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A new Rac-cGMP signaling pathway

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The small GTPase Rac and the second messenger cGMP are critical regulators of diverse cell functions. When activated by extracellular signals via membrane signaling receptors, Rac executes its functions through engaging downstream effectors such as p21-activated kinase (PAK), a serine/threonine protein kinase. However, the molecular mechanism by which membrane signaling receptors regulate cGMP levels is not known. Recently we have uncovered a signaling pathway linking Rac to the increase of cellular cGMP [1]. We show that Rac uses PAK to directly activate transmembrane guanylyl cyclases (GCs), leading to increased cellular cGMP levels. This Rac/PAK/GC/cGMP pathway is involved in platelet-derived growth factor-induced fibroblast cell migration and lamellipodium formation. Our findings connect two important regulators of cellular physiological functions and provide a general mechanism for diverse receptors to modulate physiological responses through elevating cellular cGMP levels.

References

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