NADPH oxidase 2 (NOX2) complex binds RAC1

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

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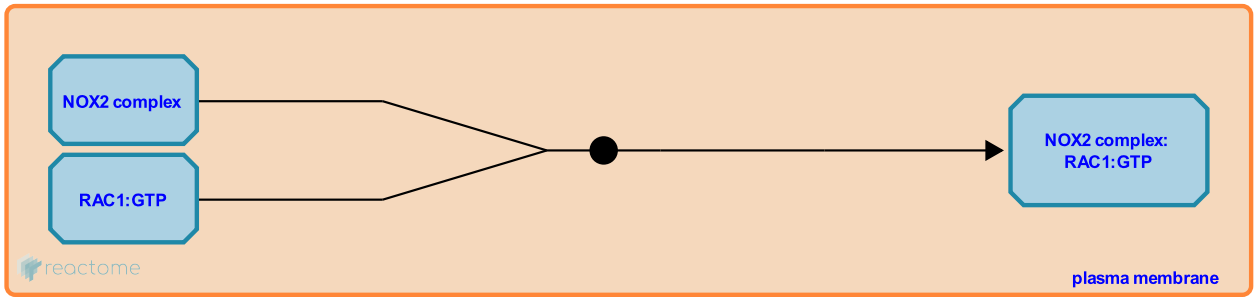
Stable identifier: R-HSA-5218827

Type: binding

Compartments: plasma membrane



Direct interaction between recombinant GTP-bound human RAC1 and human NCF2 (p67phox), a component of the NOX2 complex, leads to the activation of the NOX2 complex (Price et al. 2002). NADPH oxidase (NOX) proteins are membrane-associated, multiunit enzymes that catalyze the reduction of oxygen using NADPH as an electron donor. NOX proteins produce superoxide (O2.-) via a single electron reduction (Brown & Griendling 2009). Superoxide molecules function as second messengers to stimulate diverse redox signaling pathways linked to various functions including angiogenesis. VEGF specifically stimulates superoxide production via RAC1 dependent activation of NOX2 complex. VEGF rapidly activates RAC1 and promotes translocation of RAC1 from cytosol to the membrane. At the membrane RAC1 interacts with the NOX enzyme complex via a direct interaction with NOX2 (gp91phox or CYBB) followed by subsequent interaction with the NCF2 (Neutrophil cytosol factor 2) or p67phox subunit and this makes the complex active (reviewed in Bedard & Krause 2007). O2.- derived from Rac1-dependent NOX2 are involved in oxidation and inactivation of protein tyrosine phosphatases (PTPs) which negatively regulate VEGFR2, thereby enhancing VEGFR2 autophosphorylation, and subsequent redox signaling linked to angiogenic responses such as endothelial cell proliferation and migration (reviewed in Ushio-Fukai 2006, 2007).

Literature references

Atkinson, SJ., Price, MO., Dinauer, MC., Knaus, UG. (2002). Rac activation induces NADPH oxidase activity in transgenic COSphox cells, and the level of superoxide production is exchange factor-dependent. *J Biol Chem, 277*, 19220-8. ↗

Editions

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