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InflASD

Physiological and molecular effects of inflammation on the severity of Shank3-based ASD phenotype on mouse and hPSC model

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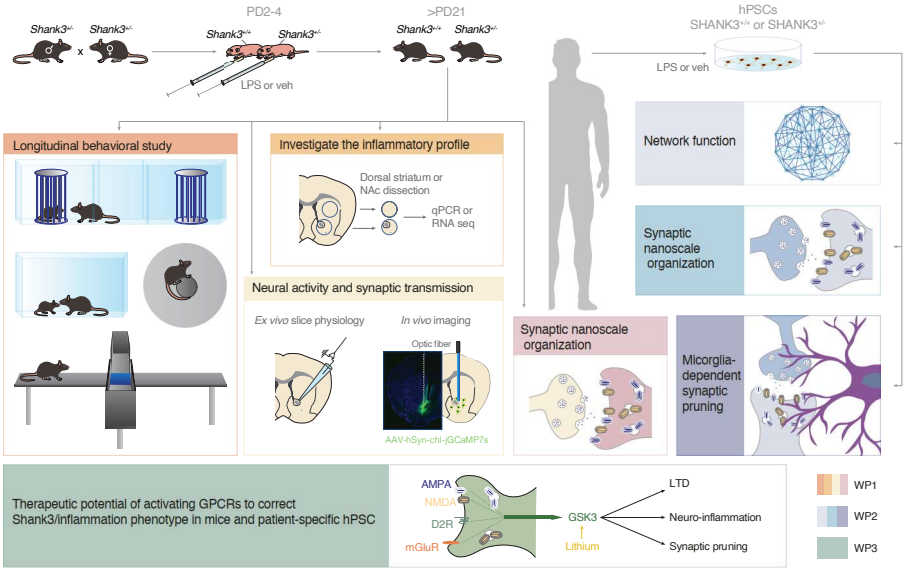
Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by impairments of social interaction and communication accompanied by a pattern of repetitive and restrictive behaviours. Since several autism risk genes affect the function of specialized structures that allow the



communication between neurons, studies in the last few years suggest that pathogenesis of ASD may be attributed to deficits in synaptic function. Mutations in the SHANK3 gene, coding for a scaffolding protein located at excitatory synapses, account for 1-2% of all ASD cases. Although autistic phenotype has been described across individuals with SHANK3 deficiency, heterogeneity in the severity of the phenotype has been reported.

Here we hypothesize that this phenotype heterogeneity is the consequence of the interplay between genetic and environmental factors (double-hits). Using human pluripotent stem cells differentiated into neurons or microglia, and exploiting genetic/environmental double hit mouse models we will identify the mechanisms underlying inflammation/gene interaction. The ultimate goal of InflASD is also to identify new strategies to treat ASD by controlling the spectrum of the inflammatory responses affecting the severity of the phenotype.