Title of Project:	Building a temporal proteomics map of the developing C. elegans nervous system
Cell Mechanism Supervisor Name	Dhanya Cheerambathur
Quantitative Supervisor Name	Tony Ly

Summary of project
The development of the nervous system is a complex process, producing a tissue highly specialized in intra- and intercellular information transfer. Central to neurodevelopment is the transformation of a neuronal precursor into a highly asymmetrically shaped neuron with unique signaling structures (e.g., axon, dendrite and synapse). The formation of these structures is a multistage, well-orchestrated process associated with significant remodeling of the neuronal proteome. Although a number of neuron-specific factors have been identified, the¬ precise proteomic alterations that facilitate neuronal morphogenesis during organismal development are poorly understood. This project aims to build a quantitative proteomic profile of neuronal morphogenesis and identify key factors underpinning neuronal structural changes. The project combines Cheerambathur-lab expertise in studying neurodevelopmental mechanisms using C. elegans and Ly-lab expertise in developing novel quantitative tools to study dynamic changes in cellular proteomes. Quantitative mass spectrometry-based proteomics have largely been restricted to sample types where cells are in abundance. Recently, the Ly lab developed a sample processing method, 'in cell digest', obtaining proteome depths of >6,000 proteins from 2,000 tissue culture cells and detection of hundreds of proteins from single cells. We aim to develop and apply this method to obtain detailed proteomic profiles of the developing nervous system in C. elegans. Its highly invariant and synchronous developmental program and simple and well-characterized neuronal tissue, comprising 30% of the organism, will highly aid this analysis. The student will combine cutting-edge quantitative proteomics with in vivo fluorescence microscopy to track neuronal structural dynamics, to identify critical determinants of neuronal morphogenesis.

What quantitative skills will the student acquire or develop during their PhD project?
• Quantitative proteomics and phosphoproteomics • Mass spectrometry • Large-scale data analysis using R and Bioconductor • Genome engineering tools in C. elegans • Biochemical methods for tissue isolation • Fluorescence microscopic methods to visualize neuronal tissue dynamics