Early life encompasses critical windows of development that can have long lasting effects on the health of the offspring. Stress during early life can critically impact development. Specifically, maternal psychological and nutritional stressors lead to suboptimal offspring health (Reynolds, 2013; Moisiadis & Matthews, 2014; Kim *et al.*, 2016). Psychological stress during pregnancy can impact fetal growth. Women with higher corticotropin-releasing hormone at midgestation, were 7.5 folds more likely to deliver preterm (Inder *et al.*, 2001). Additionally, maternal nutritional stress increases the relative risk of neonatal death by two folds for women with severe obesity (Aune *et al.*, 2014).

The placenta and mammary glands are primary sites of nutrient delivery to the developing offspring. Given their crucial role in development, the placenta and mammary glands are highly affected by maternal psychological and nutritional stressors. Studies assessing the mechanisms by which maternal stressors alter placental and lactational development and function remain limited.

My objective is to determine the role of maternal stressors on offspring health mediated through placental and mammary function. I will test the hypothesis that ***maternal psychological and nutritional stressors alter placental and mammary gland functions, ultimately affecting offspring health.***This hypothesis is supported by data showing that maternal psychological stress can lead to reduced birthweight, altered offspring hypothalamic-pituitary-adrenal axis activity, reduced milk immune components, and earlier termination of lactation (Levine, 1967; Edwards *et al.*, 1993; Matthews, 2000; Li *et al.*, 2008; Thibeau *et al.*, 2016). Furthermore, maternal nutritional stress is associated with increased risk of fetal macrosomia, increased likelihood of earlier weaning, and altered milk lipid composition (Owens *et al.*, 2010; Panagos *et al.*, 2016; Castillo *et al.*, 2016). Our preliminary data demonstrate that stressed dams exposed to glucocorticoids starting a week prior to conception give birth to small, non-viable pups. Also, hyperactivation of mammary adipocyte mechanistic target of rapamycin 1 (mTORC1) showed increased milk macronutrients. I will test my central hypothesis via the following four aims:

**Aim 1: Determine the effects of maternal glucocorticoid-induced stress on placental function.** I will expose pregnant dams to the synthetic glucocorticoid, dexamethasone, and then collect pre-term placentas in order to evaluate nutrient transport and endocrine function. In separate cohorts, I will monitor how gestational dexamethasone exposure affects offspring metabolic health.

**Aim 2: Identify the relationship between glucocorticoid exposure and mammary function.** I will expose dams to dexamethasone during lactation then assess mammary gland development, milk volume and composition. I will then monitor the growth and health of the offspring of the exposed dams.

**Aim 3: Elucidate the consequences of placental mTORC1-hyperactivation nutritional stress on placental role.** To model nutritional stress, such as that of maternal obesity I will use a genetic model of mTORC1 hyperactivation in the placenta using a trophoblast-specific driver. With this model, I will assess placental hormone production and evaluate nutrient transport, along with offspring metabolic health.

**Aim 4: Detect the effects of nutritional stress via mTORC1 hyperactivation on lactation***.* Milk volume and composition along with offspring health from dams with adipocyte mTORC1 hyperactivation will be measured.

As a result of these studies I will learn how our models of maternal psychological and nutritional stressors influence placental and mammary gland functions. I will also determine how early life exposures, demonstrated by gestational and lactational periods, affect offspring health.

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