# Independent Study Proposal

Number of credits desired: 4
Number of hours estimated to work in lab per week: 15 hours

**Research Title:** The role of the prefrontal cortex to dorsal striatum pathway in animal model of anorexia nervosa

**Project Description:**

Anorexia nervosa (AN) is an anxiety based eating disorder characterized by voluntary food restriction, excessive exercise and maladaptive decision making, usually seen in adolescent females aged 15-18 years. In addition to a higher risk of mortality, AN-afflicted individuals also are at higher risk for heart and kidney failure, anemia, and immune system complications. There is no known neurological cause for AN, but previous research has implied that prefrontal cortex (PFC) activity is partially responsible for regulating the maladaptive decision making that is a trademark of AN. Using a mouse model of AN, Activity Based Anorexia (ABA), I will partake in experiments that test the hypothesis that excitation of the PFC will curtail the maladaptively excessive running behavior and therefore decrease the severity of anorexia (SOA). We will do this using excitatory and inhibitory DREADDs (Designer Receptors Exclusively Activated by Designer Drugs), which is a minimally non-invasive way to excite or inhibit neural pathways in the brain through timed, systemic administration of agonists of G protein coupled DREADDs. In particular, we will use Cre-recombinase dependent DREADDs to target pyramidal PFC neurons that project to the dorsal striatum (DS), a region that plays a considerable role in reinforcement learning and action selection and control. In addition, I will use this technology to investigate to which regions the axon collaterals of these PFC → DS neurons travel and how they affect the behavior associated with resilient or vulnerable mice. I will also analyze the cell types that are activated or suppressed by DREADD agonists, which are expected to be the population of neurons synaptically linked to the neurons expressing DREADDs. This will involve the use of dual immunocytochemistry to determine whether the neurons expressing the immediate early gene product, cFOS, also express the markers of inhibitory neurons (glutamic acid decarboxylase) or excitatory neurons (CaMKIIalpha).

One other goal of this project in the upcoming semester is to assess the extent of correlation between depression/anxiety and ABA-vulnerability of mice. This will be done through behavioral observations, such as the elevated plus maze (EPM, to test anxiety) and tail suspension (TS, to test depression) together with measurements of the maladaptive running (to measure ABA vulnerability). We hypothesize that the running, which is driven by foraging/escape behavior displayed by mice is not only anxiolytic but also signifies resistance or the desire to "escape" a hard situation.

**Learning Objectives:**

This independent study will benefit my long term goals as it will help me collect data and get a headstart on writing my senior thesis. Specifically, the techniques I hope to become exposed to are the following:

- Animal handling, including feeding, cage cleaning, measurement of body weight, wheel running and food intake
- Analysis of the behavior of videos recording behavior during EPM and TS and ABA

- Light microscopicy, dual immunocytochemical analysis that involves capturing of images by confocal microscopy, 3-D reconstruction of images using Neurolucida and/or ImageJ software
- Training in critical reading of original scientific literature
- Practice with scientific writing and oral presentation during lab meetings

**Reading List**


1. Gabbott, P. L., Warner, T. A., Jays, P. R., Salway, P. and Busby, S. J. (2005), Prefrontal cortex in the rat: Projections to subcortical autonomic, motor, and limbic centers. J. Comp. Neurol., 492: 145-177. doi:10.1002/cne.20738
2. E. Jodoj, C. Chiang, G. Aston-Jones, Potent excitatory influence of prefrontal cortex activity on noradrenergic locus coeruleus neurons, Neuroscience, Volume 83, Issue 1, 1998, Pages 63-79, ISSN 0306-4522, https://doi.org/10.1016/S0306-4522(97)00372-2.
3. Gaykema, R. P., Van Weeghel, R. , Hersh, L. B. and Luiten, P. G. (1991), Prefrontal cortical projections to the cholinergic neurons in the basal forebrain. J. Comp. Neurol., 303: 563-583. doi:10.1002/cne.903030405


**Estimated Timeline :**

- February-March:
  - Feed mice in upcoming cohort and monitor their changes in body weight and wheel activity
  - Analyze cFos activity in the PFC through immunocytochemical analysis
  - Carry out behavioral observations through EPM (elevated plus maze) and TS (tail suspension) tests
  - Start DURF grant application
- March-April:
  - Continue to work on DURF grant application until submission date
  - Analyze previous mouse cohort's brains under confocal and fluorescent microscopy and through staining
  - Continue to work with new cohort(s) of mice
  - Analyze behavioral data (TS + EPM)
  - Begin drafting the beginnings of a senior thesis
- April-May:
  - Continue to add to senior thesis draft
  - Continue to work with new cohort(s) of mice

**Frequency with which Student plans to meet with PI + mentor:** I plan to meet with my mentor every day that I work in lab.