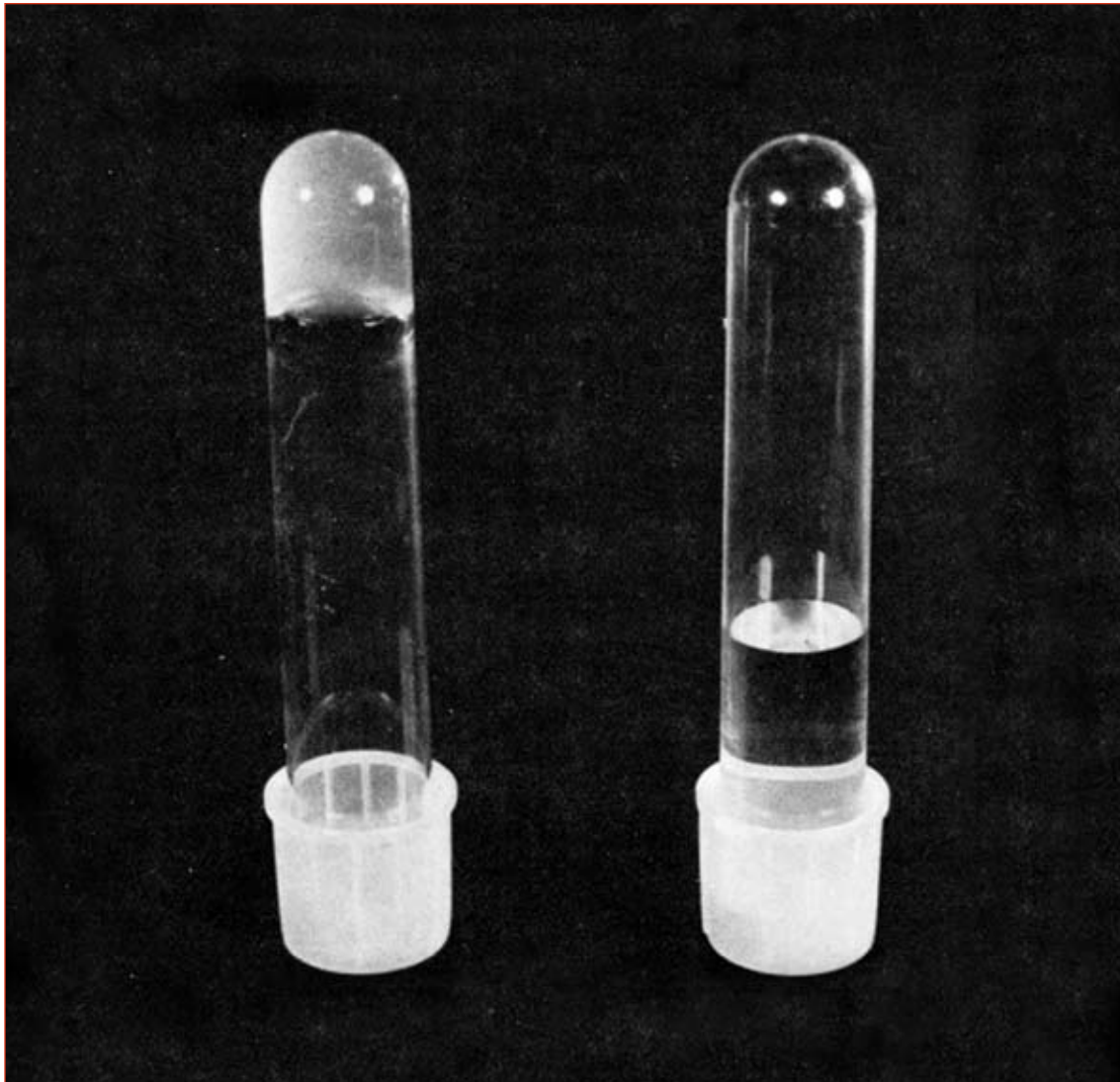


FOUNDATIONS

First Actin-binding Protein, circa 1975



Inverted tubes of gelled macrophage supernate (left) and water (right) for comparison.

It was 1975, and Thomas Stossel and John Hartwig were baffled by the “ugly precipitate” in the bottom of their test tube. Eager young biologists, the Harvard friends had set out to solve the mystery of how cells crawl. The field of cell movement was abuzz with the revelation that non-muscle cells contained actin and myosin, but no one understood the mechanism regulating those cytoskeleton proteins. Many researchers believed the protein contractions were controlled by calcium, similar to muscle cells. Stossel and Hartwig decided to purify myosin from white blood cells as a way to find the “magic calcium stuff,” recalls Stossel. Instead, their test tube was filled with some “contaminant”: A high molecular weight polymer they would soon identify as the first actin-binding protein, later called filamin A.

The pair hypothesized that their protein was responsible for the transformation of cytoplasm from a liquid to gel that occurs as cells move and engulf food, and they resolved to prove it. First, they isolated actin from macrophages. “We could only painstakingly purify small amounts of filaments,” recalls Stossel, resulting in only a few chances to get the experiment right. They added the new protein and heat; and then, with a quick flip of the tube, a gelled supernatant clung to curve of the glass. Stossel and Hartwig had proof that the actin-binding protein initiated gelation.

Though initially a controversial discovery, filamin A proved to be the first of hundreds of binding proteins that influence cell movement. ■