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Overview of lipid-sensing GPCR receptors structure and function

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Motivation and Aim: G protein-coupled receptors (GPCR) are the most important class of membrane proteins in the human body, responsible for carrying out a wide range of physiological functions, such as maintaining homeostasis of cell metabolism, modulating the transmission of nerve impulses and immune system activity, visual and olfactory perception, regulating processes in the cardiovascular system.

Endogenous ligands for GPCR represent a wide spectrum of chemical entities - amino acids and ions, proteins and peptides, nucleotides and biogenic amines, bioeffector lipids. We are aimed at structural and functional studies of lipid GPCRs that regulate various processes in the central nervous system (CNS). Examples of lipids that are ligands for GPCR are lysophospholipids, fatty acids, endocannabinoids, prostaglandins, sphingolipids, eicosanoids, leukotrienes, and other arachidonic acid derivatives.

Structural studies combined with extensive biophysical, biochemical, and pharmacological characterization help to develop a better understanding of these receptors' molecular mechanism of action and initiate rational drug development.

Methods: *X-Ray Crystallography at microfocus beamlines of synchrotron sources and X-Ray Free Electron Lasers combined with functional assays, structure-activity relationship studies, molecular modeling and docking.*

Results: In this report we will discuss the structural and functional peculiarities of lipid-sensing GPCRs, including the three representatives, for which the structure was recently obtained by our team: CysLT1 [1], CysLT2 [2], $S1P_5$ [3].

Conclusions: Further complex structural and functional studies of lipid-sensing receptors need to be carried out to find answers to fundamental questions about the molecular mechanisms of their functioning and the rational creation of drugs. A lot of works have appeared that expand the understanding of their biomedical significance, and new methods and approaches in research have been developed.

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