Project Details	
Project Code	MRCPHS26Ca John
Title	Leveraging pregnancy cohort data to investigate the link between placental hormones and adverse pregnancy outcomes
Research Theme	PHS
Project Type	Dry lab
Summary	Low birth weight (LBW) infants are at an increased risk of dying, and those who survive are more likely to experience poor health later in life. Mothers of these infants may also encounter difficulties with breastfeeding, further compounding the disadvantages faced by children. Emerging evidence suggests that placental dysfunction may underlie both LBW and breastfeeding difficulties. This PhD project will utilise data from pregnancy cohorts to investigate this hypothesis and explore the molecular origins of placental dysfunction.
Description	Fetal growth restriction is a condition where the fetus is not able to grow properly in utero resulting in a small baby. Smaller babies are at increased risk of dying. Those that survive are more likely to have developmental problems in childhood and poorer health in later life. Women who have small babies can also experience breastfeeding difficulties related to milk supply that may further adversely affect their children. We hypothesise that fetal growth restriction and poor milk supply are outcomes of the same underlying pathology - which is placental endocrine insufficiency (low placental hormones). Placental hormones drive adaptations required for a successful pregnancy which include securing nutrients for fetal growth and preparing the mammary gland for lactation. Experimental models of placental endocrine insufficiency exhibit low birth weight and deficits in mammary development supporting causality. There is evidence that human mothers with lower levels of a critical hormone called placental lactogen are more likely to deliver a small baby but there has been little investigation of placental hormones or placental characteristics in relation to breastfeeding, or exploration of co-occurrence of fetal growth restriction with breastfeeding difficulties. This project will address the deficit in our knowledge through analysis of existing pregnancy cohort data. The Grown in Wales study (GiW) is a pregnancy cohort of 355 women recruited in 2015-16 with existing measures of maternal and placental hormones alongside data on diet, lifestyle and mental health, and placental transcriptomic data for a subset of samples. The Avon Longitudinal Study of Parents and Children (ALSPAC) is a world-leading birth cohort study with a wide range of data, including genetics, on > 14,000 pregnant women (G0) and their now adult children (G1) who are having children of their own (G2). The placental transcriptome has been characterised in 270 G1/2 samples, with additional samples to be analysed over the course of this PhD. The student will use GiW data to examine the relationship between maternal antenatal serum placental lactogen, custom birth weight centiles and reported breast feeding patterns, identifying and controlling for potential confounders. They will analyse the relationship between placental gene expression and serum levels of hormones. They will also use the genetic and placental RNAseq data in ALSPAC to investigate the associations between placental hormone gene expression, fetal growth

	and breast feeding. Finally, they will have the option of steering their project towards an exploration of maternal risk factors associated with placental endocrine insufficiency and the co-occurrence of fetal growth restriction and breastfeeding difficulties. Alternatively, they may which to focus on the offspring outcomes directed by their specific interests. This work is important because, if our findings support the original hypothesis there is real potential to improve health outcome through boosting placental hormone capacity. SUSTAINABLE DEVELOPMENT GOALS • 3 Good Health and Well Being
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