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Lysosomes are digestive organelles that govern cellular metabolism and homeostasis. Despite their importance to animal health and disease, the current model of lysosome structure and function is quite simplistic: lysosomes are thought to exist mainly as discrete vesicles, each with similar degradative capacity. Recently, two early career investigators at Louisiana State University discovered a new class of lysosomes that challenges this model. In multiple species and cell types (including mammalian cells), the team has identified an interconnected, dynamic network of tubular lysosomes (TLs) that are exceptionally degradative. Notably, these TL networks suppress age-related tissue degeneration, highlighting their biomedical relevance. This study will utilize two genetically tractable model organisms, the nematode *C. elegans* and the fruit fly *Drosophila melanogaster*, to develop a comprehensive picture of this unique organelle. Live-animal imaging will be used to track TL biogenesis and activity in different tissues throughout life and in response to metabolic stimuli. In addition, the investigators will utilize fluorescent sensors to assess cargo turnover in TLs and they will perform unbiased screens to identify TL regulators. These studies have the potential to redefine

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dynamic changes in brain PG levels which, in turn, could induce changes in the expression of genes associated with sleep/wake cycles and circadian rhythms. Using mouse models, the WSU investigators have demonstrated that the mRNA of a PG-binding peptide in the brain increases after acute sleep deprivation. This peptide induces the expression of sleep regulatory cytokines involved in circadian rhythms. In this project, the WSU team plans to measure the levels of PG and of the PG-binding peptide in the mouse brain under normal circadian rhythms and sleep-wake cycles. They would determine how disrupting sleep or circadian rhythms drives changes in the levels of PG and PG-binding peptide along with other proteins related to circadian rhythms. Lastly, using *in vitro* neuronal/glial co-cultures that simulate sleeplike states, the investigators would characterize the molecular mechanisms linking PG levels to cytokines and sleep. Successful completion of this project would advance our understanding of the relationship among the micr.s1 Tf0000912 vestneuronal/glial co