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The σ_1 receptor as target for novel drugs

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Originally the opioid receptor was subclassified into three subtypes, which were termed after their prototypical ligands μ (morphine), κ (ketocyclazocine) and σ receptors (SKF-10, 047). However, this hypothesis was disproved, since the pharmacological effects of typical σ receptor drugs were not reversed by the opioid receptor antagonists naloxone and naltrexone. Finally, σ receptors were recognized as specific, non-opioid, non-PCP, but haloperidol-sensitive binding sites consisting of σ_1 and σ_2 subtypes. The two σ receptor subtypes can be differentiated by molecular weight, tissue distribution, and ligand binding profile. It has been shown that the σ_1 receptor plays an important role in several socially relevant human diseases including schizophrenia, depression, Alzheimer's disease, and drug/alcohol addiction. Antagonists at the σ_1 receptor potentiate the pain-relieving effects of opioid analgesics and, moreover, can be used for the treatment of neurogenic pain. Due to their overexpression in several human tumor cell lines, σ_1 and σ_2 receptors are interesting targets for tumor therapy and diagnosis. In the lecture the interactions of ligands with the binding site of the σ_1 receptor are analyzed. The design and synthesis of novel σ_1 receptor ligands is presented. Spirocyclic piperidines and bridged piperazines represent very promising σ_1 receptor ligands for further pharmacological evaluation. The development of a PET tracer for the imaging of σ_1 receptors in the central nervous system is shown.

Biography

Bernhard Wünsch has completed his PhD in 1987 from the University of Munich. After postdoctoral studies at the University of Berlin, he finished his habilitation in 1993. Then he moved to the University of Freiburg and finally to the University of Münster, where he is director of the Institute of Pharmaceutical and Medicinal Chemistry. He has been the dean of the faculty from 2005-2006. He is member of the collaborative research center 656 (Molecular Cardiovascular Imaging) and the Cluster of Excellence CiM (Cells in Motion). He has published more than 200 papers in reputed journals.

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