

# Unraveling the genes, pathways & systems-level interactions that control cell morphogenesis and the cytoskeleton

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## Abstract

Understanding cells as integrated systems requires that we decipher how single genes affect multiple biological processes and how processes are functionally linked. My group has pioneered the development of a live cell, 3D fluorescence high-throughput screening platform adapted to screen fission yeast (*Schizosaccharomyces pombe*) mutant libraries, in order to systematically discover the genes, pathways & systems-level interactions that control specific cellular processes.

Recently, we completed a multi-process phenotypic screen to simultaneously survey the genome with respect to three key cellular processes: cell shape, microtubule organisation and cell cycle progression. We identified, validated and functionally annotated 262 genes controlling specific aspects of those processes. Of these 62% had not been linked to these processes before and 35% are implicated in multiple processes. Importantly, we identified a conserved, novel role for DNA-damage responses in controlling microtubule stability. In addition, we have investigated systemically how these processes are functionally linked, and found unexpectedly that disruption of cell cycle progression does not necessarily impact on cell size control and that distinct aspects of cell shape regulate microtubules and vice-versa.

In a separate project, using combinatorial genetics we are currently investigating how the localisation and function of each of ~40 'core' polarity factors of *S. pombe* is affected in the absence of every other polarity factor. With that information, we are reconstructing the first topology map of the cell polarity network for any organism. This is allowing us not only to unravel numerous unknown functional relationships between polarity factors, but also to identify unexpected systems-level feedbacks between subsets of the polarity machinery, which we are probing further.

Here, I present the results of both projects and the corresponding community resources they are generating.