HBKU Thematic Research Grant 2nd Cycle– Project Highlight

Project Title: A precision medicine approach to investigate autism-related functions of altered blood proteins as potential targets for autism therapy

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Executive Summary

Autism spectrum disorder is a neurodevelopmental condition that has no cure and no single known cause, which is likely due to the broad variation in clinical symptoms and severity levels. These facts highlight a significant need for precision medicine in tackling the causes of autism and developing tailored therapies for selected groups of patients who share similar clinical features. Therefore, we have recruited a well-defined cohort of autism and control subjects and we have stratified them based on their blood proteomic profiles. Remarkably, we have identified several upregulated blood proteins in autism, which are also associated with the clinical severity of autism symptoms. Interestingly, our identified blood proteins in autism are related to neuronal functions, which include synapse assembly, cell adhesion, and neurodevelopment, which suggest a functional relevance of these blood proteins in the pathophysiology of autism.

Here, we will determine the functional impact of altered blood proteins in the pathophysiology of autism through scRNA-Seq of iPSC-derived cortical neurons generated from subjects exhibiting upregulated blood proteins. Also, we will use a gain of function approach in *Drosophila* to validate the role of these proteins in inducing autism-relevant behaviors. We expect these results to determine autism-related functions of altered blood proteins for a defined group of autism patients as an important approach towards precision medicine.

Expected Outcome

This project builds on our previous findings of upregulated blood proteins in a defined group of autism subjects. Here, we propose a new concept of studying the functional role of circulating blood proteins in the pathophysiology of autism. We will validate the functional impact of altered proteins in the blood on neuronal functions and behaviors in autism. Furthermore, we will provide a proof-of-concept for future studies to investigate autism-associated functions of other blood proteins that are altered in other subgroups of autism patients. This project outcomes could have a future application to develop an innovative strategy to target blood proteins for autism therapy, a simpler and safer approach than other therapeutics that target the brain.

Collaborating HBKU entities:

Dr. Mohamad Farhan - College of Health and Life Sciences, HBKU

Schematic: