

P023 Regulation and distribution of three splice variants of AC8
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Three alternatively spliced isoforms of the Ca^{2+} -sensitive adenylyl cyclase type 8 (AC8) have been identified. Whereas AC8 A is the full length protein, AC8 B lacks a 30 amino acid stretch in an extracellular domain, which contains two putative N-linked glycosylation sites, and AC8 C lacks 66 amino acids in a cytoplasmic domain, C1b, close to the catalytic core. We speculated that these deletions may have a profound impact on both the targeting and the regulation of these enzymes. In vivo assays in HEK 293 cells transfected with AC8 A, AC8 B or AC8 C showed that all three splice variants are robustly stimulated by capacitative Ca^{2+} entry, which is triggered by the depletion of intracellular Ca^{2+} stores. However, only AC8 A was stimulated by Ca^{2+} release from intracellular stores. Imaging GFP-tagged AC8 constructs revealed that AC8 A is exclusively localised to the plasma membrane, whereas AC8 B and AC8 C adopt a predominantly intracellular distribution. The differences in the distribution and regulation of these splice variants may enable the cell to produce cAMP in response to different types of stimuli and/or produce high local concentrations of cAMP in different cellular regions.