Optimising cell size for specialised functions: using a systems approach to understand the cell cycle during differentiation.

Supervisory team:
Main supervisor: Dr Angharad Jones (Cardiff University)
Second supervisor: Prof Jim Murray (Cardiff University)
Prof Pete Kille (Cardiff University), Dr Pete Watson (Cardiff University), Dr Daniel Pass (Cardiff University)

Collaborators: Prof Claire Grierson (University of Bristol), Dr Leah Band (University of Nottingham), Dr Richard Smith (Max Planck Institute for Plant Breeding, Cologne)

Host institution: Cardiff University

Project description:
The cell cycle is a highly conserved process, with the same major proteins controlling cell division in single-celled yeasts, plants and animals. The universality of the cell cycle underlines its evolutionary importance, but raises the question of how specialised cell divisions are produced. In multicellular organisms, one stem cell often gives rise to multiple specialised cell types with different sizes, meaning that different division rules must be followed in each lineage. This project will use the root epidermis of Arabidopsis as a model system to address how changes in gene expression during the cell cycle can result in the production of different sized cells.

The root epidermis is an important interface between the plant and its environment comprised of two distinct cell types that originate from the same stem cells; short root-hair cells that produce tube-like structures that improve water and nutrient uptake, and longer non-hair cells that play roles in transport. Although root hair growth occurs after cells have stopped dividing, differences in cell length are established much earlier and can affect the spacing between hairs as well as their development. We have previously published work showing how cell size is regulated in undifferentiated plant cells (Jones et al 201 Nat Comm 8:15060), but know little about how this mechanism changes as cells begin to differentiate or how it could be engineered to improve tissue function.

This project will use our newly developed cell-type-specific, cell-cycle markers to i) capture the dynamics of the cell cycle in the root epidermis using a state of the art light sheet microscope and ii) produce single cell transcriptomics data sets from hair and non-hair cells at different phases of the cell cycle using FACS and RNAseq. This information will be used to build a simple model of the cell cycle in differentiating cells and predict cell size under different conditions. Predictions will be tested by transiently mis-expressing genes in the opposite cell types and subjecting roots to environmental conditions that alter cell fate. The project will carried out in the Murray Lab alongside a funded project focusing on the cell cycle in undifferentiated cells. You will take part in interdisciplinary group meetings with collaborators Dr Leah Band (University of Nottingham) and Prof. Claire Grierson (University of Bristol) and receive training in cutting edge imaging and next generation sequencing technology, allowing you to develop a highly desirable skill set.

SWBio DTP

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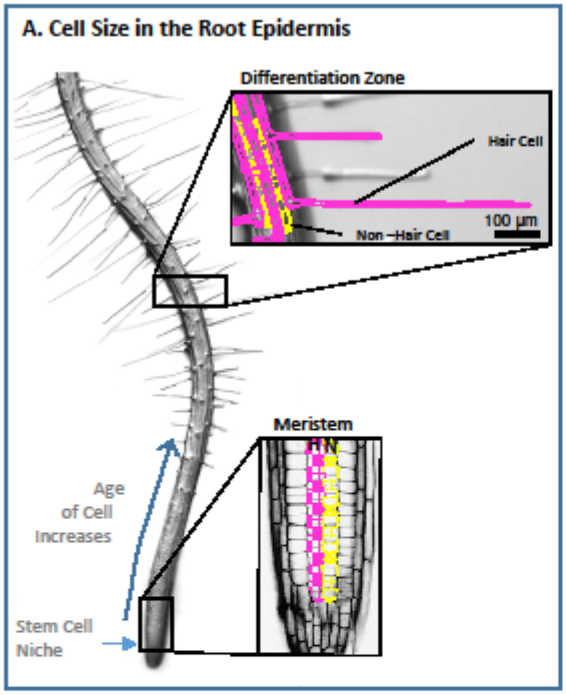

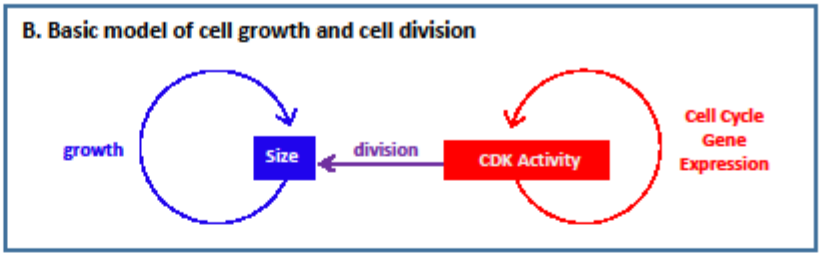

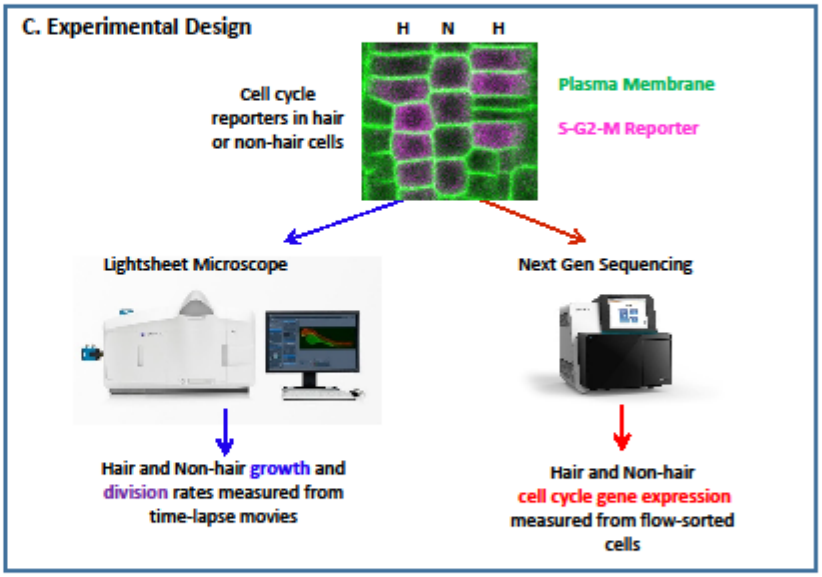

A systems biology approach to understanding cell size differentiation

A) The root epidermis of *Arabidopsis thaliana* consists of short hair cells (H-Pink) and longer non-hair cells (N-Yellow). Differences in cell length can be traced back to their actively dividing precursor cells in the meristem. This project will investigate how cell size is controlled in the two cell types and test how cell size affects the function of the epidermis by altering the normal pattern of long and short cells.

B) In dividing populations, cell size is controlled by regulating the balance between cell growth and cell division. Our model simulates this process using a growth loop (blue) and a division loop (red). With each time step the cell grows and then produces a certain amount of CDK. This process is repeated until a threshold level of CDK activity is reached at which point cell division is triggered and cell size is reduced. The model can be used to predict cell size in an individual cell or population of cells after multiple divisions. Cell growth rate and the rate of production on cell cycle regulators will the cell sizes produced.

C) To learn more about how cell size is controlled, this project will use newly produced fluorescent cell cycle reporters to collect growth, division and gene expression parameters from hair and non-hair cells. Lightsheet microscopy will be used to track cell cycle progression and growth. Fluorescence Activated Cell Sorting (FACS) will be used to isolate cells by cell type and cell cycle phase. These cells will be used to prepare transcriptomic sequencing that will show how gene expression changes through the cell cycle in the two cell types. The data will be integrated into the model and strategies to change the pattern of cell size will be developed and tested by creating new transgenic plants that mis-express key cell cycle genes.