

# Cytosolic VHL:EloB,C:CUL2:RBX1 binds hydroxyprolyl-HIF-alpha

May, B., Rantanen, K.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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08/05/2024

## 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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## 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. [↗](#)

Reactome database release: 88

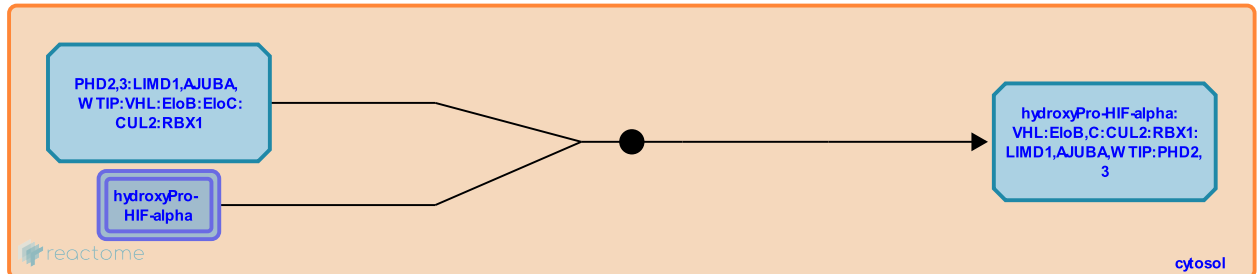
This document contains 1 reaction ([see Table of Contents](#))

## Cytosolic VHL:EloB,C:CUL2:RBX1 binds hydroxyprolyl-HIF-alpha [↗](#)

**Stable identifier:** R-HSA-1234183

**Type:** binding

**Compartments:** cytosol



VHL within the VHL:ElonginB:ElonginC:CUL2:RBX1 Complex binds HIF-alpha subunits that have hydroxylated proline residues (Cockman et al. 2000, Ohh et al. 2000, Tanimoto et al. 2000, Jaakkola et al. 2001, Ivan et al. 2001, Yu et al. 2001). VHL constitutively shuttles between the cytosol and nucleoplasm (Lewis and Roberts 2003) and though the VHL:HIF-alpha complex is predominantly nuclear, binding and degradation can occur in both the cytosol and the nucleus (Berra et al. 2001).

### Literature references

- Masson, N., Chang, GW., Mole, DR., Jaakkola, P., Maxwell, PH., Cockman, ME. et al. (2000). Hypoxia inducible factor-alpha binding and ubiquitylation by the von Hippel-Lindau tumor suppressor protein. *J Biol Chem*, 275, 25733-41. [↗](#)
- Pouysségur, J., Roux, D., Richard, DE., Berra, E. (2001). Hypoxia-inducible factor-1 alpha (HIF-1 alpha) escapes O(2)-driven proteasomal degradation irrespective of its subcellular localization: nucleus or cytoplasm. *EMBO Rep*, 2, 615-20. [↗](#)
- Poellinger, L., Pereira, T., Tanimoto, K., Makino, Y. (2000). Mechanism of regulation of the hypoxia-inducible factor-1 alpha by the von Hippel-Lindau tumor suppressor protein. *EMBO J*, 19, 4298-309. [↗](#)
- Pavletich, N., Kim, TY., Park, CW., Ivan, M., Kaelin, WG., Ohh, M. et al. (2000). Ubiquitination of hypoxia-inducible factor requires direct binding to the beta-domain of the von Hippel-Lindau protein. *Nat Cell Biol*, 2, 423-7. [↗](#)
- Lane, WS., Asara, JM., Kim, W., Salic, A., Valiando, J., Ivan, M. et al. (2001). HIFalpha targeted for VHL-mediated destruction by proline hydroxylation: implications for O2 sensing. *Science*, 292, 464-8. [↗](#)

### Editions

2011-03-09	Authored, Edited	May, B.
2012-05-19	Reviewed	Rantanen, K.