

## **MitoFit Open Seminar – Jorge Beleza – February 6<sup>th</sup>, 2020**

### ***Exercise performed during pregnancy as a preventive tool against transgenerational development of diabetes mellitus and NAFLD in the offspring. The role of epigenetic-mediated mechanisms.***

Pregnancy is associated with impaired glucose tolerance and insulin resistance, that may predispose development of gestational diabetes *mellitus* (GDM), which is a disease defined as glucose intolerance of variable degree with onset during the second or third trimester of pregnancy (2). During its development, maternal hyperglycemia stimulates overproduction of insulin that interferes with fetal homeostasis and may increase offspring risk to develop associated metabolic disorders, including diabetes *mellitus* (DB) and even non-alcoholic fatty liver disease (NAFLD) (10). Additionally, it has been recognized that an active maternal lifestyle, including regular to moderate physical exercise (PE), has a protective effect on the development of GDM. Given the deleterious impact of GDM during pregnancy on the health of the mother and her offspring, it appears crucial to work on modifiable risk factors, namely in those related with level of PE (7). Therefore, PE in all stages of life maintains and improves cardiorespiratory fitness, reduces the risk of obesity and associated comorbidities, and results in greater longevity (10). Moreover, there is growing evidence that PE in pregnancy has minimal risks and has been associated to several health-related benefits for the mother, but also for the fetus and newborn babies (1). In fact, recent data suggest that maternal exercise has the potential to activate a series of intrinsic signaling pathways, ultimately positively modulating the epigenetic mapping of the offspring and leading to a more resistant phenotype against intra-uterine and postpartum adverse insults and correspondent deleterious consequences (8,9). In addition, evidence from recent studies clearly highlights the beneficial impact of maternal exercise as a putative tool to manipulate the offspring epigenome, including the modulation of genes related with mitochondrial bioenergetics. For example, Laker and co-workers (6) reported that maternal exercise has the ability to revert highfat diet-induced hypermethylation of *Pgc-1a* in skeletal muscle. However, to our knowledge, the true impact and the putative positive modulation of physical activity on key signaling pathways associated GDM is not completely understood (5). Considering the enormous long-term benefits of exercise, namely in preventing GDM complications (3,4), behavior' changes regarding the practice of exercise during pregnancy highlights the huge parental responsibility with their offspring and with the society. Nevertheless, additional research is needed to study the effects of exercise on pregnancy-specific outcomes and to clarify the most effective behavioral counseling methods, and the optimal intensity and frequency of exercise able to counteract GDM-induced disorders and the deleterious transgenerational effect on the offspring.