Title
Exploring GPCR Biased Signaling from inside and outside the Cell

Permalink
https://escholarship.org/uc/item/6nx1z1tx

Journal
The FASEB Journal, 29(S1)

ISSN
0892-6638

Author
Trejo, JoAnn

Publication Date
2015-04-01

DOI
10.1096/fasebj.29.1_supplement.101.1

Peer reviewed

JoAnn Trejo, Ph.D.

Title: "Exploring GPCR biased signaling from inside and outside the cell"

G protein-coupled receptors (GPCRs) are the largest family of cell surface receptors expressed in the mammalian genome and mediate vast physiological responses, making this receptor class the target of most drugs used clinically. GPCRs are dynamic molecules that assume multiple active states that bias signaling towards distinct G-protein subtypes and beta-arrestins. However, the mechanisms that regulate GPCR bias signaling remains unclear. Towards understanding the molecular basis of GPCR biased signaling, we examined the role of post-translational modifications and plasma membrane compartmentalization. We discovered that N-linked glycosylation of protease-activated receptor-1 (PAR1), a GPCR for the coagulant protease thrombin, regulates preferential coupling to specific G-protein subtypes that control stress fiber formation and cellular proliferation. We also found that PAR1 distribution into caveolae in endothelial cells is critical for biased signaling induced by thrombin versus activated Protein C, an anti-coagulant protease. Thrombin-activated PAR1 coupled to G-proteins and induced endothelial barrier permeability. In contrast, APC-activated PAR1 signaled preferentially through beta-arrestins to promote endothelial barrier stabilization, which required compartmentalization in caveolae. These studies reveal two different mechanisms that regulate GPCR biased signaling from inside and outside of the cell.

In addition to her research, Dr. JoAnn Trejo is an experienced educator and leader of diversity efforts. She will also discuss the untapped potential: diversity and the advancement of science.