Metabolic Function and Regulation of Mammalian Sleep

Why do we need to sleep? Sleep is essential and sleep disorders are highly prevalent in industrialized societies, posing a massive unsolved medical and economic challenge. We humans spend about one third of our lives asleep. We all know that sleep is important for our health and wellbeing from our personal experiences of lost sleep. Despite its importance, the molecular and cellular mechanisms underlying the vital functions of sleep for promoting health and longevity are, however, not understood.

Sleep crucially requires sleep-active neurons that depolarize during sleep and that inhibit neuronal wakefulness circuits [1]. However, it is not known how sleep and wakefulness neurons are controlled to generate sleep and how sleep in turn controls cellular and organismic benefits.

Our lab studies sleep and sleep-active neurons in two animal models: 1) the nematode *Caenorhabditis elegans* and 2) the mouse [2-6]. Both animal systems have their advantages. While *C. elegans* allows for fast genetic and molecular dissection of basic sleep processes, mice recapitulate the complex stages of sleep in a way that is almost identical to these processes in humans. A key and powerful strategy of our lab is to combine *C. elegans* and Mouse work to understand the molecular mechanism by which sleep is controlled and by which sleep exerts its functions. Specifically, we solve basic mechanisms in *C. elegans* and then translate these findings into mouse models. For our studies, we use genetics, conditional mutants, optical sensors and probes, optogenetics, behavioral and electrophysiological assays. To study sleep, we generate models of sleep loss or gain and we then study the consequences of altered sleep in these animals [7].

In our previous work we have defined links between aging, immunity and gene expression[2, 3, 5]. In this project we will study how a global sleep state is generated at the metabolic and biochemical level and how this molecular sleep state exerts its life-sustaining functions via the regulation of metabolism. For this project, brain-specific mutants will be generated and analysed using EEG, behavioral, imaging and molecular approaches.

The ideal candidate for this project has already obtained experience in working with mice and has the formal requirements for work with live animals (Felasa B certificate). If not yet present, experience in animal work and formal certification can also be obtained at the TUD. In any case, we are looking for candiates that are eager to perform experiments on live mice, which present a powerful biomedial model system.

This project will thus further our molecular and mechanistic understanding of the molecular pathways that are controlled by sleep and will thus allow solving molecular and cellular mechanisms of the benefits that sleep exerts on our body.

Mouse models are useful for sleep research. The image shows a mouse sleeping in our laboratory. We are using electrophysiological, imaging-based, behavioral, and molecular (omics) approaches to understand how sleep is regulated and how it becomes beneficial to an organism.

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