There is a well-established body of literature demonstrating the effect of maternal diet and metabolic health during pregnancy on both maternal and child health outcomes, making pregnancy a critical period for both maternal metabolic health and offspring risk of chronic disease. Hyperglycemia is one of the most prevalent pregnancy-associated maternal health complications (Farrar, 2016), with 7.6% of pregnancies in the US being complicated by gestational diabetes. Furthermore, this condition is known to increase maternal risk of chronic disease morbidity (Casagrande, Linder, & Cowie, 2018) and offspring risk of obesity and cardiometabolic disease (Kaseva et al., 2019). Restriction of the eating window is a component of diet that is gaining more traction as an approach for improving metabolic health. Recent studies have detailed the benefits of time-restricted feeding (TRF) in improving chronic disease-related outcomes like insulin resistance (Halberg et al., 2005; Hatori et al., 2012; Kahleova, Lloren, Mashchak, Hill, & Fraser, 2017; Liu et al., 2019; Ravussin, Beyl, Poggiogalle, Hsia, & Peterson, 2019; Sutton et al., 2018; Woodie et al., 2018), and high blood pressure (Gabel et al., 2018; Stote et al., 2007, Sutton et al, 2018) which can occur without weight loss. To date, only one study of TRF during mouse pregnancy has been completed (Upadhyay et al., 2019); however, maternal metabolic health and offspring health in the post-natal period were not evaluated. Therefore, the effects of TRF need to be evaluated during pregnancy to characterize its ability to mitigate insulin resistance in pregnancy and long-term effects on offspring health and development.

The goal of my dissertation is to investigate how fertility and maternal metabolic health are affected by TRF, and whether or not those effects alter the developmental course and health of the resulting offspring. This will be accomplished by employing a mouse model where the early time-restricted feeding (eTRF) technique is used in pregnancy. To translate these findings to humans, I will use observational data from a human pregnancy cohort to understand feeding windows and their associations with maternal and child health outcomes. I will test the hypothesis that *in the setting of intermittent fasting, insulin resistance in pregnancy will be lessened, which will improve insulin sensitivity and confer improved glycemic health to the offspring*. This hypothesis is consistent with reduction of insulinemia and improved glycemic control without adverse effect on body weight and habitus demonstrated in the literature. To test this central hypothesis, I propose the following 3 aims:

**Model Organism Aim 1: Examine the effects of manipulation of the feeding window on female fertility, gestational health, and maternal glycemia during gestation.**

Whether or not eTRF would alter fertility and gestational health or work to alleviate insulin resistance of pregnancy in females has not yet been evaluated in mice or humans. To fill this hole in the literature, age-matched female mice will be randomized to either *ad libitum* (AL) or eTRF regimens before exposure to mating. I will assess fertility, body composition, and maternal insulin sensitivity. Furthermore, hormonal and molecular effects will be investigated to elucidate mechanisms of hypothesized improvements.

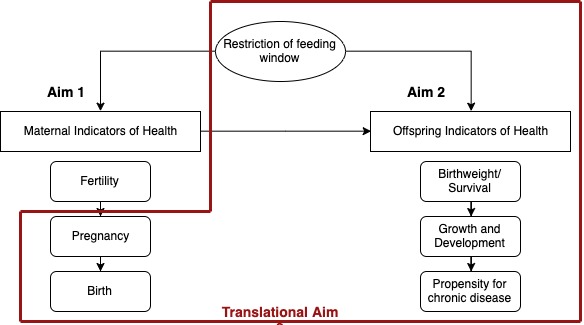
**Model Organism Aim 2: Determine the effects of gestational manipulation of the feeding window on offspring health at birth, during growth and development, and in response to Western dietary challenge.**

The pups of eTRF and AL fed dams will be evaluated for survival, litter size, and weight at birth. Further study of their body mass accretion and metabolic health will be evaluated through adulthood. Once adulthood is reached, response to high fat diet feeding and will be evaluated and molecular targets that drive differences in body mass and metabolic health will be investigated.

**Translational Aim 3: Characterize the prevalence and associations of restricted feeding with maternal and child health in humans.**

I will first characterize the prevalence of pregnancy-associated complications in the biorepository for understanding maternal and pediatric health (BUMP) cohort, then will further investigate the associations of the length of feeding window with perinatal health outcomes including: preterm birth, small for gestational age, intrauterine fetal demise, gestational diabetes, gestational weight gain, and pre-eclampsia.

The proposed study is the first of its kind to monitor eTRF in pregnancy while considering both maternal and child health outcomes. Furthermore, this is the first study of the effect of the length of eating window performed in the BUMP cohort. This work will fill critical gaps in the intermittent fasting literature; elucidating mechanisms the phenomenon of insulin sensitization and further understanding how that may affect pregnancy and the resulting offspring. Based on previous literature in non-pregnant animals and humans, we expect that employment of eTRF during gestation will improve insulin resistance during pregnancy, without effect on bodyweight or body composition, or harm to the offspring during gestation. This study will help us to understand the impacts of TRF as a feeding strategy to inform patient treatment of hyperglycemia during pregnancy; a critical period for lifelong metabolic health.



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