**Role of Bromodomain Containing Proteins BRD2-4 in GDM**

**Principal Investigator**

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In 2018, I received funding from the foundation to determine the involvement of the Bromodomain containing proteins BRD2-4in the pathophysiology of GDM. The first aim was to characterise the expression of BRD2-4 in placenta, adipose tissue and skeletal muscle from normal glucose tolerant women and women with GDM. These studies are complete. Tissues were obtained from singleton pregnancies at term (<37 weeks gestation) from lean and obese NGT women and BMI-matched women with GDM (n=10-15 patients/group). We found that BRD3 expression was significantly higher in placenta and adipose tissue from women with GDM.

Enhanced placental and adipose tissue inflammation is a central to the pathophysiology of GDM. We then assessed the effect of BRD inhibition on inflammation in human placenta and adipose tissue. Interestingly, there was no effect of specific BRD inhibition on inflammation in placenta. On the other hand, inhibition of BRDs decreased inflammation in adipose tissue.

Women with GDM also have increased peripheral insulin resistance. In particular, there are defects in the insulin signaling pathway in maternal skeletal muscle, leading to decreased glucose uptake were used to examine whether modulating BRD expression regulates insulin signaling and glucose uptake in skeletal muscle cells. Interestingly, we found no effect of BRD knockdown on the insulin signaling pathway and subsequent glucose uptake in skeletal muscle cells.

We submitted this paper for review in July 2019. The manuscripts was reviewed favourably; however, one of the reviewers asked for additional experiments. We have just completed these experiments and are in the process of analysing the data. We anticipate to re-submit the paper by end of March.

**Invited oral presentations:**

1. Invited by the Sociedad Chilena de Ciencias Fisiológicas to present at Pontificia Universidad Católica de Chile. Santiago, Chile, 28th September 2018.

2. Invited by the El Instituto de Ciencias e Innovación en Medicina (ICIM) to present at the Universidad del Desarrollo. Santiago, Chile, 1st October 2018.

3. Invited by Fondecyt to present at Universidad de Concepcion. Conception, Chile, 4th October 2018.

4. Invited by International Federation of Placenta Associations (IFPA) and the Latin American Society for Maternal-Fetal Interaction and Placenta (SLIMP) to present at the 2019 IFPA meeting. Buenos Aires, Argentina. 12 September, 2019.