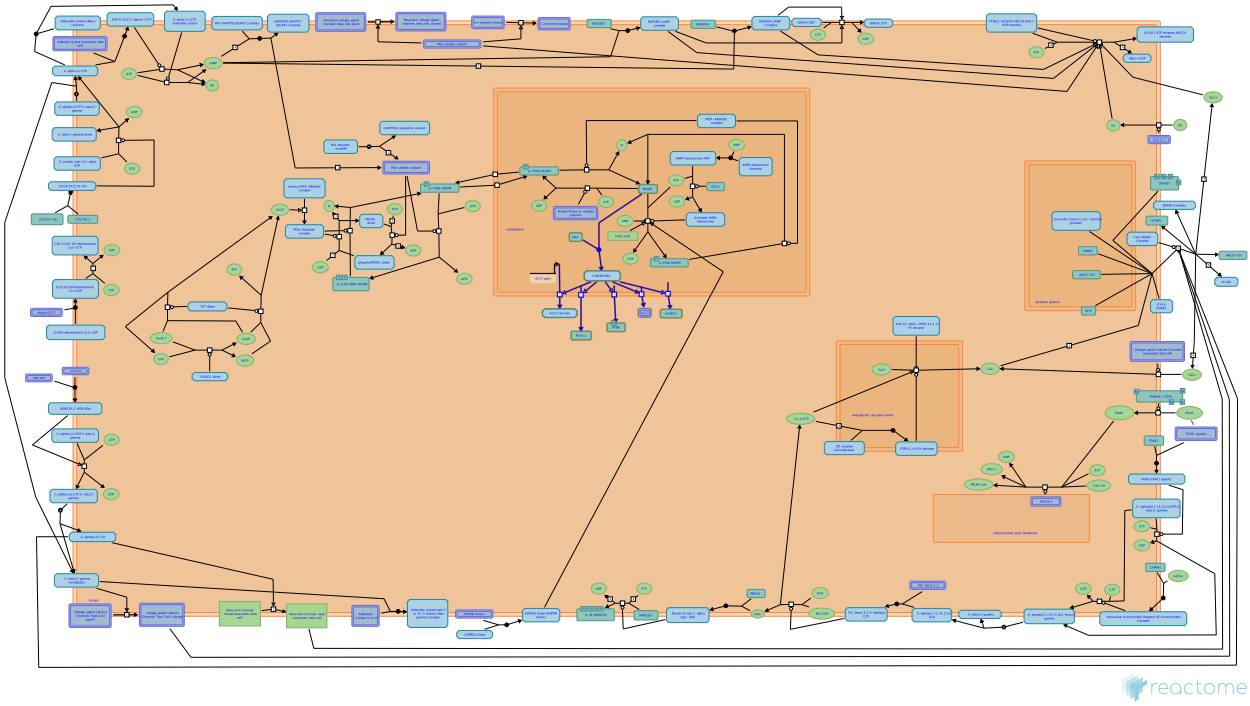
ChREBP activates metabolic gene expression



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10/09/2021

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. ↗

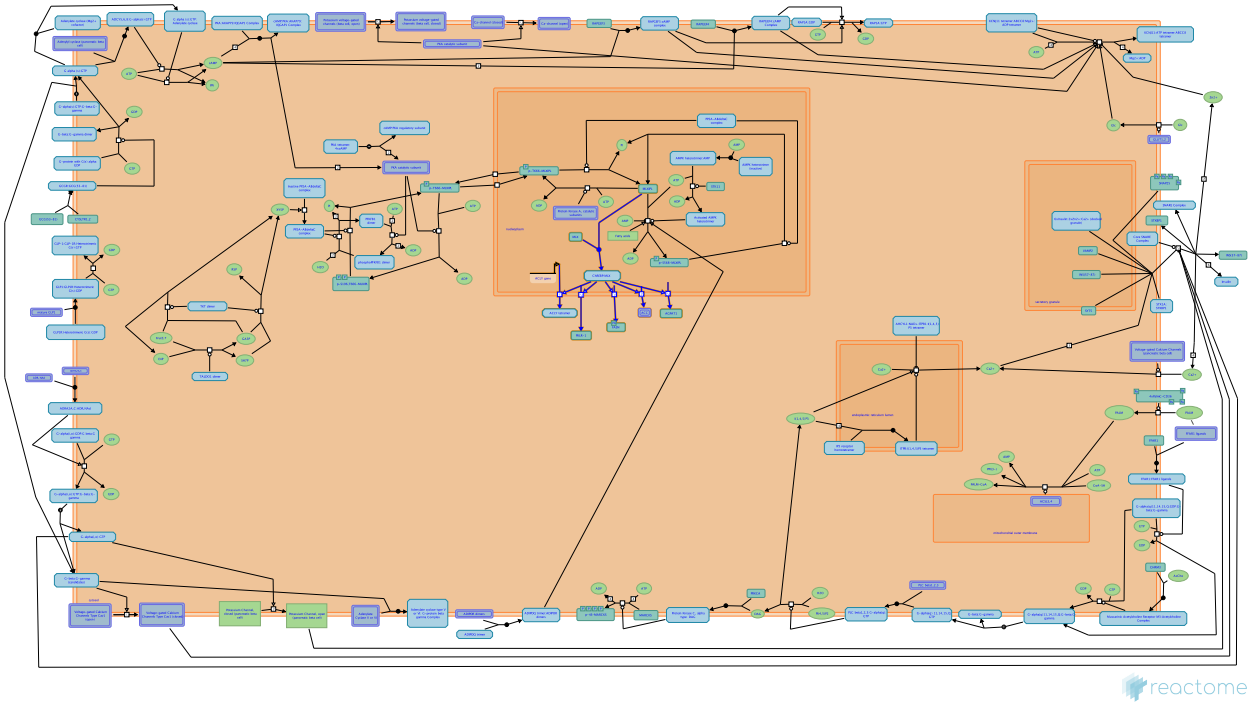
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

ChREBP activates metabolic gene expression ↗

Stable identifier: R-HSA-163765

Compartments: nucleoplasm, cytosol, endoplasmic reticulum membrane



ChREBP (Carbohydrate Response Element Binding Protein) is a large multidomain protein containing a nuclear localization signal near its amino terminus, polyproline domains, a basic helix-loop-helix-leucine zipper domain, and a leucine-zipper-like domain (Uyeda et al., 2002). Its dephosphorylation in response to molecular signals associated with the well-fed state allows it to enter the nucleus, interact with MLX protein, and bind to ChRE DNA sequence motifs near Acetyl-CoA carboxylase, Fatty acid synthase, and Pyruvate kinase (L isoform) genes (Ishi et al.2004). This sequence of events is outlined schematically in the picture below (adapted from Kawaguchi et al. (2001) - copyright (2001) National Academy of Sciences, U.S.A.).

Literature references

Kawaguchi, T., Takenoshita, M., Kabashima, T., Uyeda, K. (2001). Glucose and cAMP regulate the L-type pyruvate kinase gene by phosphorylation/dephosphorylation of the carbohydrate response element binding protein. *Proc Natl Acad Sci U S A, 98*, 13710-5. ↗

Ma, L., Tsatsos, NG., Towle, HC. (2005). Direct role of ChREBP.Mlx in regulating hepatic glucose-responsive genes. *J Biol Chem, 280*, 12019-27. ↗

Iizuka, K., Bruick, RK., Liang, G., Horton, JD., Uyeda, K. (2004). Deficiency of carbohydrate response element-binding protein (ChREBP) reduces lipogenesis as well as glycolysis. *Proc Natl Acad Sci U S A, 101*, 7281-6. ↗

Editions

2005-05-13	Authored	Gopinathrao, G.

Formation of ChREBP:MLX heterodimer ↗

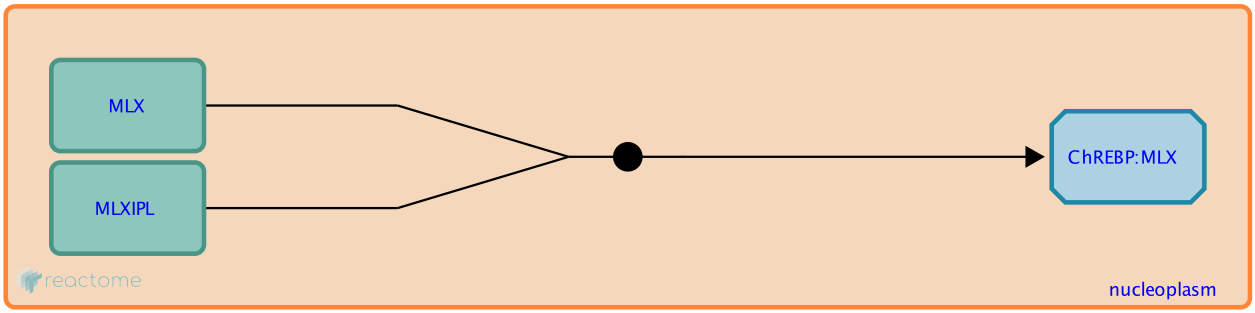
Location: ChREBP activates metabolic gene expression

Stable identifier: R-HSA-163666

Type: binding

Compartments: nucleoplasm

Inferred from: Formation of mChREBP:mMlx complex (Mus musculus)



At the beginning of this reaction, 1 molecule of 'ChREBP protein', and 1 molecule of 'MLX protein' are present. At the end of this reaction, 1 molecule of 'ChREBP:MLX' is present.

This reaction takes place in the 'nucleus'.

Followed by: Transcriptional activation of Acetyl-CoA carboxylase by ChREBP:MLX, Transcriptional activation of Citrate lyase monomer gene by ChREBP:MLX, Transcriptional activation of FAS monomer gene by ChREBP:MLX, Transcriptional activation of pyruvate kinase gene by ChREBP:MLX, Transcriptional activation of GP-acyl transferase gene by ChREBP:MLX

Transcriptional activation of pyruvate kinase gene by ChREBP:MLX ↗

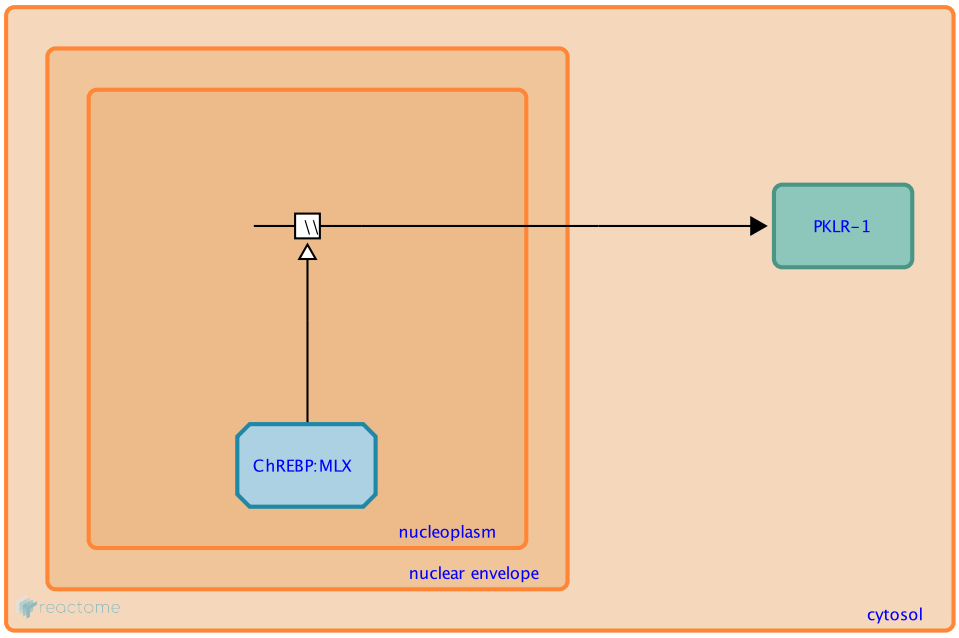
Location: ChREBP activates metabolic gene expression

Stable identifier: R-HSA-163669

Type: omitted

Compartments: nucleoplasm, cytosol

Inferred from: Transcriptional activation of pyruvate kinase L isoform gene by mChREBP:mMLX (Mus musculus)



At the end of this reaction, 1 molecule of 'pyruvate kinase, liver and RBC' is present.

This reaction takes place in the 'nucleus'.

Preceded by: Formation of ChREBP:MLX heterodimer

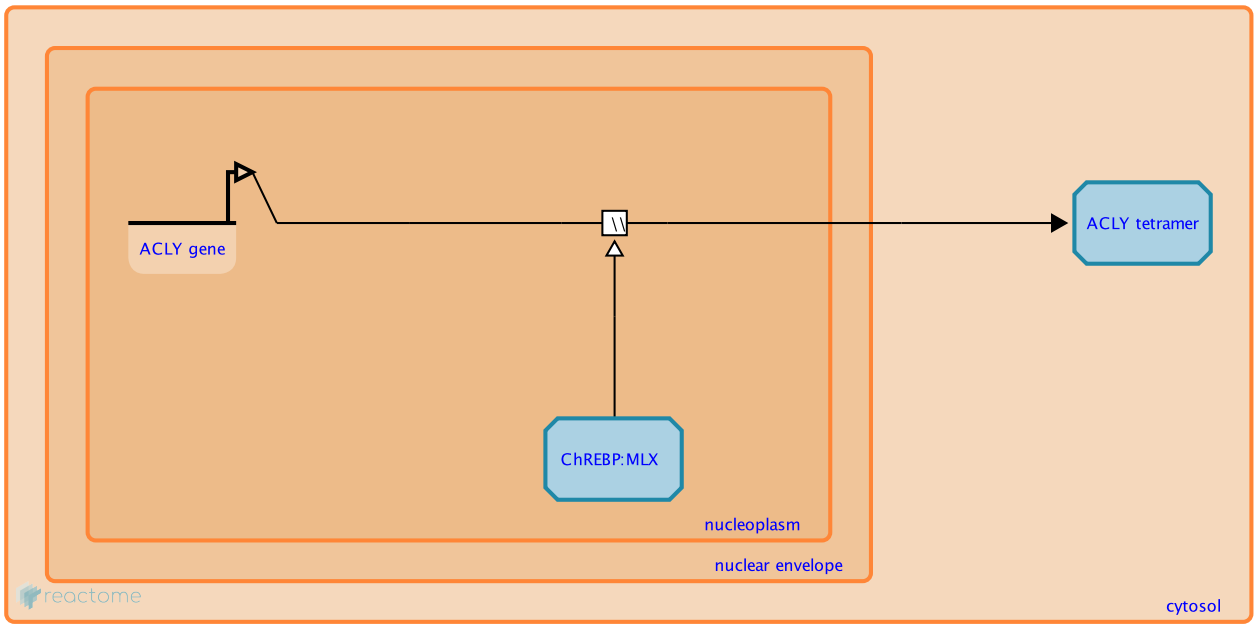
Transcriptional activation of Citrate lyase monomer gene by ChREBP:MLX ↗

Location: ChREBP activates metabolic gene expression

Stable identifier: R-HSA-163770

Type: omitted

Compartments: nucleoplasm, cytosol



At the end of this reaction, 1 molecule of 'citrate lyase monomer' is present.

This reaction takes place in the 'nucleus'.

Preceded by: Formation of ChREBP:MLX heterodimer

Literature references

Ma, L., Robinson, LN., Towle, HC. (2006). ChREBP*Mlx is the principal mediator of glucose-induced gene expression in the liver. *J. Biol. Chem., 281*, 28721-30. ↗

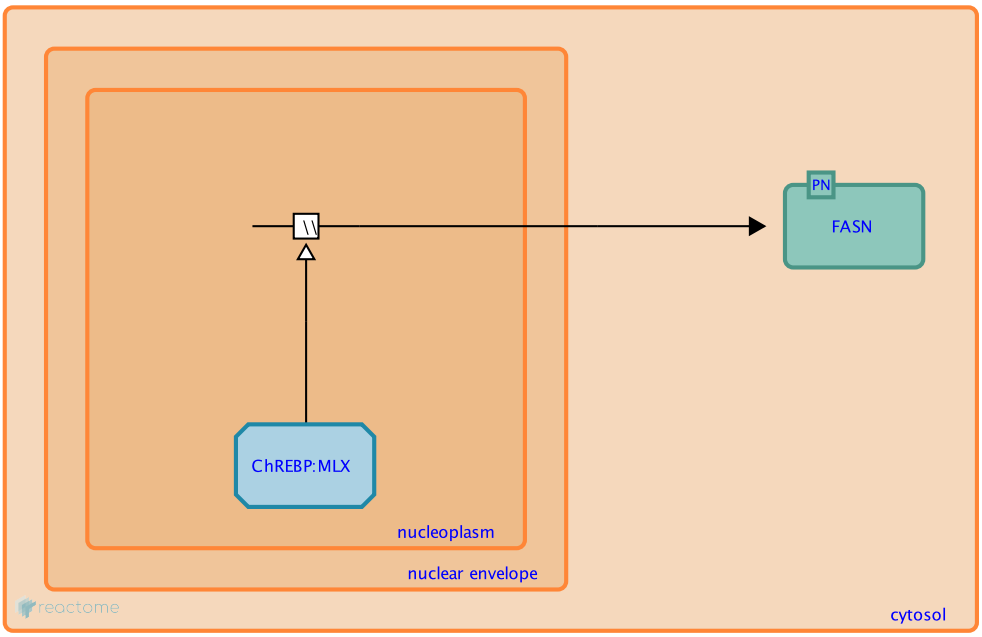
Transcriptional activation of FAS monomer gene by ChREBP:MLX ↗

Location: ChREBP activates metabolic gene expression

Stable identifier: R-HSA-163733

Type: omitted

Compartments: nucleoplasm, cytosol



At the end of this reaction, 1 molecule of 'Fatty acid synthase ' is present.

This reaction takes place in the 'nucleus' (Ma et al. 2005, Havula et al. 2012).

Preceded by: Formation of ChREBP:MLX heterodimer

Literature references

Havula, E., Hietakangas, V. (2012). Glucose sensing by ChREBP/MondoA-Mlx transcription factors. *Semin. Cell Dev. Biol., 23*, 640-7. ↗

Ma, L., Tsatsos, NG., Towle, HC. (2005). Direct role of ChREBP.Mlx in regulating hepatic glucose-responsive genes. *J Biol Chem, 280*, 12019-27. ↗

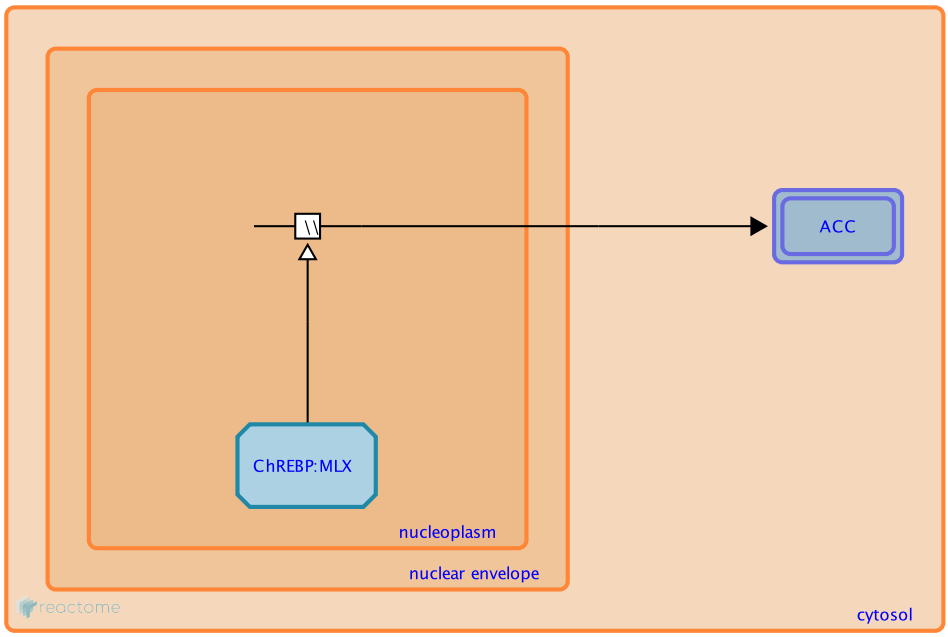
Transcriptional activation of Acetyl-CoA carboxylase by ChREBP:MLX ↗

Location: ChREBP activates metabolic gene expression

Stable identifier: R-HSA-163743

Type: omitted

Compartments: nucleoplasm, cytosol



At the end of this reaction, 1 molecule of 'Acetyl-CoA carboxylase 2 ' is present.

This reaction takes place in the 'nucleus' (Ma et al. 2006).

Preceded by: Formation of ChREBP:MLX heterodimer

Literature references

Ma, L., Robinson, LN., Towle, HC. (2006). ChREBP*Mlx is the principal mediator of glucose-induced gene expression in the liver. *J. Biol. Chem., 281*, 28721-30. ↗

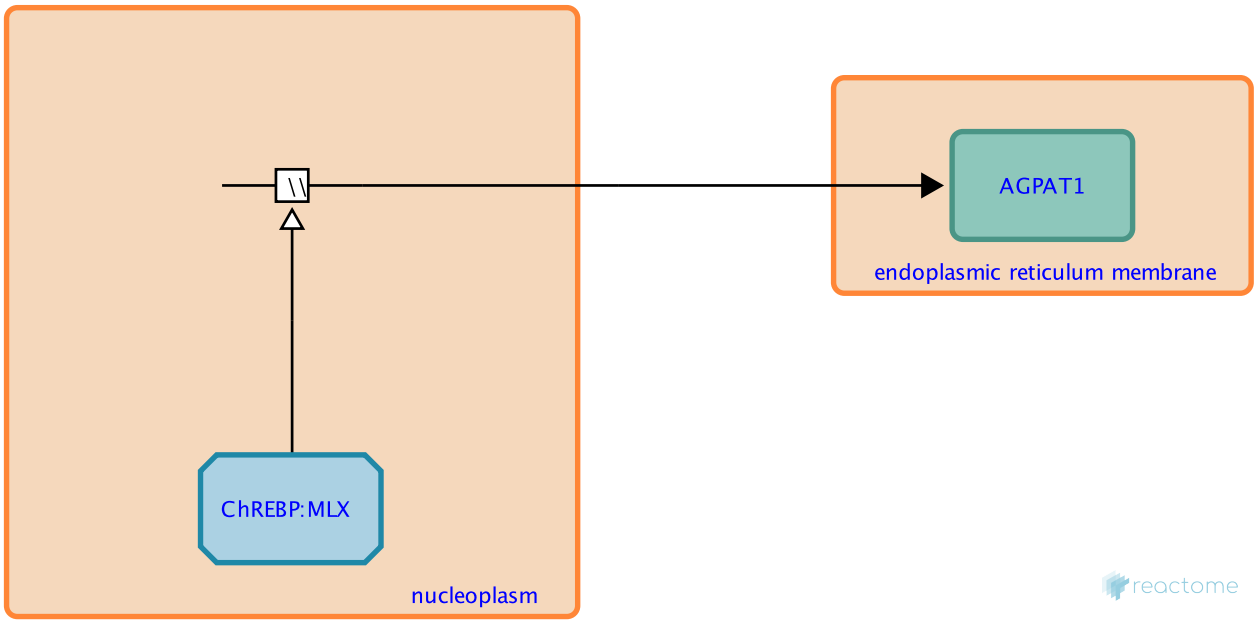
Transcriptional activation of GP-acyl transferase gene by ChREBP:MLX ↗

Location: ChREBP activates metabolic gene expression

Stable identifier: R-HSA-163748

Type: omitted

Compartments: nucleoplasm, endoplasmic reticulum membrane



At the end of this reaction, 1 molecule of '1-acyl-sn-glycerol-3-phosphate acyltransferase alpha ' is present.

This reaction takes place in the 'nucleus' (Ma et al.2007).

Preceded by: Formation of ChREBP:MLX heterodimer

Literature references

Ma, L., Sham, YY., Walters, KJ., Towle, HC. (2007). A critical role for the loop region of the basic helix-loop-helix/leucine zipper protein Mlx in DNA binding and glucose-regulated transcription. *Nucleic Acids Res., 35*, 35-44. ↗

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