**The role of stress-response pathways in intestinal stem cells regulating the gut microbiome**

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The gut microbiome is a complex ecosystem comprised of various microorganisms including bacteria, viruses, and fungi. For my project, I will focus on bacteria. Through interactions with the host, these bacteria regulate important processes, like metabolism, and help maintain tissue homeostasis. With aging, the communities that live in the gut microbiome change in composition and abundance, leading to microbial dysbiosis or unbalance, which can lead to several physiological consequences. Unpublished data from our lab done using *Drosophila melanogaster*, have shown that the knockdown of two stress-responsive transcription factors, namely Nrf2/CncC and Hsf1 in intestinal stem cells (ISC) led to an early onset of microbial dysbiosis, leaky gut and reduced survival. As both CncC and Hsf1 were found to play a role in silencing an EE-specification gene known as *asense,* an increase of enteroendocrine cell (EE) progenitors was observed in flies where both factors were knocked down. It remains unanswered how an increase in EE progenitors is responsible for microbial dysbiosis. We are interested in finding what kind of factors could be secreted by those cells resulting in alteration of the gut microbiota. The data arising from this project will help us better understand how microbial dysbiosis can influence the aging process with the long-term goal of finding new ways to extend lifespan and health span (i.e., healthy aging) of the animal.

Two projects will be done in parallel. First, we will perform an ISC-specific knockdown of Nrf2/CncC and Hsf1 to then characterize the microbial dysbiosis observed in the mutant flies compared to the control. This will be accomplished by performing a 16s rRNA sequencing of the bacterial populations found in the guts of those flies and analyzing the sequences using Rstudio. The second project is to identify the factors that are secreted by the EE progenitors responsible for microbial dysbiosis. This will be achieved by performing targeted screening of flies where specific genes will be knockdown specifically in EEs and microbial dysbiosis will be measured by Colony Forming Units (CFUs). The genes for this screening will be selected on unpublished RNAseq data where both Nrf2/CncC and Hsf1 were knocked down in ISCs.

As this is my first time working in a research lab environment, I expect to face challenges getting used to the lab culture. Moreover, since this will also be my first-time dissecting *Drosophila melanogaster* and performing 16s rRNA sequencing, I expect to face some challenges when realizing those techniques and analyzing the data. To overcome those challenges, I will be asking my mentor and my research group while also consulting the literature for help with understanding the techniques and the analyzing process.