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Mineralocorticoid Receptor Signaling in Hypertension

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Abstract

The actions of the mineralocorticoid, aldosterone, are mediated by the mineralocorticoid receptor (MR), a member of the nuclear receptor superfamily of ligand-dependent transcription factors. The MR appears in vertebrate evolution before aldosterone and indeed responds to two physiological ligands, aldosterone and cortisol (and also perhaps a third, progesterone). In epithelial tissues, aldosterone selectivity is determined by 11β-hydroxysteroid dehydrogenase type II. In other tissues cortisol is the primary ligand with multiple roles in cardiovascular function, immune cell signalling, neuronal function and adipocyte differentiation. These actions, beyond simply sodium homeostasis and hypertension, contribute to the disproportionate morbidity associated with hyperaldosteronism and the benefit observed more broadly in cardiovascular disease with the use of MR antagonists. This diversity of responses at the MR, including ligand- and tissue-specificity, is achieved through critical interactions involved in MR-mediated signal transduction. Signalling is initiated by ligand-binding which confers a ligand-specific, agonist or antagonist, conformation upon the receptor. This conformation then determines subsequent interactions within the receptor, with other transcription factors independent of DNA-binding, and with coregulatory molecules. Relatively few coregulators have however been described for the MR although our recent studies have demonstrated both ligand and/or tissue-selectivity for MR-coregulator interactions. The successful identification of the structural basis of antagonism at the MR, and of ligand-specific interactions of the MR, may provide the basis for the development of novel ligands with the ability to modulate the MR response and provide tissue specificity. *[J Assoc Clin Endocrinol Diabetol Bangladesh, 2025;4(Suppl 1): S5]*

Keywords: Mineralocorticoid receptor (MR), Aldosterone, MR antagonists

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