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Sica, Mauricio P.

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Membrane Transporters and Channels

Structural and functional characterization of human heteromeric 5-HT3 receptors.

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5-HT3 receptors are members of the Cys-loop receptor family that mediate fast excitatory transmission in central and peripheral nervous system. Genes for five different subunits (A-E) have been identified in humans, and most of the subunits have multiple isoforms. The A subunit is capable of forming functional homomeric (5-HT3A), or heteromeric receptors with the B subunit (5-HT3AB). Here we combine single-channel and macroscopic current recordings to determine if other 5-HT3 subunits, Br1, Br2, C, D and E (B-E), can combine with the A subunit to form heteromeric receptors. After co-expression of the A subunit with each of the tested subunits, single-channel events with different conductance and kinetic properties with respect to those of 5-HT3A receptors were detected, except for the Br2 subunit. These results indicate that B-E subunits can assemble into functional heteromeric receptors with the A subunit. From the corresponding recordings, the analysis of the single-channel amplitude of the opening events suggests a possible stoichiometry for each heteromeric receptor, since each subunit (B-E)