EGF is internalized and degraded

Thirty years ago, cell biologists were convinced that protein hormones and cells had a superficial relationship. Although steroid hormones such as testosterone could squeeze through the cell membrane to deliver commands, their protein counterparts never got beyond receptors on the cell’s surface. Graham Carpenter and Stanley Cohen (both then at Vanderbilt University) overturned the conventional wisdom with their study of epidermal growth factor (EGF), a protein hormone that spurs fibroblasts to duplicate their DNA and divide.

When the pair steeped human fibroblasts in EGF tagged with radioactive iodine, they found that the amount of radioactivity that spurs fibroblasts to duplicate their DNA and divide. Vanderbuilt University) wanted to know what controlled this gel–sol transformation.

At the time, the discovery that non-muscle cells contained actin and myosin was fresh. But what the pushy proteins accomplished was uncertain—researchers had just discerned that actin helps form the contractile ring that pinches cells in half during division (Schroeder, 1972). Stossel and Hartwig started by nabbing a new molecule they called actin-binding protein—the very first actin-binding protein—that spurred actin fibers in vitro to coalesce into a mesh (Hartwig and Stossel, 1975). This mesh later turned out to provide a substrate for myosin-mediated contraction.

Next, Stossel and Hartwig (1976) reproduced this phenomenon with purified proteins and linked the process with what was happening in vivo during phagocytosis. They showed that extracts of macrophages in the midst of phagocytosis solidified into a gel and did so faster than did those from cells that weren’t eating. What’s more, cytoplasm from cells that had recently swallowed an oil droplet contained more actin-binding protein than did material from resting cells. A mixture of actin, myosin, and actin-binding protein, but not the duo of actin and myosin alone, would also gel.

The idea that actin molecules can’t knit into a gel without help from actin-binding protein was controversial, Stossel recalls. In fact, the preceding paper in the same issue argued the opposite view (Pollard, 1976). Stossel says that it took about 15 years to win over most doubters, and during this time the number of participating molecules swelled. For example, Stossel’s lab discovered a protein called gelsolin, which unhooks actin filaments (Yin and Stossel, 1979). Gelsolin and the original actin-binding protein, now called filamin A, are two of the hundreds of molecules that help orchestrate cell movements. JCB

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