

PAR-1 is a novel mechanosensor for blood flow

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Atherosclerosis is readily observed in certain areas where disturbed blood flow (d-flow) is known to occur. A positive correlation between PKC ζ activation and d-flow has been reported, but the exact role of d-flow-mediated PKC ζ activation in atherosclerosis remains unclear. We found that PKC ζ -mediated p53-sumoylation is key regulator in d-flow- and peroxynitrite(ONOO \cdot)-induced EC apoptosis. *En face* confocal microscopy revealed increases in non-nuclear p53 expression and apoptosis in aortic EC located in d-flow areas compared with those present in steady laminar flow areas. We propose a novel mechanism for p53-sumoylation mediated by PKC ζ -PIASy interaction during d-flow-mediated EC apoptosis, which contributes early events of atherosclerosis. In contrast to d-flow, laminar shear stress governs anti-atherogenic responses in endothelial cells. We found that ERK5-Nrf2 cascade regulates laminar flow-mediated cytoprotective responses both in vitro and in vivo. In addition to flow-mediated endothelial signaling pathway, we recently found that PAR-1 is a novel mechanosensor for laminar flow. The related evidence will be discussed in the presentation.