PAR4 inhibition as a novel therapeutic for multiple pathophysiologies

Yukeyoung Kim
Sungho Ghil

Video Byte

Keywords: Protease-activated receptor 4, PAR4, G-protein, cell signaling, bioluminescence resonance energy transfer, cancer progression, extracellular signal-regulated kinase, phospholipase, Regulators of G-protein signaling, Cell Communication and Signaling

Posted Date: October 30th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-100890/v1

Abstract

Protease-activated receptor 4 (PAR4) is a G-protein-coupled receptor involved in platelet aggregation and immune responses. PAR4 is also overexpressed in several malignant cancers. Due to its wide array of roles, PAR4 inhibition has potential therapeutic value for managing many diseases. Regulators of G-protein signaling (RGS) modulate G-protein-coupled receptor- mediated pathways, including those of other PAR proteins. However, their specific effects on PAR4 are not fully understood. Researchers have recently investigated the network of interactions between PAR4, RGS proteins, and Gα proteins in live cells. They found that PAR4 interacted with RGS2 and RGS4 in a Gα-dependent manner, and that the formation of these complexes inhibited PAR4 signaling. Additionally, PAR4 activation promoted cell proliferation and cancer-related gene expression, and this was blocked by RGS2 and RGS4 expression. These findings suggest that both RGS2 and RGS4 selectively modulate PAR4 signaling through Gα-dependent interactions, suggesting a new drug target for treating multiple pathophysiologies.