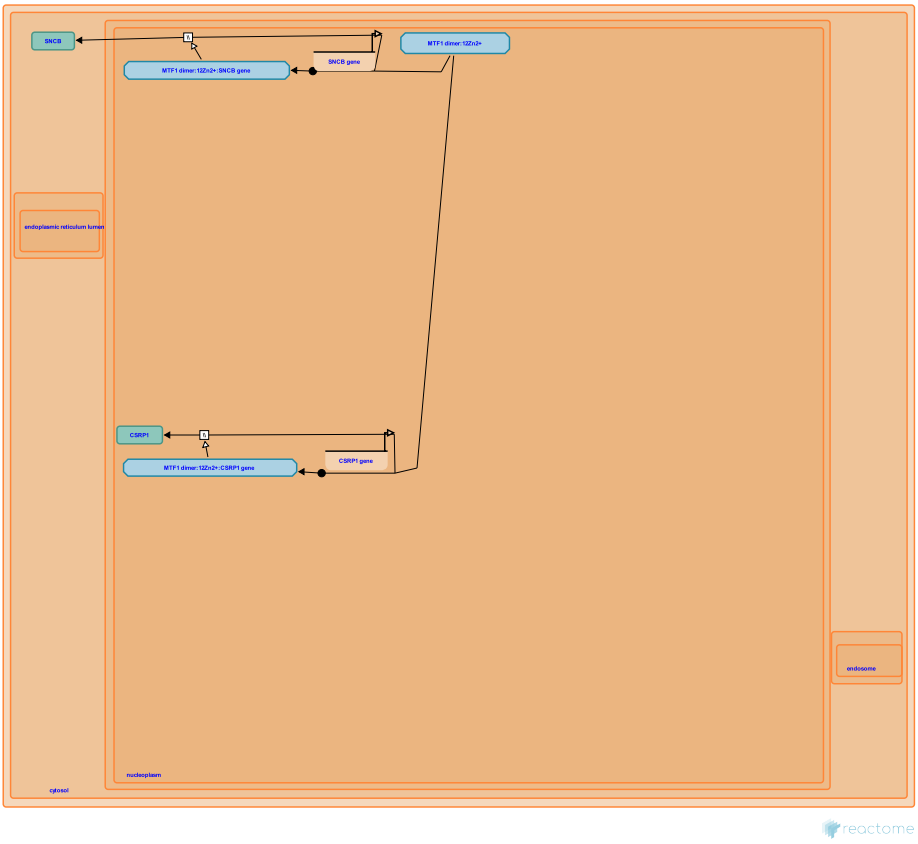
MTF1 activates gene expression



Brown, DR., Ford, D., May, B., Wang, Q.

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24/04/2024

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. ↗

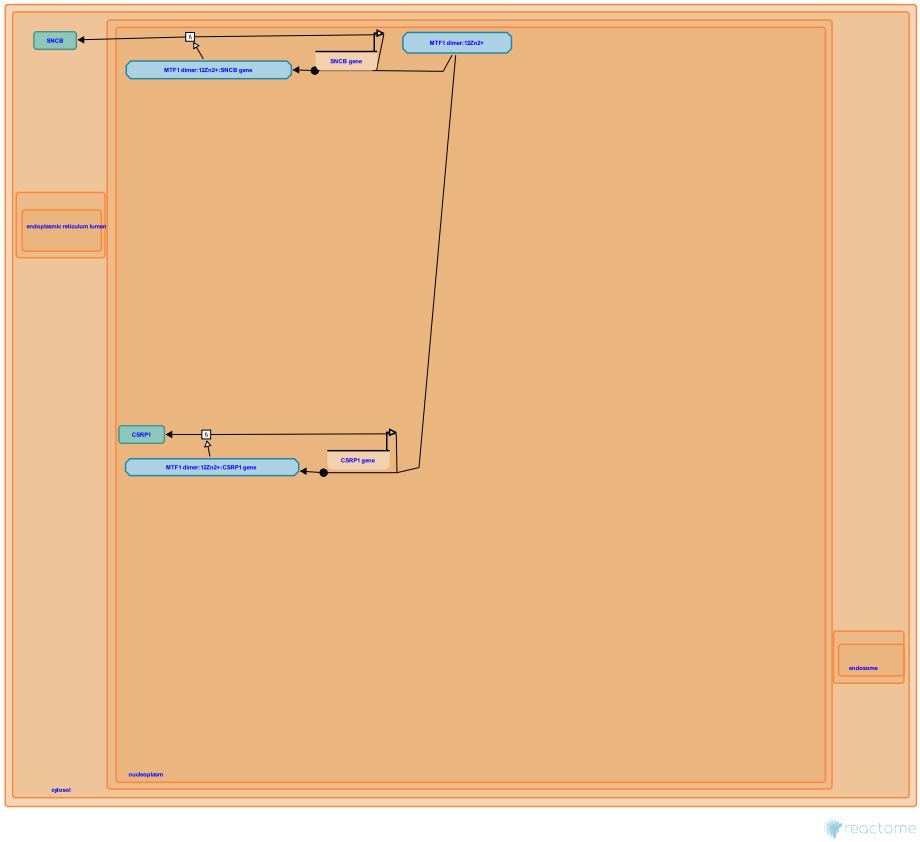
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

MTF1 activates gene expression ↗

Stable identifier: R-HSA-5660489



The MTF1:zinc complex in the nucleus binds Metal Response Elements (MREs), DNA containing the core consensus sequence 5'-TGCRCNC-3', and activates or represses transcription depending on the context of the MRE (reviewed in Laity and Andrews 2007, Jackson et al. 2008, Gunther et al. 2012, Grzywacz et al. 2015). The 6 zinc fingers of each MTF1 monomer have different affinities for zinc and evidence from the mouse homolog indicates that different concentrations of zinc, and hence different metal loads in MTF1, activate different subsets of target genes (Wang et al. 2004, Dong et al. 2015). Genes activated by MTF1 include those encoding metallothioneins, zinc transporters, and stress-response proteins (Hardyman et al. 2016).

Literature references

Opoka, W., Tyszka-Czochara, M., Grzywacz, A., Muszyńska, B., Gdula-Argasińska, J., Librowski, T. (2015). Metal responsive transcription factor 1 (MTF-1) regulates zinc dependent cellular processes at the molecular level. *Acta Biochim. Pol., 62*, 491-8. ↗

Jackson, KA., Coneyworth, LJ., Valentine, RA., Ford, D., Mathers, JC. (2008). Mechanisms of mammalian zinc-regulated gene expression. *Biochem. Soc. Trans., 36*, 1262-6. ↗

Wang, Q., Dou, Y., Dong, G., Chen, H., Qi, M. (2015). Balance between metallothionein and metal response element binding transcription factor 1 is mediated by zinc ions (review). *Mol Med Rep, 11*, 1582-6. ↗

Wakeling, LA., Hardyman, JE., Valentine, RA., Aldridge, C., Tyson, J., Jackson, KA. et al. (2016). Zinc sensing by metal-responsive transcription factor 1 (MTF1) controls metallothionein and ZnT1 expression to buffer the sensitivity of the transcriptome response to zinc. *Metallomics, 8*, 337-43. ↗

Andrews, GK., Laity, JH. (2007). Understanding the mechanisms of zinc-sensing by metal-response element binding transcription factor-1 (MTF-1). *Arch. Biochem. Biophys., 463*, 201-10. ↗

Editions

2014-12-28	Authored, Edited	May, B.
2017-01-27	Reviewed	Ford, D., Wang, Q.

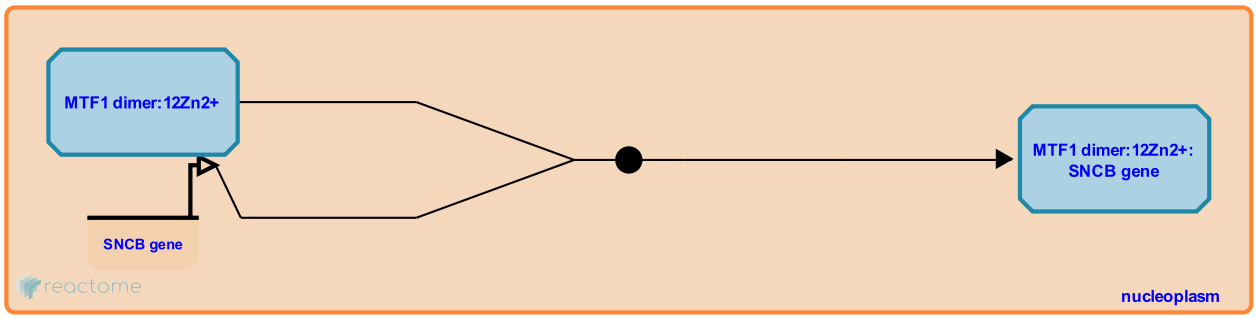
MTF1 dimer:12Zn2+ binds SNCB gene (beta-synuclein) ↗

Location: MTF1 activates gene expression

Stable identifier: R-HSA-5660479

Type: binding

Compartments: nucleoplasm



The MTF1:zinc complex binds a metal response element in the promoter of the beta-synuclein (SNCB) gene and activates transcription in response to zinc (McHugh et al. 2011).

Followed by: Expression of SNCB

Literature references

McHugh, PC., Wright, JA., Brown, DR. (2011). Transcriptional regulation of the beta-synuclein 5'-promoter metal response element by metal transcription factor-1. *PLoS ONE, 6*, e17354. ↗

Editions

2014-12-28	Authored, Edited	May, B.
2017-01-12	Reviewed	Brown, DR.

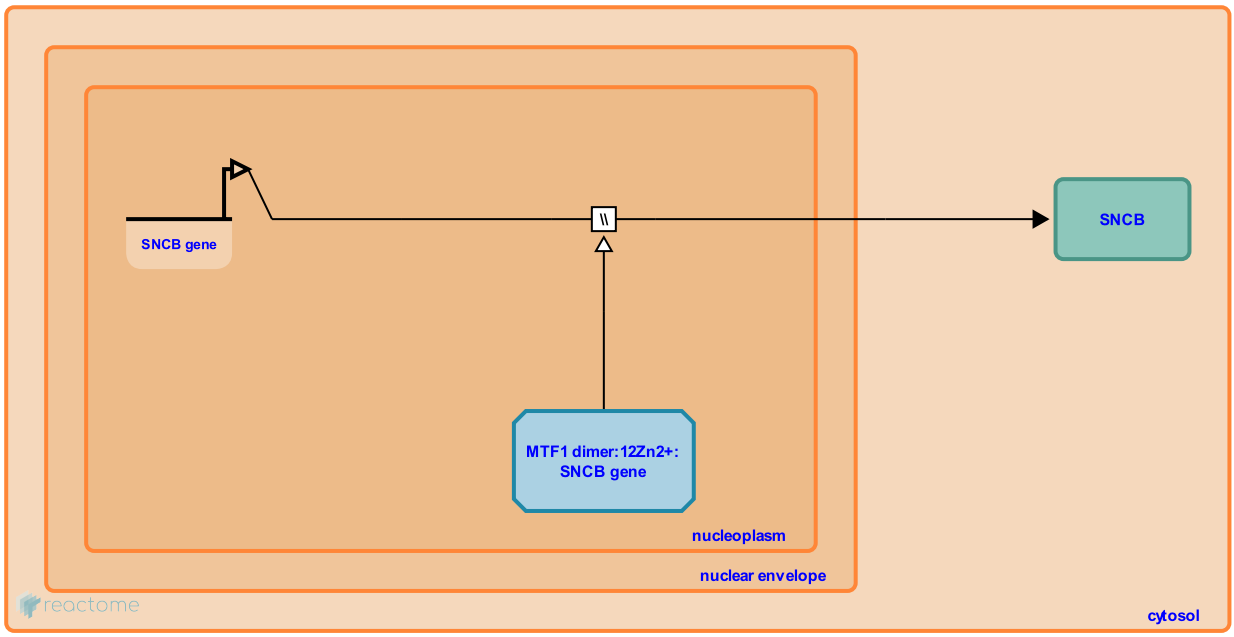
Expression of SNCB ↗

Location: MTF1 activates gene expression

Stable identifier: R-HSA-5660530

Type: omitted

Compartments: nucleoplasm, cytosol



The SNCB (beta-synuclein) gene is transcribed to yield mRNA which is translated to yield protein (Lavedan et al. 1998). Transcription of SNCB is up-regulated by copper via a metal response binding element in the 5' promoter that binds MTF1 (McHugh et al. 2011).

Preceded by: MTF1 dimer:12Zn2+ binds SNCB gene (beta-synuclein)

Literature references

McHugh, PC., Wright, JA., Brown, DR. (2011). Transcriptional regulation of the beta-synuclein 5'-promoter metal response element by metal transcription factor-1. *PLoS ONE, 6*, e17354. ↗

Nussbaum, RL., Polymeropoulos, MH., Dutra, A., Torres, R., Lavedan, C., Buchholtz, S. et al. (1998). Genomic organization and expression of the human beta-synuclein gene (SNCB). *Genomics, 54*, 173-5. ↗

Editions

2014-12-28	Authored, Edited	May, B.
2017-01-12	Reviewed	Brown, DR.

MTF1 dimer:12Zn2+ binds CSRP1 gene ↗

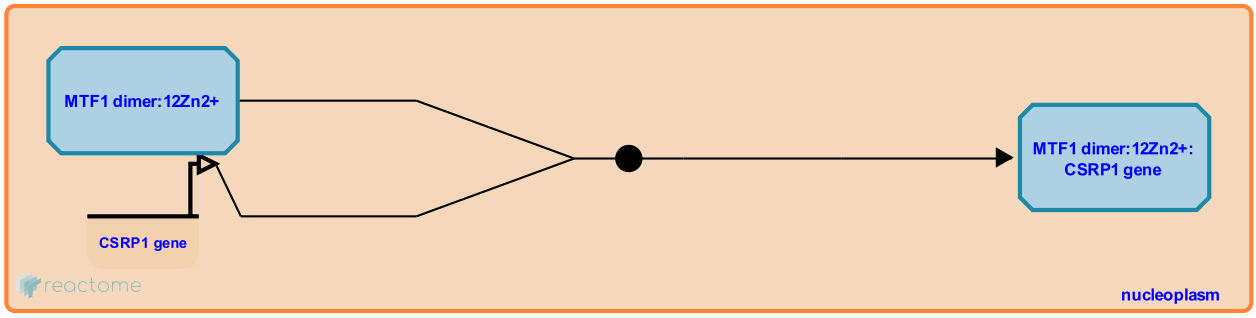
Location: MTF1 activates gene expression

Stable identifier: R-HSA-5660514

Type: binding

Compartments: nucleoplasm

Inferred from: Mtf1 dimer:12Zn2+ binds Csrp1 gene (Mus musculus)



As inferred from the mouse homolog, the promoter of the CSRP1 gene contains 3 consensus metal response elements, at least one of which binds MTF1. Expression of CSRP1 is activated by cadmium via MTF1.

Followed by: Expression of CSRP1

Editions

2014-12-28	Authored, Edited	May, B.
2017-01-27	Reviewed	Ford, D.

Expression of CSRP1 ↗

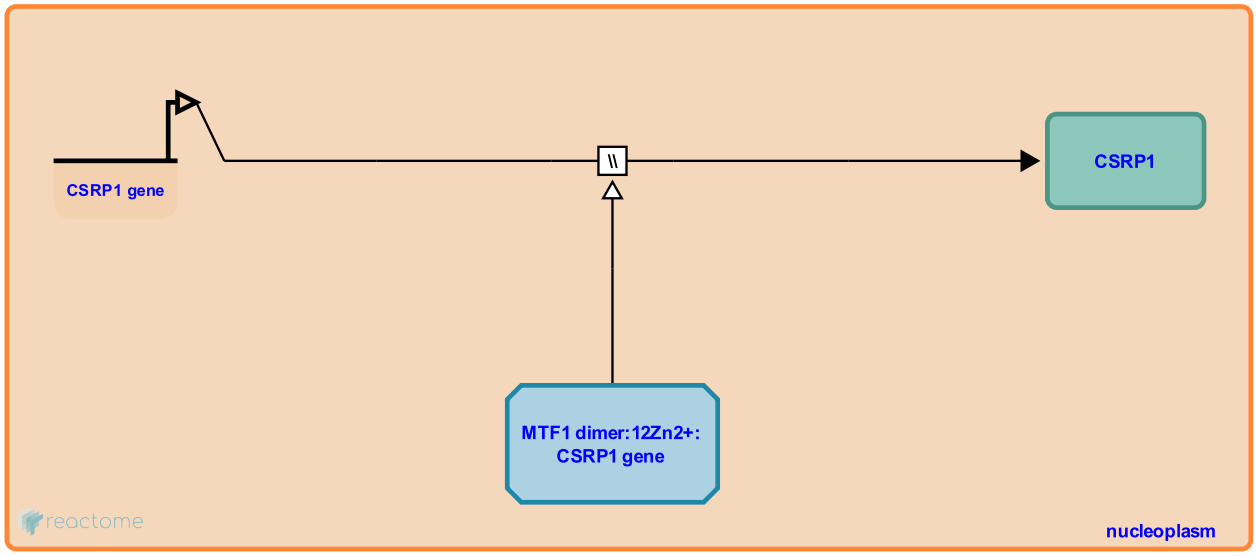
Location: MTF1 activates gene expression

Stable identifier: R-HSA-5660503

Type: omitted

Compartments: nucleoplasm

Inferred from: Expression of Csrp1 (Mus musculus)



The CSRP1 gene is transcribed to yield mRNA which is translated to yield protein. Expression of CSRP1 is activated by zinc via MTF1 (Hardyman et al. 2016). As inferred from the mouse homolog, expression of CSRP1 is activated by cadmium via MTF1.
As inferred from mouse homologs, MTF1 binds and activates the CSRP1 promoter (Wimmer et al. 2005).

Preceded by: MTF1 dimer:12Zn2+ binds CSRP1 gene

Literature references

Cooke, NE., Lee, G., Wang, X., Liebhaber, SA. (1992). Human cysteine-rich protein. A member of the LIM/double-finger family displaying coordinate serum induction with c-myc. *J. Biol. Chem., 267*, 9176-84. ↗

Wakeling, LA., Hardyman, JE., Valentine, RA., Aldridge, C., Tyson, J., Jackson, KA. et al. (2016). Zinc sensing by metal-responsive transcription factor 1 (MTF1) controls metallothionein and ZnT1 expression to buffer the sensitivity of the transcriptome response to zinc. *Metallomics, 8*, 337-43. ↗

Editions

2014-12-28	Authored, Edited	May, B.
2017-01-27	Reviewed	Ford, D.

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