

## 5. LncRNA-RP11-714G18.1 suppresses vascular cell migration via directly targeting LRP2BP.

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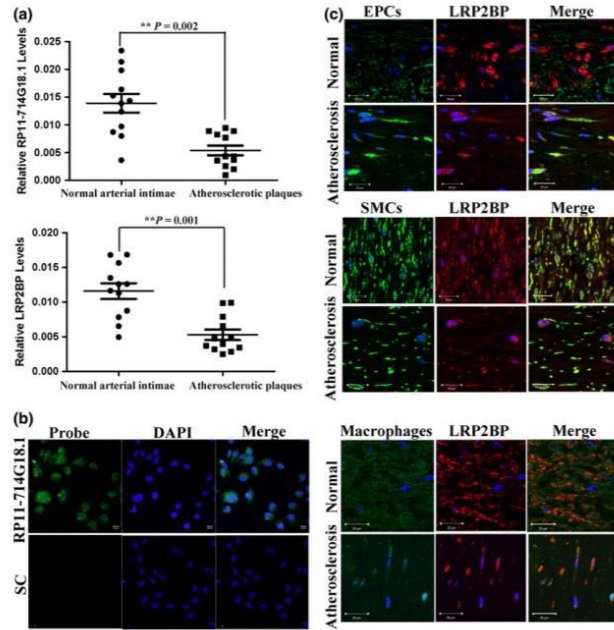
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### 作者列表

Zhang Y, Zheng L, Xu BM, Tang WH, Ye ZD, Huang C, Ma X, Zhao JJ, Guo FX, Kang CM, Lu JB, Xiu JC, Li P, Xu YJ, Xiao L, Wu Q, Hu YW , **Wang Q.**

### 文章简介

动脉粥样硬化性心血管疾病被认为是全世界死亡率和发病率的主要原因。越来越多的证据支持长链非编码 RNA (lncRNA) 在动脉粥样硬化发病机制中起重要作用, 但机制尚未阐明。本研究发现 lncRNA RP11-714G18.1 在人类晚期动脉粥样硬化斑块组织中表达显著降低。在人血管平滑肌细胞 (VSMCs) 和内皮细胞 (ECs) 中过表达 RP11-714G18.1 能抑制细胞迁移, 降低 ECs 与单核细胞的粘附, 抑制新生血管形成, 减少 VSMCs 的凋亡并促进一氧化氮的产生。RP11-714G18.1 可以直接与其附近的基因 LRP2BP 结合并增加 LRP2BP 的表达。此外, RP11-714G18.1 通过 LRP2BP 介导 EC 和 VSMC 中基质金属蛋白酶 1 (MMP1) 的下调而抑制细胞迁移。在动脉粥样硬化患者血清中 LRP2BP 的水平与高密度脂蛋白胆固醇水平呈正相关, 与肌钙蛋白水平呈负相关。这表明 RP11-714G18.1 可通过 RP11-714G18.1 / LRP2BP / MMP1 信号通路抑制血管细胞迁移而发挥抗动脉粥样硬化作用, 该通路是动脉粥样硬化防治潜在新靶点。



**Fig. .** Expression of lncRNA RP11-714G18.1 and LRP2BP in advanced atherosclerotic plaques and normal tissues. (a) The relative expression of lncRNA RP11-714G18.1 and LRP2BP in advanced atherosclerotic plaque tissues (cohort 1, n = 12) compared with normal arterial intima (cohort 1, n = 12) by qRT-PCR. Data are shown as mean  $\pm$  SEMs for three independent experiments. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 versus those in normal arterial intima in Student's t-test. (b) Detection of RP11-714G18.1 by RNA-FISH. Green represents FISH probes of RP11- 714G18.1. Nucleus are counterstained with DAPI (blue). The scramble control probe was used as negative control. (c) Detection of cellular sources of LRP2BP expression in human plaques (cohort 2, n = 3) or in normal arterial intima (cohort 2, n = 3). Images are taken from the fibrous cap area (ECs and VSMCs) or in the shoulder area close to intraplaque microvessels (macrophages) of atherosclerotic plaques. Double immunofluorescence staining for LRP2BP (red, Alexa-594-tagged) and cell type markers (green, Alexa-488-tagged), CD34 (marker for endothelial progenitor cells<sup>46</sup>), SMC-a-actin (SMC marker), CD68 (macrophage marker). Nucleus was stained with DAPI (blue). White scale bar: 20  $\mu$ m. SC, scramble control; LRP2BP, the low-density lipoprotein related receptor 2 binding protein; qRT-PCR, quantitative reverse transcription PCR; SEM, standard error of mean; EC, endothelial cell; VSMC, vascular smooth muscle cell; DAPI, 40 ,6-diamidino-2-phenylindole