

**P015** Are functionally important contacts established between the N-terminus and extracellular loop-1 of the  $V_{1a}$  vasopressin receptor?

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The  $V_{1a}$  vasopressin receptor ( $V_{1a}R$ ) is a Family A G-protein-coupled receptor (GPCR), activated by the neurohypophysial peptide hormone [arginine<sup>8</sup>]vasopressin (AVP). We have previously shown that Arg<sup>46</sup> in the N-terminus of the  $V_{1a}R$  is essential for the high affinity binding of AVP to the  $V_{1a}R$ . This arginyl residue is conserved in all members of the neurohypophysial peptide hormone receptor family suggesting an important role in the functioning of these receptors. The exact function and mechanism of action of Arg<sup>46</sup> has yet to be elucidated, although it is believed to play a role in constraining the inactive state or the  $V_{1a}R$ . Furthermore, Arg<sup>46</sup> can not be functionally substituted by any other residue, including Lys. Residues in extracellular loop-1 (ECL1) have also been implicated in high affinity agonist binding using a range of approaches including peptide mimetics, mutagenesis and direct labelling by a photoaffinity analogue of AVP. This study investigates if there is any functional interaction between Arg<sup>46</sup> in the N-terminal domain and specific residues in ECL1 using a combination of reciprocal mutagenesis and pharmacological characterisation.