**Mechanisms of epithelial symmetry-breaking during mammalian morphogenesis.**

A focus of 21st century anatomical research is how anatomy arises in development. Straight lines and smooth outlines are relatively uncommon in our anatomy, at least at a small-scale. Much more common are corrugations (intestine wall), branching trees (ducts of glands) and branching networks (blood vessels). The 'hills' and 'valleys' of corrugated structures, and the 'tips' and 'stalks' of branched structures, begin as the same cell type. So why do some cells advance to be hills or tips while others do not? This creation of differences where there were none is an example of 'symmetry breaking'. Understanding it is important for understanding how natural tissues form, and also pathological anatomy (for example, the spiky crab-like shape that gives 'cancer' its name).

Some years ago, there was a proposal that cells secrete something that slows cell advance, but any protruding cells experience less of it, allowing them to advance faster and breaking the symmetry of the system. A previous AS-funded student conducted experiments that refuted this hypothesis but raised an alternative mechanical hypothesis involving the internal protein skeletons of cells and the junctions between them. Technology has now advanced enough to allow us to control the behaviour of these skeletons with directed light, on a cell-by-cell basis using a special microscope. This project will test the hypothesis that causing a local change in cytoskeletons with light will be sufficient to break the symmetry of the system and cause stimulated cells to lead branches, even when the light is switched off.

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| **Figure:** This figure shows symmetry breaking, in which one cell in an epithelial clone is advancing while others remain behind - the first stage in emergence of a new branch.  Photo credit: Dr Kim Martin (from her AS-funded PhD in the lab hosting this current studentship). |  |