

Epigenetics and arterial hypertension: the challenge of emerging evidence

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Abstract

Epigenetic phenomena include DNA methylation, post-translational histone modifications, and noncoding RNAs, as major marks. Although similar to genetic features of DNA for their heritability, epigenetic mechanisms differ for their potential reversibility by environmental and nutritional factors, which make them potentially crucial for their role in complex and multifactorial diseases. The function of these mechanisms is indeed gaining interest in relation to arterial hypertension (AH) with emerging evidence from cell culture and animal models as well as human studies showing that epigenetic modifications have major functions within pathways related to AH. Among epigenetic marks, the role of DNA methylation is mostly highlighted given the primary role of this epigenetic feature in mammalian cells. A lower global methylation was observed in DNA of peripheral blood mononuclear cells of hypertensive patients. Moreover, DNA hydroxymethylation appears modifiable by salt intake in a Dahl salt-sensitive rat model. The specific function of DNA methylation in regulating the expression of AH-related genes at promoter site was described for hydroxysteroid (11-beta) dehydrogenase 2 (HSD11B2), somatic angiotensin converting enzyme (sACE), Na⁺/K⁺/2Cl⁻ cotransporter 1 (NKCC1), angiotensinogen (AGT), α -adducin (ADD1), and for other crucial genes in endocrine hypertension. Post-translational histone methylation at different histone 3 lysine residues was also observed to control the expression of genes related to AH as lysine-specific demethylase-1 (LSD1), HSD11B2, and epithelial sodium channel subunit α (SCNN1A). Noncoding RNAs including several microRNAs influence genes involved in steroidogenesis and the renin-angiotensin-aldosterone pathway. In the present review, the current knowledge on the relationship between the main epigenetic marks and AH will be presented, considering the challenge of epigenetic patterns being modifiable by environmental factors that may lead toward novel implications in AH preventive and therapeutic strategies.