Study finds biomarkers for psychiatric symptoms in patients with rare genetic condition 22q

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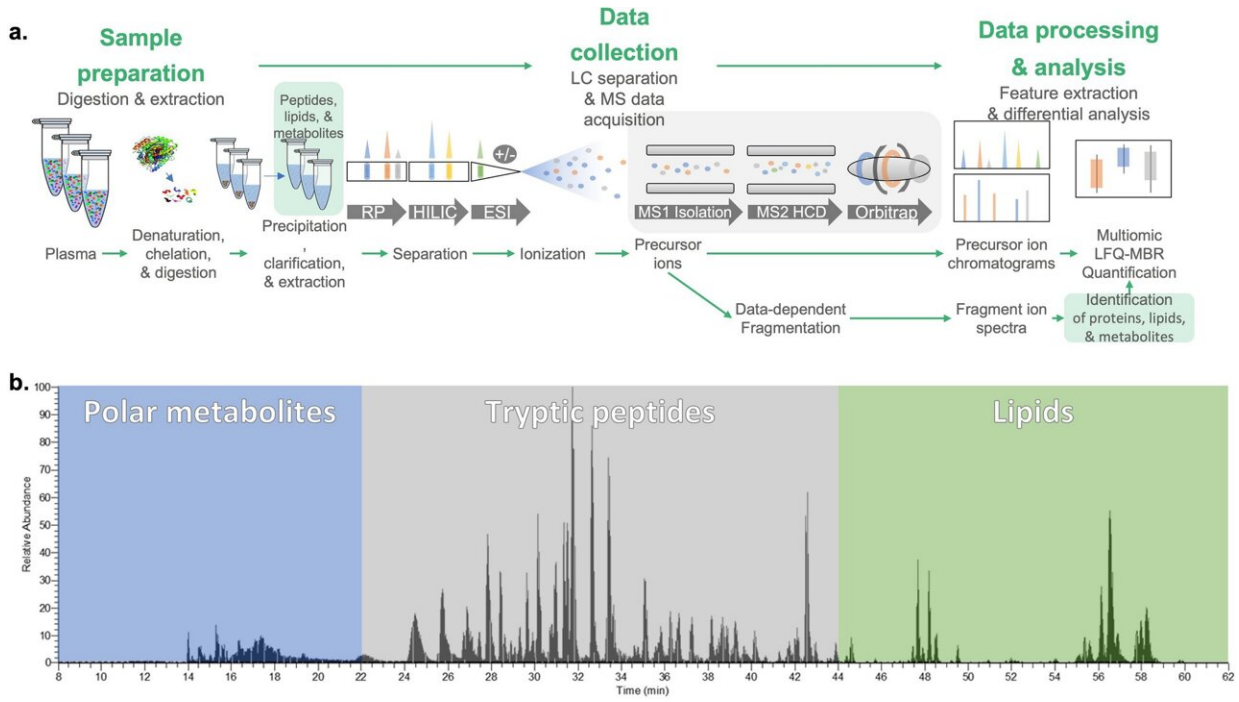

a) Multiomics analysis with the Omni-MS workflow. b) Multiomic LC–MS separation. Credit: *Metabolomics* (2024). DOI: 10.1007/s11306-024-02088-0

A recent study led by UC Davis Health researchers provides new insights into the molecular changes linked to the rare genetic condition 22q11.2 deletion syndrome, or 22q. It found unique biomarkers that could identify patients with 22q who may be more likely to develop schizophrenia or psychiatric conditions, including psychosis, which is commonly associated with 22q. The research was published in the journal *Metabolomics*.

People with 22q are missing a piece of chromosome 22 that contains more than 30 genes. This loss can lead to a variety of health challenges, including heart issues, psychosis, attention-deficit/hyperactivity disorder (ADHD), autism and other conditions. However, it is not clear which genes in the deleted region lead to these symptoms.

The research team focused on the likelihood of patients with 22q developing psychosis, a condition characterized by difficulty recognizing what is real and what is not. This condition can affect up to 20% of patients with 22q in their late teens to mid-twenties. Without good diagnostic tests, it is almost impossible to predict which patients face these risks. Early detection would help patients start treatments when most helpful.

"The molecular changes we found clearly distinguish patients with 22q from those who don't have this condition. These findings could help predict psychosis risk in these patients before symptoms manifest," said Flora Tassone, a professor in the Department of Biochemistry and Molecular Medicine. Tassone is an investigator at the UC Davis MIND Institute and the senior author of the paper. "This work could also help identify targets to aid prognosis and develop future treatments."

While genetic testing can identify specific deletions, the researchers

wanted to investigate how these genetic losses affect the expression of proteins and metabolites (compounds produced by chemical reactions in cells).

Taking advantage of a long-term 22q study

The team used a variety of techniques to identify proteins and metabolites that can be linked to 22q. They examined plasma samples from 10 male and six female participants with 22q and six male and eight female controls. The participants' ages ranged between 7 and 17 years, with an average age of 12.7 years for those with 22q and 12.9 years for controls.

Participants with 22q had a follow-up visit to assess various medical conditions, including psychosis.

"Longitudinal studies are crucial to understanding the course of this condition," Tassone said. "They help us detect symptoms at their earliest stages and possibly identify corresponding biomarkers. Also, participants who were children or early teens when the study began are now late teens or young adults and are at greater risk of developing symptoms of psychosis."

By focusing on changes in proteins and metabolites, the researchers could view the syndrome's molecular readout through two distinct lenses. The protein studies could generate promising drug targets, and the metabolite studies are already producing potential diagnostic markers.

"Looking at the metabolic profile can help us identify compounds that could act as biomarkers and possibly predict disease development," said Marwa Zafarullah, now a postdoctoral researcher at Stanford University and the first author of the study. "We saw that specific metabolites showed significant differential expression in the individuals with the

condition compared to controls."

Specifically, the researchers identified two metabolites, taurine and arachidonic acid, which could serve as markers for likelihood of psychosis.

Taurine is the most abundant metabolite in the brain and spinal cord. Reduced taurine has been linked to neurodegenerative conditions, including psychosis. Studies have found that taurine supplementation could offer protection against these conditions. Arachidonic acid is an unsaturated fatty acid that plays a central role in neurodevelopment.

The study also identified a set of proteins that were expressed differently in patients with 22q. This suggests that these proteins may contribute to the development of the syndrome.

The team plans to confirm and expand on these results in an ongoing, larger study, which will include as collaborators developmental-behavioral pediatrician Kathleen Angkustsiri and researcher and psychologist Andrea Schneider, both of the MIND Institute. The long-term goal is to identify molecular changes that improve early detection and lead to effective treatments.

"By better understanding how 22q functions, we can start moving towards precise diagnostic tests and even therapies. We can also work on developing strategies that may delay or prevent the psychiatric challenges that often occur with this genetic condition," Tassone said. "This knowledge would give clinicians new and better tools to personalize treatment for each patient."

More information: Marwa Zafarullah et al, Untargeted metabolomic, and proteomic analysis identifies metabolic biomarkers and pathway alterations in individuals with 22q11.2 deletion syndrome, *Metabolomics*

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