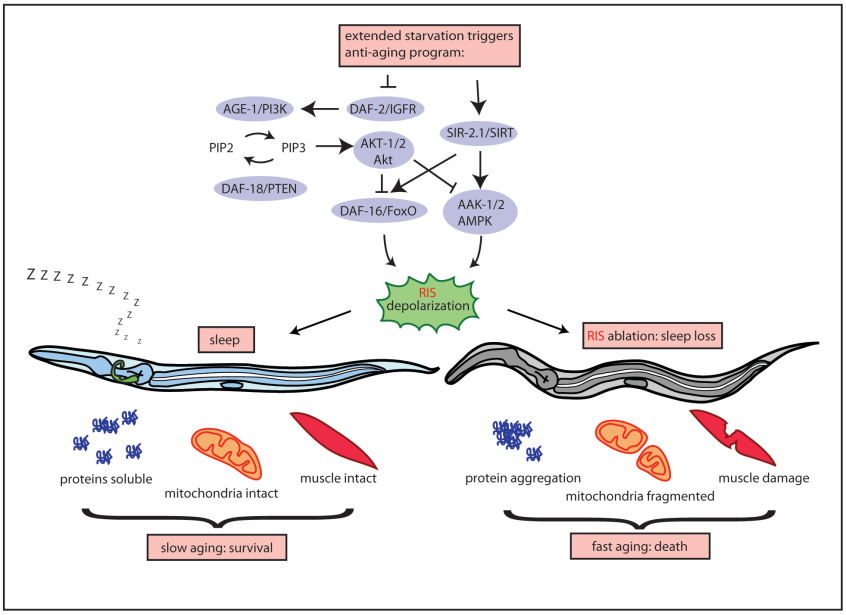
Sleep control of aging

The molecular and cellular mechanisms underlying the vital functions of sleep in promoting health and longevity are not well 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. The nematode *Caenorhabditis elegans* is an important model system to study basic biological processes including aging, stress resistance, and sleep at the cellular and molecular level. Like many other animals, *C. elegans* displays sleeping behavior. We previously showed that *C. elegans* possesses a key sleep-active neuron called RIS[1,2]. Impairing RIS genetically or optogenetically leads to virtually complete and highly specific sleep loss. RIS impairment dramatically shortens survival and increases the progression of aging, but the underlying signaling pathways, effectors, and mechanisms through which RIS supports survival and counteracts aging phenotypes are not understood[3,4]. In this project we will study how the RIS neuron supports survival and counteracts aging. We will test the hypothesis that RIS impacts signaling pathways and effectors that are known to control starvation resistance and longevity. We will investigate, which of the signaling pathways and effectors that control aging interact with RIS by performing genetic survival screening. We will study which of the signaling pathways and effectors that are crucial for aging are controlled by RIS and solve underlying mechanisms. This project will thus result in a molecular and mechanistic understanding of the signaling pathways and effectors that are controlled by sleep-active neurons during starvation and will thus allow solving molecular and cellular links between sleep and aging.



Sleep counteracts the progression of aging phenotypes. Cartoon summary of the link between aging, starvation and sleep. Nutrient starvation triggers arrest and sleep through a conserved longevity gene network to depolarize RIS, which in turn is required to counteract aging phenotype progression[3]. How sleep-active neurons act to control aging phenotype progression and promote longevity is not well understood in any system.

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3. Wu, Y., Masurat, F., Preis, J., and Bringmann, H. (2018). Sleep Counteracts Aging Phenotypes to Survive Starvation-Induced Developmental Arrest in C. elegans. Curr Biol *28*, 3610-3624 e3618. 10.1016/j.cub.2018.10.009.
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