# Haesun Kim Laboratory

Myelin is a lipid-rich cellular structure that surrounds axons. It is produced by special glial cells: the oligodendrocyte in the Central Nervous System (CNS) and the Schwann cell in the Peripheral Nervous System (PNS). Myelin integrity is crucial as it enables fast nerve conduction, modulates nerve impulse conduction velocity, and promotes neuronal survival.

Abnormal myelin formation and maintenance, myelin breakdown, and demyelination are common pathological features found in many CNS neurodegenerative disorders such as Multiple Sclerosis, Krabbe leukodystrophy, and traumatic brain injury, and PNS disorders including Charcot-Marie-Tooth disease, Guillain-Barré syndrome, diabetic, and chemo-induced neuropathies. These diseases are caused by various factors (inflammation, infection, metabolic changes, and genetic mutations) that affect myelination, myelin maintenance, and/or myelin repair. Understanding the molecular mechanisms that regulate these processes is important for developing therapeutic strategies to improve the prognosis of the patients.

We use mouse models and cell culture systems to decipher the intricate molecular and metabolic processes that are responsible for these myelin defects in human neuropathologies. The Beckman Scholar joining my lab will have an opportunity to participate in the following research projects:

1. **Investigating the impact of choline metabolism in regulating myelination and myelin repair:** Prenatal choline deficiency is linked to abnormalities in brain white matter, regions of the brain that are heavily myelinated. A choline-rich diet has been proposed as a strategy to promote myelination and myelin repair in the CNS. Choline is an important precursor to myelin membrane lipids. Choline also feeds into biosynthetic pathways that generate signaling lipids important for myelination. Despite the importance of choline, the mechanism by which Schwann cells and oligodendrocytes import choline is currently unknown. We have identified Choline-like transporter 1 (CTL1) protein as a choline transporter in Schwann cells. CTL1 is also expressed in oligodendrocytes. Using transgenic mouse models with targeted deletion of CTL1 in Schwann cells and oligodendrocytes, we are currently investigating how choline import and metabolism regulate myelination and myelin repair, as well as trophic support of neurons in the nervous system. The project involves the use of various imaging techniques and biochemical and molecular analyses combined in models of in vivo and in vitro myelination and nerve injury.
2. **Investigating the function of transcription factor TFEB in promoting peripheral nerve repair:** Following peripheral nerve injury, the regeneration process depends on the plasticity of the Schwann cells, which convert into stem cell-like repair Schwann cells that direct axonal regrowth, re-myelinate, and allow functional recovery. This makes Schwann cells one of the very few regenerative cell types in adult bodies. Recently, we showed that the transcription factor TFEB governs the repair Schwann cell generation in injured nerves. To this end, we are currently investigating TFEB-dependent cellular processes associated with the regenerative function of repair Schwann cells. An aberrant increase in TFEB activity has been reported in human patients with Charcot-Marie-Tooth (CMT) disease, a genetic disease that affects Schwann cell myelination and peripheral nerve function. Using a CMT mouse model combined with genetic deletion of TFEB in Schwann cells, we are investigating the role of TFEB during CMT pathogenesis.