

Ph.D. Proposal Abstract

Title: Elucidating HOXA10 Driven Gene Regulatory Networks in the Endometrium

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ABSTRACT

Embryo implantation is a complex biological process that depends on endometrial receptivity, embryo attachment, invasion, and stromal cell decidualization. Disruptions in these processes can lead to infertility and recurrent implantation failure (RIF). The homeobox transcription factor HOXA10 is crucial for uterine development, and its expression affects receptivity, decidualization, and trophoblast invasion in the adult endometrium. Dysregulation of HOXA10 can result in implantation failure, impaired decidual responses, and abnormal trophoblast invasion. It is also linked to various endometrial disorders, including endometriosis, unexplained infertility, RIF, endometrial hyperplasia, and cancer.

Although HOXA10 is recognized as a major regulator of these cellular transformations, the precise molecular mechanisms underlying these changes remain poorly understood. While some studies have identified a limited set of direct HOXA10 target genes and transcriptomic alterations following HOXA10 disruption, these findings are fragmented and lack comprehensive network-level interpretations. Furthermore, implantation is regulated not only by protein-coding genes but also by non-coding RNAs, including miRNAs, lncRNAs, and circRNAs, whose coordinated regulation by HOXA10 has largely been unexplored.

This study aims to elucidate the molecular mechanisms through which HOXA10 regulates endometrial function using integrative multi-omics approaches. We will identify HOXA10 regulated coding and non-coding transcriptomes, map its chromatin occupancy, reconstruct HOXA10 centered gene regulatory networks, and examine their dysregulation in the endometrium of women with recurrent implantation failure. This research will provide a systems-level understanding of the HOXA10 driven gene regulatory network that underlies the process of implantation.