Title of Project	Investigating genome-proteome disequilibrium in polyploid human and drosophila cells
Cell Mechanism Supervisor Name	Hiro Ohkura
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Summary of project

Polyploidy is a physiological cellular state occupied by important cell types in the human body. Precursors of platelets and trophoblast cells undergo a cyclical process of genome reduplication and unfinished mitoses, called endomitoses, to form polyploid cells. Multi-nucleated polyploid hepatocytes are not uncommon in adult human livers, and are thought to function as a quiescent reserve of cells poised to rapidly divide in response to tissue injury.

Compared to mitotic cell division, less is known about endomitosis regulation. Several important questions emerge: how do cells tolerate increased genome dosage? Is spindle assembly differentially regulated in endomitosis? How do cells maintain quiescence in the polyploid state?

The aim of the PhD project is to test the hypothesis that polyploid cells tolerate increased genome dosage by asymmetric scaling of the proteome.

Technological advances in mass spectrometry have revolutionised the analysis of cellular proteomes. Quantitative information can be obtained for thousands of proteins in a single analysis, including protein copy numbers.

State of the art mass spectrometry technology will be applied to study protein copy number dynamics proteome-wide in human and drosophila cell types that undergo endomitosis as part of their maturation. The aim of the proteomic analyses will be to identify candidate protein pathways important for maintaining the polyploid state. Candidate pathways will be further characterised mechanistically using genetic approaches to test whether attenuation is required for maintaining polyploidy.

The PhD project will provide opportunities to train in quantitative protein analysis using complementary techniques, including mass spectrometry-based proteomics, single cell flow cytometry, and fluorescence microscopy. The PhD project will also involve training in the analysis and visual representation of large, quantitative datasets using scripting languages (e.g. R).