Cigarette smoking induces vascular proliferative disease through the activation of Egr-1

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Vascular proliferative diseases such as atherosclerosis, restenosis after arterial injury, and hypertensive vascular diseases are commonly associated with the proliferation of vascular smooth muscle cells (VSMCs). Multiple stimuli such as shear stress,1 hypoxia,2 arterial injury, and angiotensin II (Ang II)3 are associated with the development of vascular proliferative diseases by the activation of early growth response (Egr)-1 as a master regulator for the proliferation of VSMCs.

The zinc finger transcription factor Egr-1 is an 80 to 82 kDa nuclear phosphoprotein consisting of 533 amino acids. The DNA-binding domain of Egr-1 consists of three zinc finger motifs located between amino acids 332 and 416 towards the carboxy-terminal region of the protein. Via these zinc finger motifs, Egr-1 binds to GC-rich DNA sequences to activate or repress gene transcription.4

Egr-1 activated by shear stress, mechanical injury, or Ang II, for example, stimulates transcription of several proinflammatory genes, including TNF-α,5 IL-2,5 MCP-1, and ICAM-1,6 to induce atherosclerosis. Egr-1 also stimulates expression of growth factors such as PDGF, TGF-β,7 bFGF,8 and tissue factor9 to induce arterial proliferation. Many of these genes also stimulate the expression of Egr-1 in vascular cells. These positive feedback loops amplify and sustain gene transcription through Egr-1-mediated mechanisms in vascular proliferative diseases.

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References