Nature Reviews Nephrology **11**, 255 (2015); published online 17 March 2015; doi:10.1038/nrneph.2015.32

HYPERTENSION

Redox-sensitive transcription factors regulate the renal dopamine receptor

Aberrant functioning of the renal dopamine receptor (D1R) under conditions of oxidative stress has been associated with elevated blood pressure. New research led by Anees Banday has now identified a mechanism by which D1R might become dysregulated under conditions of oxidative stress.

The researchers used *in vivo* and *in vitro* analyses to examine the role of the redox-sensitive transcription factors AP1 and SP3 in regulating D1R. Rats and cultured HK2 cells were exposed to the pro-oxidant L-buthionine sulfoximine (BSO), to induce oxidative stress. BSO treatment caused downregulation of *D1R* mRNA in both models compared to controls, paralleled by an increase in the nuclear expression of SP3 and AP1. A reduction in D1R membrane expression following BSO treatment was illustrated by the inability of a D1R agonist to inhibit Na/K–ATPase activity in cultured cells. Treatment with tempol, an antioxidant, abolished the effects of BSO.

Transfection studies using small interfering RNAs (siRNAs) led the researchers to determine that AP1 is located upstream of SP3 in the D1R redox signalling cascade. BSO failed to downregulate D1R in cells treated with either AP1 or SP3-specific siRNA, implicating the necessity of an intact AP1–SP3 transcriptional axis in this process.

"Loss of renal D1R function because of oxidative stress could be a significant risk factor for oxidative stress-associated hypertension," propose the researchers. They say that these new data highlight the importance of the renal dopamine system in blood pressure regulation.

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Original article Banday, A. A. *et al.* Transcriptional regulation of renal dopamine D1 receptor function during oxidative stress. *Hypertension* doi:10.1161/HYPERTENSIONAHA.115.05255

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