MILESTONE 10

Sharing the actin' limelight

> These papers gave the textbook view of the cell cytoskeleton.
> *Jonathon Howard*

We take for granted our ability to see various components of the cytoskeletal network; however, back in 1969, the presence of actin in cells other than muscle cells came as a surprise.

The ability of heavy meromyosin (HMM) to bind to isolated actin filaments and form arrowhead complexes was shown by Huxley in 1963. Ishikawa, Bishoff and Holtzer used this information to investigate whether intermediate filaments were related to actin filaments in sections of myotubes. Their electron micrographs showed that these filaments did not bind HMM, and so were unlikely to contain actin. However, they noticed that fibroblasts, which were also present, seemed to have a filamentous network in which arrowhead-complex formation was evident. They verified this finding in chondrocytic cells and reasoned that these 'mesenchymal-like cells' might require such filaments for amoeboid movement. However, the addition of HMM to epithelial cell preparations confirmed a similar network. Therefore, actin was not restricted to contractile or motile cells.

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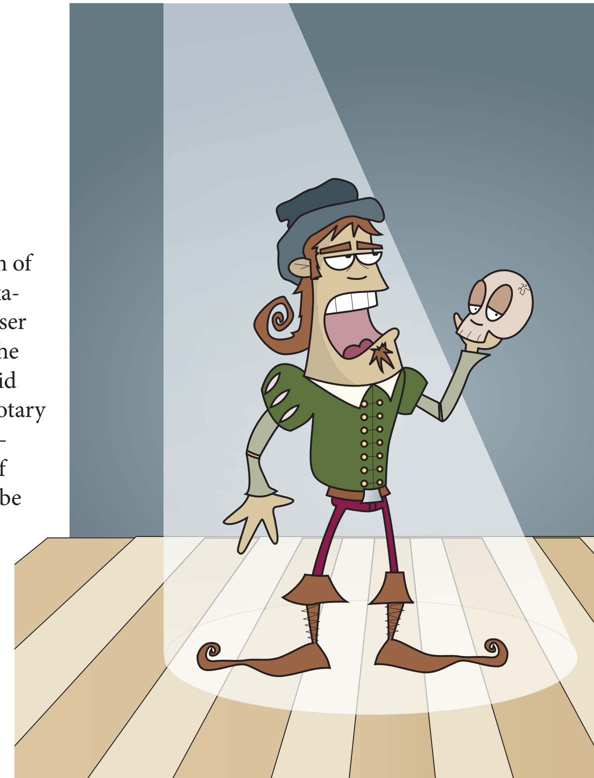
Visualization of the spatial arrangement of the actin network was achieved in 1974, thanks to Lazarides and Weber. They purified actin from mouse fibroblasts and used it to raise an antibody. Indirect immunofluorescence revealed the now famous actin stress-fibre network that is common to cells in tissue culture, as well as several of what the authors termed 'focal points' where actin fibres converge. Although indirect immunofluorescence had already been used to show the localization of myosin and troponin, this paper demonstrated the ease with which it is possible to visualize the actin network.

Examination of the intact cytoskeleton at the electron microscopic level remained difficult owing to disruption of the network by chemical fixation; however, in 1980, Heuser and Kirschner — through the use of rapid freezing in liquid helium, freeze drying and rotary platinum–carbon coating — produced an exact replica of the cytoskeleton that could be effectively viewed using scanning or high-voltage electron microscopy. This made possible the detailed analysis of the cytoskeleton in specific areas of the cell, and furthered our understanding of its importance in all aspects of cellular function.

Nicola McCarthy, Chief Editor,
Nature Reviews Cancer



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