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NBDS Seminar
Seminar Title:  5-Fluorouracil chemotherapy upregulates cytokines and alters hippocampal dendritic complexity in aged mice

Date and Time: Thursday, May 18th at 9:00 a.m.
Site:  BioMed-II Building, Rayford Auditorium, Rm. 106

**Seminar Abstract**

***5-Fluorouracil chemotherapy upregulates cytokines and alters hippocampal dendritic complexity in aged mice***

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Approximately 1 in 2 adults will be diagnosed with cancer during their lifetime with a median age at diagnosis of 66 years. Improvements in cancer therapy have helped a growing number of patients to survive. Due to this survivorship, there has been a greater focus on researching the long-term adverse effects of treatment and the impact this treatment can have on the daily lives of patients. Chemotherapy is the most commonly implemented treatment, often used in conjunction with local therapies such as surgery and radiotherapy. However, neurotoxicity is a frequent accompaniment of cancer chemotherapy. Chemobrain, also known as “chemofog,” is a cognitive impairment consisting of deficits in attention, executive and motor function, memory, and speed of information processing, following chemotherapy for a multitude of cancers. These deficits can persist for several years in patients and can dramatically affect many aspects of daily living, such as employment, social functioning, and community integration. 5-FU, an anti-metabolite and pyrimidine analogue, was developed in 1957 and has been used to treat breast, bowel, prostate, gastrointestinal, vaginal, and cervical cancer. 5-FU interacts with nucleic acids within the DNA sequence and interferes with RNA and DNA synthesis. Animal studies that have examined intraperitoneal injections of 5-FU have shown a disruption of learning and memory across multiple tasks, including object recognition, avoidance conditioning, cue-specific and contextual fear condition tasks, and Morris water maze. 5-FU passes through the blood brain barrier (BBB) by simple diffusion and can affect proliferating cells in neurogenic zones, like the subgranular zone (SGZ) of the hippocampus. It is proposed that these altered neurogenic zones may contribute heavily to the cognitive deficits seen in those with chemobrain. Cytokines and chemokines are secreted signaling proteins derived from many different types of cells that help determine and regulate immune responses. Several clinical studies have demonstrated that administering a standard dose of chemotherapeutic drugs causes an increase in cytokine levels for a variety of cytokines. The present investigation was designed to assess how a relatively low dose of 5-Fu would affect dendritic spine density and morphology. Such data might provide critical information regarding the mechanism of disruption of neural circuitry following chemotherapeutic treatment.