The Predicted Three-Dimensional Structure of the Rat Somatostatin II Receptor

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The Somatostatin II receptor is a member of a family of 5 distinct membrane bound G-Protein Coupled Receptors which bind the neuroendocrine peptides Somatostatin-14, Somatostatin-28 and Cortistatin. They have important physiological roles in inhibiting hormone secretion, particularly the secretion of growth hormone, Insulin, Glucagon and Gastrin, inhibiting exocrine secretion by the pancreas and stomach, and modulating neuronal excitability and smooth muscle contraction. Somatostatin further acts as a regulator of function in diabetes mellitus, epilepsy, Alzheimer and Huntington Disease and even AIDS. Additionally, many neuroendocrine tumors express high levels of Somatostatin receptors and, because of their ability to inhibit tumor cell secretion as well as proliferation, Somatostatin analogs are now used to target these receptors both for cancer therapy and diagnosis. Using MembStruk, the structure of the Rat Somatostatin II receptor has been predicted from first principle. The structure is further validated through the use of HierDock to predict the binding site of a synthetic antagonist. The predicted site is an appropriate surface for somatostatin and analogues of somatostatin and encompasses both experimentally determined as well as novel residues essential for ligand binding.