Title of Project:	Shaping the meiotic spindle by phase separation
Cell Mechanism Supervisor Name	Hiro Ohkura
Quantitative Supervisor Name	Cait MacPhee

Summary of project

The spindle is a molecular machinery which segregates chromosomes in dividing cells. Although centrosomes play a central role in assembling spindles in mitotic cells, oocytes assemble the bipolar spindle without centrosomes. A new report revealed that liquid-liquid phase separation plays an important role in establishing a bipolar spindle in oocytes. In recent years, phase separation has attracted much attention in biology as a mean to dynamically compartmentalise cellular components. Gaps remain to be bridged between the biophysics of phase separation in vitro and protein behaviours/function in a complex cell environment.

This project aims to understand how the biophysical properties of phase separation shapes the bipolar spindle in oocytes by combining in vitro and in vivo assays. The TACC protein accumulates to the spindle poles and is important for spindle bipolarity in oocytes. It is shown in vitro that this protein can phase-separate on its own in solution. Dynamics of TACC will be measured by live microscopy in both in vitro and in oocytes. Regulation of phase separation in vitro and TACC accumulation in oocytes will be further studied. Other proteins whose localisation depends on TACC in oocytes will be identified and tested for accumulation in phase separated TACC compartments in vitro. Mutants which change the property of phase separation in vitro will be tested in protein localisation and spindle bipolarity/chromosome segregation in oocytes.

What quantitative skills will the student acquire or develop during their PhD project?

Cell Biology skills: immunostaining, live imaging, confocal microscopy, super resolution microscopy.
Quantitative skills: quantitative imaging analysis, determining the turnover rates from FRAP (fluorescence recovery after photobleaching) or photoconversion data