Aging before birth: identifying prenatal influences of lifestyle on telomeres and the epigenetic clock

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Project description:

Being born biologically "aged" may contribute to higher risk of disease later in life. Importantly, premature placental aging has been suggested as a mechanism contributing to fetal growth restriction and an increased the risk of stillbirth and preterm delivery. Evidence to support accelerated aging in utero comes from studies of two biomarkers of aging – telomere length and DNA methylation. Shortened telomeres have been reported in diabetic pregnancies, growth-restricted fetuses, prenatal depression and pregnancies ending in stillbirth. DNA methylation age acceleration has been linked to prenatal exposure to tobacco smoke, lower socioeconomic status and prenatal depression, factors also linked to fetal growth restriction and poor outcomes for children. These data support a modifiable aging process that starts before we are born. However, little is known about maternal lifestyle factors that protect against premature aging.

This study will novelly explore the hypothesis that healthier lifestyles in pregnancy protect against the accelerated aging associated with exposure to prenatal adversity. Precision biomolecular analysis of telomeres and DNA methylation in placenta and cord blood will be combined with the analysis of biological, dietary and biosocial data from two Welsh pregnancy cohort studies with >500 samples to identify factors modifying these biomarkers of aging. The Grown in Wales Study is a data rich longitudinal cohort study of pregnancy-related mood disorders with data on maternal lifestyle in pregnancy including dietary data, alongside measurements of free fatty acids (FFAs) present in the mother's blood. There is a rich body of literature that suggests some FFA protect against aging in adults while other FFAs are associated with inflammation which could accelerate aging. This component is therefore particularly unique and relevant to the study.

Telomere length will be measured using Single Telomere Length Analysis (STELA), a technique developed at Cardiff University which provides high-resolution single molecule data. DNA methylation age will be determined from Illumina Infinium MethylationEPIC BeadChip array data. The student will receive extensive training in multivariate statistics and analysis of longitudinal data through formal courses and supervision, and undertake a secondment to Bristol University to train in epigenetic epidemiology ultimately integrating and validating findings across multiple international datasets.

While many studies report associations between biomarkers of aging and pregnancy complications, this will be the first study to explore whether modifiable lifestyle factors such a maternal diet influence biomarkers of placental aging and, most importantly, obtain evidence that healthy diets, exercise or omega 3 protect against premature placental aging supporting lifelong health.