

Expression of SERPINE1 (PAI-1)

Albrecht, U., D'Eustachio, P., Delaunay, F., Hirota, T., Kay, SA., May, B.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](https://creativecommons.org/licenses/by/4.0/). For more information see our [license](https://reactome.org/licenses/).

30/04/2024

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

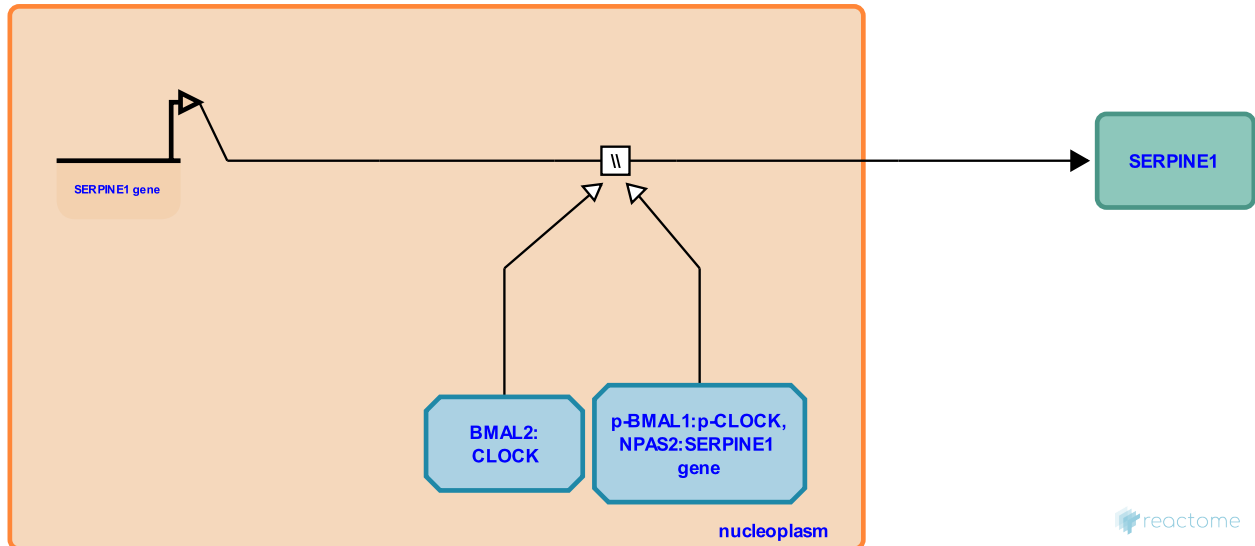
This document contains 1 reaction ([see Table of Contents](#))

Expression of SERPINE1 (PAI-1) ↗

Stable identifier: R-HSA-549364

Type: omitted

Compartments: nucleoplasm, extracellular region



The phosphorylated BMAL1:CLOCK (ARNTL) heterodimer binds an E-box in the promoter of the PAI-1 gene and activate transcription of PAI-1. NPAS2 is predicted to act redundantly with CLOCK.

The PAI-1 gene is transcribed to yield mRNA and the mRNA is translated to yield protein. The PAI-1 gene shows circadian expression due to direct transcriptional activation by the BMAL1:CLOCK (ARNTL:CLOCK) heterodimer and the BMAL2:CLOCK (CLIF:CLOCK, ARNTL2:CLOCK) heterodimer.

BMAL2 (ARNTL2, CLIF) forms a heterodimer with CLOCK, binds E-boxes in the PAI-1 promoter and activates transcription of the PAI-1 gene. BMAL2 shows constitutive rather than circadian expression.

Literature references

- de la Monte, SM., Yet, SF., Layne, MD., Chin, MT., Maemura, K., Lee, ME. et al. (2000). CLIF, a novel cycle-like factor, regulates the circadian oscillation of plasminogen activator inhibitor-1 gene expression. *J Biol Chem*, 275, 36847-51. ↗
- Samani, NJ., Chong, NW., Codd, V., Chan, D. (2006). Circadian clock genes cause activation of the human PAI-1 gene promoter with 4G/5G allelic preference. *FEBS Lett*, 580, 4469-72. ↗
- van der Bom, JG., Bots, ML., Kluft, C., Haverkate, F., Grobbee, DE. (2003). The 4G5G polymorphism in the gene for PAI-1 and the circadian oscillation of plasma PAI-1. *Blood*, 101, 1841-4. ↗
- Eren, M., Smith, LH., Vaughan, DE., Johnson, CH., Painter, CA., Schoenhard, JA. (2003). Regulation of the PAI-1 promoter by circadian clock components: differential activation by BMAL1 and BMAL2. *J Mol Cell Cardiol*, 35, 473-81. ↗

Editions

2009-05-27	Reviewed	D'Eustachio, P.
2010-03-19	Authored, Edited	May, B.
2010-06-23	Reviewed	Hirota, T., Kay, SA., Delaunay, F., Albrecht, U.