CELL POLARITY

Polar exploration

Many bacteria show polar characteristics, such as the positioning of a flagellum at one end of the cell. However, the mechanisms involved in establishing this polarity are poorly understood. A recent study from Lucy Shapiro and colleagues has made important progress in understanding these processes by identifying a master regulator of polarity in *Caulobacter crescentus*.

The *C. crescentus* life cycle involves two different cell types, both with specialized structures located at one pole of the cell. Several proteins that are involved in the development of these structures and that have corresponding polar distributions have been identified, providing useful markers of polarity. Shapiro and colleagues made use of these features to investigate whether the actin-like protein MreB is required for polarization in *C. crescentus*.

MreB has a distinctive localization pattern, forming a spiral structure that extends along the length of *C. crescentus* cells. By analogy to eukaryotic actin, MreB molecules might have an intrinsic polarity, so the spirals they form could be used for the asymmetric localization of molecules required for the development of polar structures. To test this, the authors analysed the effect of MreB depletion on the distribution of four signalling proteins — PleC, DivJ, CckA and DivK — that are required for polar development in *C. crescentus*. Depletion of MreB abolished the polar foci that are usually formed by all four proteins at certain points in the cell cycle, consistent with a role for MreB as a global regulator of polarity.

Importantly, MreB seems to be actively required for specifying polarity, rather than having a passive role in protein localization. Unlike CckA and DivK, which form foci at both poles of *C. crescentus* cells, PleC and DivJ are asymmetrically distributed at certain points in the cell cycle, localizing to only one pole. When

CYTOKINESIS

A good place to start

A new report in *Science* describes the rapid identification and characterization of proteins that function in cytokinesis, using an approach that combines functional-proteomic and comparative-genomic analysis.

From synchronized Chinese hamster ovary (CHO) cells, Ahna Skop and colleagues isolated midbodies — microtubule-rich, transient structures that are derived from the spindle midzone and that exist after cell division, just before the daughter cells detach. The proteins in the midbody preparation were identified by a protein identification technology — MudPIT — that is used for the analysis of proteins in complex protein mixtures.

After eliminating proteins that have general housekeeping functions, 160 candidate midbody proteins remained, of which 57 were known cytokinesis proteins. Most candidate midbody proteins seemed to be conserved in evolution as 147 out of 160 proteins had clear *Caenorhabditis elegans* homologues. The functional relevance of the candidate midbody proteins became apparent when the authors analysed gene function by RNA interference using double-stranded (ds)RNA that corresponded to each of the *C. elegans* genes. Most of these dsRNAs produced a disrupted cytokinesis phenotype.

By analysing the various mutant phenotypes, the authors found that a significant percentage of midbody proteins that function in cytokinesis also produce defects in germline development when they are disrupted. They went on to show that gonad development and sterility mutant phenotypes are, in fact, frequently caused by defects in cytokinesis in the germline or in early embryos. In addition, 16 proteins that are essential for embryo and germline cytokinesis were also required for polar-body extrusion (the polarized, asymmetric cell division that occurs during meiosis). So, cytokinesis, gonad organization and polar-body extrusion seem to use a common set of proteins.

Although membrane and cytoskeletal proteins are known to be involved in cleavage-furrow formation, among other cytokinesis processes, how these proteins are recruited to the cleavage plane has been unclear. Skop and co-workers identified 40 membrane and cytoskeletal proteins, which include proteins that are involved in lipid-raft formation and vesicle trafficking. They suggest that raft-associated factors could target and activate specific membrane events in cytokinesis.

Among the midbody proteins, 24% were Golgi-associated proteins, which led the authors to speculate that there might be some parallels between cytokinesis in animals and plants, as Golgi-derived vesicles are involved in cell-wall formation after cell division in plants.

Finally, the functional analysis of midbody proteins revealed some unexpected phenotypes — 20% of the identified proteins caused defects in coordination, which implicates these proteins in muscle or neuronal development. In addition, 14% of the mammalian proteins that were identified are known to have a role in human diseases, mostly those that are associated with membrane and cytoskeletal pathologies. So this study provides plenty of starting points for further investigations — including into cytokinesis, development or disease mechanisms.

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References and links

ORIGINAL RESEARCH PAPER Skop, A. R. *et al.* Dissection of the mammalian midbody proteome reveals conserved cytokinesis mechanisms. *Science* 27 May 2004 (doi:10.1126/science.1097931)