**INVOLVEMENT OF STROMAL INTERACTION MOLECULE-1 IN ANGIOTENSIN-II-INDUCED EXPRESSION OF EARLY GROWTH RESPONSE PROTEIN-1 IN VASCULAR SMOOTH MUSCLE CELLS**

E.R. Simo-Cheyou, **A.K. Srivastava**

CRCHUM, University of Montreal, Montreal, Quebec, Canada

The early growth response protein 1 (Egr-1) is a zinc finger transcription factor that has been suggested to regulate the expression of genes linked with inflammation and cell cycle regulation. An up-regulation of Egr-1 expression has been reported in models of atherosclerosis and intimal hyperplasia. Various vasoactive peptides and growth promoting stimuli have been shown to induce the expression of Egr-1 in VSMC. Angiotensin-II (Ang-II) is a critical vasoactive peptide implicated in the pathogenesis of vascular diseases. Ang-II elevates the intracellular level of calcium through activation of store-operated calcium entry involving inositol-3-phosphate receptor (IP3R)-coupled depletion of endoplasmic reticular calcium and stromal interaction molecule 1 (STIM-1). However, an involvement of IP3R/STIM-1- induced calcium pathway in Ang-II-induced Egr-1 expression remains unexplored. Therefore in the present studies we have examined the role of Ang-II-induced calcium release in Egr-1 expression in VSMC and investigated the contribution of STIM-1 in this process. Calcium chelation with BAPTA-AM as well as pharmacological blockade of IP3R with 2-aminoethoxydiphenyl borate (2-APB) decreased Ang-II-induced calcium release measured in cells loaded with Fura-2. Consistent with this, both BAPTA-AM and 2-APB attenuated Ang-II-induced enhanced expression of Egr-1 protein and mRNA levels. Furthermore, silencing of STIM-1 via RNA interference significantly abrogated STIM-1 protein and mRNA expression and resulted in an attenuation of Ang-II-induced Egr-1 expression. Our data demonstrate that Ang-II-induced Egr-1 expression is mediated by STIM-1 and calcium release in A-10 VSMC and suggest an implication of STIM-1 in the pathogenesis of vascular proliferative diseases. (Supported by a grant from CIHR).