

P023 Pharmacological characterisation of the rat corticotropin-releasing factor (CRF) type 2 β receptor (CRF-R_{2 β}) in transfected CHO cells and identification of a novel splice variant (CRF2del)

Julie M.-N. Rainard, Stewart E. Mireylees and Mark G. Darlison

School of Biomedical and Natural Sciences, Nottingham Trent University, Clifton Lane, Nottingham NG11 8NS

A full-length CRF-R_{2 β} complementary DNA (cDNA) was cloned from rat heart and transiently transfected into Chinese Hamster Ovary (CHO) cells. These were used to determine the effects of rat/human CRF, mouse urocortin I, rat urocortin II and mouse urocortin III on intracellular cAMP levels using a chemiluminescent assay. CRF ($pEC_{50} = 7.4 \pm 0.09$; 41.4nM), urocortin I ($pEC_{50} = 9.8 \pm 0.08$; 0.17nM), urocortin II ($pEC_{50} = 6.23 \pm 0.07$; 0.6mM) and urocortin III ($pEC_{50} = 9.55 \pm 0.11$; 0.3nM) stimulated cAMP accumulation in a concentration-dependent manner. During cloning, an alternatively-spliced variant of CRF-R_{2 β} (CRF2del) was found, which has an in-frame deletion of 21 amino acids that includes most of the fourth transmembrane domain. As expected, loss of this sequence resulted in a receptor with no pharmacological response to any of the ligands previously tested. Furthermore, co-transfection with CRF2del did not appreciably alter the pharmacology of the wild-type CRF-R_{2 β} . However, CRF2del mRNA was shown to be present, together with the wild-type receptor transcript, in a range of neonatal and adult rat tissues suggesting that it has an, as yet, undiscovered physiological function.