Animal Bioresource in Japan

Subcellular Localization of Dystrophin Isoforms in Cardiomyocytes and Phenotypic Analysis of Dystrophin-deficient Mice Reveal Cardiac Myopathy is Predominantly Caused by a Deficiency in Full-length Dystrophin

Nami Masubuchi, Yuichi Shidoh, Shunzo Kondo, Jun Takatoh, Kazunori Hanaoka
Laboratory of Molecular Embryology, Department of Bioscience, Kitasato University School of Science, 1–15–1 Kitasato, Minami-Ku, Sagamihara, Kanagawa 252-0373, Japan

Abstarc :

Duchenne muscular dystrophy (DMD) is an X-linked recessive progressive muscle degenerative disorder that causes dilated cardiomyopathy in the second decade of life in affected males. *Dystrophin*, the gene responsible for DMD, encodes full-length dystrophin and various short dystrophin isoforms. In the mouse heart, full-length dystrophin Dp427 and a short dystrophin isoform, Dp71, are expressed. In this study, we intended to clarify the functions of these dystrophin isoforms in DMD-related cardiomyopathy. We used two strains of mice: *mdx* mice, in which Dp427 was absent but Dp71 was present, and *DMD*-null mice, in which both were absent. By immunohistochemical staining and density-gradient centrifugation, we found that Dp427 was located in the cardiac sarcolemma and also at the T-tubules, whereas Dp71 was specifically located at the T-tubules. In order to determine whether T tubule-associated Dp71 was involved in DMD-related cardiac disruption, we compared the cardiac phenotypes between *DMD*-null mice and *mdx* mice. Both *DMD*-null mice and *mdx* mice exhibited severe necrosis, which was followed by fibrosis in cardiac muscle. However, we could not detect a significant difference in myocardial fibrosis between *mdx* mice and *DMD*-null mice. Based on the present results, we have shown that cardiac myopathy is caused predominantly by a deficiency of full-length dystrophin Dp427.

Key Word :
cardiomyopathy, dp427, dp71, dystrophin, heart

Volume 62, Number 3, - 2013