

SPECIFICITY OF DNA METHYLATION PATTERNS IN THE HYPERTENSIVE KIDNEY

Wise IA^a, Prestes P^a, Tomaszewski, M^b, Charchar FJ^{a,c}

^aFederation University Australia, Ballarat, Victoria, Australia; ^bUniversity of Manchester, Manchester, UK; ^cUniversity of Melbourne, Parkville, Victoria, Australia

Background: Evidence suggests that DNA methylation (5mC) is important in the development of essential hypertension (EH). The 5mC percentage, a measurement for global methylation studies, in peripheral blood leukocytes (PBL) has been previously associated with hypertension. Methylation patterns are tissue-specific, contributing to differences in transcriptional regulation and cellular differentiation. So far, there have been no studies of 5mC in the kidney – an important effector organ in EH. Furthermore, there has been no investigation of the relationship between 5mC patterns in the hypertensive kidney and PBLs.

Aims: (i) To determine if global 5mC in the kidney is correlated to hypertension diagnosis and blood pressure (BP) regulation. (ii) To determine whether PBLs provide a surrogate for cross-tissue patterns of 5mC in the kidney.

Methods: We used 96 human kidney and 76 human PBL samples from the TRANSLATE study to investigate global 5mC percentage. TRANSLATE consists of carefully characterized collections of “apparently healthy” specimens of human kidneys. Global methylation was determined using the 5mC ELISA kit (Zymo Research) that measures the total amount of 5mC present in a sample.

Results: We found no association of global 5mC percentage in kidney ($P=0.18$) and PBL ($P=0.54$) with hypertension diagnosis, nor between PBL 5mC percentage and BP. However, a negative correlation was found between kidney 5mC percentage and systolic BP ($r=-0.246$; $P<0.05$), and diastolic BP ($r=-0.319$; $P<0.01$). This association was still evident after adjustment for antihypertensive medication for systolic BP ($r=-0.210$; $P<0.05$) and diastolic BP ($r=-0.273$; $P<0.01$). Furthermore, we found a strong positive correlation between normotensive kidneys and leukocyte 5mC percentages ($r=0.864$; $P<0.01$). Similarly, a strong positive correlation was evident for hypertensive kidneys and leukocyte 5mC percentages ($r=0.916$; $P<0.01$).

Conclusion: Our findings show that kidney 5mC, but not PBL 5mC, is correlated to BP regulation. No relationship was evident for global 5mC and hypertension diagnosis, regardless of the tissue type studied. Furthermore, PBL 5mC global methylation percentage was highly correlated to kidney 5mC percentage. These results highlight the importance of further studies on the involvement of kidney DNA methylation in hypertension, as well as further investigation of the relationship between methylation patterns in the kidney and blood.