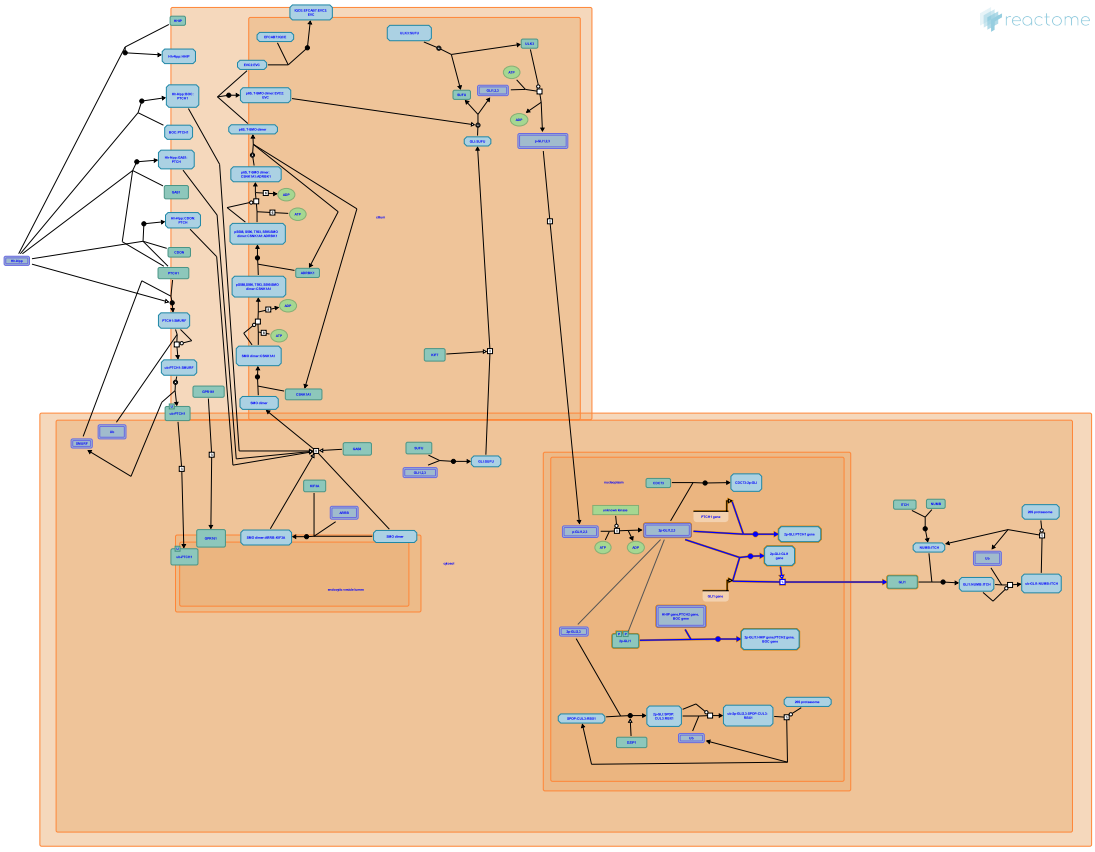
GLI proteins bind promoters of Hh responsive genes to promote transcription



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06/05/2024

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. ↗

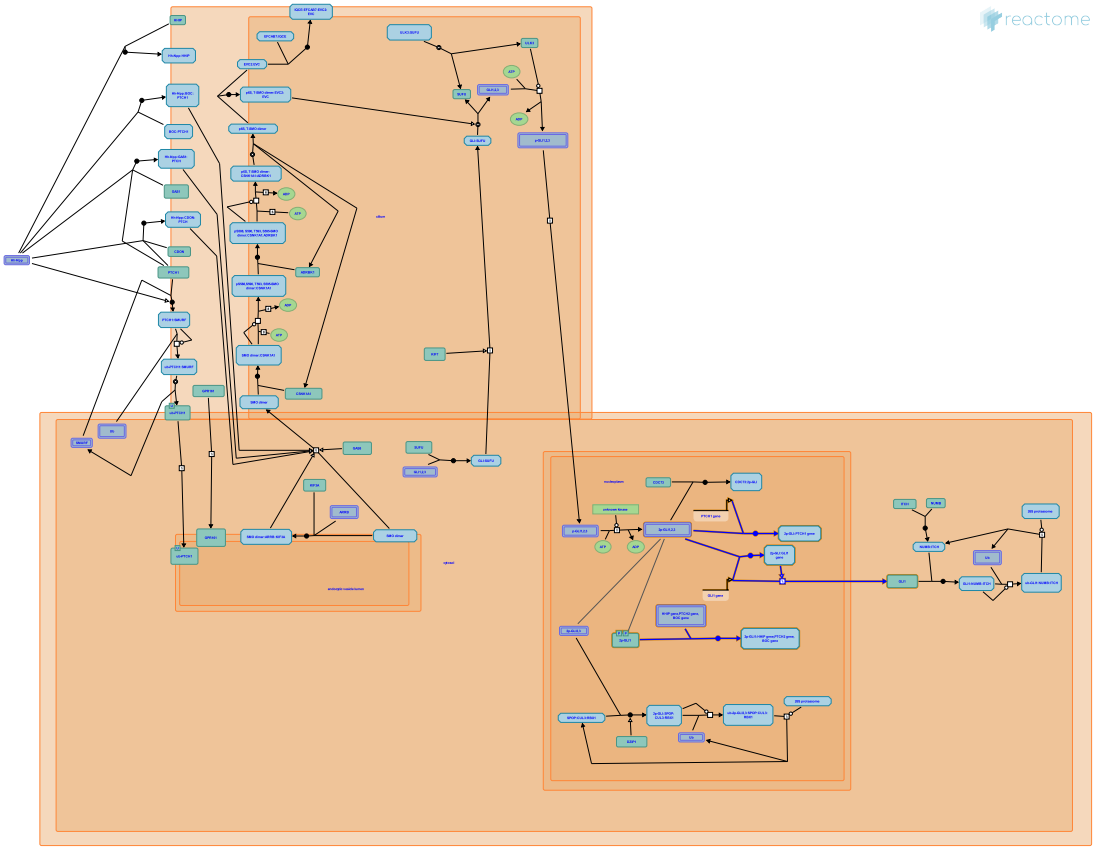
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

GLI proteins bind promoters of Hh responsive genes to promote transcription ↗

Stable identifier: R-HSA-5635851



GLI proteins are bifunctional DNA-binding proteins that recognize consensus GLI sites 5'-GACCACCC-3' in the promoters of target genes (Kinzler and Vogelstein, 1990). Pathway induction upon ligand-binding diverts the GLI proteins from the processing/degradation pathway that generates the truncated repressor form and promotes the formation of the full-length transcriptional activator (reviewed in Hui and Angers, 2011; Briscoe and Therond, 2013). GLI-dependent target genes have been identified by a number of ChIP based screens, and well-established, direct targets include a number of Hh pathway members including PTCH1, PTCH2, GLI1, HHIP and BOC (Lee et al, 2010; Vokes et al, 2007; Vokes et al, 2008; Agren et al, 2004; Bai et al, 2004; Bai et al, 2002; Dai et al, 1999). Full-length GLI proteins nucleate the assembly of a transcriptional activation complex at target gene promoters, but the details of interacting partners are not well known. The C-terminus of GLI3 has been shown to interact with a number of transcriptional activators including the histone acetyltransferase CBP, the Mediator component Med12 and the TATA-box recognition protein TAF31, but the detail of how and when these binding partners interact is not known (Dai et al, 1999; Zhou et al, 2006; Yoon et al, 1998; reviewed in Hui and Angers, 2011). Each of the GLI proteins has been shown to bind to CDC 73, a component of the PAF complex that has roles in RNA polymerase II-mediated transcription (Mosimann et al, 2009; reviewed in Tomson and Arndt, 2013).

Literature references

Hui, CC., Angers, S. (2011). Gli proteins in development and disease. *Annu. Rev. Cell Dev. Biol., 27*, 513-37. ↗

Stephen, D., Joyner, AL., Bai, CB. (2004). All mouse ventral spinal cord patterning by hedgehog is Gli dependent and involves an activator function of Gli3. *Dev. Cell, 6*, 103-15. ↗

Ishii, S., Dai, P., Nakafuku, M., Maekawa, T., Akimaru, H., Tanaka, Y. (1999). Sonic Hedgehog-induced activation of the Gli1 promoter is mediated by GLI3. *J. Biol. Chem., 274*, 8143-52. ↗

Davidson, EH., Giles, S., Wong, WH., Longabaugh, WJ., McCuine, S., McMahon, AP. et al. (2007). Genomic characterization of Gli-activator targets in sonic hedgehog-mediated neural patterning. *Development, 134*, 1977-89. ↗

Kinzler, KW., Vogelstein, B. (1990). The GLI gene encodes a nuclear protein which binds specific sequences in the human genome. *Mol. Cell. Biol., 10*, 634-42. ↗

Editions

2014-10-31	Edited	Gillespie, ME.
2014-10-31	Authored	Rothfels, K.
2014-11-09	Reviewed	Liu, Y C.

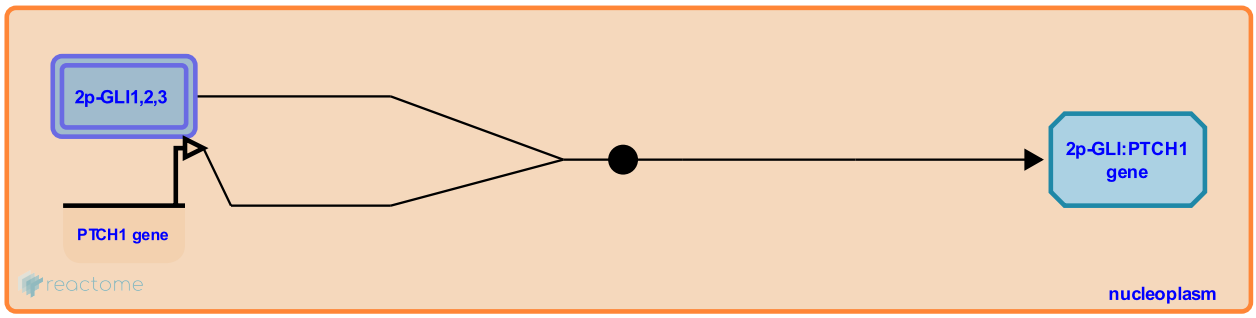
GLI proteins bind PTCH1 gene ↗

Location: GLI proteins bind promoters of Hh responsive genes to promote transcription

Stable identifier: R-HSA-5635848

Type: binding

Compartments: nucleoplasm



PTCH1 has been identified as a Hh-responsive target in a number of genome-wide ChIP-based screens and each of the GLI proteins enhances transcription through a consensus GLI-binding site in a ligand-dependent manner (Vokes et al, 2007; Vokes et al, 2008; Lee et al, 2010; Agren et al, 2004). Expression of PTCH1 in response to Hh stimulation establishes a negative feedback loop that limits the duration of pathway activation (reviewed in Hui and Angers, 2011).

Literature references

Hui, CC., Angers, S. (2011). Gli proteins in development and disease. *Annu. Rev. Cell Dev. Biol., 27*, 513-37. ↗

Davidson, EH., Giles, S., Wong, WH., Longabaugh, WJ., McCuine, S., McMahon, AP. et al. (2007). Genomic characterization of Gli-activator targets in sonic hedgehog-mediated neural patterning. *Development, 134*, 1977-89. ↗

Wong, WH., McMahon, AP., Ji, H., Vokes, SA. (2008). A genome-scale analysis of the cis-regulatory circuitry underlying sonic hedgehog-mediated patterning of the mammalian limb. *Genes Dev., 22*, 2651-63. ↗

Kogerman, P., Wessling, M., Toftgård, R., Agren, M., Kleman, MI. (2004). Expression of the PTCH1 tumor suppressor gene is regulated by alternative promoters and a single functional Gli-binding site. *Gene, 330*, 101-14. ↗

Wong, WH., McMahon, AP., Ji, H., Scott, MP., Lee, EY., Vokes, SA. et al. (2010). Hedgehog pathway-regulated gene networks in cerebellum development and tumorigenesis. *Proc. Natl. Acad. Sci. U.S.A., 107*, 9736-41. ↗

Editions

2014-10-31	Edited	Gillespie, ME.
2014-10-31	Authored	Rothfels, K.
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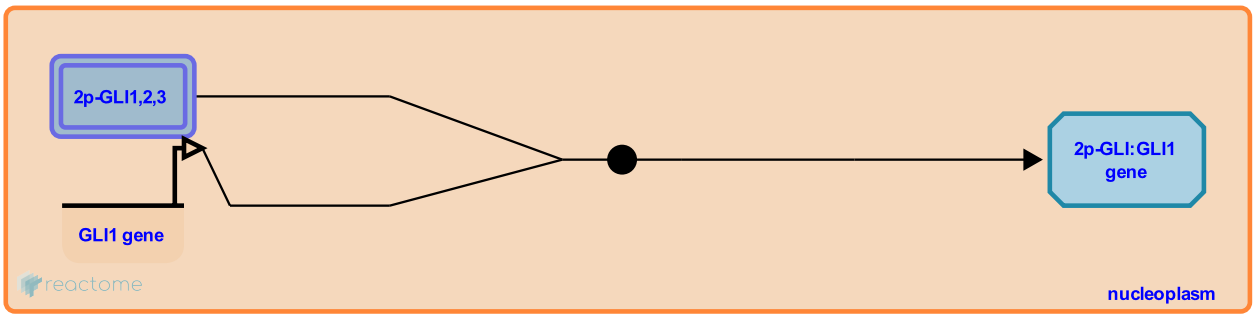
GLI proteins bind GLI1 gene ↗

Location: GLI proteins bind promoters of Hh responsive genes to promote transcription

Stable identifier: R-HSA-5635846

Type: binding

Compartments: nucleoplasm



GLI1 is a direct target of the GLI transcription factors and its expression is absolutely dependent on Hh pathway activation (Dai et al, 1999; Bai et al, 2002; Bai et al, 2004; Vokes et al, 2007; Vokes et al, 2008; Lee et al, 2010). GLI1 is an obligate transcriptional activator and its expression downstream of Hh stimulation establishes a positive feedback loop (reviewed in Briscoe and Therond, 2013).

Followed by: Hh-dependent expression of GLI1 gene

Literature references

Stephen, D., Joyner, AL., Bai, CB. (2004). All mouse ventral spinal cord patterning by hedgehog is Gli dependent and involves an activator function of Gli3. *Dev. Cell, 6*, 103-15. ↗

Ishii, S., Dai, P., Nakafuku, M., Maekawa, T., Akimaru, H., Tanaka, Y. (1999). Sonic Hedgehog-induced activation of the Gli1 promoter is mediated by GLI3. *J. Biol. Chem., 274*, 8143-52. ↗

Davidson, EH., Giles, S., Wong, WH., Longabaugh, WJ., McCuine, S., McMahon, AP. et al. (2007). Genomic characterization of Gli-activator targets in sonic hedgehog-mediated neural patterning. *Development, 134*, 1977-89. ↗

Wong, WH., McMahon, AP., Ji, H., Vokes, SA. (2008). A genome-scale analysis of the cis-regulatory circuitry underlying sonic hedgehog-mediated patterning of the mammalian limb. *Genes Dev., 22*, 2651-63. ↗

Thérond, PP., Briscoe, J. (2013). The mechanisms of Hedgehog signalling and its roles in development and disease. *Nat. Rev. Mol. Cell Biol., 14*, 416-29. ↗

Editions

2014-10-31	Edited	Gillespie, ME.
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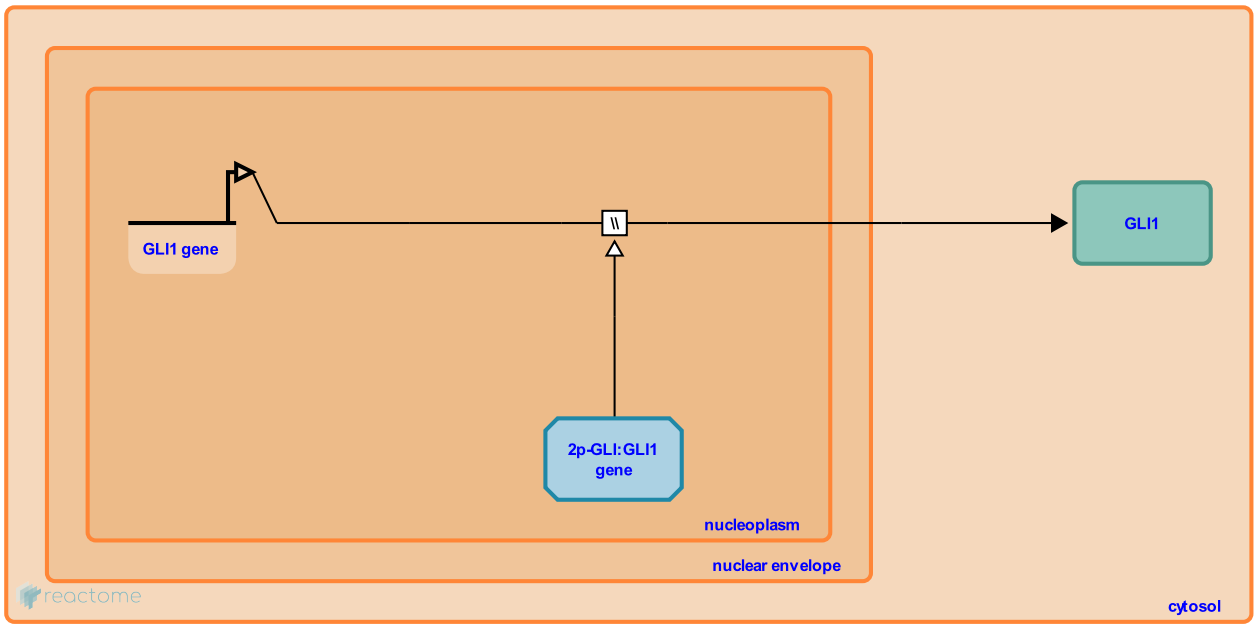
Hh-dependent expression of GLI1 gene ↗

Location: GLI proteins bind promoters of Hh responsive genes to promote transcription

Stable identifier: R-HSA-5635853

Type: omitted

Compartments: nucleoplasm, cytosol



GLI1 expression is promoted by the binding of the full-length GLI transcription factors to consensus GLI sites in the promoter in response to Hh signaling (Dai et al, 1999; Bai et al, 2002; Bai et al, 2004; Vokes et al, 2007; Vokes et al, 2008; Lee et al, 2010).

Preceded by: GLI proteins bind GLI1 gene

Literature references

Stephen, D., Joyner, AL., Bai, CB. (2004). All mouse ventral spinal cord patterning by hedgehog is Gli dependent and involves an activator function of Gli3. *Dev. Cell, 6*, 103-15. ↗

Ishii, S., Dai, P., Nakafuku, M., Maekawa, T., Akimaru, H., Tanaka, Y. (1999). Sonic Hedgehog-induced activation of the Gli1 promoter is mediated by GLI3. *J. Biol. Chem., 274*, 8143-52. ↗

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Wong, WH., McMahon, AP., Ji, H., Vokes, SA. (2008). A genome-scale analysis of the cis-regulatory circuitry underlying sonic hedgehog-mediated patterning of the mammalian limb. *Genes Dev., 22*, 2651-63. ↗

Stephen, D., Joyner, AL., Auerbach, W., Bai, CB., Lee, JS. (2002). Gli2, but not Gli1, is required for initial Shh signaling and ectopic activation of the Shh pathway. *Development, 129*, 4753-61. ↗

Editions

2014-10-31	Edited	Gillespie, ME.
2014-10-31	Authored	Rothfels, K.
2014-11-09	Reviewed	Liu, Y C.

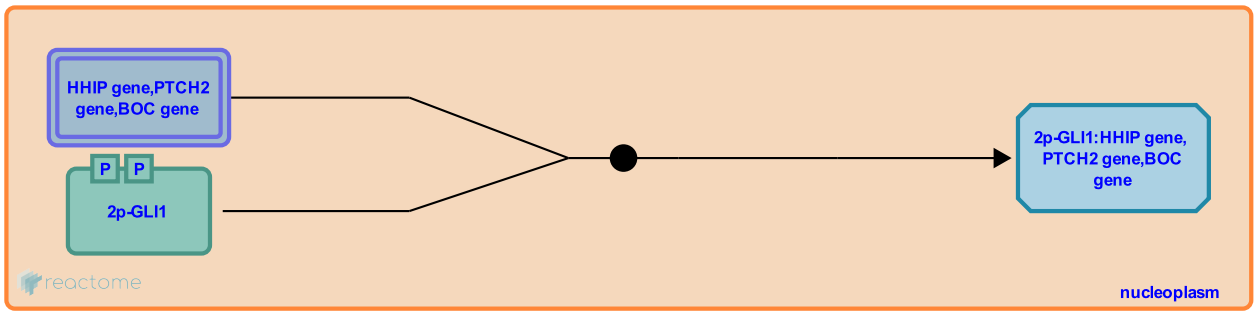
GLI1 binds HHIP gene, PTCH2 gene and BOC gene promoters ↗

Location: GLI proteins bind promoters of Hh responsive genes to promote transcription

Stable identifier: R-HSA-5635850

Type: binding

Compartments: nucleoplasm



Genome-wide ChIP studies have identified Hh pathway members HHIP, PTCH2 and BOC as direct targets of GLI1 downstream of pathway activation (Vokes et al, 2007; Vokes et al, 2008; Lee et al, 2010).

Literature references

Davidson, EH., Giles, S., Wong, WH., Longabaugh, WJ., McCuine, S., McMahon, AP. et al. (2007). Genomic characterization of Gli-activator targets in sonic hedgehog-mediated neural patterning. *Development, 134*, 1977-89. ↗

Wong, WH., McMahon, AP., Ji, H., Vokes, SA. (2008). A genome-scale analysis of the cis-regulatory circuitry underlying sonic hedgehog-mediated patterning of the mammalian limb. *Genes Dev., 22*, 2651-63. ↗

Wong, WH., McMahon, AP., Ji, H., Scott, MP., Lee, EY., Vokes, SA. et al. (2010). Hedgehog pathway-regulated gene networks in cerebellum development and tumorigenesis. *Proc. Natl. Acad. Sci. U.S.A., 107*, 9736-41. ↗

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