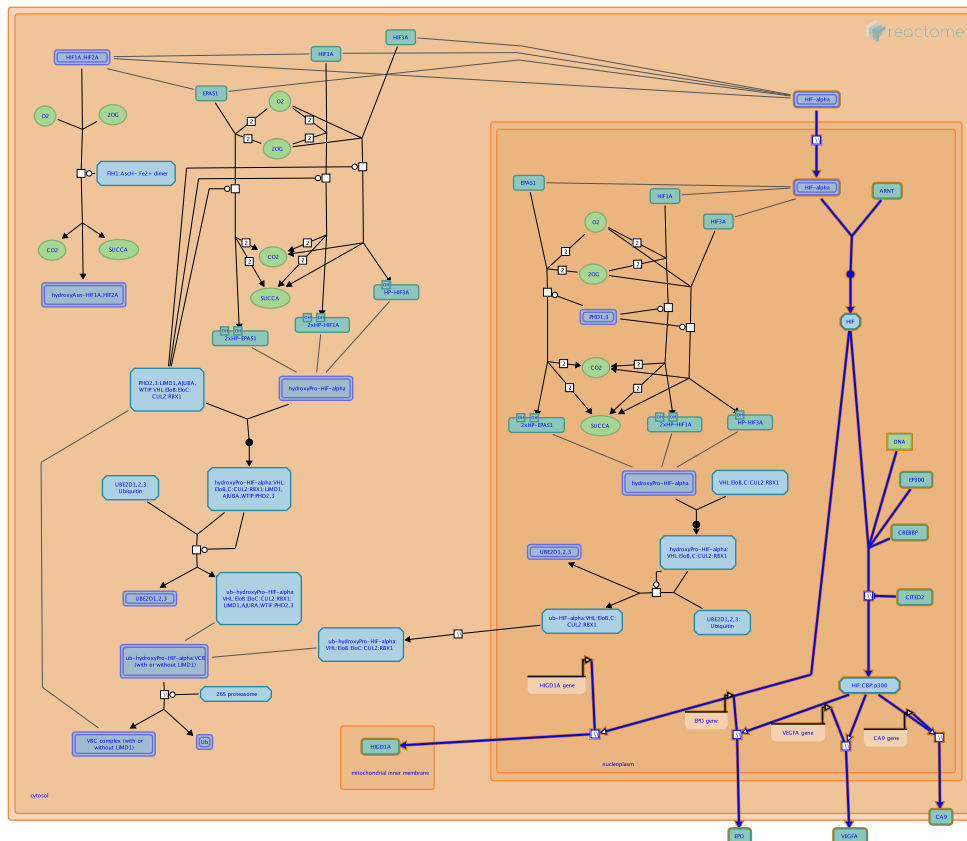


Regulation of gene expression by Hypoxia-inducible Factor



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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

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Reactome database release: 77

This document contains 1 pathway and 7 reactions ([see Table of Contents](#))

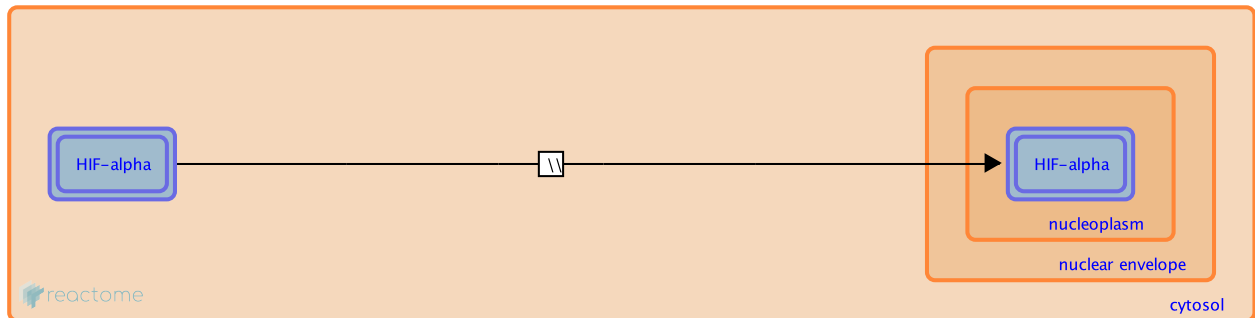
HIF-alpha translocates from cytosol to nucleus ↗

Location: [Regulation of gene expression by Hypoxia-inducible Factor](#)

Stable identifier: R-HSA-1234161

Type: omitted

Compartments: cytosol, nucleoplasm



HIF-alpha (HIF1A, EPAS1, HIF3A isoform 1) is translocated into the nucleus (Kallio et al. 1998, Depping et al. 2008, Chachami et al. 2009, Heikkilä et al. 2011). Importin 4 and importin 7 (Chachami et al. 2009) as well as the importin alpha/beta pathway (Depping et al. 2008) appear to be capable of interacting with HIF-alpha. During hypoxia HIF-alpha accumulates in the nucleus where it associates with CBP and p300 (Kallio et al. 1998).

Followed by: [HIF-alpha binds ARNT \(HIF1-beta\) forming HIF-alpha:ARNT](#)

Literature references

- Chachami, G., Paraskeva, E., Mingot, JM., Braliou, GG., Görlich, D., Simos, G. (2009). Transport of hypoxia-inducible factor HIF-1alpha into the nucleus involves importins 4 and 7. *Biochem Biophys Res Commun*, 390, 235-40. ↗
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Editions

2011-03-18	Authored, Edited	May, B.
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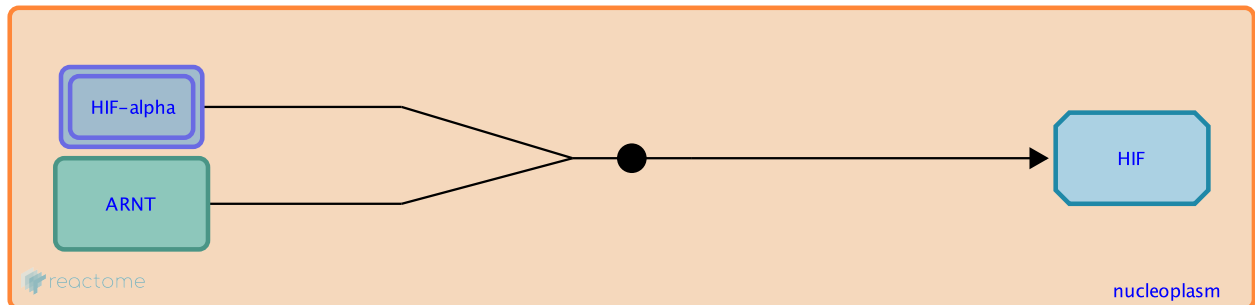
HIF-alpha binds ARNT (HIF1-beta) forming HIF-alpha:ARNT ↗

Location: [Regulation of gene expression by Hypoxia-inducible Factor](#)

Stable identifier: R-HSA-1234171

Type: binding

Compartments: nucleoplasm



HIF-alpha (HIF1A, HIF2A (EPAS1, MOP2), HIF3A isoform 1) forms a heterodimer with ARNT (HIF1-beta) (Wang et al. 1995, Jiang et al. 1996, Hogenesch et al. 1997, Tian et al. 1997, Gu et al. 1998, Erbel et al. 2003, Heikkilä et al. 2011, Zhang et al. 2014, Kim et al. 2015).

Preceded by: [HIF-alpha translocates from cytosol to nucleus](#)

Followed by: [Expression of HIGD1A](#), [Formation of HIF:CBP:p300 complex at promoters](#)

Literature references

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- Jiang, BH., Rue, E., Wang, GL., Roe, R., Semenza, GL. (1996). Dimerization, DNA binding, and transactivation properties of hypoxia-inducible factor 1. *J Biol Chem*, 271, 17771-8. ↗
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Editions

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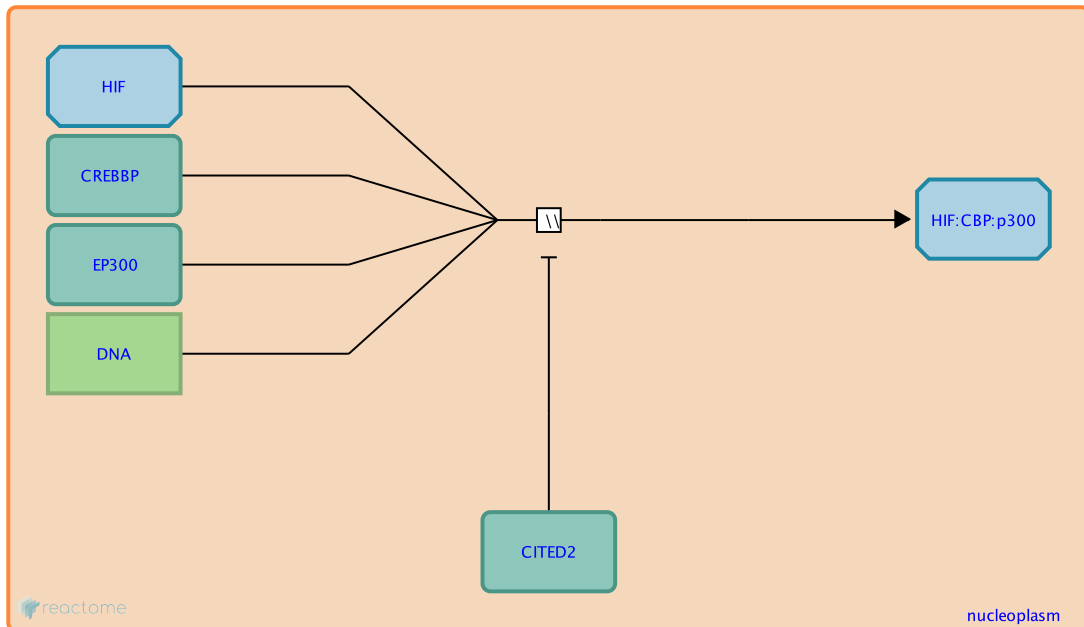
Formation of HIF:CBP:p300 complex at promoters ↗

Location: [Regulation of gene expression by Hypoxia-inducible Factor](#)

Stable identifier: R-HSA-1234167

Type: omitted

Compartments: nucleoplasm



HIF (heterodimer of HIF-alpha and HIF-beta) recruits p300 and CBP to the promoters of target genes (Kallio et al. 1998, Ebert and Bunn 1998, Ema et al. 1999, Gu et al. 2001, Dames et al. 2002, Freedman et al. 2002).

Preceded by: [HIF-alpha binds ARNT \(HIF1-beta\) forming HIF-alpha:ARNT](#)

Followed by: [Expression of VEGFA](#), [Expression of Erythropoietin \(EPO\)](#), [Expression of Carbonic Anhydrase IX \(CA9\)](#)

Literature references

- Ema, M., Hirota, K., Mimura, J., Abe, H., Yodoi, J., Sogawa, K. et al. (1999). Molecular mechanisms of transcription activation by HIF and HIF1alpha in response to hypoxia: their stabilization and redox signal-induced interaction with CBP/p300. *EMBO J*, 18, 1905-14. ↗
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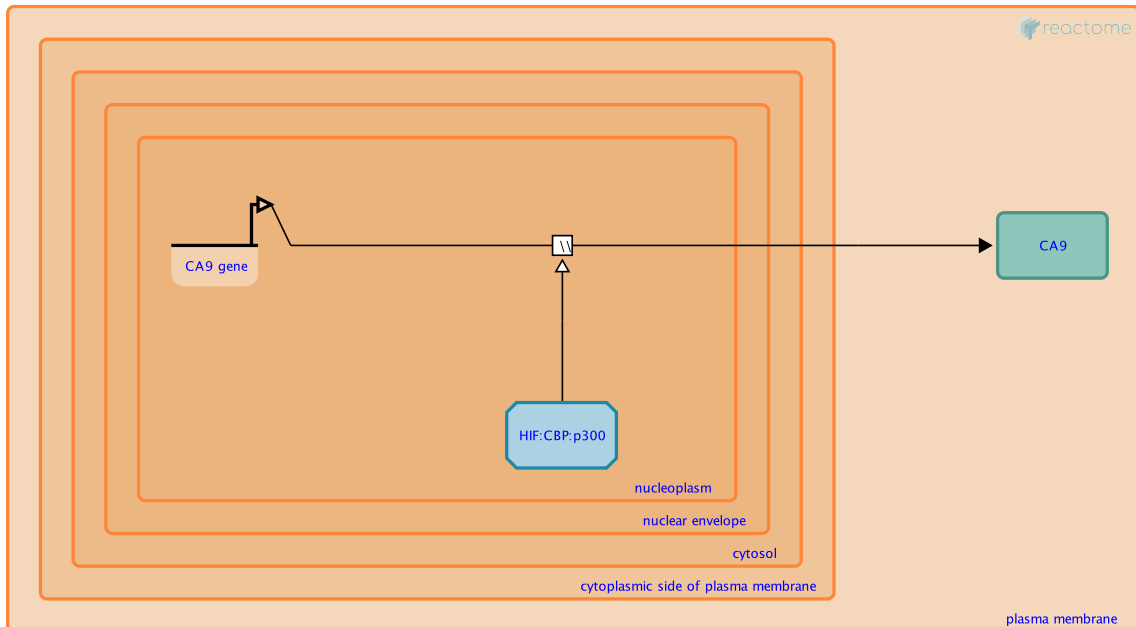
Expression of Carbonic Anhydrase IX (CA9) ↗

Location: [Regulation of gene expression by Hypoxia-inducible Factor](#)

Stable identifier: R-HSA-1235035

Type: omitted

Compartments: nucleoplasm, plasma membrane



The gene encoding carbonic anhydrase IX (CA9) is transcribed to yield mRNA and the mRNA is translated to yield protein. Hypoxia-inducible factor binds the promoter of CA9 and enhances expression of CA9.

Preceded by: [Formation of HIF:CBP:p300 complex at promoters](#)

Literature references

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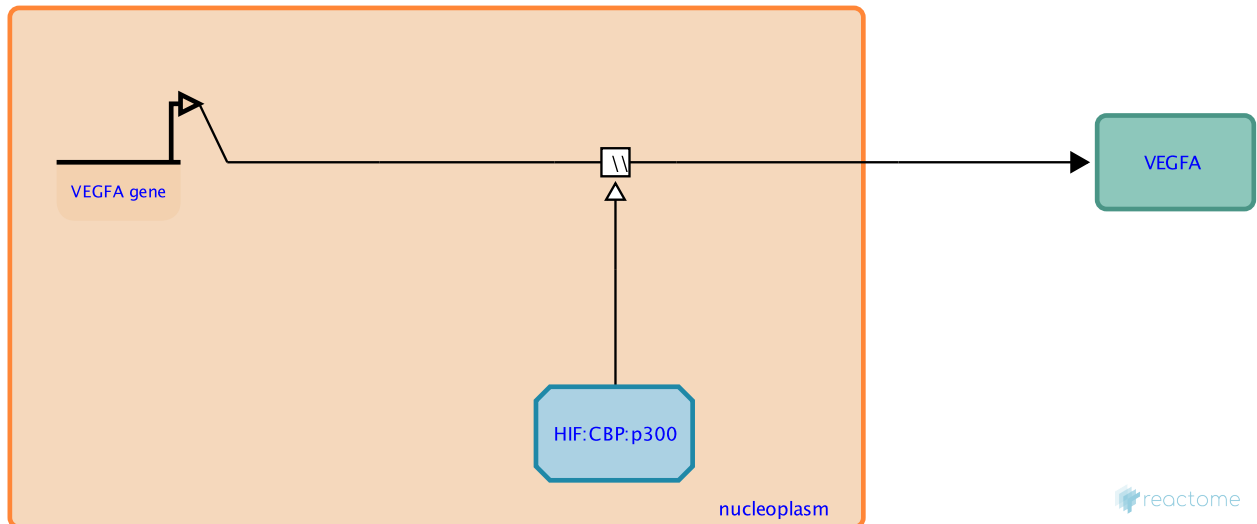
Expression of VEGFA ↗

Location: Regulation of gene expression by Hypoxia-inducible Factor

Stable identifier: R-HSA-1235037

Type: omitted

Compartments: nucleoplasm, extracellular region



The VEGFA (VEGF) gene is transcribed to yield mRNA and the mRNA is translated to yield protein. Hypoxia-inducible factor binds the VEGF promoter, recruits p300 and CBP, and enhances transcription.

Preceded by: Formation of HIF:CBP:p300 complex at promoters

Literature references

Forsythe, JA., Jiang, BH., Iyer, NV., Agani, F., Leung, SW., Koos, RD. et al. (1996). Activation of vascular endothelial growth factor gene transcription by hypoxia-inducible factor 1. *Mol Cell Biol*, 16, 4604-13. ↗

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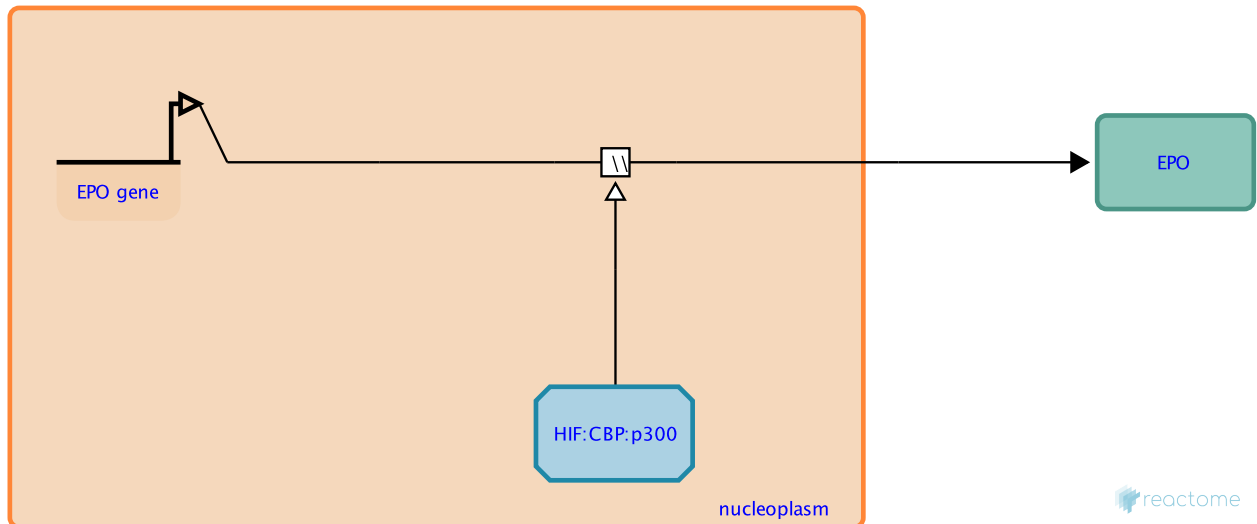
Expression of Erythropoietin (EPO) ↗

Location: Regulation of gene expression by Hypoxia-inducible Factor

Stable identifier: R-HSA-1235070

Type: omitted

Compartments: nucleoplasm, extracellular region



The EPO gene is transcribed to yield mRNA and the mRNA is translated to yield protein. Transcription of EPO is enhanced by Hypoxia-inducible factor, which binds to the EPO promoter.

Preceded by: Formation of HIF:CBP:p300 complex at promoters

Literature references

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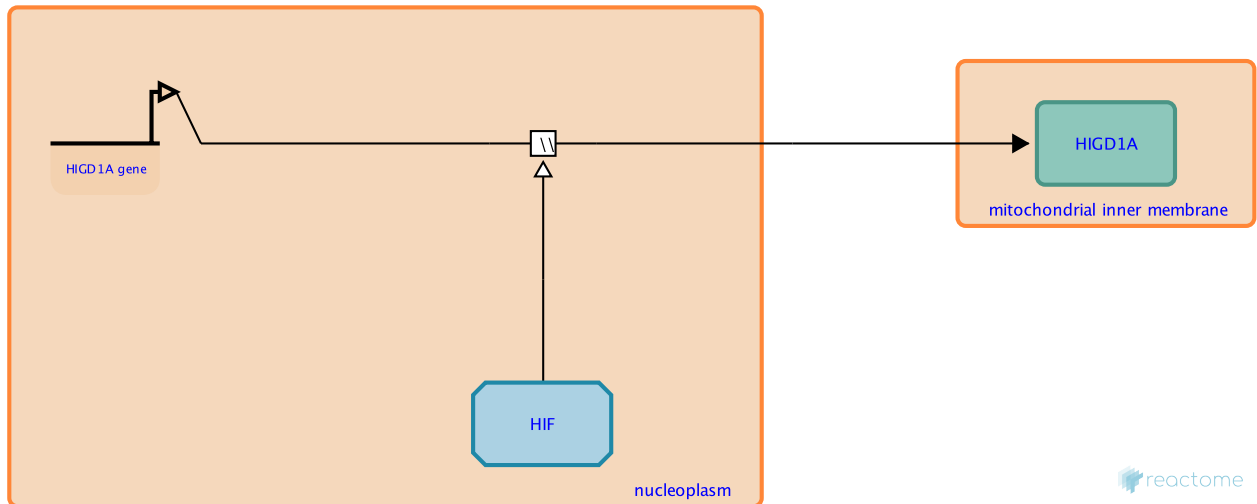
Expression of HIGD1A ↗

Location: Regulation of gene expression by Hypoxia-inducible Factor

Stable identifier: R-HSA-8932184

Type: omitted

Compartments: nucleoplasm, mitochondrial inner membrane



The HIGD1A (RCF1A, HIG1) gene is transcribed to yield mRNA and the mRNA is translated to yield protein (Ameri et al. 2015). Expression of HIGD1A is transactivated by HIF in response to hypoxia (Ameri et al. 2015).

Preceded by: HIF-alpha binds ARNT (HIF1-beta) forming HIF-alpha:ARNT

Literature references

Ameri, K., Jahangiri, A., Rajah, AM., Tormos, KV., Nagarajan, R., Pekmezci, M. et al. (2015). HIGD1A Regulates Oxygen Consumption, ROS Production, and AMPK Activity during Glucose Deprivation to Modulate Cell Survival and Tumor Growth. *Cell Rep.* ↗

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