Abstract:
Spinocerebellar ataxia1 or SCA1 is an autosomal dominant neurodegenerative disorder characterized by loss of balance and motor coordination due to primary dysfunction of the cerebellum and is caused by CAG repeat expansion in ATAXIN1 (Orr et al. 1993). The protein Ataxin1 is known to play a role in transcription and RNA metabolism (Orr 2012). Transcriptional deregulation is an early occurrence in the pathogenesis of the disease and is known to precede behavioral and morphological changes in mice models of SCA1 (Lin et al. 2000; Serra et al. 2004).

In India, SCA1 accounts for 22% of Autosomal Dominant Cerebellar Ataxia (Mittal et al. 2005). Majority of SCA1 studies in India are hospital-based and hence cross-sectional; thus they fail to reveal characteristic clinical features of disease progression. Studies conducted in patient cohorts, where progression of the disease can be monitored over a period of time, will help in better understanding the varied effects of Ataxin1 during SCA1 pathogenesis.

In my thesis, I have conducted a longitudinal study on genetic and clinical characteristics of SCA1 in a south Indian cohort in Tamil Nadu. Pre-symptomatic, symptomatic patients and normal individuals living in the same geographic location were checked for SCA1 mutation. Individuals with shared genetic founders were selected for exploring transcriptional changes by next generation sequencing. In this thesis I have shown alterations in microRNA and mRNA expression captured from PBMCs of these patients. This study, thus, paves way for further studies in understanding SCA1 pathogenesis using surrogate markers found in blood.