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论著

Cx43基因对近端流出道隔心肌化过程的调控机制

赵晓晴[1],黄国英[1△],谢利剑[1],彭涛[1],陈萍[2],周国民[3]

1复旦大学附属儿科医院心血管中心， 上海 200032;2 复旦大学附属妇产科医院超声室， 上海 200011;3 复旦大学上海医学院解剖与组胚教研室， 上海 200032

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摘要 目的:探讨connexin43（Cx43）基因在小鼠近端流出道隔心肌化的作用及其机制。 方法:选用胚胎（ED）11.5 d至出生后1 d的Cx43基因剔除（KO）纯合型（Cx43-/-）、杂合型（Cx43+/-）及野生型（Cx43+/+）C57/BL6小鼠作为研究对象；采用PCR方法鉴定基因型；HE染色观察心脏结构，免疫组化法测定横纹肌肌动蛋白α-SCA、凋亡相关分子active caspase-3及神经嵴细胞的标志物AP-2的表达。 结果:①Cx43-/-小鼠大多出生后24 h内即死亡。大体解剖见明显的右室流出道圆锥部异常膨隆，右心房扩张；组织切片HE染色示右室流出道壁大量异常小梁状组织增生突起，形成多个囊状结构，右室流出道腔明显狭窄，右室腔扩张。Cx43+/-和Cx43+/+心脏无明显异常。②Cx43-/-小鼠近端流出道隔中央区域α-SCA的表达明显滞后。③Active caspase-3组化显示Cx43+/+凋亡细胞主要出现在近端流出道隔，ED12.5至ED15.5均可见到；Cx43+/-凋亡减少，Cx43-/-则仅见很少凋亡细胞。④Cx43-/-流出道AP-2的表达增多，且表达位置异常。 结论:Cx43 KO小鼠以右室流出道异常增生引起的梗阻性畸形为主要特征，该病变过程可能与胚胎期近端流出道隔心肌化迟滞有关，其近端流出道隔细胞凋亡减少和神经嵴细胞表达异常很可能参与了流出道心肌化异常的形成，表明Cx43在近端流出道隔心肌化过程中具有重要作用。

关键词 基因,Cx43 基因敲除 细胞凋亡 神经嵴

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Role of Cx43 gene in the process of myocardialization of proximal outflow tract septum in the mouse heart

ZHAO Xiao-qing[1],HUANG Guo-ying[1],XIE Li-jian[1],PENG Tao[1],CHEN Ping[2],ZHOU Guo-min[3]

1Pediatric Heart Center, Children’s Hospital of Fudan University, Shanghai 200032, China.E-mail:gyhuang@shmu.edu.cn;2 Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200032, China;3 Department of Anatomy, Histology and Embryology, Shanghai Medical College of Fudan University, Shanghai 200032, China

Abstract

<FONT face=Verdana>AIM:To investigate the role of Cx43 in the myocardialization of the proximal outflow tract (OFT) septum in the mouse heart.
METHODS:C57/BL6 mice of ED11.5 to 1 day after birth were used in this study, which included Cx43 knockout homozygotes (Cx43-/-), heterozygotes (Cx43+/-) and wildtypes (Cx43+/+). Pathohistological analysis was used to examine the structure of the hearts. The expression of alpha-sarcomeric actin (α-SCA), active caspase-3 and activator protein-2 (AP-2) were detected by immunohistochemistry.
RESULTS:Most Cx43-/- mice died within 24 h after birth with a swelling and blockage of the conotruncal region, which led to the obstruction of OFT and enlargement of right ventricle. HE staining showed plenty of abnormal tissues in this region forming many pouches. No apparent malformations were observed in Cx43+/- and Cx43+/+ mice. The expression of α-SCA in the proximal OFT septum was delayed obviously in Cx43-/-. The apoptotic cells existed in the proximal OFT septum of Cx43+/+ mostly during ED12.5 to ED15.5. However, there were less apoptotic cells observed in Cx43+/-, and few in Cx43-/-. The expression of AP-2, marker of neural crest cells, was increased in Cx43-/- and abnormally located in the proximal OFT septum.
CONCLUSIONS:Cx43 KO mice are characterized by hyperplasia in conotruncal region, which may be associated with the delayed myocardialization of OFT septum. The decreased apoptosis and the abnormal distribution of cardiac neural crest cells are likely to contribute to the abnormal myocardialization in mice with Cx43 defects. </FONT>

Key words Genes Cx43 Gene knockout Apoptosis Neural crest

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通讯作者 黄国英 gyhuang@shmu.edu.cn