MILESTONE 21

The prokaryotic cytoskeleton

> The first glimpse of filamentous proteins inside bacteria. Arguably the beginning of 'bacterial' cell biology.
> *Jan Lowe*

Actin and tubulin are the major components of the eukaryotic cytoskeleton. It was previously thought that prokaryotes lacked a cytoskeleton. However, research in the 1990s firmly established that, in fact, the cytoskeleton originated in prokaryotes, with the discovery that filamentation temperature-sensitive protein Z (FtsZ) is the bacterial homologue of tubulin and MreB is the homologue of actin.

FtsZ is a key player in bacterial cell division and acts at an early point in the pathway. The functional relationship between FtsZ and tubulin was uncertain because they share low sequence identity at the amino-acid level. FtsZ does, however, contain a short tubulin signature sequence, which is known to be involved in the binding of GTP to tubulin. The group of Lutkenhaus initially showed FtsZ to form a filamentous ring structure during cell division and predicted it to be a cytoskeletal element. Then, two independent groups led by Rothfield and Park set out to test whether FtsZ can also function as a GTP-binding protein. Using biochemical assays, they demonstrated that FtsZ purified from bacterial cells can bind and hydrolyse GTP just like eukaryotic tubulin. Furthermore, GTP binding was essential for the function of FtsZ in cell division and also for its propensity to form filaments *in vitro*, as was shown a little later.

However, the most convincing demonstration that FtsZ was the bacterial counterpart of tubulin came when its crystal structure was solved by Löwe and Amos. They revealed that FtsZ has an overall three-dimensional structure that is similar to eukaryotic α-tubulin and β-tubulin. FtsZ and tubulin also share the way in which they initially assemble into linear polymers with a longitudinal interface between two subunits that contains the GTPase active site.

While the connection between FtsZ and tubulin was being established, the origin of actin remained obscure. In 2001, two papers by van den Ent *et al.* and Jones *et al.* demonstrated that MreB is the bacterial homologue of eukaryotic actin. Based on sequence similarities, actin belongs to a large superfamily of proteins of unrelated function that includes the chaperone heat-shock protein-70 (Hsp70). Jones and colleagues showed that MreB and the closely related protein Mbl are important for regulating the rod shape of *Bacillus subtilis*. Using light microscopy, they found that MreB and Mbl form large spirals under the cell membrane. Both proteins contribute to the determination of cell shape. These proteins are conserved, with the existence of homologues in a wide range of bacteria. In general, spherical bacteria lack *MreB*, whereas those with complex shapes, including rod and filamentous forms, have one or more such genes.

The helical bands observed by Jones *et al.* were suggestive of a cytoskeleton. van den Ent *et al.* provided direct evidence for this by showing that purified MreB forms polymers under various conditions *in vitro*. Electron microscopy showed that the polymers resembled one of the helical strands of filamentous actin. They then determined the crystal structure of MreB and found that it is remarkably similar to actin. These papers provided strong evidence that MreB and actin are homologues.

In the past decade, the discovery of bacterial homologues of actin and tubulin revolutionized our view of bacterial cell architecture. The coming period will address important questions about the function and regulation of the bacterial cytoskeleton, and allow comparisons with the eukaryotic system.

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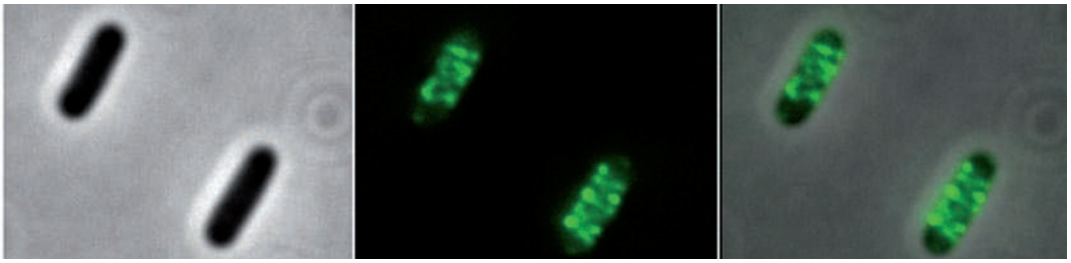

Cells that contain green fluorescent protein (GFP) fusion to the MreB paralogue Mbl in *B. subtilis*. Image courtesy of R. Carballido-López and J. Errington. University of of Newcastle, UK.

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