



## Altered Translation in Autism (ALTRUISM)

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Autism spectrum disorder (ASD) is a complex lifelong neurodevelopmental condition of high prevalence with atypical social, behavioral and cognitive function, which creates a high economic burden for public health. The extraordinary complexity and heterogeneity of genotypes and phenotypes are major challenges when investigating ASD. In spite of elusive etiology, dysregulated protein synthesis has emerged as a point of convergence among mechanisms underlying ASD. This project aims to understand the pathophysiology of ASD downstream of mutations in FMR1, PTEN, TSC1/2 and RPL10, which directly impinge on protein synthesis. Molecular understanding of ASD will enable efficient patient stratification and identification of predictive biomarkers for a possible drug repurposing of already existing therapies targeting translational regulators. This will be achieved by using a combination of modern high-throughput technologies (-omics) for quantification of transcriptomes and proteomes along with morphological and functional studies in iPSC derived neurons and brain organoids harboring distinct mutations. As proof-of-principle, we will screen blood samples from deeply phenotyped patients for newly identified biomarkers. The personalized medicine approach proposed here will pave the way for new ASD treatments, significantly ameliorating life quality of patients and their families, and benefitting dramatically on the health systems worldwide.