A NOVEL ROLE OF PERINATAL MYOSIN IN CARDIAC AND SKELETAL MUSCLE DEVELOPMENT

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Cardiac myxomas are the most common primary cardiac tumors in adults. Approximately 7% occur in the familial disorder known as Carney complex (CNC). In CNC, familial cardiac myxomas occur in the setting of spotty skin pigmentation, extracardiac myxomas, endocrinopathy, and other neoplasms. Previously, we identified an R674Q missense mutation in the MYH8 gene encoding the myosin heavy chain perinatal isoform (MyHCpn) in individuals with a rare CNC variant who exhibit typical CNC findings along with the trismus pseudocamptodactyly limb contracture syndrome. To define the role of MyHCpn in mammalian development, we established a genetically engineered mouse line carrying the orthologous R674Q mutant MYH8 allele. Myh8R674Q/+;EIIa-Cre mice die within minutes after birth. Gross examination of these mice at embryonic day (E)18.5 revealed smaller embryos with abdominal bulges (A). Upon histological examination of E18.5 Myh8R674Q/+;EIIa-Cre cardiac and skeletal muscles, we observed fiber size variability, signs of apoptosis and increased muscle degeneration/regeneration (B). Electron microscopic images of striated muscles showed enlarged mitochondria, focal absence of myofibrils, loosely arrayed fiber bundles, and regional Z-line irregularities (C). We also observed the presence of nemaline rods indicative of nemaline myopathy (D). Together, these findings suggest a novel and important role of MyHCpn in cardiac and skeletal muscle development.