Regulation of Sleep Homeostasis by the Translational Repressor Pumilio in *Drosophila melanogaster*

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Numerous studies have shown that sleep deprivation increases synaptic proteins; nevertheless, the effects of reducing the translation of synaptic proteins on sleep behavior have not been thoroughly explored. Pumilio (Pum) is an RNA binding protein involved in neuronal homeostasis that repress the translation of many synaptic proteins and decrease neuronal excitably during chronic patterns of neuronal activity. We show that knocking down Pum in *Drosophila melanogaster* timeless neurons abolishes sleep rebound. Our data shows that Pum is recruited during sleep deprivation and prevent the uncontrolled synthesis of synaptic proteins at the translational level. Consistent with the idea that these effects are due to exaggerated translation of synaptic proteins, oral administration of the translational blocker, Rapamycin, completely rescues the sleep rebound in Pum knockdown flies. Conversely, exaggerating synaptic translation by overexpressing the eukaryotic initiation factor 4E (eIF4E), which is a known target of Pum repression, decreased the sleep rebound. These results suggest that unregulated translation impairs sleep rebound, making translation of synaptic proteins an important regulator of sleep homeostasis. We expect to expand this research to other homeostatic processes such as those controlling the development of tolerance to drugs such as alcohol. For this, we will examine the role of Pum in alcohol tolerance, initiating with pharmacological manipulation of wild type *Drosophila melanogaster* and later on with Pum knockdown and overexpression.