

Serotonin Club Satellite Meeting

Plenary Lectures

SC Plenary 1

How the serotonin story is being rewritten by new gene-based discoveries

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Discovered over 50 years ago, serotonin's important functions in brain and body became identified over the next years by neurochemical, physiological and pharmacological investigations. This 2008 Rapport Lecture will focus on some of the most recent historical developments in serotonin science that are based on genetic methodologies. These include the consequences resulting from direct serotonergic gene manipulation (gene deletion or overexpression) in mice and other species; on phenotypes related to functional human serotonergic gene variants; and on pharmacogenomic investigations of serotonergic drugs, including both their therapeutic actions and their side effects. The serotonin transporter (SERT) has been the best studied of serotonin system molecular components, and will be the primary focus of this Lecture, providing a prime example of gene-based discoveries that have clarified serotonin's many important homeostatic functions in humans and other species.

SC Plenary 2

5-HT₄ receptors: history, molecular pharmacology and brain functions

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Twenty years ago, we started the characterization of a 5-HT receptor coupled to cAMP production in neurons. This receptor obviously had a pharmacology different to the other 5-HT receptors described at that time, i.e. the 5-HT₁, 5-HT₂, 5-HT₃ receptors. We proposed to name them 5-HT₄ receptors. Nowadays, 5-HT₄ receptors are one of the most studied GPCRs of the 'rhodopsin' family. Thanks to the existence of a great variety of ligands with inverse-agonist, partial agonists, agonists and antagonist profiles, the pharmacological and physiological properties of this receptor are slowly emerging. Although some 5-HT₄ partial agonists have been on the market for gastro-intestinal pathologies, no 5-HT₄ receptor drugs have been commercialized yet for brain disorders. However, since 5-HT₄ receptors have recognized effects on memory, depression and feeding in animal models, there is still hope for a therapeutic destiny of this interesting target, in brain disorders.