Characterization of the cellular and molecular mechanism that support the heterogenic excitability pattern of dorsoventral hippocampal pyramidal neurons

Primary Guide: Dr. Giriraj Sahu
Co-Guide: Prof. Deepak Nair

Summary of the Research Problem: The hippocampus is a critical brain region widely involved in various memory and cognition tasks. The functions of the hippocampus are principally mediated by the pyramidal and granule cells arranged in the form of a trisynaptic circuit named CA1, CA3, and dentate gyrus. Though the trisynaptic structural organization pattern of the hippocampus remains identical throughout, the circuit connectivity pattern, cellular anatomy, physiology, and functional properties vary along its dorsoventral longitudinal axis. The dorsal hippocampal neurons are responsible for episodic and spatial cognitive functions, whereas ventral hippocampal neurons are involved in emotional and fear memory. Intriguingly, the excitability pattern which determines the functional characteristics of individual neurons differs along the hippocampal longitudinal axis. The ventral hippocampal neurons are intrinsically more excitable than the dorsal hippocampal neurons for a given stimulus. Notably, in temporal lobe epilepsy, recurrent seizures generally originate in the ventral hippocampus before spreading to other brain regions including the dorsal hippocampus. The hyperexcitability phenotype of ventral hippocampal neurons is proposed to be the causative factor that induces the generation of recurrent epileptic seizures, which makes the ventral hippocampus a potential target for the treatment of temporal lobe epilepsy. However, the cellular mechanisms that lead to this varied excitability pattern between the dorsal and ventral neuronal populations remained a mystery to date. Among the various neuronal excitability control mechanism, calcium-dependent afterhyperpolarization (AHP) events intrinsically regulate the pattern and frequency of hippocampal pyramidal neuronal firing patterns. Preliminary findings further depict a heterogenic development of AHP magnitudes between the dorsal and ventral hippocampal pyramidal neurons.

The major aim of this project is to elucidate the molecular, cellular, and neuronal connectivity mechanisms that support the heterogenic development of AHP events and excitability patterns between dorsal and ventral hippocampal pyramidal neurons. We will be targeting the AHP-generating primary ion channel protein complexes and their secondary cellular modulators to study the processes and factors that support the heterogenic excitability pattern of dorsoventral hippocampal pyramidal neurons. For this, we will be employing brain slice electrophysiological recordings, protein biochemistry, immunohistochemistry, super-resolution microscopy, and computational methodologies. The outcome of the research will provide critical insights into the excitability pattern of hippocampal pyramidal neurons and the mechanisms that support the hyperexcitability and seizure-prone nature of the ventral hippocampal neurons.

Eligibility: The project seeks a highly motivated and research-driven candidate interested in experimental and computational neuroscience. As the project requires a multidisciplinary approach, basic experience in one or more of the following molecular biology/ protein biochemistry/ immunohistochemistry/ physiology/ machine learning/ coding is desirable but is not mandatory.