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ALDOSTERONE AS AN ADAPTIVE REGULATOR OF ELECTROLYTE HOMEOSTASIS BEYOND CLASSICAL GENOMIC MECHANISMS

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Aldosterone is historically perceived as a steroid hormone that controls the electrolyte balance by activating an intracellular mineralocorticoid receptor which results in gene transcription in a time range of several hours. This classical genomic framework however falls short in explaining the high-rate physiological responses needed to adapt to changing environmental conditions including change in hydration status, temperature, and salinity. There is growing evidence of a more significant and active role of aldosterone in environmental adaptation (Guinn et al., 2024).

This review summarizes the existing evidence regarding three complementary processes that widen the knowledge of aldosterone physiology. To begin with, aldosterone has been demonstrated to cause non-genomic effects that are fast in action and involve membrane-associated receptors. These processes are done in a few seconds to minutes and include the stimulation of intracellular signaling pathways, such as calcium-dependent cascades and mitogen-activated protein kinases (Guinn et al., 2024). These pathways control ion-binding transporter proteins in kidney epithelial cells, which can instantly adjust the sodium and protons exchange regardless of transcriptional action.

Second, tissue-specific sensitivity to aldosterone is influenced by local corticosteroid metabolism. The local supply of active glucocorticoids and mineralocorticoids is controlled by enzymatic systems and in particular by the 11β-hydroxysteroid dehydrogenase isoforms. This generates microenvironmental disparities in nephron segments and other tissues, which permits the electrolyte movements and fluid balance to be fine-tuned (Good, 2007).

Third, new evidence indicates that environmental exposures can cause changes in the epigenetics of adrenal zona glomerulosa cells, which produce aldosterone. Moving shifts in chromatin accessibility and histone modification patterns at important steroidogenic genes, including cytochrome CYP11B2 and steroidogenic acute regulatory protein, can be part of a kind of metabolic memory (Parati et al., 2026). This process offers a possible explanation of long-term adaptation to recurrent environmental stresses, such as dehydration and thermal stress.

Recent discoveries of mechanosensitive ion channels, especially type PIEZO2, in renal juxtaglomerical cells provide another connection of physical forces to hormonal regulation. These channels react to alterations in blood volume and blood pressure, and they affect renin release, thus, altering the renin-angiotensin-aldosterone system. This result indicates one of the direct pathways according to which mechanical stimuli can influence the aldosterone dynamics.

Together, these processes contribute to a revised conceptual framework where aldosterone can be considered an integrative controller of both short and long-term physiological adjustments to environmental changes. This view can be used to understand the variability in individual salt sensitivity and can help in enhancing the understanding of hypertension disorders and fluid balance disorders. Future studies of these pathways can offer novel treatment targets to the dysregulated diseases related to aldosterone signaling.