

## Chen Institute Symposium 2025

**Speaker:** Amita Sehgal

**Talk title:** *Trimming brain fat with sleep*

**Abstract:** There is universal agreement that lack of sleep impairs performance, especially cognitive ability, during waking hours and considerable evidence supports adverse effects of sleep loss on other physiological parameters as well. Thus, sleep may be regarded as important for waking function. However, what happens during sleep to facilitate wake performance and promote health?

Driven by the successful use of *Drosophila* for deciphering molecular mechanisms of the circadian clock, we developed a *Drosophila* model to address molecular and cellular underpinnings of sleep. Through the use of forward genetic screens, we have identified genes and tissues that affect sleep amount. Coupled with tests of candidate hypotheses for sleep function, we are starting to get a handle on cellular functions of sleep that may be broadly relevant for the brain, and perhaps even the body. In general, we find that sleep is important for metabolic homeostasis, which includes clearance of metabolic waste via autophagy and endocytosis through the blood brain barrier (BBB). Our ongoing work implicates sleep in lipid metabolism, in particular. We find that specific lipids accumulate under conditions of high sleep need e.g. when endocytosis through the BBB is blocked. And lipids are transferred from neurons to glia in a daily cycle that helps to maintain mitochondrial integrity in neurons. Clearance of lipids from the brain also involves circulating cells from the periphery, in a sleep-dependent manner. Together this work suggest that sleep is important for the regulation of lipids, which in turn broadly impact cellular metabolism.