Study discovers connection between between heart and brain in KBG syndrome

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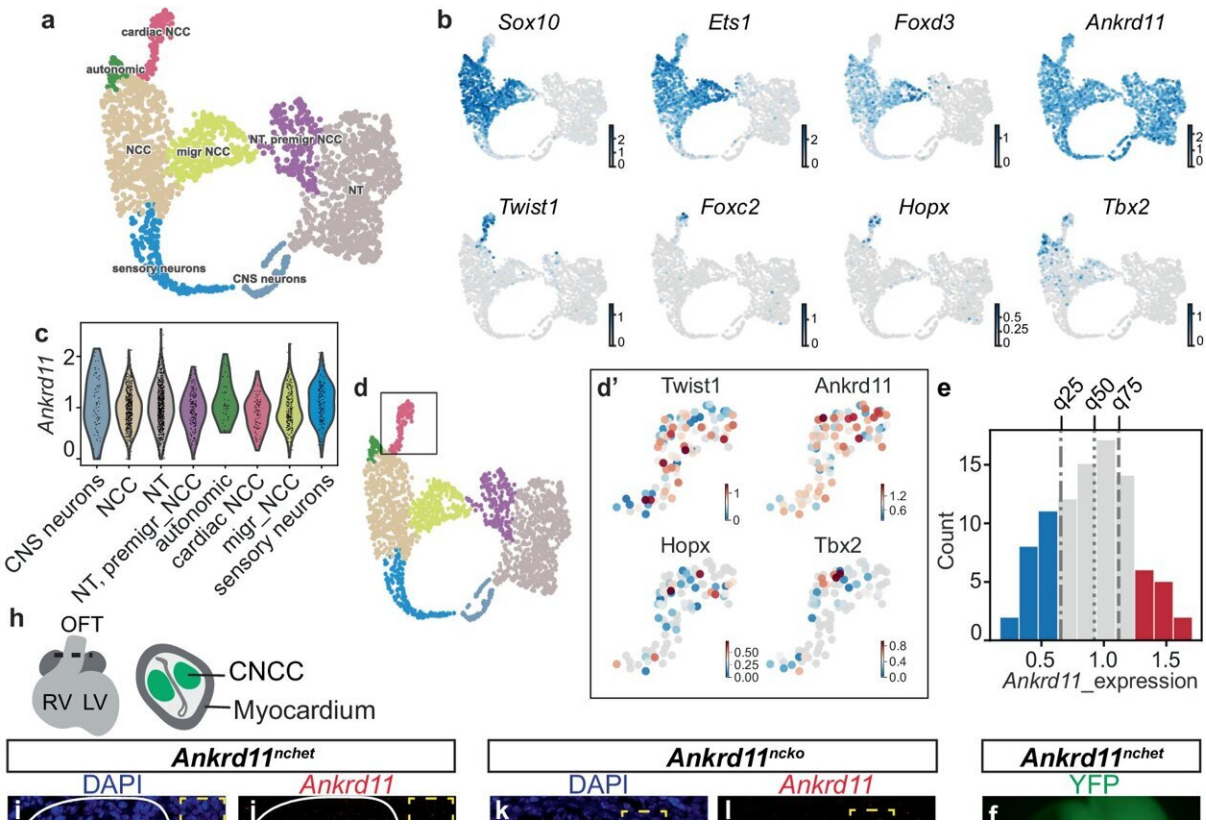

Ankrd11 is expressed in cardiac neural crest cells and ablated in the *Ankrd11*^{ncko} mouse model. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-48955-1

A new study sheds light on a medical question scientists have long

wondered: why do 40% of children with the rare neurodevelopmental disorder KBG syndrome have heart defects? The research now points to a critical link between the heart and the brain. The research is published in the journal *Nature Communications*.

KBG syndrome can cause unusual facial development, skeletal abnormalities, intellectual underdevelopment and heart defects. The syndrome is caused by mutations in the ANKRD11 gene, which plays a crucial role in brain development, but it wasn't until now that researchers at the University of Alberta also found a tie between the gene and the heart, including problems with heart valves and the walls between heart chambers.

Anastassia Voronova, an associate professor in the Faculty of Medicine and Dentistry, led the study, with cutting-edge Vizgen Merscope technology and the U of A's Core Research Facilities team.

Voronova's team observed that mice with the ANKRD11 gene removed from their neural crest cells—a critical part of heart development—had abnormal heart formation and function, including inefficient blood circulation due to the heart's outflow tract not properly forming, and enlarged heart ventricles which affected the heart's ability to pump blood. Several important signaling pathways were also affected, impacting cell function and development.

This team's research follows their previous work published earlier this year, which showed the importance of ANKRD11 to the development of brain cells. These findings in mice were also found in KBG syndrome patients, leading to the discovery of a novel clinical phenotype—the absence of smell.

The next steps are to investigate how the heart and brain influence each other's development in children with KBG syndrome to develop better

clinical care and treatment. The study's findings, along with other recent work in this area, have already started to influence clinical practices: heart evaluations are now recommended for children diagnosed with KBG syndrome.

"The problem with rare disorders is that not all patients are evaluated the same way across the world," says Voronova.

"By showing a clear role of ANKRD11 in heart development, our work paves the way for including heart evaluations in clinical guidelines across the world. This will help to ensure every child diagnosed with KBG syndrome will have their heart evaluated and corrected in a timely manner if needed."

More information: Yana Kibalnyk et al, The chromatin regulator Ankrd11 controls cardiac neural crest cell-mediated outflow tract remodeling and heart function, *Nature Communications* (2024). DOI: 10.1038/s41467-024-48955-1

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