Special issue “role of G-proteins and GPCR-mediated signaling in the pathophysiology and treatment of psychiatric disorders”

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G-protein-coupled receptors (GPCRs), also known as seven transmembrane receptors, are the largest and most diverse group of membrane receptors in eukaryotes that are used by cells to convert extracellular signals into intracellular molecular events, including responses to hormones, neurotransmitters, as well as responses to vision, olfaction and taste signals. They comprise almost a thousand genes which regulate virtually all known physiological processes in living organisms including homo sapiens. Moreover, these receptors are the targets for drugs accounting for more than half of all prescription drug sales in the world. At the beginning of the twentieth century, J.N. Langley described the concept of the receptor as “receptive substance”. However, Langley’s idea was generally either ignored or derided, and knowledge of the chemical nature of the “receptor” and how it affected cell function had to wait a bit longer.

The pharmacological studies using radioligand binding techniques initiated in the late 1960s and developed in the 1970s provided new and deeper insights into the molecular identity and properties of GPCRs. Along with this line of pharmacological studies, molecular studies of rhodopsin, a light receptor in rod photoreceptor cells of the retina, have paved the way to understanding a large family of GPCRs such as β -adrenoceptors in 1980s. Undoubtedly, the

discovery of G-proteins by Alfred G. Gilman and Martin Rodbell, the Nobel Prize winners in 1994, was also groundbreaking work to understand fundamental molecular mechanisms for signal transduction pathways from a receptor activated by chemical messages, such as hormones, autacoids, and neurotransmitters, to cellular function. Ever since then, work on this important family of GPCRs and G-proteins has generated new insights into physiological and pathophysiological signaling mechanisms and continues to produce new drug targets through the translation of fundamental biology into therapeutic applications.

GPCRs are the most common targets of the neuropharmacological drugs in the central nervous system, and dysregulation of GPCR-mediated signaling is postulated to result in disorganization of brain function such as sensation, perception, memory, cognition, association, thought, affect and volition. Then, it has been conceived they are deeply involved in multiple mental disorders such as schizophrenia and depression. The essential abnormalities in mental disorders are, however, still unknown. To add updated knowledge concerning the GPCR-mediated signaling implicated in mental disorders or neuropsychological functionality, we planned to edit a special issue on this theme and advertised the scope of the issue as follows:

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“Pharmacological Reports plans to launch a special issue devoted to outline advances on involvement of GPCR pathways in the nature, causes, mechanisms and treatments of mental disorders. Contributions may include a broad range of topics related to experimental and clinical pharmacology addressing molecular, cellular, neurochemical, circuitries, neuroimaging, behavioral and drug discovery areas. Translational investigations whose primary focus deals with involvement of GPCR signaling in mental disorder mechanisms and treatments are encouraged....”

In response to our invitation, many researchers have had much interest in contributing to the issue. Lots of

manuscripts had been submitted to the issue, of which 19 papers have been accepted for publication after ordinary strict peer-review process. As listed in Table 1, this issue consists of nine reviews, five articles, and five short communications. Although the topics and targeted proteins are varied, from basic understanding of molecular function involved in fundamental physiology and neural network to investigations into possible molecular abnormalities

in patients, all articles provide us with invaluable hints to understand the implications of GPCR-mediated signaling in pathophysiology of mental disorders.

As guest editors, we sincerely wish the researchers in this field enjoy reading the articles included in this special issue. Hopefully, this issue would encourage the readers to endeavor further to gain more understanding of GPCR-signaling pathways implicated in the pathophysiology of

Table 1 Summary of the papers published in this Special Issue

Article type	Chemical substrate, GPCRs or G-proteins	(Patho)physiological relevance	Author(s)	DOI
Review	GABA receptor/ δ - and μ -opioid receptor	Dopamine efflux in nucleus accumbens	Tadashi Saigusa et al.	https://doi.org/10.1007/s43440-021-00249-9
	Endocannabinoids	Fear memory/posttraumatic stress disorder (PTSD)	Ikumi Mizuno and Shingo Matsuda	https://doi.org/10.1007/s43440-021-00246-y
	Formyl peptide receptors	Immune-related brain disorders	Kinga Tylek et al.	https://doi.org/10.1007/s43440-021-00271-x
	Glucagon-like peptide-1 receptor	Depression	Jan Detka and Katarzyna Głombik	https://doi.org/10.1007/s43440-021-00274-8
	G protein-biased opioid agonist	Opioid addiction/analgesia	Lucja Kudła and Ryszard Przewlocki	https://doi.org/10.1007/s43440-021-00251-1
	Chemokine CCL2 and CCR2	Depression	Katarzyna Curzytek and Monika Leśkiewicz	https://doi.org/10.1007/s43440-021-00280-w
	Chemokine CX3CL and CX3CR1	Schizophrenia	Katarzyna Chamera et al.	https://doi.org/10.1007/s43440-021-00269-5
	Multiple GPCRs and G α subtypes	Pharmacological methodology	Rebeca Diez-Alarcia et al.	https://doi.org/10.1007/s43440-021-00253-z
	A2AR-mGluR5 and A2AR-FGFR1 heteroreceptor complexes	Striatal-enriched protein tyrosine phosphatase (STEP)	Dasiel O. Borroto-Escuela et al.	https://doi.org/10.1007/s43440-021-00314-3
Article	Pituitary adenylate cyclase-activating polypeptide	Fear learning and memory	Yuji Kambe et al.	https://doi.org/10.1007/s43440-021-00222-6
	α_{2A} -adrenoceptor and CB $_1$ receptor/G α_{i2} and G α_z	MEK-ERK and FADD cascades	Alfredo Ramos-Miguel et al.	https://doi.org/10.1007/s43440-021-00240-4
	Dopamine D $_2$ receptor	Schizophrenia	Iker Eguskiza et al.	https://doi.org/10.1007/s43440-021-00305-4
	Opioid and cannabinoid receptor	Tolerance and physical dependence to opioids	Agata Szymaszkiewicz et al.	https://doi.org/10.1007/s43440-021-00291-7
	5-HT $_{2A}$ and M $_1$ muscarinic acetylcholine receptor/G $\alpha_{q/11}$	Opiate addict	Yuji Odagaki et al.	https://doi.org/10.1007/s43440-021-00248-w
Short communication	Chlorpromazine	Adult neurogenesis	Jakub Skałbania et al.	https://doi.org/10.1007/s43440-021-00259-7
	5-HT $_{2C}$ and 5-HT $_{2A}$ receptor	Maternal diet and a risk of mental illnesses of offspring	Kinga Gawlińska et al.	https://doi.org/10.1007/s43440-021-00298-0
	G α_{i2} , G α_{i3} , RhoA, and Rac1	Chronic restraint stress	Katarzyna Rafa-Zabłocka et al.	https://doi.org/10.1007/s43440-021-00294-4
	Olanzapine/Phoenixin, spexin and nesfatin-1	Effect of long-term treatment with olanzapine	Artur Pałasz et al.	https://doi.org/10.1007/s43440-021-00267-7
	Cannabidiol	Antidepressant-like effect of cannabidiol in a rat model of early-life stress	Cristian Bis-Humbert et al.	https://doi.org/10.1007/s43440-021-00285-5

mental disorders. We appreciate all the authors contributing to the issue as well as all the reviewers of the submitted manuscripts. Special thanks are also due to the presidents of the Japanese Pharmacological Society, the Japanese Society of Neuropsychopharmacology, and the Japanese Society of Biological Psychiatry, for their kind notifying the society

members of the advertisement of “Call for papers” for this special issue.

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