

P005 Identification Of Assembly Signals Within GABA_A Receptor Subunits

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γ -Aminobutyric acid type A (GABA_A) receptors are the major sites of fast synaptic inhibition in the brain. In mammals, they are constructed as pentameric structures from multiple subunits selected predominantly from the following distinct classes: α (1-6), β (1-3), γ (1-3), δ , ϵ , θ and σ , creating an incredible (16^5) potential for structural diversity. In support of the existence of differential assembly signals, GABA_A receptor assembly appears to be strictly controlled, producing receptors with a fixed stoichiometry of 2 α , 2 β and 1 γ . Furthermore, GABA_A receptor assembly signals have been identified in the α 1, α 1 β 2/3 and γ 3 subunits. Consistent with the location of these assembly signals to intersubunit contact points, the α/γ signals are located proximal to the GABA and benzodiazepine binding sites formed at subunit interfaces between the α - β and α - γ subunits respectively. Using site-directed mutagenesis, we have determined that the conversion of a single amino acid is sufficient to alter the assembly profile of the α 1 subunit. Furthermore, we present evidence for the existence of alternative assembly signals, which may permit the formation of diverse receptor types, dependent upon subunit availability.