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Gabbiani G, Ryan G B & Majno G. Presence of modified fibroblasts in granulation tissue and their possible role in wound contraction. *Experientia* 27:549-50, 1971. [Department of Pathology, University of Geneva, Switzerland]

This work reported for the first time the presence of fibroblastic cells with contractile features (myofibroblasts) in different granulation tissues and suggested that these cells are responsible for the phenomenon of wound contraction. [The *SCI*® indicates that this paper has been cited in over 290 publications.]

Giulio Gabbiani
Department of Pathology
Centre Medical Universitaire
University of Geneva
1211 Geneva 4
Switzerland

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Thanks to a fellowship of the Canadian Medical Research Council, I spent the year from October 1967 to September 1968 in three different laboratories in order to improve my knowledge of electron microscopic techniques. I worked for most of that time with G. Majno at the Department of Pathology of Harvard Medical School, where I became familiar with the concept of nonmuscle-cell contraction, in particular, endothelial contraction. In addition, I spent brief periods with W.S. Hartroft at the Department of Pathology of the Hospital for Sick Children, University of Toronto, Ontario, Canada, and with C.A. Baud at the Department of Morphology, University of Geneva, Switzerland. The project with Hartroft was on the formation of the pigment ceroid induced by different fatty acids in the model of the "granuloma pouch," developed previously by H. Selye, the chairman of my department at the University of Montreal, Quebec, Canada.

While studying the wall of the pouch (a typical pyogenic membrane) under the electron microscope, I was impressed by the morphology of the fibroblasts, which appeared very different from the usual fibroblastic cells seen in normal rat dermis. Their cytoplasm was loaded with filamentous structures 40 to 80 Å in diameter, a feature typical of smooth-muscle cells. Of course, there were still differences between granulation tissue fibroblasts and smooth-muscle cells, but at first I was attracted by the similarities and by the possibility that these cells were responsible for the phenomenon of granulation tissue contraction. Selye encouraged me to continue on this line and so did Majno, with whom I was negotiating to move to the University of Geneva as an assistant professor in the Department of Pathology, where he had just been appointed cochairman.

I arrived in Geneva at the end of 1969 and, together with G.B. Ryan (now chairman of the Department of Anatomy, University of Melbourne, Parkville, Australia) and Majno, extended the preliminary observations to three more experimental models of granulation tissue and defined the ultrastructural features of these modified fibroblasts. Thus, we felt entitled to suggest the hypothesis that such cells are responsible for wound contraction. The paper was written rapidly and sent to *Nature*, which also rapidly refused it. We were, of course, discouraged but decided to send practically the same manuscript to *Experientia*, where it was published. We then (in collaboration with P.R. Statkov and B.J. Hirschel) showed that strips of granulation tissue were retracting or relaxing, when treated with appropriate pharmacological agents, similarly to smooth-muscle strips[1,2] and described these modified fibroblasts in the nodule of human palmar fibromatosis (Dupuytren's disease).[3] Meanwhile, this special cell had received a name: "the myofibroblast."[1-3] Since then, the biology of myofibroblasts and their distribution in several animal and human normal and pathological tissues have been the object of research in many laboratories.[4-5] Moreover, more recent work has shown that there is a correlation between the phenotypical features of myofibroblasts and the clinical behavior of lesions containing these cells.[6]

Our work is a typical example of an advance made by applying a new technique to an old problem. In my opinion the interest stimulated by our observation is due to the fact that it correlates well with the previous assumption that the centripetal force exerted during granulation tissue contraction is localized within the tissue itself and involves cellular elements.[5] Moreover, the identification of the myofibroblast makes this cell a good target for potential therapeutic agents. Many features of the myofibroblast, such as its origin, are yet unknown, but further work on this cell will probably shed new light on the mechanism of normal and pathological wound healing and on the possibility of influencing soft tissue contracture.

1. **Majno G, Gabbiani G, Hirschel B J, Ryan G B & Statkov P R.** Contraction of granulation tissue *in vitro*: similarity to smooth muscle. *Science* 173:548-50, 1971. (Cited 200 times.)
2. **Gabbiani G, Hirschel B J, Ryan G B, Statkov P R & Majno G.** Granulation tissue as a contractile organ. A study of structure and function. *J. Exp. Med.* 135:719-34, 1972. (Cited 350 times.)
3. **Gabbiani G & Majno G.** Dupuytren's contracture: fibroblast contraction? An ultrastructural study. *Amer. J. Pathol.* 66:131-46, 1972. (Cited 220 times.)
4. **Seemayer T A, Lagacé R, Schürch W & Thelmo W L.** The myofibroblast: biologic, pathologic and theoretical considerations. *Pathol. Annu.* 15(Pt. I):443-70, 1980. (Cited 50 times.)
5. **Skalli O & Gabbiani G.** The biology of the myofibroblast. Relationship to wound contraction and fibrocontractive diseases. (Clark R A F & Henson P M, eds.) *The molecular and cellular biology in wound repair*. New York: Plenum, 1988. p. 373-402.
6. **Skalli O, Schürch W, Seemayer T, Lagacé R, Montandon D, Pittet B & Gabbiani G.** Myofibroblasts from diverse pathological settings are heterogeneous in their content of actin isoforms and intermediate filament proteins. *Lab. Invest.* (In press.)

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