**NATRIURETIC PEPTIDE RECEPTOR-C IMPROVES VASCULAR REMODELING INSPONTANEOUSLY HYPERTENSIVE RATS**

**M.B. Anand-Srivastava**

University of Montreal, Montreal, QC, Canada

**Objective:** Hypertrophy and hyperproliferation of vascular smooth muscle cells are important contributors of vascular remodelling and hallmarks of vascular disease such as atherosclerosis, restenosis and hypertension. Vascular smooth muscle cells (VSMC) from spontaneously hypertensive rats (SHR) exhibit hyperproliferation and hypertrophy. We earlier showed that a specific agonist of natriuretic peptide receptor-C (NPR-C), C-ANP4-23, attenuates the development of high blood pressure in SHR. The present study investigated if C-ANP4-23could also attenuate the hyperproliferation and hypertrophy of VSMC from SHR and to explore the underlying signaling pathways contributing to this inhibition.

**Method:** The proliferation and hypertrophy of VSMC was determined by [3H] thymidine and [3H]leucine incorporation respectively and the expression of proteins was determined by Western blotting.

**Results:** VSMC from SHR exhibit hyperproliferation and hypertrophy and overexpression of cyclin D1, cyclin A, cyclin E, cyclin-dependent kinase 2 (cdk2), phosphorylated retinoblastoma protein (pRb), Giα, Gqα and PLCβ1 proteins and enhanced phosphorylation of ERK1/2 and AKT and all these were attenuated to control levels by C-ANP4-23. Furthermore, PD98059, wortmannin and pertussis toxin, the inhibitors of MAP kinase, PI3kinase and Giα proteins respectively, also attenuated the hyperproliferation of VSMC from SHR and overexpression of cell cycle proteins to control levels.

**Conclusion:** These results indicate that NPR-C activation by C-ANP4-23 attenuates the enhanced levels of cell cycle proteins through the inhibition of enhanced expression of Giα proteins, enhanced activation of MAPkinase/PI3kinase and results in the attenuation of hyperproliferation of VSMC from SHR whereas C-ANP4-23-mediated inhibition of Gqα and PLCβ1 proteins attenuates VSMC hypertrophy, It may be suggested that C-ANP4-23could be used as a therapeutic agent in the treatment of vascular complications associated with hypertension, atherosclerosis and restenosis.

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