LETTER TO THE EDITOR

Function of human mineralocorticoid receptor splice variant

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In their recent paper, Pascual-Le Tallec et al. (1) state that a publication by Bloem et al. (2) describes that a mineralocorticoid receptor (MR) splice variant with a 12 bp insertion coding for a protein with four additional amino acids (MR+4) shows no functional difference to the MR without insertion. This evidence is not produced in the publication by Bloem et al. or to our knowledge anywhere else. On the contrary Bloem et al. propose that the additional four amino acids residues in the DNA binding domain could alter binding to a glucocorticoid response element (GRE) and transcription activation. Because this splice variant shows considerable concentrations in various human tissues (3), we have compared transactivation mediated by MR and MR+4. The plasmid pchMR+12 coding for hMR+4 was created by in vitro PCR mutagenesis of pchMR coding for hMR. Transactivation of both variants by aldosterone was analysed in CV-1 cells by measuring firefly luciferase activity of an inducible reporter gene normalised to the activity of constitutively expressed renilla luciferase (Fig. 1) (4).

References


Received 23 April 2004
Accepted 3 May 2004

Figure 1 Aldosterone produced a concentration-dependent transactivation of the reporter gene. Half the maximal transactivation (ED50) was achieved near log 11 M aldosterone regardless of whether hMR or hMR+4 was expressed. There was a tendency toward a slightly lower ED50 (higher sensitivity) and somewhat weaker transactivation when MR+4 was expressed. The data justify the statement by Pascual-Le Tallec et al. (1) that the function of hMR+4 is comparable to that of hMR.