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Epigenetic regulation of phosphodiesterase 4d in restrictive cardiomyopathy mice with cTnI mutations

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Epigenetic regulations play an important role in disease development. In this study, we have investigated epigenetic regulations in restrictive cardiomyopathy mice with cTnI193 His mutation. Our results demonstrated that phosphodiesterase (PDEs) 4d was down-regulated in the heart of these mice. Further studies showed that the epigenetic modifications were associated with enhanced acetylation of histone 3 lysine 4 and lysines 9, whereas tri-methylation of histone 3 lysine 4, were decreased in histones near the PDE4d gene promoter regions. The binding levels of histone transmethylase SMYD1 and histone deacetylase HDAC1 were increased in the gene promoter regions in cTnI193His

transgenic hearts. Using immune-fluorescent labeling we found an evidence of cTnI existence in the nucleus of cardiomyocytes and Western blotting further confirmed that both wild type and mutated cTnI could be detected in the cell nucleus of the hearts. Furthermore, an interaction between cTnI and SMYD1, or cTnI and HDAC1 was observed. Overexpression of the mutated cTnI in cultured cardiomyocytes reduced the expression of PDE4d. Our data suggest that the decrease of PDE4d expression in RCM mice caused by cTnI mutations may be related to epigenetic regulation, i.e. histone acetylation and methylation, and cTnI might be involved in this procedure via an interaction with HDAC1 and SMAD1 in the hearts.

Biography

Zhao Weian now is a PhD student from Chongqing Medical University, China.

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