

**P020** The role of second extracellular loop of the CGRP receptor in ligand recognition

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Calcitonin-gene related peptide (CGRP) is a 37 amino acid neuropeptide. The CGRP receptor is a heterodimer of a family B G-protein coupled receptor, calcitonin receptor-like receptor (CLR) and a single-pass transmembrane protein, receptor activity modifying protein 1 (RAMP1). Receptor activation is likely to require an interaction between the N-terminus of CGRP and the extracellular loops of CLR. We have investigated the residues within the second extracellular loop of CLR needed for receptor activation by means of an alanine scan. Point mutants were introduced into CLR by the Stratagene Quikchange mutagenesis kit. The ability of CGRP to stimulate cAMP production in the mutated receptor was measured. following transfection into Cos 7 cells. For R252A, Y255A, D256A, C260A, W261A, S263A and T266A, there was a significant decrease in the pEC<sub>50</sub> for CGRP, indicating that these all contributed, either directly or indirectly to the recognition of CGRP by the receptor.

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