Sleep disorders affect millions of people worldwide and despite the importance of sleep, we have a poor understanding of its molecular basis. *Drosophila melanogaster* (the fruit fly) is an excellent model organism for sleep research due to the powerful genetic techniques available. Like humans, *Drosophila* have a circadian clock that regulates sleep/wake cycles. While the molecular components of the circadian clock in flies are well-studied, the mechanisms by which these molecules regulate sleep are unclear. A recent large-scale screen by the Wu Lab identified a novel *Drosophila* gene, *wide awake* (*wake*), that acts downstream of the circadian clock to promote sleep onset. Flies lacking WAKE exhibit a dramatic increase in sleep latency (the time it takes to fall asleep). In addition, WAKE is expressed in the lateral ventral neurons (LNvs), which include the master circadian pacemaker cells in *Drosophila*[1].WAKE levels cycle throughout the day, and this cycling is dependent on an intact circadian clock as well as the presence of light. Interestingly, the LNvs that express WAKE have been shown to be light-sensitive[2].

In my proposed project, I plan to study the light-dependent regulation of WAKE. To explore this mechanism, I will determine if 1) both light and the circadian clock are required for WAKE to cycle normally, or 2) if light is sufficient by itself. First, I will perform western blot analysis of the effects of light on WAKE protein levels. The levels WAKE protein would be compared between flies in three days constant light (LL) and three days constant dark (DD) conditions. In addition to increasing light, LL conditions also disrupt the circadian clock. Thus, if light is sufficient to induce WAKE expression, then I hypothesize that there will be increased WAKE expression in the flies from the LL condition vs the flies from the DD condition. However, if WAKE levels are not increased in flies from LL, this would suggest that both the circadian clock and light are necessary for WAKE expression. The second set of experiments

would involve a behavioral assay to determine the effect of various light intensities on sleep latency. I predict that an increase in light intensity during the daytime will reduce sleep latency due to higher levels of WAKE expression. To do these experiments, I will use the automated tracking systems in the Wu Lab that allow us to measure sleep in individual flies on a large-scale. Importantly, WAKE has a single homolog in mice and humans, and this mammalian WAKE homolog is enriched in the superchiasmatic nucleus of mice, which is light sensitive and the master circadian pacemaker in mammals. Thus, insights we gain from studying the light-dependent regulation of WAKE may serve to deepen our understanding of how sleep is regulated in humans.

I first became interested in neuroscience in sixth grade, when I read a book about Phineas Gage, a man whose frontal lobe was severely damaged by an iron rod. I remember being astounded by the fact that his personality and social behavior were irreversibly changed, while leaving other mental faculties intact. Since then, I've become a neuroscience major here at Johns Hopkins, and have thoroughly enjoyed my neuroscience courses. Furthermore, I've had the opportunity to do research with the Neurology Department at the Johns Hopkins Hospital. Being a research assistant has given me an invaluable chance to experience firsthand exciting aspects of neuroscience research. When not in class or doing research I enjoy volunteering at the Baltimore Rescue Mission Clinic, which offers experience working directly with patients. My ultimate goal is to become a neurologist, allowing me to use my interest in neuroscience to help people. The Woodrow Wilson Fellowship would provide great assistance in accomplishing this goal.

References

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