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ORAL PRESENTATION

Open Access

Genetic modifiers of hypertension in sGC-deficient mice

Emmanuel Buys

From 6th International Conference on cGMP: Generators, Effectors and Therapeutic Implications
Erfurt, Germany. 28-30 June 2013

Background

Hypertension is an important modifiable risk factor for coronary heart disease, congestive heart failure, stroke, end-stage renal disease, and peripheral vascular disease. Many of the molecular mechanisms and genetic factors underlying the development of the most common forms of human hypertension remain to be defined. Nitric oxide (NO) and one of its primary targets, the cyclic guanosine monophosphate (cGMP) generating enzyme soluble guanylate cyclase (sGC), play an essential role in regulating blood pressure, in part by modulating relaxation of vascular smooth muscle.

Results

Male mice deficient in the $\alpha 1$ subunit of soluble guanylate cyclase (sGC $\alpha 1^{-/-}$ mice) are prone to hypertension in some, but not all, mouse strains, suggesting that additional genetic factors contribute to the onset of hypertension associated with sGC $\alpha 1$ -deficiency. Using linkage analyses, we discovered quantitative trait loci (QTL) that were linked to mean arterial pressure (MAP) in sGC $\alpha 1^{-/-}$ mice. One locus is syntenic with previously identified blood pressure-related QTLs in the human and rat genome and contains the genes coding for renin. Hypertension in sGC $\alpha 1^{-/-}$ mice was associated with increased activity of the renin-angiotensin-aldosterone system (RAAS) and RAAS inhibition normalized MAP and improved endothelium-dependent vasorelaxation in sGC $\alpha 1^{-/-}$ mice.

Conclusion

These data identify the RAAS as a blood pressure-modifying mechanism in a setting of impaired NO/cGMP signaling [1].

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Reference

1. Buys ES, Raheer MJ, Kirby A, Mohd S, Baron DM, Hayton SR, Tainsh LT, Sips PY, Rauwerdink KM, Yan Q, Tainsh RET, Shakartzi HR, Stevens C, Decaluwé K, Rodrigues-Machado MDG, Malhotra R, Van de Voorde J, Wang T, Brouckaert P, Daly MJ, Bloch KD: **Genetic modifiers of hypertension in soluble guanylate cyclase $\alpha 1$ -deficient mice.** *J Clin Invest* 2012, **122**:2316-2325.

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