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# This Week's Citation Classic™

**Wessells N K, Spooner B S, Ash J F, Bradley M O, Luduena M A, Taylor E L, Wrenn J T & Yamada K M.** Microfilaments in cellular and developmental processes. *Science* 171:135-43, 1971.
[Department of Biological Sciences, Stanford University, CA]

This paper reported the correlations between cytoplasmic microfilaments and motile activities in an array of cellular and developmental systems using the mold metabolite cytochalasin B as the experimental probe. Cytochalasin B concomitantly disrupted microfilament arrays and inhibited motile activities. This activity identified microfilaments as fundamental cytoplasmic structures in cellular and morphogenetic movements. [The *SCI*® indicates that this paper has been cited in over 1,325 publications since 1971.]

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"By the late 1960s, electron microscopic analyses had led to the recognition that cytoplasmic arrays of microfilaments were present where they could provide the basis for the cell-shape changes involved in cytokinesis, cell motility, and morphogenetic movements of epithelia. In fact, the structural similarity between microfilaments and the thin filaments of muscle suggested that they could be components of a contractile apparatus powering various nonmuscle motility phenomena. However, experimental demonstration of the necessity of microfilaments in this process was lacking. Then, in 1967, Carter[1] published results showing that mold metabolites called cytochalasins caused binucleation of cultured cells. Next, a seminal experiment by Schroeder, which was first reported in 1969 and appeared later as a major publication in 1972,[2] demonstrated that cytochalasin caused disappearance of the 'contractile ring' of microfilaments normally present in the cleavage furrow, leading to failure of the furrow to form or progress, thus producing binucleation.

"In the late fall of 1969, I was a postdoctoral fellow analyzing tissue interactions in organ morphogenesis in N.K. Wessells's laboratory at Stanford University. Wessells had already published on microfilaments in developing epithelia. He had a graduate student, J.T. Wrenn, who discovered that the early event in estrogen-induced tubular gland formation in the chick oviduct was the appearance of arrays of microfilaments followed by cell-shape changes and tubular gland invaginations. The potential application of cytochalasin to this system was obvious from Schroeder's key discovery, and a supply was obtained. In addition, it was clear that microfilaments could act in the branching morphogenesis systems I was working on. Furthermore, another student, K.M. Yamada (presently chief, Membrane Biochemistry, Laboratory of Molecular Biology, National Cancer Institute), was investigating sensory ganglia neurite extension, a motile activity that could also involve microfilaments. Cytochalasin effects on these systems were dramatic, resulting in a series of papers in *Proceedings of the National Academy of Sciences of the USA* in 1970 showing disruption of microfilament systems and inhibition of salivary branching,[3] tubular gland formation,[4] and neurite extension.[5]

"Wessells's laboratory was a remarkable environment in which to work. He had an outstanding array of graduate students, including Wrenn and Yamada, M.O. Bradley, J.F. Ash, and M. Anderson (Luduena), and he ran his laboratory in a supportive and collaborative way. One worked with, rather than for, Wessells. His attitude was contagious and, in short order, these people had extended the motility-microfilament-cytochalasin correlation to a variety of systems. In addition to the organ systems and neurite extension, microfilament involvement was established for single-cell locomotion, ascidian metamorphosis, cytoplasmic streaming, contractions of egg cortices, platelet contraction, and other motile phenomena, all of which were reported in this *Citation Classic* manuscript.

"Response to the publication was rapid and sustained. There was controversy over the mode of action of cytochalasin, but, in general, microfilament involvement in motile phenomena was accepted and has been further documented. The succeeding decade saw an explosion of research[6] that continues today in the general area of microfilaments, cytoplasmic contractile proteins, and the cytoskeleton. The citation frequency of this paper stems from its timely appearance and the breadth of its coverage of motile phenomena involving microfilaments."

1. **Carter S B.** Effects of cytochalasins on mammalian cells. *Nature* 213:261-4, 1967. (Cited 665 times.)
2. **Schroeder T E.** The contractile ring. II. Determining its brief existence, volumetric changes, and vital role in cleaving *Arbacia* eggs. *J. Cell Biol.* 53:419-34, 1972. (Cited 160 times.)
3. **Spooner B S & Wessells N K.** Effects of cytochalasin B upon microfilaments involved in morphogenesis of salivary epithelium. *Proc. Nat. Acad. Sci. US* 66:360-4, 1970. (Cited 140 times.)
4. **Wrenn J T & Wessells N K.** Cytochalasin B: effects upon microfilaments involved in morphogenesis of estrogen-induced glands of the oviduct. *Proc. Nat. Acad. Sci. US* 66:904-8, 1970. (Cited 100 times.)
5. **Yamada K M, Spooner B S & Wessells N K.** Axon growth: roles of microfilaments and microtubules. *Proc. Nat. Acad. Sci. US* 66:1206-12, 1970. (Cited 245 times.)
6. **Korn E D.** Biochemistry of actomyosin-dependent cell motility (a review). *Proc. Nat. Acad. Sci. US* 75:588-99, 1978. (Cited 455 times.)