Lilli P. Ziegler
Rising Senior, Ben Franklin High School, New Orleans

Mentor: Alison J. Quayle
Collaborators: John Lammons and Li Shen
LSUHSC, Department of Microbiology, Immunology and Parasitology

Could members of the maternal vaginal microbiome aid in the optimal maturation of their newborn infant's gastrointestinal microbiome?

The bacterial metabolite Indole-3-lactic acid (ILA) has an important role in maturing, and preventing inflammation in, a newborn infant's gastrointestinal (GI) tract. ILA is a predominant metabolite produced by *Bifidobacter longum* subsp. *infantis* (*B.infantis*), a major 'pioneer' bacterium in a healthy infant GI microbiome. These *Bifidobacter* make ILA by metabolizing tryptophan, an essential amino acid found in high concentrations in breastmilk. My lab recently observed a significant concentration of ILA in the vaginal secretions of some, but not all, young reproductive age women. We hypothesize that vaginal bacteria, transferred to newborns at birth, could aid in the optimal early development of their infant's GI tract. The objectives of my study were (1) first to determine if there was an association of ILA with specific vaginal bacterial species in this clinical cohort and (2) second, to determine if ILA concentrations found in the vaginal secretions can ligate the aryl hydrocarbon receptor (AHR), which is reported to play a key role in maintaining homeostasis and preventing inflammation at mucosal sites.

For objective (1) I found that (i) ILA abundance was significantly increased in the vaginal secretions of participants with a vaginal microbiome categorized as community state type I (CST I, an optimal CST which is dominated by *Lactobacillus crispatus*) compared to participants categorized with CSTs defined by low *Lactobacillus* abundance, CST IV-A and CST IV-B (p-value < 0.001). Analysis of subCSTs found that participants categorized as CST I-A (highest *L.crispatus* dominance) had significantly greater ILA abundance compared to participants categorized as CST III-A (*L.iners* dominance) ($p = 0.02$), CST III-B ($p = 0.01$), CST IV-A ($p < 0.001$), and CST IV-B ($p < 0.001$). *L. crispatus* relative abundance was found to be positively associated with ILA abundance ($p < 0.001$). For objective (2) I became proficient at cell culture, expanding and utilizing the HT29-Lucia AhR Cell line (InvivoGen), which is an epithelial cell line engineered to express endogenous AhR, and which allows the screening of potential AHR ligands by measuring secreted Lucia luciferase reporter protein in the culture supernatant. I determined that ILA ligated the AHR receptor, with activity in the concentration range found in the vaginal secretions of women with *L. crispatus*-dominant CST I.

This preliminary data suggest that (i) ILA may be a metabolic marker of a healthy vaginal microbiome, potentially produced by *Lactobacillus crispatus*, and ii) having read a recent study of mothers and their infants indicating that members of mom's vaginal microbiome are transiently shared with their infant, this raises the possibility that an optimal, lactobacillus dominant microbiome in mom may play a role in seeding their infant's gut, and potentially contribute to early ILA production in the infant.