**NITRIC OXIDE, GI PROTEINS AND REGULATION OF BLOOD PRESSURE**

E. Hossain, O. Sarkar, Y. Li, **M.B. Anand-Srivastava**

University of Montreal, Montreal, Quebec, Canada

Nitric oxide (NO) donors are used as promising therapeutic agents for the treatment of cardiovascular diseases such as angina pectoris, myocardial infarction and congestive heart failure, however, the molecular mechanisms underlying the therapeutic activities remains poorly understood. We previously showed that nitric oxide (NO) donor, SNAP, decreased the enhanced expression of Gialpha proteins and associated functions in aortic vascular smooth muscle cells (VSMC) from spontaneously hypertensive rats (SHR). Since the enhanced expression of Gialpha proteins is implicated in the pathogenesis of hypertension, the present study was undertaken to investigate the effect of in vivo treatment of SHR with NO donor; sodium nitroprusside (SNP) on the development of high blood pressure (BP) and to explore molecular mechanisms responsible for this response. 8 week-old SHR and Wistar-Kyoto (WKY) rats were intraperitoneally injected with SNP at a concentration of 0.5mg/kg body weight twice a week for two weeks. Western blotting was used to determine the expression of various proteins. Intraperitoneal injection of SNP attenuated the high BP by about 50 mmHg; however, this treatment did not affect BP in WKY rats. In addition, increased production of superoxide anion, peroxynitrite, NAD(P)H oxidase activity, overexpression of different subunits of NAD(P)H oxidase, superoxide dismutase 1 /2, Gialpha proteins, AT1 receptor, increased phosphorylation of growth factor receptors, c-Src, and ERK1/2 in aortic VSMC from SHR were attenuated to WKY levels by SNP treatment. Furthermore, the hyperploliferation of VSMC from SHR was also inhibited by SNP treatment. In conclusion, we show that in vivo treatment of SNP attenuates the high BP in SHR through the inhibition of enhanced levels of Gialpha proteins, oxidative stress, and oxidative stress-mediated signaling pathways and suggest that the new therapies targeting Gialpha proteins may be developed for the treatment of hypertension

(Supported by grant from CIHR).