Abstract: Antibiotic-resistant bacteria are a major and rising global health threat. Although this threat affects all ages, pediatric patients and aged individuals are at increased risk of antibiotic-resistant bacterial infections. Currently, vaccines and therapeutic antibodies are unavailable for most antibiotic-resistant bacteria. To generate these antibodies, B cells must be activated by T cells to form germinal centers, which are sub-anatomical structures in the B cell follicles of lymph nodes. In germinal centers, B cells rapidly proliferate and mutate to form somatically mutated high-affinity antibody secreting cells, such as plasma cells, and memory B cells. However, emerging evidence suggests that conditions like aging and alterations to gut microbiome can diminish the ability to generate germinal center-mediated B cell immunity. In this talk, I will discuss my laboratory’s effort in developing ex vivo immune organoids using cells from both young and aged individuals to generate antibody secreting cells in a dish against viral infections and antibiotic-resistant bacteria. We further elucidate the role of epigenetic modifiers, such as EZH2, in these responses. Finally, I will discuss how alterations to the gut microbiome from metabolic disorders affects germinal center and thereby vaccine response, which can then be improved through nanomaterial vaccines.