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P37. ANALYSIS OF CORTICAL GENE EXPRESSION VARIABILITY IN A MOUSE MODEL OF X-LINKED INFANTILE SPAMS SYNDROME

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Background: Infantile Spasms Syndrome (ISS) is a early-onset epileptic encephalopathy characterized by epileptic spasms during early infancy and severe global developmental delay. A GCG triplet repeat expansion in X-linked Aristaless-related homeobox gene (ARX) is the most commonly inherited error found in patients with X-linked ISS. Although a growing number of studies have been done on the identification of the complete subset of ARX targets, the effect of repeat instability remains unknown.
Objectives: Here we describe a single-cell RNA sequencing study design aimed to identify transcriptome landscapes in the epileptogenic cortex of the Arx mouse compared to the wild type one. The Arx model develops severe tonic-clonic seizures in a phenotype that well recapitulates the chronic epilepsy associated to the c.304ins(GCG)7 mutation in ISS children. We have isolated cortical Arx and wild type neurons from the developing brains and set up the experimental conditions to proceed with the scRNA-seq protocol. Our main objective is to define how the activity of the expanded-polyalanine ARX TF perturbs directly or indirectly transcriptome profiles in distinct inhibitory and excitatory sub-types. The generation of these datasets will constitute a valuable resource to probe cellular composition and molecular features of the epileptogenic cortex associated to ARX defects. Understanding all these aspects may help us to identify cell-specific epileptic-biomarkers linked to the disease-response that could be used as druggable targets in anti-epileptic drug discovery research.