BIOCHEMICAL JOURNAL LETTERS

Homology between neurohypophyseal hormone receptors

The hormones [Arg^8]vasopressin and oxytocin generate a wide range of physiological effects, including antidiuresis, vasoconstriction, milk ejection and uterine contraction (Michell et al., 1979; Soloff et al., 1979). Research addressing how these neurohypophyseal peptides function at the molecular level has recently been advanced by the cloning of several receptor proteins which mediate the multifarious actions of these hormones (Morel et al., 1992; Lolait et al., 1992; Birnbaumer et al., 1992; Kimura et al., 1992).

During our studies on rat testes (M. Wheatley, J. Howl, R. Lavis, S. Rudge, C. J. Kirk and A. R. L. Davies, unpublished work), we have isolated a full-length clone of a vasopressin V_{1a} receptor, using the PCR with primers based on the recently published sequence of the rat liver V_{1a} receptor (Morel et al., 1992). Sequencing revealed the clone from testes to be identical with the published sequence, except that it possessed three additional bases. Re-sequencing the original clone of the liver V_{1a} receptor (both sense and antisense strands) established that the three extra bases were also present in this clone. The difference between the sequence of the V_{1a} receptor from testes and the reported sequence of the liver V_{1a} receptor was therefore a sequencing error in the original report (Morel et al., 1992), and was not due to tissue-specific receptor subtypes or to an error introduced into the testes' vasopressin-receptor sequence by *Taq* polymerase. This is not a trivial finding, as, in addition to the protein being 395 amino acids (M_r 44478) rather than 394, the extra bases change the reading frame of part of the V_{1a} receptor sequence (Figure 1). This sequence corresponds to the N-terminal half of the first extracellular loop of the receptor. As it has been hypothesized that this domain may have a role in ligand binding/recognition (Sharif and Hanley, 1992), it is noteworthy that this loop of the V_{1a} receptor displays a far greater sequence homology with other members of the neurohypophyseal hormone receptor family than was previously thought (Figure 2), but it is not homologous among G-protein-coupled receptors in general. Consequently, this may constitute part of the molecular basis for the well-documented lack of receptor-specificity exhibited by many analogues of vasopressin and oxytocin (Manning et al., 1987).

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325                                   357
CTATGCTGGGACATCACCTACCGCTTCCGCGGG
LeuCysTrpAspIleThrTyrArgPheArgGly
109                                   119
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Figure 1 Corrected sequence of the V_{1a} receptor

Bases in **bold** were omitted in the original report (Morel et al., 1992); the subsequent amino acid changes are underlined. Only the relevant domain is shown, with its position in the full sequence indicated by the number of the base and amino acid residue.

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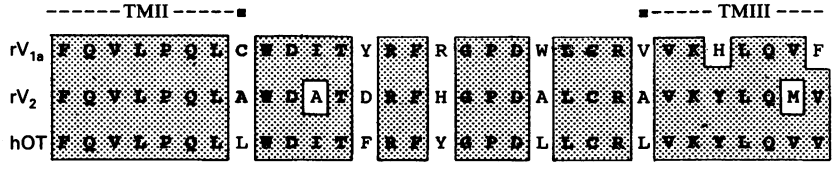

Figure 2 Alignment of neurohypophyseal hormone receptor sequences

Only the sequence of the first extracellular loop is shown between putative transmembrane domain (TM) II and III. Abbreviations: rV_{1a}, rV_2, rat V_{1a} and V_2 vasopressin receptors (Lolait et al., 1992); hOT, human oxytocin receptor (Kimura et al., 1992). Identical residues are enclosed in shaded boxes.