Papers of the Week

Designer Protein Allows Better Understanding of the Role of a Particular G Protein-coupled Receptor

* See referenced article, J. Biol. Chem. 2016, 291, 7809–7820

A G Protein-biased Designer G Protein-coupled Receptor Useful for Studying the Physiological Relevance of Gq/11-dependent Signaling Pathways

Approximately one-third of all drugs target G protein-coupled receptors (GPCRs). The drugs may also affect a different class of proteins called β-arrestins. But it is difficult to tell when a drug is targeting GPCR- or β-arrestin signaling. In this Paper of the Week, a team led by Jürgen Wess at the National Institute of Diabetes and Digestive and Kidney Diseases engineered a designer receptor that falls into a category of designer proteins known by the acronym DREADDs. The receptor only activates a certain G protein and does not interact with β-arrestins. By analyzing the engineered receptor in cell cultures and mice and by comparing the receptor’s activity to another designer receptor that only interacts with the β-arrestin 2 protein, the investigators found that the newly engineered receptor promotes glucose release in liver cells by activating Gq-type G proteins. The investigators say studies with their engineered receptor “should guide the development of novel classes of functionally biased ligands that show high efficacy in various pathophysiological conditions but display a reduced incidence of side effects.”

DOI 10.1074/jbc.P115.702282

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