Research Summary of the c gene in the Mexican Axolotl

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Humphrey (1968, 1972) reported the discovery of a mutation in the axolotl which he called c for cardiac lethal. Embroyos homozygous recessive for this trait lack functional hearts. Affected embryos develop without apparent abnormalities to stage 34 (heartbeat stage). At this time, the heart fails to beat. Cardiac lethal animals show normal swimming movements indicating that skeletal muscle is uneffected by the mutation. Mutants never eat and die soon after hatching. Parabiosis of normal and mutant embryos does not correct the cardiac lethal trait, nor does this procedure effect the normal twin. Transplants of heart mesoderm from mutant embryos into normal hosts produce functional hearts. The reciprocal transplant, that is, normal into mutant, fails to produce functional hearts.

Justus and Hollander (1971) and Hollander and Justus (1971) reported electrophysiology studies on cardiac lethal embryos. In these studies, transmembrane potentials were recorded by impaling heart cells with microelectrodes. Resting potentials of 24 mV were found in mutant heart cells. The magnitude of these potentials were similar to that found for other inexcitable tissues. Direct stimulation of mutant hearts failed to produce heartbeats. Acetylcholine, norepinephrine and serotonin had no effect on heart tissue in mutant embryos; these drugs did alter heart action in normal embryos at the same stage of development. These results suggest that myogenic factors which are required to produce action potentials may be absent in hearts of cardiac lethal embryos.

Lemanski, Bertke and Justus (1970) reported preliminary studies on the ultrastructure of heart cells in cardiac lethal embryos. Mutant heart cells appeared less differentiated than cardiac cells in normal embryos. Myofibrillar material was completely lacking in some mutant heart cells. Although 60 A myofilaments appeared to be present in some mutant heart cells, very few 140 A filaments were observed. Lemanski (1973 a,b) reported more detailed electron microscope studies of cardiac mutant heart cells. Partial organization of myofibrils were occasionally seen. Sarcomeres and intercalated disc were rarely seen in heart cells of affected embryos. Heavy meromyosin binding studies of myocardial cells from mutant embryos has demonstrated the presence of actin; myosin may not be present in these cells.

We are continuing our analysis of the cardiac lethal mutation in my laboratory. In addition, we are studying other parameters in the development of the salamander cardiovascular system, for example, changes in lactate dehydrogenase before and after the initiation of the heartbeat and changes in hemoglobins before and after metamorphosis. More recently, we have initiated studies on the development of mammalian cardiac tissue. Summaries of this work will be presented in a future edition of the newsletter.

References:

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