

Manasek F J. Embryonic development of the heart. I. A light and electron microscopic study of myocardial development in the early chick embryo. *J. Morphology* 125:329-66, 1968.
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Embryonic chick myocardium, stages 8+ to 12-, was examined with the electron microscope. The myocardium was shown to consist of a homogeneous population of myogenic cells, each at about the same level of cytodifferentiation, organized into an epithelium. The developing muscle cells have the ultrastructural appearance of secretory cells as well as muscle. [The *SCI*® indicates that this paper has been cited in over 150 publications.]

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This work was done while I was a postdoctoral fellow in the Department of Anatomy at Harvard Medical School. I was learning the technique of electron microscopy, and, despite Don Fawcett's gentle encouragement to apply the instrument to problems in reproductive biology, I began to look at other developing systems. Embryo ultrastructure was still largely unexplored, a situation soon to change as a result of the recent introduction of aldehyde fixatives, and virtually every section I examined with the electron microscope revealed new things. I recall how delighted and excited I was to discover that not "everything had been done already."

It soon became clear that a systematic study correlating events at the ultrastructural level with those at higher levels of organization could provide a link between cell activity and tissue and organ morphogenesis. This strategy succeeded well for the myocardium. Two major papers resulted from this study; the first was a brief note in the *Journal of Cell Biol-*

*ogy*¹ reporting that differentiated cardiac muscle cells undergo mitosis. This paper presented some of the first hard evidence proving that differentiated muscle cells are able to divide. I still feel that this was my most important single contribution to the field, although I never followed up on the work personally. My *Journal of Morphology* paper, the *Classic*, was another outcome of that same study. It began as an attempt to document myocardial development from anlage to hatching, but that was a bit of hubris I soon lost. The paper, after the referees got through with it, ultimately covered only a few hours of development.

Those few hours, however, were very important. I reported several findings whose significance was not clear at that time but have since proven instrumental in altering the way we think about early myocardial development and myogenesis. For the first time, early embryonic cardiac muscle was appreciated as being a homogeneous epithelial tissue with the ability to perform many seemingly diverse tasks such as contracting and secreting connective tissue simultaneously. This demonstration proved important later in understanding the relationship between myocardial shape and connective tissue² and ultimately led to a new understanding of early cardiac morphogenesis.³

This paper marks a division between "old" and "new" cardiac embryology, and I believe that it was responsible, in part at least, for introducing a cell biological perspective to subsequent studies of heart development. It continues to provide an intellectual interface where studies at the organ, tissue, cellular, biochemical, and, more recently, molecular levels can meet. My own current work, continuing at Dartmouth Medical School, is a direct outgrowth of this paper. The work leading to this publication is now about 20 years old, and it gives me a great sense of personal satisfaction to see the influence this modest descriptive study continues to have on the field.

1. Manasek F J. Mitosis in developing cardiac muscle. *J. Cell Biol.* 37:191-6, 1968. (Cited 105 times.)
2. Nakamura A & Manasek F J. An experimental study of the relation of cardiac jelly to the shape of the early chick embryonic heart. *J. Embryol. Exp. Morphol.* 65:235-56, 1981.
3. Manasek F J, Kulikowski R R, Nakamura A, Nguyenphuc Q & Lactitis J W. Early heart development: a new model of cardiac morphogenesis. (Zak R, ed.) *Growth of the heart in health and disease*. New York: Raven Press, 1984. p. 105-30.