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Vasiliev Ju M, Gelfand I M, Domnina L V, Ivanova O Y, Komm S G & Olshevskaya L V. Effect of colcemid on the locomotory behaviour of fibroblasts. *J. Embryol. Exp. Morphol.* 24:625-40, 1970.
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Fibroblasts in culture can crawl directionally on the substratum. Colcemid and other microtubule-depolymerizing drugs inhibit this movement by abolishing division of the cell edge into active and nonactive zones. It was suggested that microtubules are necessary for stabilization of the nonactive state of certain parts of the cell surface. [The *SCI*® indicates that this paper has been cited in over 170 publications.]

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This paper was a result of an analysis of unexpected observations made in the course of a systematic investigation of the reactions of cultured cells to alterations in density of cell population. Wishing to imitate the wound healing process, we mechanically removed a part of the dense culture and examined the cells that had migrated directionally into the "wound."[1] One particular result of this migration is activation of cell replication. To count the mitotic cells, we used a standard procedure, namely, we incubated the cultures with colcemid or other drugs blocking mitosis at the stage of metaphase. To our disappointment, this experiment was not successful; besides blocking mitosis, colcemid also inhibited cell migration into the wound. We then realized that this unpredicted effect of colcemid might be interesting on its own, because its analysis might help us to learn something about the mechanisms of cell migration.

It was already known that a normal fibroblast moves by extending and attaching pseudopods from its edge. These reactions are polarized, that is, pseudopods are extended only from the anterior part of the edge, while lateral edges remain nonactive. Naturally, our first suggestion was that colcemid paralyses migration by paralysing these locomotory reactions. However, when we performed microcinematography of our cultures, we found that the nature of the effect was quite different and much more interesting. The drug-treated cells were not paralysed but, in contrast, extended pseudopods from all the parts of their edges; stable, nonactive edges were not formed. These cells could not migrate in one particular direction because they tried to move simultaneously in all possible directions. Colcemid and other metaphase-inhibiting drugs had been known to act selectively upon microtubules, and electron microscopy of colcemid-treated fibroblasts had confirmed that microtubules disappeared from their cytoplasm.

We came to the conclusion that fibroblasts have a special microtubule-dependent mechanism that prevents extension of pseudopods from certain parts of the cell surface. External factors, such as contacts with another cell, produce nonstable changes of pseudopodial activity, while an intracellular mechanism stabilizes the cessation of activity. In other words, this microtubule-dependent mechanism, named "stabilization," memorizes the effects of external factors on the cell shape and movement.

At the time of this research our group worked in almost complete isolation. We first met Michael Abercrombie (from Cambridge) and other leading specialists on cell behaviour during the Moscow Embryology Conference held in August 1969. It was a great moral support for us when Michael approved our results and recommended their prompt publication.

We think that the paper has been frequently cited because it describes a process regulating one of the most complex cellular functions, directional locomotion, and because it links this regulation with a specific structure, the microtubule. At present, it is clear that regulations of this type play essential roles in locomotion and morphogenesis. However, the molecular mechanisms of these regulations still remain almost as obscure as in 1970.[2,3]

1. **Vasiliev J M & Gelfand I M.** *Neoplastic and normal cells in culture.* Cambridge, UK: Cambridge University Press, 1981. 372 p.
2. **Domnina L V, Rovensky J A, Vasiliev J M & Gelfand I M.** Effects of microtubule-destroying drugs on the spreading and shape of cultured epithelial cells. *J. Cell Sci.* 74:267-82, 1985.
3. **Dugina V B, Svitkina T M, Vasiliev J M & Gelfand I M.** New type of morphological reorganization induced by phorbol ester: reversible partition of cell into motile and stable domains. *Proc. Nat. Acad. Sci. USA* 84:4122-5, 1987.