JPS-ASCEPT Lecture 2025

3 月 19 日（水）9:30～10:20 第 5 会場（第 98 回日本薬理学会年会 3 日目）
座長：橋本　均（大阪大学／日本薬理学会理事長）

Illuminating Insights into Receptor Complexes

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日本薬理学会とオーストラリア薬理学会（ASCEPT）の講師交換プログラムで Kevin Pfleger 先生が講演されます。Pfleger 先生は、Edinburgh 大学で博士号を取得し、2002 年 10 月に西オーストラリア大学に異動しました。過去 20 年間にわたり、特に GPCR に関わる分子レベルおよび細胞レベルでの受容体の結合と機能のプロファイリングに関する幅広い専門知識を培ってきました。2021-2023 には ASCEPT president をお務めです。ASCEPT から交換プログラム講師としてご推薦いただき、薬理学会年会での講演をお願いすることになりました。
多数の会員の皆様のご参加をお待ちしています

Receptors that respond to hormones, neurotransmitters, chemokines and growth factors traffic to the cell surface where they are activated by ligands and signal via coupling to molecules such as G proteins or Grb2. For most G protein-coupled receptors (GPCRs), arrestins then bind and inhibit plasma membrane G protein coupling, facilitate internalization via clathrin-mediated endocystosis, and potentially generate a secondary signalling complex. Signalling potentially continues in endosomes, and receptors are then either recycled to the cell surface or are targeted for degradation. Furthermore, heteromerization can lead to transactivation, transinhibition, or modulation of receptor signalling pathways. Because of the importance of kinetics, being able to measure receptor function in live cells and in real time is highly advantageous, and this can be achieved by using technologies such as bioluminescence resonance energy transfer (BRET). BRET uses a donor luciferase enzyme fused to a protein of interest that transfers resonance energy to an acceptor, such as a small fluorescent moiety like BODIPY, or a derivative of green fluorescent protein like Venus. This only occurs if donor and acceptor are within 10 nm of each other. We have utilised BRET to monitor ligand binding, G protein and Grb2 coupling, arrestin recruitment and receptor trafficking. We have done this both with transient transfection and through tagging endogenous receptors with luciferase using CRISPR/Cas9 gene editing. As a result of developments by our laboratory and others, BRET has now been widely adopted across academia and industry for the study of receptors. We have also assessed numerous heteromer complexes, and our molecular pharmacology investigations have provided the rationale for both pre-clinical and clinical studies. The most advanced of these is a Phase 3 clinical trial for the treatment of chronic kidney disease focal segmental glomerulosclerosis (FSGS) being undertaken by Dimerix.