ABSTRACT

Name of Trainee: Jessica Toothaker (jessica.toothaker@yale.edu)
Mentor: Liza Konnikova (liza.konnikova@yale.edu)
Type of Trainee: Graduate Student

Title: Human placental villi immune cells contribute to homeostasis in utero.
J. Toothaker, Yale University

Background: Novel insights suggest that the fetal and neonatal immune systems are more mature and developed than previously appreciated, though potentially with altered function. Perhaps, the most critical site to regulate a mature and developed fetal immune system during pregnancy is at the fetal-maternal interface (placenta) itself. We hypothesized that fetal immune cells in the placenta are mature and functional but suppressed at mid-gestation to prevent in utero inflammation.

Methods: We used both suspension (CyTOF) and imaging mass cytometry to survey immune populations in the mid-gestation placenta taken from elective terminations of healthy pregnancies. Moreover, we identified immunosuppressive and activation signatures based on surface marker expression with mass cytometry, mRNA transcription with in situ hybridization, and cytokine production measured by flow cytometry after immune cell stimulation.

Results: We demonstrate that the healthy second trimester placenta contains a diverse immune landscape comprised of innate cells including macrophages, NK cells and ILCs, as well as antigen presenting cells (APCs) and antigen experienced T cells. Moreover, we determined that the immune cells in the placenta are likely capable of eliciting an inflammatory response but maintain immune homeostasis at baseline through a variety of mechanisms. The mechanisms described include limiting chemotaxis by reduced expression of chemokine receptors on innate cells and low transcription of chemokine ligands in the placenta overall. Furthermore, placental APCs constitutively express PD-L1, likely regulated by the high expression of IFNg by placental immune cells. This PD-L1 expression by APCs is potentially needed to prevent the activation of antigen-experienced placental T cells which can be activated through the TCR pathway by antigens present in the uterine environment.

Conclusions: Fetal immune cells within the placenta are functionally mature and capable of eliciting an inflammatory response, however multiple immunosuppressive mechanisms prevent improper immune activation in utero.

Word Count: 239