

3. Long non-coding RNA NEXN-AS1 mitigates atherosclerosis by regulating the actin-binding protein NEXN

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文章简介

NEXN 蛋白是一种肌动蛋白结合蛋白,可调控细胞粘附及迁移。王前教授团队前期基因芯片发现动脉粥样斑块组织中 NEXN 及 lncRNA NEXN-AS1 的表达下调,为进一步探讨 NEXN 与 NEXN-AS1 对动脉粥样硬化进程的影响和相关机制,该团队进行了一系列体内外实验。ChIRP-PCR 及荧光素酶报告基因实验证实 lncRNA NEXN-AS1 可直接上调 NEXN 基因的表达;ChIRP-MS 及 RIP 实验提示显示 NEXN-AS1 可与 BAZ1A 蛋白结合;体外实验过表达 NEXN-AS1 可上调 NEXN 水平且下调 BAZ1A 表达;此外过表达 NEXN-AS1 后可以使 TLR4 寡聚化及 NF- κ B 活性下降,减少细胞炎症因子的表达,该效应在干扰 NEXN 后减弱,而在干扰 BAZ1A 后得到恢复。结果提示 NEXN-AS1 可通过下调 BAZ1A 及上调 NEXN 水平以抑制 TLR4 蛋白寡聚化及 NF- κ B 的活性,减少内皮细胞粘附分子和细胞炎症因子的表达,进而抑制单核细胞对内皮的粘附作用,降低 VSMC 的迁移能力,从而减缓动脉粥样硬化进程。

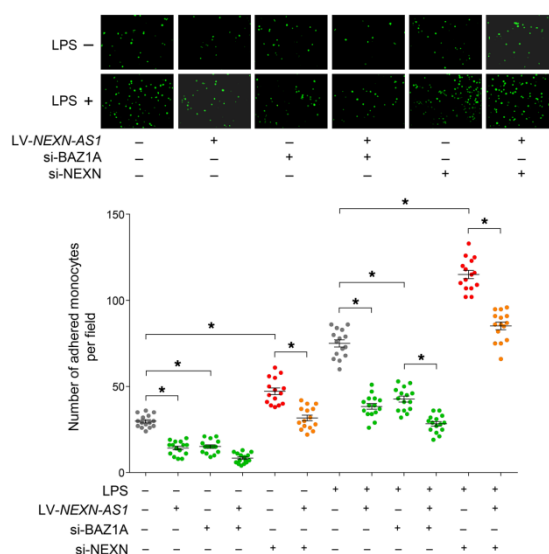


Fig. NEXN-AS1 and NEXN inhibit monocyte adhesion to endothelial cells. Cultured human vascular endothelial cells were transfected with either NEXN-AS1-expressing lentivirus (LV-NEXNAS1), BAZ1A siRNA (si-BAZ1A), or NEXN siRNA (si-NEXN), then either treated or not treated with lipopolysaccharides (1 μ g/ml) for 4 hours and subsequently cocultured with fluorescently labeled monocytes for 1 hour, followed by fluorescent microscopy. Upper panel shows representative images of adhered monocytes. Original magnification, $\times 200$. The graph shows mean \pm SD number of adhered monocytes per microscopic field, from 5 independent experiments with each experiment performed in triplicate. * $P < 0.05$, ANOVA with post hoc analysis and Bonferroni's correction