Structures and dynamics of PAC1 receptor visualised in 3D animations: staying "in the loop"

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Class B1 peptide hormone G protein-coupled receptors (GPCRs) have a broad range of regulatory metabolic effects and are therefore important drug targets. The PAC1R, a Class B1 GPCR, is a potential drug target for the treatment of migraine and other central nervous system (CNS) disorders yet remains underutilized as a target.
More interestingly, PAC1R exists as multiple splice variants, including PAC1nR ('null' variant) and PAC1sR ('short' variant, missing 21 amino acids), which can be activated by endogenous peptide agonists VIP and PACAP. VIP signaling and regulatory functions are globally enhanced at PAC1sR relative to PAC1nR, yet the pharmacology of other PAC1R agonists is similar between these two splice variants. Using cryo-EM structures, MD simulations and mutagenesis, we propose mechanisms for the altered VIP-mediated signaling by distinct interactions in these receptor variants.
Furthermore, we load our structural data into Blender, an open-source 3D computer graphics software, to develop 3D animations based on our experimental data, and tell visual stories about how these receptor variants work.