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# 心肌细胞过表达miR-27b导致小鼠发生心肌纤维化和线粒体损伤

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摘要 以往的miRNA芯片研究结果显示, miR-27b在人类心脏疾病标本和压力负荷引起的小鼠心肌肥厚模型中表达水平明显升高, 提示其在心脏疾病发生过程中发挥了重要功能。为研究miR-27b在心脏组织中的功能, 文章建立了在心肌细胞特异性 a-肌球蛋白重链(a-MHC)启动子(5.5 kb)控制下过表达miR-27b的转基因小鼠。通过Real-time PCR检测, 发现miR-27b前体和成熟体表达水平在转基因小鼠心脏组织中明显升高。miR-27b转基因小鼠不仅出现心肌肥厚, 还表现出明显的心肌纤维化。进一步研究表明心肌纤维化的关键调节分子金属基质蛋白酶13(MMP13)是miR-27b的靶分子, 在miR-27b转基因小鼠中MMP13显著下调, 胶原分子I和 III则显著上调。此外, 还发现miR-27b转基因小鼠会出现心脏超微结构的损伤。以上研究结果表明, miR-27b可能通过抑制MMP13促进心肌纤维化。

关键词： miR-27b 心肌细胞 转基因小鼠 心肌纤维化 MMP13

Abstract： Previous microRNA array results have shown that miR-27b is upregulated in heart tissue from human cardiomyopathy and pressure-overloaded hypertrophic mouse model, implying that miR-27b might play important role in heart diseases. To study the in vivo function of miR-27b, we generated a transgenic mouse line overexpressing miR-27b under the control of the 5.5 kb promoter of ?-myosin heavy chain (?-MHC). Real-time PCR results demonstrated that miR-27b precursor and mature miR-27b were significantly increased in the heart tissues of miR-27b transgenic mice. miR-27b transgenic mice not only displayed cardiac hypertrophy, but also exhibited significant cardiac fibrosis. Further study showed that MMP13, a key regulator involved in cardiac fibrosis, was the target of miR-27b, and miR-27b transgenic mice displayed decreased expression of MMP13 and increased expression of Col I and III. In addition, defects in ultrastructral architecture were also found in miR-27b transgenic mice. The above results demonstrated that miR-27b might inhibit MMP13 to promote cardiac fibrosis.

Keywords： miR-27b, cardiomyocyte, transgenic mice, cardiac fibrosis, MMP13

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