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INVESTIGATING SIGNALING PATHWAYS INVOLVING THE HCA RECEPTOR FAMILY

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Investigating Signaling Pathways Involving the HCA Receptor Family

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ABSTRACT

Increasing obesity rates have put the American population at higher risk for developing obesity-related medical conditions such as hypertension, heart disease, and diabetes. The hydroxycarboxylic acid (HCA) receptor family is a family of G protein-coupled receptors (GPCRs) that are expressed in adipose tissue and function as metabolic sensors, making them potential pharmaceutical targets in the treatment of obesity and other metabolic disorders. The HCA receptor family consists of the HCA1, HCA2, and HCA3 receptors, which are activated by hydroxycarboxylic acids such as lactate and 3-hydroxybutyric acid. We utilized bioluminescence resonance energy transfer (BRET) to study agonist-induced coupling of luciferase-tagged HCA receptors to Venus fluorescent protein-tagged G protein heterotrimers or arrestins. Our results indicate that the three HCA receptors couple to the Gi/o subfamily of G proteins. The data additionally confirms a lack of coupling to the other G protein subfamilies (Gs, Gq, and G12) and lacks evidence of arrestin recruitment to HCA receptors. Overall, our study highlights the use of BRET as a powerful tool for analysis of GPCR signaling and demonstrates its possible use for future studies to determine the potency of potential drugs targeting HCA receptors as a therapy for health-related problems such as obesity.

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