(Epi)genetic variants of the sarcomere-desmosome are associated with premature utero-contraction in spontaneous preterm labor

Jie Wang[1], Xiucui Luo[2], Jing Pan[3], Xiaoyan Dong[4], Xiujun Tian[5], zhihua Tu[1], Weina Ju[6], Meijiao Zhang[2], Mei Zhong[7], Charles Chen[8], Michael Flory[6], Yong Wang[9], William Brown[6], and Nanbert Zhong[6]

[1]Hainan Provincial Hospital for Maternal and Children's Health
[2]Center of Translational Research, Lianyungang Municipal Hospital for Maternal and Children's Health
[3]Lianyungang Municipal Hospital for Maternal and Children's Health
[4]Shanghai Children's Hospital, Shanghai Jiaotong University
[5]Sanya Maternity and Child Care Center Affiliated to Hainan Medical University
[6]New York State Institute for Basic Research in Developmental Disabilities
[7]Nanfang Hospital, Southern Medical University
[8]The Third Affiliated Hospital of Guangzhou Medical University
[9]Washington University in Saint Louis Department of Obstetrics and Gynecology

April 28, 2020

Abstract

Background: Spontaneous preterm birth (sPTB) is a syndrome with clinical and genetic heterogeneity. Few studies have focused on genetic and epigenetic defects and pathogenic mechanisms associated with premature uterine contraction (PUC) of sPTB. Objective: To investigate the (epi)genetic variations associated with premature uterine contraction (PUC) of sPTB. Design: An integrated omics approach of systems biology was employed. Genomics, transcriptomics, methylomics, and proteomics were employed to focus on genetic loci/genes related to uterine muscle contraction, and specifically on genes associated with sarcomeres and desmosomes. Methods: Pregnant cohort with biobank of pregnant tissues was subjected to multiomic studies. Results: Thirteen SNVs and pathogenic variants were identified in the sarcomere gene, TTN, from 146 women with sPTL. DEPs of five lncRNAs were identified from loci that overlap with four sarcomeric genes. Longitudinally, the lncRNA TPM3 was found to significantly regulate the messenger RNA (mRNA) of TPM3 in the placenta, compared to maternal blood. The majority of GMPs related to PUC were also identified in the CpG promoters of sarcomeric genes/loci. DEP of PCU mRNAs showed 22 genes associated with the sarcomere and three with the desmosome. Conclusion: The results demonstrated that PUC was associated mainly with pathogenic variants of the TTN gene and that transcription of sarcomeric PUC genes is likely regulated by epigenetic factors, including methylation and lncRNA.

Hosted file

`WangJ_Multiomics of premature contraction in sPTB .pdf` available at https://authorea.com/users/308262/articles/439307--epi-genetic-variants-of-the-sarcomere-desmosome-are-associated-with-premature-utero-contraction-in-spontaneous-preterm-labor