ABSTRACT

Placental ageing is associated with the gestation period and leads to cellular and molecular changes that promote fetal independence as the placental function is reduced towards labour. However, premature ageing can compromise pregnancy outcomes, affecting fetal growth and development. Premature placental ageing has been associated with stillbirth. Research on the use of circular RNAs (circRNAs) in other species as indicators of cellular ageing and senescence is emerging, with their stability and regulatory functionality in samples making them promising candidates for this purpose.

My study aimed to quantify circRNA in blood samples collected from mothers who experienced unexplained fetal deaths compared with those who went on to have healthy pregnancies, to determine the biomarker potential of a panel of circRNAs for stillbirth screening. As *in vitro* studies are required to determine the biological mechanism involved with circRNAs in placental ageing, and Dr Arthurs is currently culturing placental organoids which have been genetically edited to overexpress candidate circRNAs, my project also aimed to optimise the process of *in situ* localisation of antigens in placental organoids via fluorescence microscopy.

Elevated levels of candidate circRNAs were found in maternal blood samples from women who experienced unexplained stillbirths compared to controls, suggests that a diagnostic threshold could be established for early intervention. This approach could enhance prenatal care, improve pregnancy outcomes, promote fetal health and development monitoring, and support better-informed pregnancy-related decisions. Furthermore, the immunofluorescence protocol for *in situ* localisation was successfully optimised, allowing for further investigation into the biological mechanisms underpinning placental ageing pathology due to circRNA accumulation.