Studying early human embryo development using stem cell models

Supervisory team:
Main supervisor: Dr Ge Guo (University of Exeter)
Second supervisor: Dr Fabrice Gielen (University of Exeter)
Prof Rosalind M John (Cardiff University), Prof Austin Smith (University of Exeter)

Collaborators: Prof Mark Goodfellow (University of Exeter), Prof Jennifer Nichols (MRC Human Genetics Unit, Edinburgh), Prof Peter Zandstra (University of British Columbia, Canada), Dr Alex Corbett (University of Exeter)

Host institution: University of Exeter (Streatham)

Project description:
How a complex structure, an embryo, forms from a single cell is a fascinating fundamental biology question. Understanding early human embryo development will also have applications in reproductive medicine. However, research is limited by availability of human embryos and ethical considerations. Therefore, our concept of human early embryo development draws heavily on mouse studies. However human embryos differ in many respects including timescale and formation of a bilaminar embryonic disc as the substrate for gastrulation. We recently established a stem cell based human blastocyst model (the "blastoid"), that recapitulates the morphology and cellular composition of natural human blastocysts.

This blastocyst model provides a unique experimental platform to investigate human developmental dynamics using genetic, molecular and bioengineering approaches. In this project the PhD student will implement a microfluidic system to mimic the in utero biophysical environment and empower further development of the blastoid. You will then undertake high resolution 3D time-lapse imaging using a cutting edge advanced light sheet microscope. You will map the developmental dynamics at cellular resolution by live cell tracking using fluorescent lineage reporters that you will create using CRISPR/Cas 9 technology. Building on this technical platform you will explore the molecular regulatory mechanism of human hypoblast differentiation and bilaminar disc formation, involving single cell transcriptomic analyses. The project integrates embryology, stem cell biology, molecular biology, transcriptomics, biophysics and bioimaging.

Reference: Yanagida A. et al, Naive stem cell blastocyst model captures human embryo lineage segregation. Cell Stem Cell 28, 1016-102. Guo G. etal, Human naive epiblast cells possess unrestricted lineage potential. Cell Stem Cell 28, 1040-1056 e1046.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.