

ケミカルバイオロジー研究所

Research Institute for Chemical Biology

第 50 回 ケミカルバイオロジー研究所セミナー
第 134 回 生物科学フロンティアセミナー

Prof. Annette G. Beck-Sickinger

(独) ライプチヒ大学・生化学科

Institute of Biochemistry, Faculty of Life Sciences,

Leipzig University

G PROTEIN-COUPLED PEPTIDE RECEPTORS: STATE OF THE ART AND INNOVATIVE THERAPEUTIC CONCEPTS

令和 5 年 11 月 7 日 (火) 10:45~11:45

A13 棟 323 号室 (講義室 B)

Peptides hormones play an important role in the regulation of manifold activities in the body. Many of them transmit their activity through G protein-coupled receptors (GPCR), which are among the most promising drug targets nowadays. However, in addition to their direct activity, indirect mechanisms have been shown to play an important role, e. g. as drug shuttles in tumour targeting. Accordingly, in addition to ligand binding, internalization has to be addressed and to be studied, including arrestin recruitment. The neuropeptide Y/pancreatic polypeptide family contains 36 amino acid peptides, which bind to four different so-called Y-receptors in human. By a combination of X-ray analysis, cryo-EM, NMR, molecular modelling and crosslinking combined with mass spectrometry, we have recently identified the distinct binding modes of NPY peptides to their Y-receptors. Neuropeptide Y receptors have been shown to play a relevant role in the regulation of food intake. Furthermore, they participate in adipogenesis and some of them are overexpressed in tumours. By knowing the receptor bound structure, specific ligands as well as peptide-drug conjugates have been designed to selectively address Y receptors in different tissues including allo-steric modulators.

大阪公立大学 研究推進機構 協創研究センター
ケミカルバイオロジー研究所・所長 中瀬 生彦

〒599-8531 大阪府堺市中区学園町 1-1

大阪公立大学大学院理学研究科

(連絡先) 藤井 郁雄

TEL: 072-254-9834, fujii@omu.ac.jp



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