Dynamics of PDGFRα^{+} Mesenchymal Cells in Oviductal Regeneration

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The oviduct comprises epithelial cell types and a stromal microenvironment that together facilitate oviduct function, including gamete transport, fertilization and early embryonic development. Although it is known that the oviductal epithelium experiences significant damage during ovulatory cycles, key progenitor cells involved in post-ovulatory oviductal regeneration are largely unknown. Defining progenitors and underlying mechanisms involved in oviductal regeneration and homeostasis is pivotal for understanding and addressing infertility and malignancy. In particular, progenitors in the stroma that may participate in oviductal regeneration remain tenuous and underexplored. In the uterus and mammary gland, mesenchymal cells expressing Platelet-Derived Growth Factor Receptor alpha (PDGFRα) are reported to contribute to epithelial lineages during regeneration. The objective of our study is to characterize PDGFRα^{+} cells in the oviduct and determine their fate and function in oviductal regeneration.

Using immunofluorescence and flow cytometry analysis of oviducts from wild-type and *Pdgfra*$^{H2B\text{-}eGFP}$ reporter female mice, we have observed that PDGFRα expression is restricted to mesenchymal stromal cells in the murine oviduct microenvironment, and absent from epithelial cells including secretory and ciliated cells. PDGFRα^{+} oviduct cells also express hormone receptors as detected by immunofluorescence and published single cell RNA-seq data, suggesting that these mesenchymal cells are likely hormone responsive. Further, we found that the proportion of H2B-GFP^{+} cells, representing *Pdgfra*-expressing cells, in reporter mice fluctuates during the hormone-driven estrous cycle. Specifically, PDGFRα^{+} cells were found to be elevated in mouse oviducts in the post-ovulatory phase. Notably, the H2B-GFP^{+} oviductal stromal population from reporter mice gave rise to more colonies compared to the H2B-GFP-negative fraction in colony forming cell assays *in vitro*, indicating that *Pdgfra*-expressing cells enrich for stromal progenitors in the oviduct. Preliminary findings utilizing a tamoxifen-inducible *Pdgfra*^{CreERT}*R26*^{mTmG} lineage tracing mouse model demonstrate that PDGFRα^{+} mesenchymal progenitors in the stroma have the capacity to generate epithelial lineages in the oviduct during ovulatory cycles.

Our findings illuminate novel progenitor characteristics of PDGFRα^{+} cells in the murine oviduct, and a dynamic role for this stromal population during oviductal regeneration. We envision that this work will lay a foundation for the development of novel cell-targeted therapeutics for oviductal regenerative medicine and cancer.