

## **Kidney DNA methylation as a driver of genetic changes in hypertension**

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**Objectives:** Hypertension is associated with various physiological changes that result in an increased risk of stroke, cardiovascular events and chronic kidney disease. Here we conducted a genome-wide analysis of methylation changes in the human kidney to identify epigenetic signatures of hypertension using the largest collection of apparently healthy human renal tissue. As the first analysis of its kind in the human kidney we also determined whether these changes have functional consequences at the gene expression level. **Methods:** We examined DNA extracted from a total of 94 human kidneys to investigate methylation patterns in hypertension. We also examined RNA-sequencing to characterise the transcriptome of 180 human kidneys to uncover interactions between DNA methylation and gene expression. **Results:** Our methylation analysis identified one hypertension-associated CpG site, three systolic blood pressure-associated CpG sites and 19 diastolic blood pressure-associated CpG sites; including four CpG sites previously identified in peripheral blood studies of hypertension. DNA methylation is a known regulator of gene expression; therefore, we investigated whether differential DNA methylation in proximity to hypertension-associated renal genes correlated with their renal expression. Methylation of two genes (FAM50B, PC) showed an association with renal expression. The transcriptome analysis of 180 kidneys revealed 14 hypertension-associated genes, 1 gene associated with systolic blood pressure and 6 genes associated with diastolic blood pressure; including those involved in smooth muscle response to blood pressure fluctuation and blood pressure response to salt intake in humans. **Conclusion:** Our study uncovered DNA methylation as a new regulatory mechanism underpinning hypertension-related changes in renal gene expression.

**Keywords:** hypertension, kidney, epigenetics, DNA methylation, RNA-seq, blood pressure