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Utilizing Emerging Technology to Identify Non-Coding Regulatory Elements in Human Myometrial Tissues

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Purpose:
The myometrium is the muscular compartment of the uterus made of smooth muscle that maintains the structural integrity before and generates force at parturition. Dysregulated myometrial actions may lead to pregnancy complications such as preterm birth and dystocia. Homeostasis of the myometrium is governed by genetic networks, in part, though non-coding regulatory elements. The present study aims to identify cis-acting elements in the myometrial biopsies of healthy term pregnant participants.

Methods:
Three human myometrial specimens were obtained from lower segment uteri at term pregnancy prior to the onset of labor, followed by RNAseq and H3K4me1, H3K27ac, CTCF and PGR (progesterone receptor) ChIP-seq to profile transcriptome, enhancers, potential DNA looping anchors and PGR occupancy. Parturition association genome variants from literature were to establish their association with findings in the present study.

Results:
The 3 human subjects share 13090 active and 540 super enhancers. Approximately one third of active and 40% super enhancers are located nearby high-level expressing genes. Myometrial active enhancers exhibit over-representation of binding motifs of transcription factors known for myometrial homeostasis, hormone signaling mediators and smooth muscle gene regulation, including AP-1, PGR and SRF. Enriched functional annotations on cell-cell adhesion junction and steroid hormone receptor activities are found among the 355 active genes that are in close proximity of super enhancers. Notably, over 70% of super enhancers show the PGR occupancy, in accordance with the critical role of progesterone signaling in maintaining uterine quiescence before parturition. Parturition association genome variants in the non-coding genome have also been found in the myometrial enhancers, with some in a lustered pattern.

Conclusion:
We have successfully mapped and cataloged cis-acting elements in the myometrial genome. Our work identifies regulatory elements that may function to control expression of myometrial active genes, partly through interacting with progesterone signaling during pregnancy. The findings also implicate an impact of gestational duration-associated single nucleotide polymorphisms (SNPs) on myometrial gene expression and the genome topology.

Title:

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Keywords:
Enhancer, Myometrium and Parturition-associated genome variants

Abstract Summary:
This study is to demonstrate a collaborative model for nursing researchers to participate in a multidisciplinary team obtaining various types of data emerging in modern biomedical research.

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