

Mouse models of sleep loss

Why do we need to sleep every night? We all know that sleep is important for our health and wellbeing. The molecular and cellular mechanisms underlying the vital functions of sleep in promoting health and longevity are not understood. This is surprising since sleep is essential and sleep disorders are highly prevalent in industrialized societies, posing a massive unsolved medical and economic challenge.

Sleep crucially requires sleep-active neurons that depolarize during sleep and that inhibit neuronal wakefulness circuits [1]. However, it is not known how sleep neurons control 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 strategy of our lab is to generate genetic models of sleep loss and we then study the consequences of lost sleep in these animals [7].

In this project we will study how sleep neurons in mice support survival, health, and counteracts aging. For this project, mice will be generated that lack specific populations of sleep-active neurons and we will test for the consequences of sleep loss on many health-related parameters and on cellular and molecular processes. This project will thus result in a molecular and mechanistic understanding of the signaling pathways and effectors that are controlled by sleep-active neurons 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 becomes beneficial to an organism.

References:

1. Bringmann H. Sleep-Active Neurons: Conserved Motors of Sleep. *Genetics*. 2018;208(4):1279-89. Epub 2018/04/06. doi: 10.1534/genetics.117.300521. PubMed PMID: 29618588; PubMed Central PMCID: PMC5887131.
2. Koutsoumparis A, Welp LM, Wulf A, Urlaub H, Meierhofer D, Börno S, et al. Sleep neuron depolarization promotes protective gene expression changes and FOXO activation. *Current Biology*. 2022. doi: <https://doi.org/10.1016/j.cub.2022.04.012>.
3. Sinner MP, Masurat F, Ewbank JJ, Pujol N, Bringmann H. Innate Immunity Promotes Sleep through Epidermal Antimicrobial Peptides. *Curr Biol*. 2021;31(3):564-77 e12. Epub 2020/12/02. doi: 10.1016/j.cub.2020.10.076. PubMed PMID: 33259791.
4. Maluck E, Busack I, Besseling J, Masurat F, Turek M, Busch KE, et al. A wake-active locomotion circuit depolarizes a sleep-active neuron to switch on sleep. *PLoS biology*. 2020;18(2):e3000361. Epub 2020/02/23. doi: 10.1371/journal.pbio.3000361. PubMed PMID: 32078631.
5. Wu Y, Masurat F, Preis J, Bringmann H. Sleep Counteracts Aging Phenotypes to Survive Starvation-Induced Developmental Arrest in *C. elegans*. *Curr Biol*. 2018;28(22):3610-24 e8. Epub 2018/11/13. doi: 10.1016/j.cub.2018.10.009. PubMed PMID: 30416057; PubMed Central PMCID: PMC6264389.
6. Hu Y, Korovaichuk A, Astiz M, Schroeder H, Islam R, Barrenetxea J, et al. Functional Divergence of Mammalian TFAP2a and TFAP2b Transcription Factors for Bidirectional Sleep Control. *Genetics*. 2020;216(3):735-52. Epub 2020/08/10. doi: 10.1534/genetics.120.303533. PubMed PMID: 32769099; PubMed Central PMCID: PMC67648577.
7. Bringmann H. Genetic sleep deprivation: using sleep mutants to study sleep functions. *EMBO Rep*. 2019;20(3). Epub 2019/02/26. doi: 10.15252/embr.201846807. PubMed PMID: 30804011; PubMed Central PMCID: PMC6399599.