

HBKU Thematic Research Grant 2nd Cycle– Project Highlight

Project Title: Drug screening for autism spectrum disorder using human induced pluripotent stem cells (iPSCs)



LPI: Dr. Yongsoo Park

Executive Summary

Background: Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder, characterized by repetitive behaviors and deficits in reciprocal social interaction and communication. ASD often co-occurs with attention deficit hyperactivity disorder and epilepsy, which are associated with hyperexcitability of neurons. However, currently there are no available ASD therapeutics to treat hyperexcitability.

Objectives: My team has investigated the pathophysiological mechanisms underlying hyperactivity ASD phenotype using human induced pluripotent stem cell (iPSC)-derived cortical neurons and found out that TRPC6 mutations associated with ASD can lead to hyperexcitability of neurons. In this proposal, we aim to identify small molecule(s) that reverse hyperexcitability of neurons as an ASD therapeutic approach. We will use TRPC6 knockout (KO) human iPSC-derived cortical neurons as a disease model system of ASD in collaboration with Dr. Ayman Al Haj Zen.

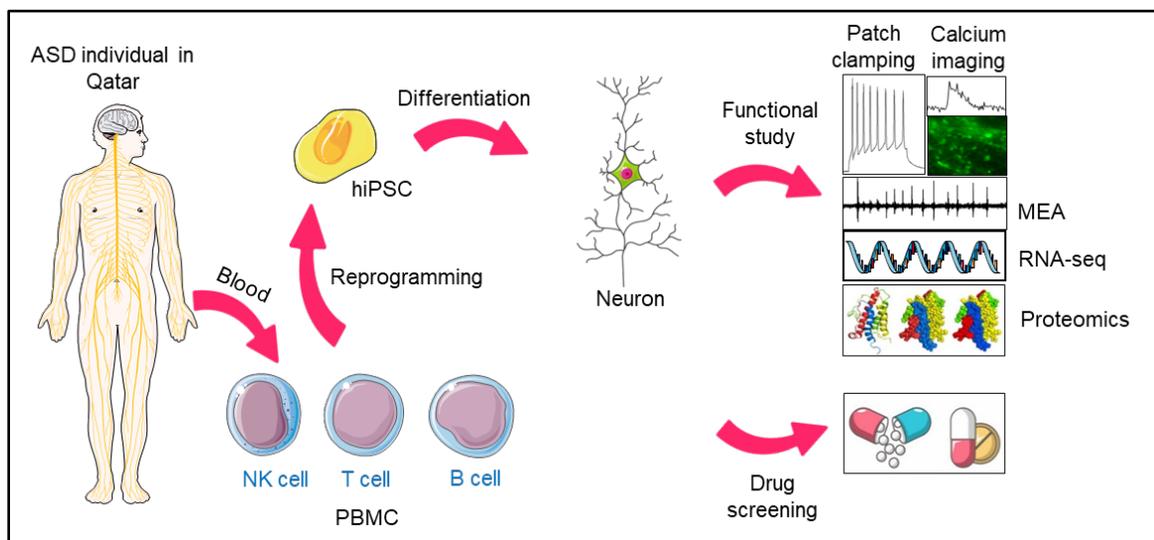
Significance and motivation: Our modeling of ASD using human iPSC-derived cortical neurons that carry mutations of ASD risk genes can provide a platform to study the pathophysiological mechanisms of ASD. Furthermore, modeling ASD using patient-specific human iPSC-derived cortical neurons will be a valuable tool to screen drugs for ASD therapeutics.

Expected Outcome

Our successful project will lead to the outcomes of 1~2 IP disclosure including i) ASD-specific human iPSC-derived cortical neurons as a ASD model to study the pathophysiology and ii) drugs that rescue calcium signaling and hyperexcitability as the ASD treatment.

Collaborating HBKU entities: Dr. Ayman Al Haj Zen, College of Health & Life Sciences (CHLS)

Schematic:



Schematic diagram to model the neuropathology of ASD using human iPSC-derived cortical neurons. Patient-specific cortical neurons that carry mutation of ASD risk genes, e.g., TRPC6, has great potential utility studying pathophysiology in neurogenesis caused. It is creative and novel to study the pathophysiological mechanisms underlying ASD phenotype using patient-specific human iPSC-derived neurons with focus on calcium signaling. ASD-specific cortical neurons will be used for the functional study to understand the pathophysiology of ASD and for drug screening to develop treatment of ASD by rescuing calcium signaling.