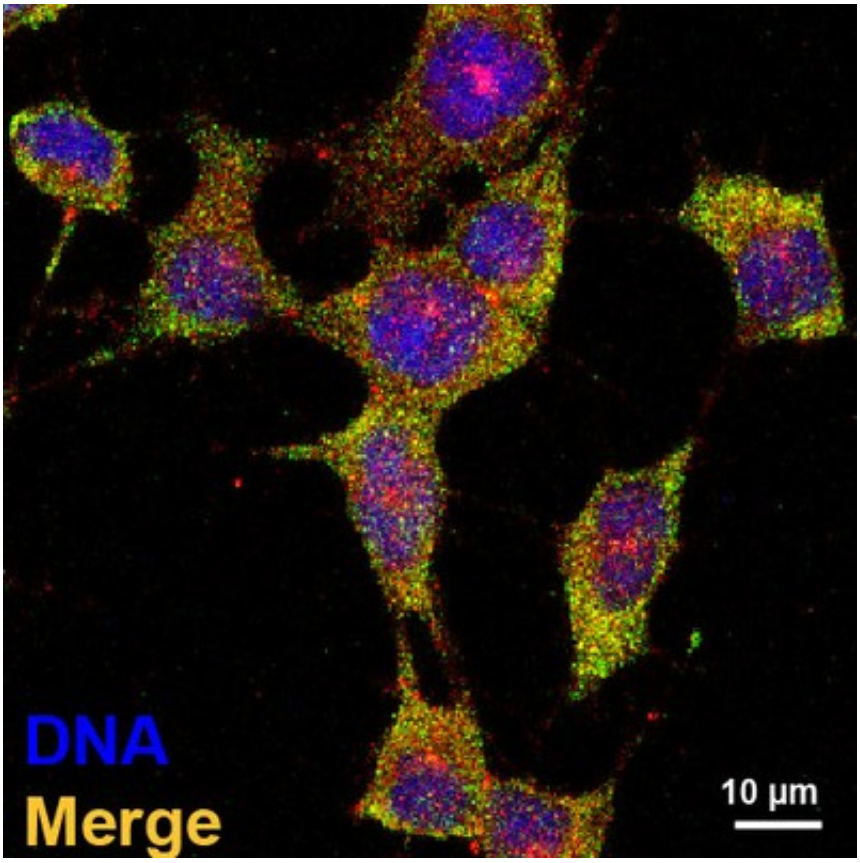
Gene associated with schizophrenia risk regulates neurodevelopment

September 25 2017



The ZNF804A protein and ribosomal protein RPSA, co-localized in mouse nerve cells, were stained with fluorescent dyes and merged into a single image. Both are involved in the translation of proteins from RNA. A new study demonstrates the role of ZNF804A during proliferation and migration of neurons in the brain as well as its contribution to psychiatric disorders like schizophrenia. Credit: Pennsylvania State University

A gene associated with the risk of schizophrenia regulates critical components of early brain development, according to a new study led by researchers from Penn State University. The gene is involved in the translation of proteins from RNA and in the proliferation and migration of neurons in the brain. Understanding the function of this gene—described in a paper that appears online in the journal *Molecular Psychiatry*—could lead to more effective treatments for schizophrenia.

"A recent study identified over 100 genes associated with schizophrenia risk, but their functions are largely unknown," said Yingwei Mao, associate professor of biology at Penn State and lead author of the study. "We investigated one of these genes that is known to be significantly associated with schizophrenia: ZNF804A. In this study, we provide molecular evidence showing that ZNF804A could contribute to psychiatric disorders like schizophrenia."

Schizophrenia is a severe mental disorder that affects approximately one percent of the world's population. Treatments tend to focus on alleviating symptoms, which include delusions and hallucinations, rather than addressing the underlying causes. Like many human diseases, schizophrenia is complex, and no single genetic or environmental factor has been identified as the cause of the disease.

"We found that ZNF804A affects brain structure and function during early fetal development," said Mao. "This supports the idea that changes early in neurodevelopment can produce effects that may not be triggered until adulthood. Although schizophrenia symptoms typically appear in late adolescence or early adulthood, genetic mutations affecting early neurodevelopment could embed risk for future behavioral changes."

The research team identified genes that interact with ZNF804A, which include nine genes involved in controlling the translation of RNA to proteins. This suggests an influential role of ZNF804A in this important

decoding process. Using a mouse model, the team also demonstrated that two processes during neurodevelopment are regulated by the gene: proliferation—the replication of neuronal stem cells that have the potential to become multiple different kinds of cells, including neurons—and migration—the movement of neurons to specific locations in the brain during development.

"ZNF804A is critical to regulating proliferation and migration," said Mao. "Disturbances to these processes may cause neuronal stem cells to develop into different type of cells or may cause neurons to migrate to different locations in the brain, changing neuronal circuitry and potentially leading to behavioral disorders like schizophrenia."

ZNF804A also interacts with and modulates expression of other genes known to be associated with schizophrenia. "Determining the role of ZNF804A is the first step in understanding how schizophrenia-associated genes contribute to abnormal brain development," said Mao. "Understanding how these genes interact to contribute to the development of schizophrenia may allow us to identify the general pathway of the disease, potentially providing a better target for treatment."

More information: Y Zhou et al, Interactome analysis reveals ZNF804A, a schizophrenia risk gene, as a novel component of protein translational machinery critical for embryonic neurodevelopment, *Molecular Psychiatry* (2017). dx.doi.org/10.1038/mp.2017.166

O Durak et al. Ankyrin-G regulates neurogenesis and Wnt signaling by altering the subcellular localization of β-catenin, *Molecular Psychiatry* (2014). DOI: 10.1038/mp.2014.42

Medical Xpress

Provided by Pennsylvania State University

Citation: Gene associated with schizophrenia risk regulates neurodevelopment (2017, September 25) retrieved 10 April 2024 from https://medicalxpress.com/news/2017-09-gene-schizophrenia-neurodevelopment.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.