REVIEW

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MULTIDISCIPLINARY

Mechanobiology in vascular remodeling

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ABSTRACT

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Keywords: , , , , , A

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INTRODUCTION

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VASCULAR CELLS RESPOND TO MECHANICAL STRESSES

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MECHANOTRANSDUCTION NETWORK BASED ON HIGH-THROUGHPUT BIOTECHNOLOGY

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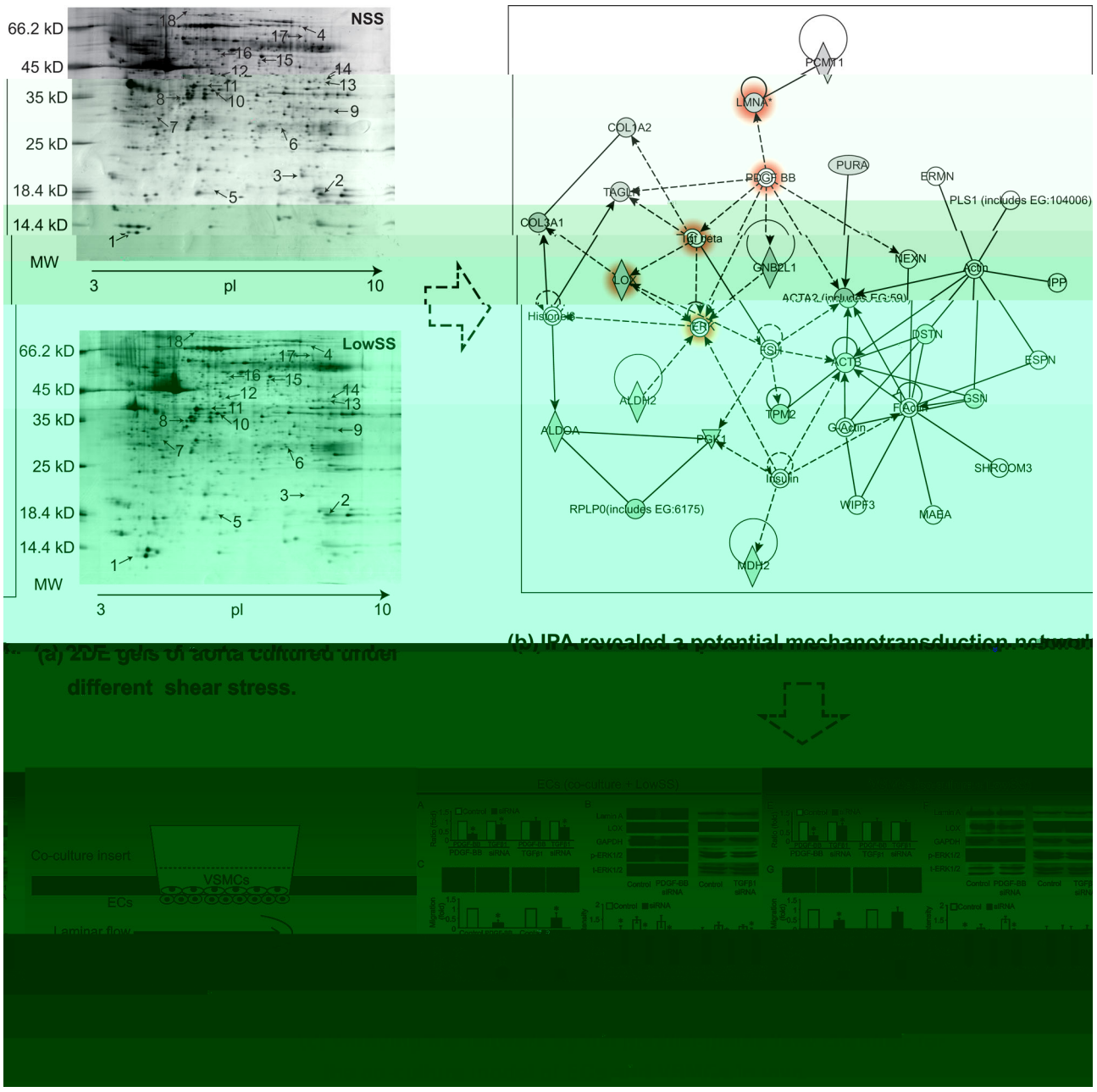

Figure 2. Schematic drawing outlining the vascular cell mechanotransduction network based on mechano-vascular proteomics. (a) 2D electrophoresis (2DE) gels of aorta cultured under different shear stresses. The protein profiles of rat aorta cultured under NSS (15 dyn/cm^2) and LSS (5 dyn/cm^2) are compared by using comparative proteomic techniques, 2DE and MALDI-TOF mass spectrometry. (b) IPA reveals a potential mechanotransduction network. Differentially expressed proteins are analyzed by IPA and a signaling network that is highly correlated with mechanotransduction of LSS, involving PDGF-BB, TGFβ1, lamin A, LOX and ERK 1/2. (c) Validation of the network by the parallel-plate flow chamber (left panel) for the co-culture model of ECs and VSMCs *in vivo*. In the EC/VSMC co-culture parallel-plate flow chamber, ECs and VSMCs are grown on opposite sides of a 10-μm-thick polyethylene terephthalate (PET) membrane, and the ECs are subjected to SS. The interactions of ECs and VSMCs are able to occur through 0.4-μm diameter PET membrane pores. Using this system, the expressions of molecules involved in the networks, namely, PDGF-BB, TGFβ1, lamin A, LOX and phospho-ERK1/2, and the migration and proliferation of ECs and VSMCs separately under two levels of shear stress at 5 and 15 dyn/cm^2 are studied.

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MECHANOREGULATION OF NON-CODING RNAS IN VASCULAR REMODELING

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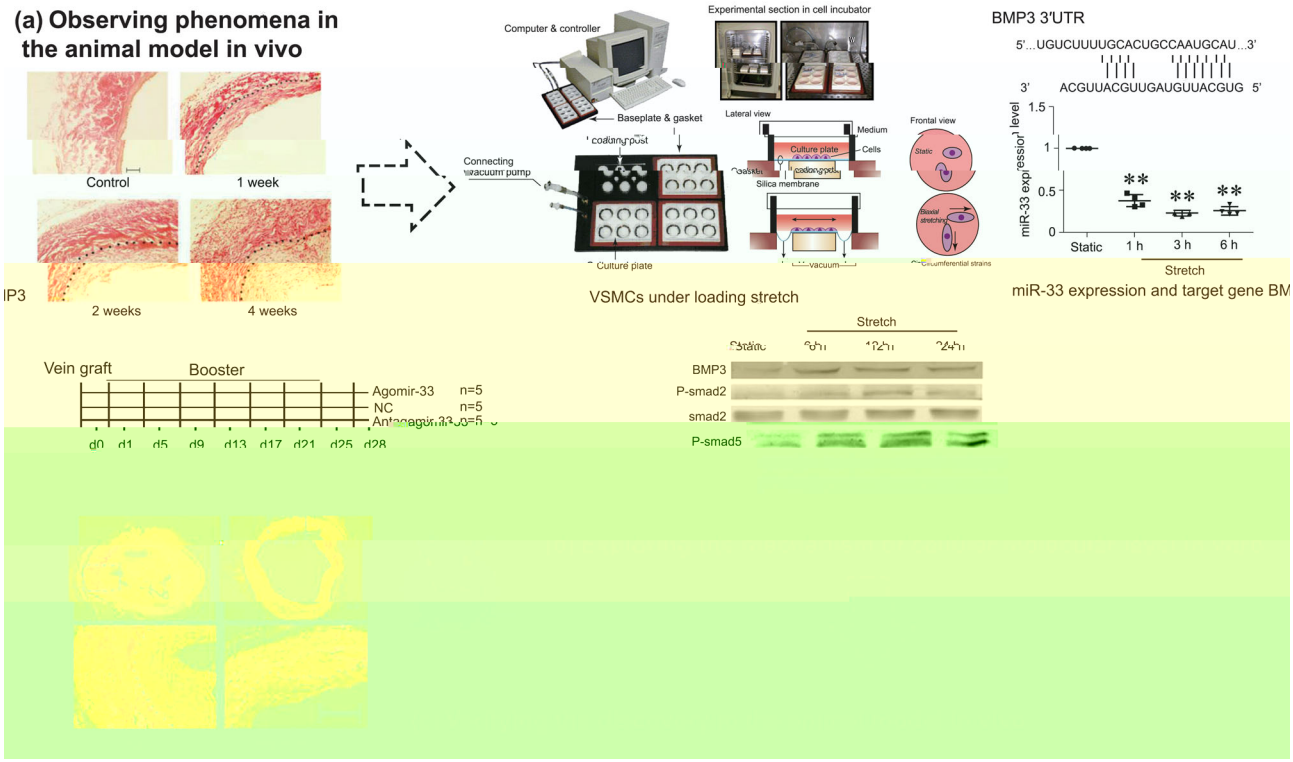

Figure 3. Schematic outlining the mechanobiological study of the roles of miRNAs and their target gene for exploring biomarkers. (a) Pathological outcomes in an animal model *in vivo*. Neointimal hyperplasia and cell proliferation are increased significantly, and miR-33 expression is decreased in rat vein grafts one, two and four weeks post-surgery. (b) Exploration of the biomechanical mechanism at the cellular and molecular levels *in vitro*. Use of a cyclic strain loading model of venous VSMCs and computation prediction of the miRNA target gene. The arterial stretch increases venous VSMC proliferation, represses miR-33 expression, and enhances target gene, BMP3, expression and phosphorylation of its downstream molecules smad2 and smad5, which are involved in VSMC proliferation. (c) Verifying the discovery in the animal model *in vivo*. The perivascular multi-point injection in the graft vein rat model demonstrates that agomiR-33 not only attenuates BMP3 expression and smad2 and smad5 phosphorylation, but also attenuates neointimal formation and cell proliferation in grafted veins.

SUMMARY AND PERSPECTIVES

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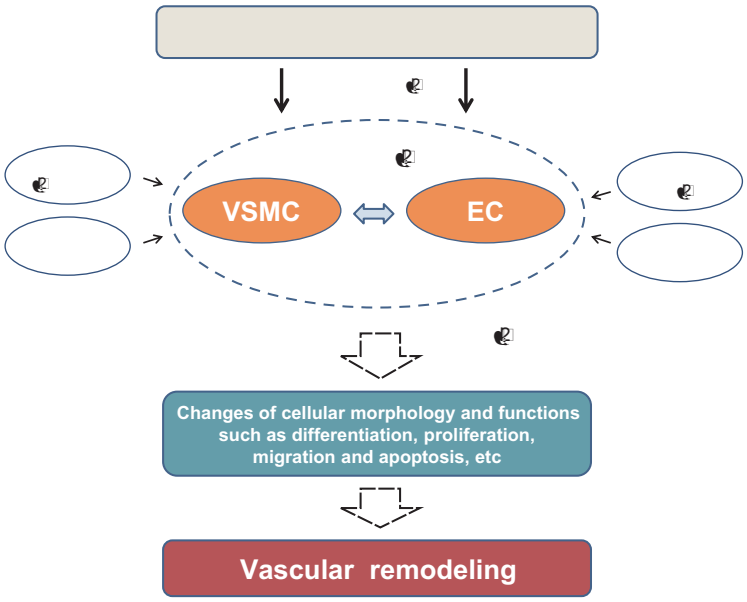

Figure 4. Schematic outlining mechanobiology in vascular remodeling. Mechanical forces, including SS and cyclic strain, are critically important factors regulating vascular remodeling. Vascular cells, mainly ECs and VSMCs, can sense the various forms of mechanical signals, transform them into intracellular biochemical signals, i.e., mechanotransduction, and then initiate cascades of cellular responses that ultimately regulate vascular functions. The interaction between ECs and VSMCs is also involved in vascular remodeling, in addition to chemical factors, microparticles, thrombocytes and the floating cells in the blood flow, as well as extracellular matrix and cells in the adventitia.

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