

International Union of Basic and Clinical Pharmacology. Guidelines for GPCR ligand bias

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Abstract

G protein-coupled receptors modulate a plethora of physiological processes and mediate the effects of one-third of FDA-approved drugs. Notably, depending on which ligand has activated a particular receptor, it can engage different intracellular transducers. This paradigm of ligand-dependent ‘biased signaling’ dictates a need to advance beyond the level of receptors to consider the combined ligand-receptor pair in order to understand physiological signaling. Bias signaling also has the potential to improve medicines by reducing adverse effects. However, this is challenged by inconsistent interpretation of results and lack of commonly agreed guidelines. Here, we present recommended terminology and guidelines to conduct, report and quantify bias in a comparable and reproducible fashion. We expect these recommendations will facilitate a common understanding of experiments and findings across basic receptor research and drug discovery, while the area and the analytical methods to measure bias are still evolving, especially in complex cellular, tissue and organismal systems.

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