Different angiogenic capacity of endothelial cells in male and female mice

Obesity is a major global health problem and is considered a consequence of changes in food composition/consumption and is exacerbated by inactive lifestyle. It is well established that there is a sex specific difference in development of obesity related cardiometabolic disorders such as type 2 diabetes. In obesity, the normal balance between adipose tissue expansion and angiogenesis (production of new blood vessels from the pre-existing ones) is disturbed. Recently published data from our lab indicates higher angiogenesis in adipose (fat) tissue of high fat fed female mice compared to males. This could contribute to the sex related differences in susceptibility to develop obesity related disorders. For my master’s project, I have been studying the inherent sex differences in endothelial cells (cells lining the blood vessel) capacity to form new blood vessels. To achieve this objective, visceral adipose tissue was harvested from male and female C57BL/6J mice and was used for endothelial sprouting assays and endothelial cell isolation. Consistent with higher angiogenesis observed in female adipose tissue, endothelial cell outgrowth from 3D collagen adipose explant cultures indicated that 85% of female explants developed new capillary sprouts compared to 50% for male explants. However, the sprouting area and cell density was greater in male compared to female explants, suggesting a higher number of endothelial cells. In cell proliferation assay, male endothelial cell growth was 1.5-fold greater than that of females. These data unexpectedly demonstrate that male endothelial cells have higher capacity to proliferate compared to female cells. In migration/invasion assay, female cells showed higher migration capacity compared to males. Protein measurements of pathways involved in angiogenic capacity in endothelial cells, indicate higher activation of p38 and higher expression of FoxO1 proteins in females compared to males. p38 is involved in cell migration and is also activated in cell stress. FoxO1 is essential in endothelial cell homeostasis, metabolism and inhibits cell proliferation. These results indicate that the higher vascularization of adipose tissue previously observed in high-fat-fed female mice may not result from sex-differences in the proliferative capacity of endothelial cells. Further experiments will examine contributions of different signaling pathways such as Notch to the observed sexual dimorphism in the angiogenic capacity of adipose tissue. By comparing the angiogenic capacity of male and female endothelial cells, we may understand the role of endothelial cells in the sexual dimorphism observed in pathophysiology of obesity related metabolic disorders.