

P003 Pharmacological characterisation of the AMY_{1(a)} receptor
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Calcitonin (CT) receptors dimerise with receptor activity modifying proteins (RAMPs) to create high affinity amylin (AMY) receptors. Although characterised by binding, the functional effects of different antagonists at these receptors have not been evaluated in detail. Here, we transiently transfected COS-7 cells with the human (h) CT_(a) receptor with or without hRAMP1 and assessed the effects of antagonists through assay of cAMP responses. Agonist potency at CT_(a) was, hCT >> rAMY = βCGRP, all other agonists tested were very weak. At AMY_{1(a)} (CT_(a)/RAMP1) the order was, hCT = rAMY = αCGRP > βCGRP > Tyr⁰αCGRP = [Cys(Et)^{2,7}]hαCGRP = [Cys(ACM)^{2,7}]hαCGRP > adrenomedullin. At CT_(a), the rank order of antagonism of hCT and rAMY responses was salmon CT₈₋₃₂ > AC187 ≥ AC413. AMY₈₋₃₇, CGRP₈₋₃₇ and adrenomedullin₂₂₋₅₂ were without effect. At AMY_{1(a)}, a similar profile was observed with hCT as the agonist. With rAMY, however, the profile changed to, salmon CT₈₋₃₂ = AC187 = AC413 > CGRP₈₋₃₇, AMY₈₋₃₇, and adrenomedullin₂₂₋₅₂ were again without effect. The affinity of CGRP₈₋₃₇ that we report for AMY_{1(a)} is comparable with that for putative CGRP₂ receptors. This potential explanation for CGRP₂ receptors is consistent with previous reports that CGRP₈₋₃₇ is an antagonist of amylin receptors and early reports that amylin was acting via CGRP receptors to produce its biological effects.