Aging before birth: identifying early-life influences on telomeres and the epigenetic clock

Supervisory team:
Main supervisor: Prof Rosalind John (Cardiff University)
Second supervisor: Prof Duncan Baird (Cardiff University)
Dr Gemma Sharp (University of Bristol)

Host institution: Cardiff University

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 a stillbirth. 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 and pregnancies ending in still birth. DNA methylation age acceleration has been linked to prenatal exposure to tobacco smoke and lower socioeconomic status, factors also linked to fetal growth restriction and poor outcomes for children. These data support a modifiable aging process that start before we are born but 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 biosocial and biological data from the Grown in Wales Study to identify factors modifying these biomarkers of aging. Grown in Wales 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 a technique developed by Prof Duncan Baird called Single Telomere Length Analysis (STELA) which provide high-resolution single molecule data. DNA methylation age will be determined from Illumina Infinium MethylationEPIC BeadChip array data. The student will additionally 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. 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.