

Nuclear PHD1,3 hydroxylates proline residues on EPAS1 (HIF2A)

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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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. [↗](#)

Reactome database release: 88

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

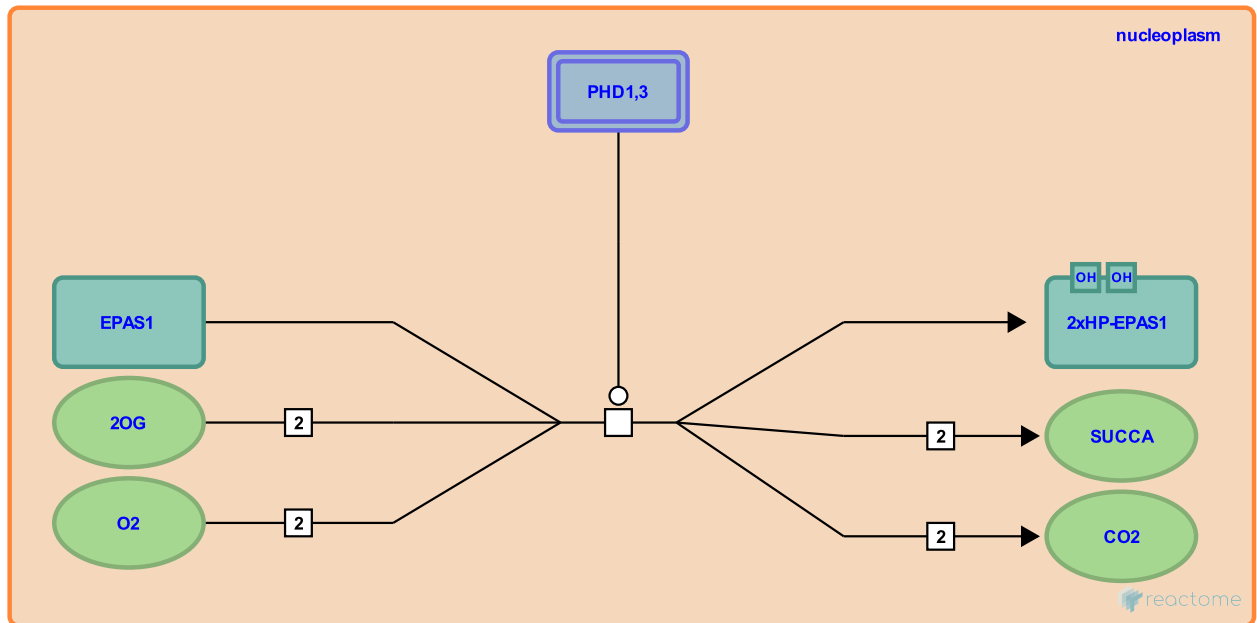
Nuclear PHD1,3 hydroxylates proline residues on EPAS1 (HIF2A) ↗

Stable identifier: R-HSA-1234166

Type: transition

Compartments: nucleoplasm

Inferred from: Nuclear PHD1,3 hydroxylates proline residues on HIF1A (Homo sapiens)



Proline hydroxylases PHD1 (EGLN2) and PHD3 (EGLN3) located in the nucleus hydroxylate HIF2A (EPAS1) at proline-405 and proline-531 (Hirsila et al. 2003, Percy et al. 2008, Furlow et al. 2009). The amount of hydroxylation occurring in the nucleus is controversial. Most hydroxylation is believed to be cytosolic.

Literature references

- McMullin, MF., Furlow, PW., Percy, MJ., Lappin, TR., Bierl, C., Master, SR. et al. (2009). Erythrocytosis-associated HIF-2alpha mutations demonstrate a critical role for residues C-terminal to the hydroxylacceptor proline. *J Biol Chem*, 284, 9050-8. ↗
- McMullin, MF., Furlow, PW., Li, X., Lucas, GS., Percy, MJ., Lappin, TR. (2008). A gain-of-function mutation in the HIF2A gene in familial erythrocytosis. *N Engl J Med*, 358, 162-8. ↗
- Stengel, P., Klinger, M., Acker, H., Hellwig-Bürgel, T., Fandrey, J., Wotzlaw, C. et al. (2003). Intracellular localisation of human HIF-1 alpha hydroxylases: implications for oxygen sensing. *J Cell Sci*, 116, 1319-26. ↗
- Hirsilä, M., Günzler, V., Koivunen, P., Myllyharju, J., Kivirikko, KI. (2003). Characterization of the human prolyl 4-hydroxylases that modify the hypoxia-inducible factor. *J Biol Chem*, 278, 30772-80. ↗

Editions

2011-03-09	Authored, Edited	May, B.
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