Research Area of Interest: The distribution of white adipose tissue (WAT) plays an important role in the development of obesity-associated pathologies, such as diabetes and heart disease. While accumulation of visceral WAT (VWAT) is detrimental for metabolic health, accumulation of subcutaneous WAT (SWAT) may confer protection against these pathologies. Interestingly, females have an SWAT accumulation bias while males accumulate more VWAT. This differential WAT accumulation appears to be sex-hormone dependent, with estrogen being essential for SWAT expansion. Therefore, my research program will focus on dissecting the role of estrogen signaling in the sexual dimorphic WAT expansion, specifically how it affects the activation of adipocyte precursor (AP) cells. The Rodeheffer lab at Yale, a world leader institution in metabolism research, is a pioneer in AP biology that has developed novel tools and technologies to address this question.

Relevant Coursework: The coursework taken at Yale have prepared me to think critically about science and how to target research questions and effectively develop them into grant proposals. The cell biology and genetics courses were key to understand the cellular mechanisms underlying physiological processes and how genetic tools can be accurately used to answer fundamental biological questions. Furthermore, in biophysics I learned the underlying principles of spectroscopy methods, confocal microscopy, and mass spectrometry; all of which will be essential techniques during my PhD research. In order to be adept at bioinformatics analysis, I will enroll in a genomics course specifically tailored to teach RNAseq data analysis. Finally, the graduate seminar required every year of my training at Yale will further develop my presentation skills, which are central for success in science.

Methods and Theoretical Framework: We have shown that estrogen is crucial for the activation of APs in SWAT but not VWAT in male and female mice. Once APs are activated they commit differentiation into mature adipocytes and thus contribute significantly to WAT mass**.** I hypothesize that estrogen receptor alpha (ERα) is required for APs activation and expansion of SWAT and there are distinct molecular mechanisms driving WAT expansion in VWAT and SWAT, with VWAT expansion being independent of ERα activity.

Aim1: Determine if ERα is required for AP activation in SWAT. We will generate AP-specific *ERα* knockout mice using inducible systems developed in the Rodeheffer lab. We will then measure the proliferation of APs in both fat depots of *ERα-APKO* mice upon periods of high-fat diet (HFD) using an established flow cytometry-based proliferation assay. We expect to see impaired AP activation only in SWAT of *ERα-APKO* mice.

Aim 2: Establish if *ERα* is essential for increased adipocyte formation in diet-induced obesity. The Rodeheffer lab has pioneered an in vivo adipogenesis assay that tracks adipocyte formation via incorporation of the nucleoside analog BrdU. We will use this assay to assess adipocyte formation in female *ERα-APKO* mice fed a HFD. We expect to see impaired AP differentiation only in SWAT of *ERα-APKO* mice.

Aim 3: Determine the transcriptional mechanisms driving AP activation in female SWAT. Preliminary data (not shown) indicates FOXM1, a transcription factor, is important in male VWAT AP activation. It is known that ERα and FOXM1 work together on breast cancer cells to promote the expression of a different gene program than FOXM1 alone. We hypothesize FOXM1 is important in AP activation in both males and females, but it acts through distinct molecular mechanisms depending on the presence of estrogen. To asses this we will perform RNAseq on APs from VWAT and SWAT under HFD and standard diet conditions of WT female mice. We expect to see an increase in gene expression in FOXM1-ERα targets only in SWAT of HFD females. We can further assess this FOXM1-ERα interaction in SWAT APs via chromatin immunoprecipitation assays.

Project relation to society and career goals: Obesity is one of the most pressing public health concerns in modern society. This project is designed to increase our understanding of a central issue of the obesity phenotype – how fat mass expansion differs between men and women. I am confident this research program will prepare me extensively to secure a postdoctoral position at a major research institution and thus, pursue my goal of becoming a leading independent principal investigator in academia. Lastly, my participation in several minority-oriented organizations at Yale will prepare me to become an advocate of minorities in STEM, an essential part of my goals in academia.