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Angiotensin type 1 receptors regulate a specific set of micro RNA's in cardiovascular tissues including human arteries

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The Angiotensin II type 1 receptor (AT1R) is a key regulator of blood pressure and cardiac contractility and it is profoundly involved in development of cardiac disease as illustrated by the widespread use of AT1R blockers. Since several microRNAs (miRNAs) have been implicated in cardiac disease, we asked whether miRNAs might be regulated by AT1R signals *in vitro* using primary cardiac myocytes and fibroblasts and *in vivo* using aortas from rats with AngII induced hypertension and isolated arteries from patients with cardiovascular disease.

We first performed global miRNA microarray analysis of angiotensin II (Ang II) mediated miRNA regulation in HEK293N cells over-expressing the AT1R followed by verification with quantitative PCR in HEK293N cells, cardiac myocytes and fibroblasts. These experiments revealed several miRNAs (miRNA-7, miRNA-29b, miRNA-129-3p, miRNA-132, and miRNA-212) that were upregulated by Ang II. We next infused AngII in Wistar rats to investigate in vivo regulation. All candidate miRNA's except miR-29b were also up-regulated in rat aortas after chronic AngII infusion. Strongly supporting differentially expressed candidate miRNA's and securing human relevance, we extended these findings to human arteries. Relevant candidate miRNA's were measured in human arteries from 16 patients treated with and 16 not treated with AT1R blockers. Remarkably, we found a robust decrease in a set of miRNA's including miR-7. We are currently examining target molecules in our different experimental systems.

The perspective is that the identified miRNAs may be involved in Ang II-mediated cardiac biology and disease. This is important since modified miRNA and anti-miRNA molecules have been reported to work directly as drugs opening novel pharmacological venues.

Keywords: Renin Angiotensin System, Angiotensin type 1 receptor blockers, microRNA, cell signalling, cardiovascular disease, human arteries.