

Mechanically-induced cell competition among epithelial cells

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Abstract

Cell competition is a process whereby defective or less fit cells are selectively recognised and eliminated by their relatively fitter wild-type neighbours. It is thought to act as a cellular quality control mechanism and has additionally been linked to cancer development. The mechanisms of cell competition however are still largely unidentified; it is not known whether a single pathway exists, to sense cellular fitness and eliminate the weaker population, or whether different pathways are responsible for competition.

We are investigating the mechanisms involved in cell competition using a recently established *in vitro* assay, where MDCK cells silenced for the tumour suppressor *scribble* (*scribbleKD*) are eliminated by wild-type cells (Norman *et al* 2012). Our work shows that wild-type cells actively compact *scribbleKD* cells into a high cell density arrangement and this compaction is both necessary and sufficient to induce their elimination through cell death and delamination. Time-lapse video microscopy shows a 'chase and run' behaviour between the wild-type and *scribbleKD* cells, which is initiated upon cell-cell contact between the populations and is responsible for forcing the *scribbleKD* cells into a high density configuration. In addition, we show that *scribbleKD* cells have heightened sensitivity to high-density compaction compared to wild-type cells, which is accompanied by an intrinsic elevation of p53 levels. Compaction further increases p53 activation and this results in their elimination. Overall we show that cells, traditionally known to compete through molecular signals, can also compete exclusively through mechanical insults.