Pregnancy is a critical period of development, for both mother and fetus, and is accompanied by transient insulin resistance and adipose tissue accumulation (Musial et al., 2016; Pipe et al., 1979). This insulin resistance and propensity for energy conservation also may be modified by maternal diet and environmental stressors. The timing of feeding is an aspect of diet that is gaining more consideration as a modifiable behavior for improving metabolic health, including establishing a subcommittee on eating frequency for the next iteration of the dietary guidelines for Americans (dietaryguidelines.gov). Recent studies have detailed the benefits of time-restricted feeding (TRF) in improving chronic disease-related outcomes like insulin resistance (Gabel et al., 2018; Sutton et al., 2018), and high blood pressure (Gabel et al., 2018; Stote et al., 2007, Sutton et al, 2018). Only one study of TRF during pregnancy has been completed thus far in rodents (Upadhyay, 2019); however, maternal insulin resistance, energy conservation and offspring health in the post-natal period were not evaluated.

It is likely that women experience time-restriction of food intake during pregnancy in many

contexts; including food insecurity, hyperemesis gravidarum, observing Ramadan, engaging in shift work and voluntary changes in food intake. I aim to evaluate the mechanism of insulin resistance and energy conservation in normal mouse pregnancy and to investigate how these phenomena respond to time-restricted feeding. I will test the hypothesis that insulin resistance in pregnancy will drive energy conservation and improved absorptive capacity compared to non-pregnant animals. Further, in the setting of early time-restricted feeding (eTRF), insulin resistance in pregnancy will be lessened, which will improve insulin sensitivity and confer resistance to high fat diet feeding in the offspring.

**Aim 1: Identify the physiological mechanisms contributing to energy conservation and insulin resistance during pregnancy**. Age matched pregnant and non-pregnant female mice will be compared in this study. Energy expenditure, insulin sensitivity, and macronutrient absorptive efficiency will be evaluated.

**Aim 2: Examine the effect of early time-restricted feeding in the perinatal period on maternal health.** Dams exposed to time-restricted feeding during gestation will be compared to age-matched *ad libitum* fed controls. Food intake, body composition, energy expenditure, gestation length, and mechanisms of insulin sensitivity will be evaluated. Based on ELISA results from maternal blood samples, candidate hormones (GDF15 and corticosterone) will be further evaluated for their mechanistic contribution to energy expenditure and insulin resistance.

**Aim 3: Determine the effect of early time-restricted feeding in the perinatal period on offspring health.** Pups of dams exposed to time-restricted feeding will be compared to pups of ad libitum fed dams. Survival rates, birthweight, body composition, insulin sensitivity and sensitivity to a high fat diet will be measured.

**Aim 4: Utilize the Michigan Medicine central biorepository obstetrics cohort to investigate human maternal health during pregnancy.** I will evaluate pregnancy-related glycemia and gestational weight gain in relation to hormone candidates determined in aim 2. I will also determine the prevalence of intentional and unintentional fasting in this sample and examine its associations with perinatal health outcomes; including: preterm birth, low birthweight/small for gestational age, intrauterine fetal demise, gestational diabetes, gestational weight gain, and pre-eclampsia.

Figure 1: the aims of this proposed thesis research