

1. **Project Title:** Age-related loss of neuropeptide Y in the auditory midbrain and hippocampus. Jeffrey Mellott, PhD. NEOMED; Building E; Rooms 41/57/147/153
2. **Abstract:** Recent studies demonstrated that sensory processing deficits may be a precursor to pathologies such as Alzheimer's Disease. Our long-term goal is to determine biomarkers that contribute to brain health across multiple nuclei as aging progresses from normal into pathological. Neuropeptide Y (NPY), a neurotransmitter that is co-released by GABAergic cells in the hippocampus and the inferior colliculus (IC) and, may be such a biomarker. In the hippocampus, NPY is considered neuroprotective as it can modulate oxidative stress, protect neurons from A $\beta$  neurotoxicity and prevent spatial memory loss. Recent studies of the IC have demonstrated that NPY is expressed exclusively in GABAergic cells and its receptors are expressed by glutamatergic cells, just as it is in the hippocampus. However, our understanding of age-related changes to NPY function in the IC serving as an early biomarker for functional changes in the hippocampus is inadequate due to the lack of information regarding how NPY expression and release occurs across the same time course of these two structures.
3. **Significance:** The project will identify if NPY is downregulated in the auditory midbrain during aging, and if so, does the downregulation occur before, simultaneously, or after the loss in the hippocampus.
4. **Goals and objectives:** The student will examine IC and hippocampal tissue for the presence of NPY at 4 different ages.
5. **Methods used:** We will use electron microscopy, immunohistochemistry, fluorescent microscopy, in situ fluorescence hybridization, traditional tract-tracing, neuron reconstruction.
6. **Proposed methods of data analysis:** Most analysis will be conducted with NeuroLucida Explorer (MicroBrightField) for fluorescent microscopy and SerialEM for Electron Microscopy.
7. **Impact of findings:** Our long-term goal is to determine shared mechanisms within auditory and hippocampal circuitry that are affected by aging and contribute to presbycusis and cognitive decline.

#### Student Mentoring Plan

1. The student will be expected to attend weekly lab meetings and journal club. The student will be tasked to present their findings to the lab towards the end of the 8 week period
2. Most of the tissue necessary to conduct the data collection and analysis is already "on slide/grid". Generating the cases needed will be minimal or absent from the 8-week term, which will help maximize the student's time. All needed elements to complete the study are fully function and routinely used in the lab. Microscopy training will come

from the PI. Training on the needed software will be a combination of the PI and Research Assistants.

3. All experiments will be conducted and analyzed in E-147/E153 and E-41/57.