



**PI: Traci Testerman**

Institution: University of South Carolina School of Medicine

Award Year: 2017

Project Title: "Novel animal models for the study of PMP etiology and treatment"

Project Status: Active

**Update 1 (12-2018)**

We believe that *Helicobacter pylori*, a bacterium that causes stomach cancer, and certain other bacterial species contribute to growth of PMP tumors and to their resistance to chemotherapy. This hypothesis is bolstered by the fact that the tumors of PMP patients treated with antibiotics have molecular characteristics associated with more benign disease than tumors from patients not treated with antibiotics. We have cultured several bacterial species from PMP tumors, including at least one new species. Replicating PMP in mice can speed up the discovery process, leading to improved treatment methods for PMP patients. To this end, we are growing PMP tumors directly in immunodeficient mice and culturing PMP tumor cells *in vitro*. Tumor material injected directly into mice will contain tumor-associated bacteria, whereas cells grown *in vitro* in the presence of antibiotics will not. Cells grown *in vitro* can then be injected into groups of mice with and without specific PMP-associated bacteria to determine which bacteria increase the tumor growth rate or mucus production. We have just begun such an experiment. We are also testing the effects of bacteria by treating some mice with antibiotics following injection of human tumors. Thus far, mice have developed tumors from material derived from seven PMP patients. Injecting this tumor material into new mice has succeeded in generating new tumors. It is critical to have enough cells or tumor material to inject into a large number of mice in order to get statistically-significant results. Our methods facilitate larger experiments and more consistent results. As an alternative to cultured cells, a large amount of tumor/mucin obtained from one mouse can be divided and injected into multiple mice with and without bacteria. We have also been able to culture tumor cells from three mice. In cases where we have cultured cells from both the primary tumor and the mouse tumor, we will be able to compare characteristics to determine whether growth in mice or exposure to antibiotics/bacteria changes the tumor phenotype. The phenotype includes the physical appearance of tumors and the presence of certain tumor antigens or other molecules that are associated with more aggressive cancers. As our research progresses, we expect to gain a better understanding of which bacteria most strongly impact tumor growth. From this, we can determine which combination of antibiotics will be most effective for treating patients. In the future, we will also be able to use our model to test different chemotherapy regimens. Our goal is to determine the optimal combination of surgery, antibiotics, and chemotherapy to cure more PMP patients.