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Using iPSC derived neurons to study the cellular basis of Timothy syndrome, a multisystemic disorder associated with autism

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Autism Spectrum Disorders (ASDs) are a highly heritable and heterogenous group of neurodevelopmental disorders characterized by language impairments, deficits in social interaction and the presence of stereotyped and repetitive behaviors. The underlying cellular and biochemical defects that lead to ASD are still unknown. We used induced pluripotent stem cell (iPSC) technology to investigate the cellular basis of Timothy Syndrome (OMIM: 601005), a multisystemic disorder caused by a mutation in the calcium channel CACNA1C that includes autism. We generated five iPSC lines from fibroblasts harvested from two patients with TS. We differentiated several lines of iPSC from the TS patients and healthy controls into forebrain neurons and cardiomyocytes and studied their phenotypes using a variety of approaches including immunocytochemistry, single cell gene expression, calcium imaging and patch clamp electrophysiology. We have identified several interesting and robust phenotypes in patient derived neurons and myocytes indicating that this is a promising approach for studying the underlying cellular defects that lead to neurodevelopmental disorders.