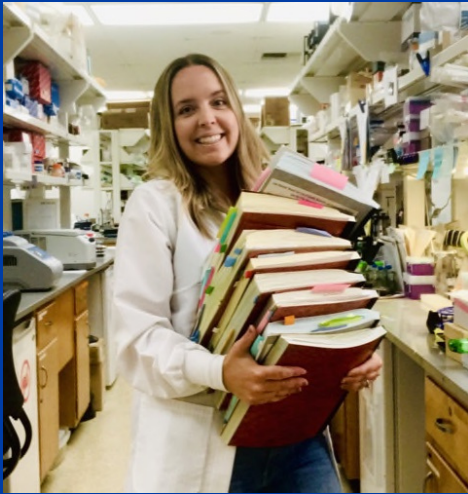


PH.D. DISSERTATION DEFENSE OF



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Prolactin Effect in the Murine Oviduct

The most common and deadly form of ovarian cancer is High-Grade Serous Ovarian Carcinoma (HGSOC). Most cases of HGSOC are now known to arise from epithelial cells of the fallopian tube and not the ovary. Lesions arise only in the fimbrial region, known as the infundibulum in the mouse. Prolactin (PRL) has been described in many studies to be a potent serum analyte in the detection of ovarian cancer. However, unknown is whether elevated PRL initiates disease or is the result of disease, although once cancer is present, it is clear that PRL promotes cancer cell survival and migration. In human ovarian cancer cell lines, the long form of the PRL receptor (LF Prlr) mediates increased cell survival, proliferation and migration, whereas signaling through the short forms (SF) counteracts these effects and promotes differentiation; thus, the ratio of LF/SF Prlr is important to PRL's end effects. To gain insight into the normal biological role of PRL in the oviduct as well as to examine PRL's potential for disease initiation, Prlr expression and effects of elevated PRL were assessed. The ratio of LF to SF3 Prlr varied by region of the oviduct (mRNA and protein), suggesting different effects of PRL in the different oviductal segments. Interestingly, the only segment that showed changes in this ratio in response to hormones of the estrous cycle was the infundibulum. In addition, the mucosal epithelium of the infundibulum was the most responsive to acutely elevated PRL. Whole transcriptome sequencing of the infundibulum following a 7-day PRL treatment in vivo showed downregulation of genes involved in multi-ciliated cell (MCC) function. This suggests that prolonged elevated PRL reduces the function of the ciliated cells, a novel additional mechanism whereby elevated PRL negatively impacts fertility. Longer term treatments with PRL will be necessary to determine whether de-differentiation of ciliated cells contributes to lesion formation in the infundibulum.

Tuesday, September 7, 2021

10:00AM (PST)

<https://ucr-edu-hipaa.zoom.us/j/9178908500>