The Effect of Myocyte Enhancer Factor 2A Gene on proliferation, migration and phenotype of Vascular Smooth Muscle Cells

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Aims: The genetic basis for vascular smooth muscle cells (VSMCs) phenotypic switching is unclear. Recent studies showed that 21-base pair deletion mutation (△21) in myocyte enhancer factor 2A (MEF2A) gene could be an inherited marker for coronary artery disease. The effect of MEF2A gene mutation on the VSMCs phenotypic switching was studied.

Methods: Human aortic VSMCs were used. Four groups VSMCs transfected with Green fluorescent protein plasmid (control group), with MEF2A wild-type (WT) plasmid (WT group), with MEF2A △21 plasmid (△21 group) or with MEF2A siRNA (siRNA group) were studied. VSMCs proliferation was determined by MTT. The migration of VSMCs was measured by Millicell chamber. The expression of MEF2A protein, α-SM-actin, SM22α, osteopontin and p38 mitogen-activated protein kinase (MAPK) signaling pathway were detected by western blotting.

Results: MEF2A protein expression was knockdown by siRNA transfection. MEF2A protein was overexpressed in WT and △21 groups. Compared to WT group, △21 and siRNA groups showed higher VSMCs proliferation (MTT 0.31 vs 0.63 vs 0.66, P<0.01) and more migration (21.2 vs 52.6 vs 58.0, P<0.01). In addition, transfection of △21 and siRNA could induce downregulation of α-SM-actin and SM22α (P<0.01) and upregulation of osteopontin (P<0.01) in VSMCs. The phosphorylated p38 signaling pathway expression was significantly enhanced in the △21 and siRNA groups as compared to WT group (P<0.01).

Conclusions: These results demonstrate that MEF2A dominant negative mutation and RNA silence can induce phenotype switching of VSMCs, leading to its increased proliferation and migration, which may involve in p38 MAPK signaling pathway.

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