Ultrastructural Studies on the Formation of Myofilaments and Myofibrils in the Human Embryonic and Adult Hypertrophied Heart

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Summary. The myofibrillogenesis in the human embryonic heart is described. The synthesis of thin filaments, which are the first to appear, takes place in close proximity to smooth surfaced SR tubules. Z-band material is closely related to the thin filaments and appears first as irregularly distributed patches in the filamentous mass. Further cellular differentiation includes an organization of the thin filaments/Z-band material. The synthesis of thick filaments, which follows that of the thin filaments, takes place in ribosome rich areas of the cell. They are rapidly incorporated into the strings of organized thin filaments/Z-band material. The periodic binding sites on both kinds of filaments are believed to play an important role in the precise ordering of the filaments.

The formation of myofilaments in the adult hypertrophied human heart is also described. The similarities between this process and that observed in the embryonic heart are striking, and we believe it to be the same process.

Key words: Myofibrillogenesis – Human heart – Electron microscopy.

Introduction

The process of myoblast differentiation to form functional muscle cells involves the formation and precise spatial ordering of two kinds of filaments. Ultrastructural aspects of this process in myocardial cells have been reported by Muir (1957), Wainrach and Sotello (1961), Cedergren and Harary (1964), Schiebler (1966), Allen and Carstens (1967), Huang (1967), Manasek (1968), Hagopian and Spiro (1970), Legato (1970), Sako, (1975), and Rønnau (1977).

The same process has also been described in skeletal muscle cells (Allen and Pepe, 1965; Heuson-Stiennon, 1965; Fischman, 1967), and although Manasek (1968) has described differences between the differentiating process in the two kinds of muscle cells, the process seems to progress in a comparable manner.

Although described in detail in these reports, there is still disagreement about basic features in myofibrillogenesis. The present paper describes this process in the
human embryonic heart. Special attention is paid to the sequential appearance of the two kinds of filaments, the role of the Z-band material, and the organization of free myofilaments into myofibrils. Furthermore, myofibrillogenesis, as described in the embryonic tissue, is compared with filament synthesis in the adult hypertrophied human heart.

Material and Methods

1. Embryonic Tissue. The materials used were embryos obtained from pregnancies of women where therapeutic abortion for social reasons was performed. All the women were healthy and had regular menstrual periods. The time elapsed from start of the last menstrual period till termination of pregnancy varied from 7 to 13 weeks, and only apparently normal pregnancies were selected.

In general anesthesia the cervix was dilated and the uterine content was removed by use of a ring-forceps followed by curettage. The fetuses, totalling 8, were isolated and dissected under an operating microscope. The hearts were immediately transferred to ice-cold Karnovsky fixative (Karnovsky, 1965) to which 5% sucrose was added. After 3 h of fixation the tissue was washed overnight in a cacodylate-buffered 1% sucrose solution and then treated with 1% cacodylate-buffered OsO₄ solution for 1.5 h. After one wash in the same buffer and a wash in distilled water, the tissue was stained for 1.5 h in a 2% uranyl acetate solution before dehydration through an ethanol series. The ultrathin sections were grid-stained with lead citrate (Reynolds, 1963).

2. Adult Tissue. Myocardial biopsies were obtained from the left ventricular wall by the Vim Silvermann technique (Rake et al., 1969) using a Tru-Cut biopsy needle. The biopsies were taken at the time of open heart surgery, prior to aortic or mitral valve replacement, from 22 patients with acquired heart disease. A heavy hypertrophy of the left ventricular wall was present in all patients. The biopsies were immediately transferred to ice-cold Karnovsky fixative. The further treatment of the tissue was identical with that of the embryonic tissue.

Results

Embryonic Tissue

All ages are characterized by a sequence of cellular differentiation from the epi- and endocardial sides toward the middle of the ventricular wall where the most differentiated cells are located.

At an early stage the myoblasts contain few filaments embedded in the dense cytoplasm and, characteristic of many immature cells, a large number of ribosomes, both free and membrane-associated (Fig. 1). An active synthesis of myofilaments appears in later stages of development, and the first to appear are the thin filaments, having a diameter of about 90 Å. The synthesis of these filaments takes place in close proximity to a network of smooth-surfaced sarcoplasmic reticulum tubules (Figs. 2 and 3). Free ribosomes, few in number, are randomly scattered in the cytoplasm. The first signs of primitive Z-band substance appear as faint electron dense patches (Fig. 3).

Fig. 1. Undifferentiated heart muscle cells. No myofilaments are visible. Note the well developed granulated SR. N: Nucleus, Embryonic tissue. × 11,200

Fig. 2. Early stage of thin filament synthesis. Scattered thin filaments are seen among tubules of smooth-surfaced SR tubules (arrow). M: Mitochondrion. Embryonic tissue. × 44,000