reactome

Pathway Analysis Report

Gene names from liver

This report contains the pathway analysis results for the submitted sample 'Gene names from liver'. Analysis was performed against Reactome version 67 on 14/12/2018. The web link to these results is:

https://reactomedev.oicr.on.ca/PathwayBrowser/#/ANALYSIS=MjAxODEwMDQxMDA3MDhfMw%3D%3D

Please keep in mind that analysis results are temporarily stored on our server. The storage period depends on usage of the service but is at least 7 days. As a result, please note that this URL is only valid for a limited time period and it might have expired.

Table of Contents

1. Introduction

Reactome is a curated database of pathways and reactions in human biology. Reactions can be considered as pathway 'steps'. Reactome defines a 'reaction' as any event in biology that changes the state of a biological molecule. Binding, activation, translocation, degradation and classical biochemical events involving a catalyst are all reactions. Information in the database is authored by expert biologists, entered and maintained by Reactome's team of curators and editorial staff. Reactome content frequently cross-references other resources e.g. NCBI, Ensembl, UniProt, KEGG (Gene and Compound), ChEBI, PubMed and GO. Orthologous reactions inferred from annotation for Homo sapiens are available for 17 non-human species including mouse, rat, chicken, puffer fish, worm, fly, yeast, rice, and Arabidopsis. Pathways are represented by simple diagrams following an SBGN-like format.

Reactome's annotated data describe reactions possible if all annotated proteins and small molecules were present and active simultaneously in a cell. By overlaying an experimental dataset on these annotations, a user can perform a pathway over-representation analysis. By overlaying quantitative expression data or time series, a user can visualize the extent of change in affected pathways and its progression. A binomial test is used to calculate the probability shown for each result, and the p-values are corrected for the multiple testing (Benjamini–Hochberg procedure) that arises from evaluating the submitted list of identifiers against every pathway.

To learn more about our Pathway Analysis, please have a look at our relevant publications:

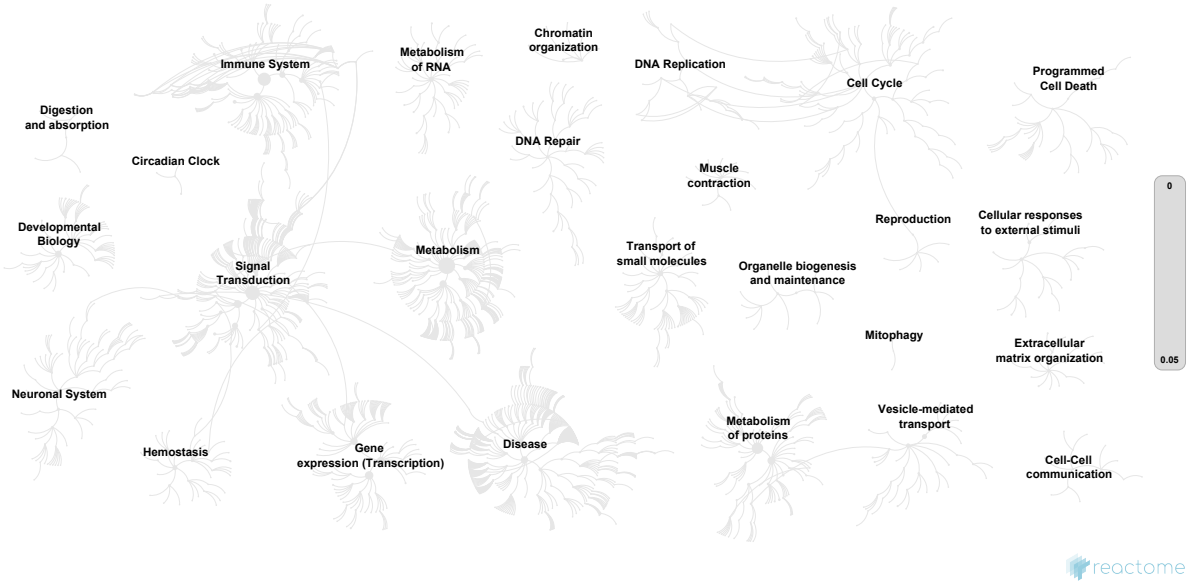
Fabregat A, Sidiropoulos K, Garapati P, Gillespie M, Hausmann K, Haw R, DEustachio P (2016). The reactome pathway knowledgebase. Nucleic Acids Research, 44(D1), D481D487. https://doi.org/10.1093/nar/gkv1351.

Fabregat A, Sidiropoulos K, Viteri G, Forner O, Marin-Garcia P, Arnau V, Hermjakob H (2017). Reactome pathway analysis: a high-performance in-memory approach. BMC Bioinformatics, 18.

2. Properties

- This is an **overrepresentation** analysis: A statistical (hypergeometric distribution) test that determines whether certain Reactome pathways are over-represented (enriched) in the submitted data. It answers the question 'Does my list contain more proteins for pathway X than would be expected by chance?' This test produces a probability score, which is corrected for false discovery rate using the Benjamani-Hochberg method.
- 178 out of 209 identifiers in the sample were found in Reactome, where 12909 pathways were hit by at least one of them.
- IntAct interactors were included to increase the analysis background. This greatly increases the size of Reactome pathways, which maximises the chances of matching your submitted identifiers to the expanded pathway, but will include interactors that have not undergone manual curation by Reactome and may include interactors that have no biological significance, or unexplained relevance.
- This report is filtered to show only results for species 'Homo sapiens' and resource 'all resources'.
- The unique ID for this analysis (token) is MjAxODEwMDQxMDA3MDhfMw%3D%3D. This ID is valid for at least 7 days in Reactome's server. Use it to access Reactome services with your data.

3. Genome-wide overview



This figure shows a genome-wide overview of the results of your pathway analysis. Reactome pathways are arranged in a hierarchy. The center of each of the circular "bursts" is the root of one top-level pathway, for example "DNA Repair". Each step away from the center represents the next level lower in the pathway hierarchy. The color code denotes over-representation of that pathway in your input dataset. Light grey signifies pathways which are not significantly over-represented.

4. Most significant pathways

The following table shows the 10 most relevant pathways sorted by p-value.

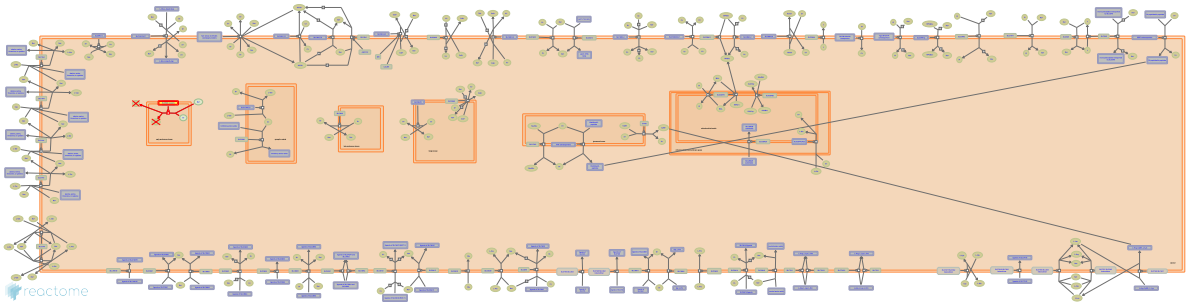
Pathway name	Entities				Reactions	
	found	ratio	p-value	FDR*	found	ratio
Defective SLC9A6 causes X-linked, syndromic mental retardation,, Christianson type (MRXSCH)	1 / 3	1.59e-04	0.324	1	1 / 1	8.48e-05
Defective SLC5A1 causes congenital glucose/galactose malabsorption (GGM)	1 / 3	1.59e-04	0.324	1	1 / 1	8.48e-05
Defective LARGE causes MDDGA6 and MDDGB6	1 / 3	1.59e-04	0.324	1	1 / 1	8.48e-05
Transport of glycerol from adipocytes to the liver by Aquaporins	1 / 3	1.59e-04	0.324	1	1 / 2	1.70e-04
E2F-enabled inhibition of pre-replication complex formation	2 / 9	4.76e-04	0.328	1	1 / 1	8.48e-05
Signaling by FGFR2 IIIa TM	5 / 30	0.002	0.354	1	2 / 2	1.70e-04
Glycogen storage disease type II (GAA)	1 / 4	2.12e-04	0.407	1	1 / 1	8.48e-05
Defective SLCO1B3 causes hyperbilirubinemia, Rotor type (HBLRR)	1 / 4	2.12e-04	0.407	1	1 / 1	8.48e-05
Laminin interactions	5 / 33	0.002	0.43	1	12 / 15	0.001
Defective CYP19A1 causes Aromatase excess syndrome (AEXS)	1 / 5	2.65e-04	0.479	1	1 / 1	8.48e-05

* False Discovery Rate

5. Pathways details

For every pathway of the most significant pathways, we present its diagram, as well as a short summary, its bibliography and the list of inputs found in it.

1. Defective SLC9A6 causes X-linked, syndromic mental retardation,, Christianson type (MRXSCH) (R-HSA-5619092)



Diseases: syndromic intellectual disability.

SLC9A6 encodes the sodium/hydrogen exchanger 6 NHE6, a protein ubiquitously expressed but most abundant in mitochondria-rich tissues such as brain, skeletal muscle and heart. It is located on endosomal membranes and thought to play a housekeeping role in pH homeostasis in early endosomes. It mediates the electroneutral exchange of protons for Na+ and K+ across the early and recycling endosome membranes. Defects in SLC9A6 can cause mental retardation, X-linked, syndromic, Christianson type (MRXSCH; MIM:300243), a syndrome characterised by profound mental retardation, epilepsy, ataxia and microcephaly. MRXSCH shows phenotypic overlap with Angelman syndrome (Gilfillan et al. 2008, Schroer et al. 2010, Kondapalli et al. 2014).

References

Kondapalli KC, Prasad H & Rao R (2014). An inside job: how endosomal Na(+)/H(+) exchangers link to autism and neurological disease. Front Cell Neurosci, 8, 172.

Gilfillan GD, Selmer KK, Roxrud I, Smith R, Kyllerman M, Eiklid K, ... Strømme P (2008). SLC9A6 mutations cause X-linked mental retardation, microcephaly, epilepsy, and ataxia, a phenotype mimicking Angelman syndrome. Am. J. Hum. Genet., 82, 1003-10.

Schroer RJ, Holden KR, Tarpey PS, Matheus MG, Griesemer DA, Friez MJ, ... Schwartz CE (2010). Natural history of Christianson syndrome. Am. J. Med. Genet. A, 152, 2775-83.

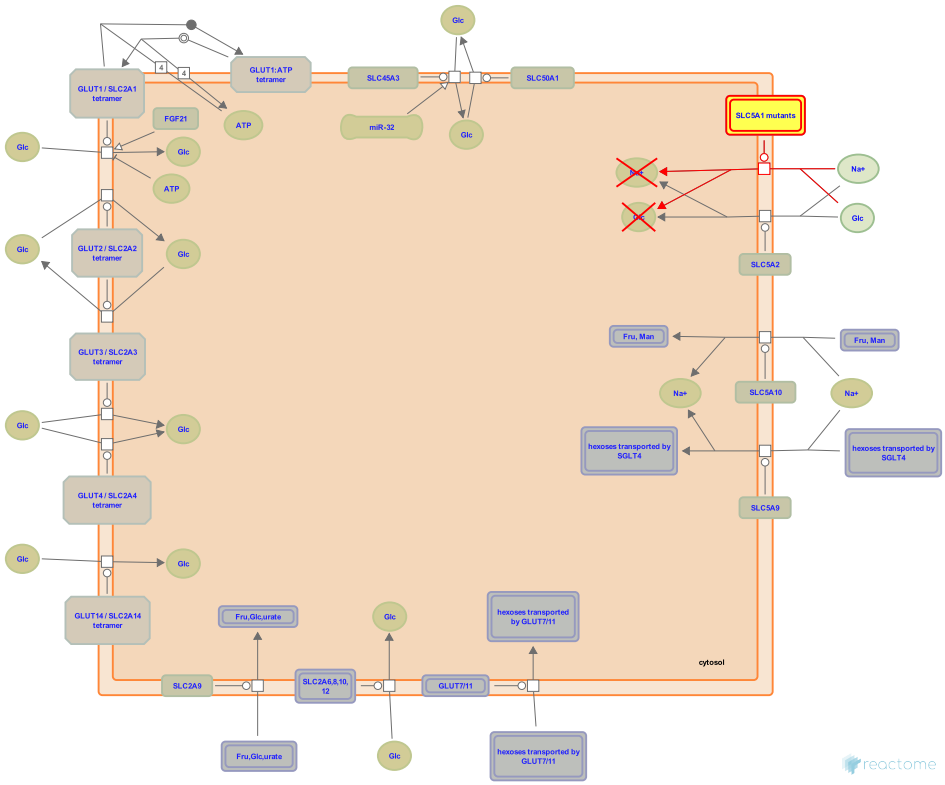
Edit history

Date	Action	Author
2014-08-22	Edited	Jassal B
2014-08-22	Authored	Jassal B
2014-08-22	Created	Jassal B
2015-08-04	Reviewed	Broer S
2018-12-05	Modified	Croft D

Entities found in this pathway (1)

Input	UniProt Id
SLC9A6	Q92581

2. Defective SLC5A1 causes congenital glucose/galactose malabsorption (GGM) (R-HSA-5656364)



Diseases: glucose intolerance.

Sodium/glucose cotransporter 1 (SLC5A1 aka SGLT1) actively and reversibly transports glucose (Glc) into cells by Na+ cotransport with a Na+ to glucose coupling ratio of 2:1. SLC5A1 is mainly expressed in the microvilli of intestine and kidney and responsible for the absorption of sugars. Overexpressed SLC5A1 has been found in various cancers, possibly playing a role in preventing autophagic cell death by maintaining intracellular glucose levels. Defects in SLC5A1 can cause congenital glucose/galactose malabsorption (GGM; MIM:606824), an autosomal recessive disorder manifesting itself in newborns characterised by severe, life-threatening diarrhea which is usually fatal unless glucose and galactose are removed from the diet (Wright et al. 2002, Bergeron et al. 2008, Wright et al. 2007, Wright 2013).

References

Wright EM, Turk E & Martin MG (2002). Molecular basis for glucose-galactose malabsorption. Cell Biochem. Biophys., 36, 115-21.

Wright EM, Hirayama BA & Loo DF (2007). Active sugar transport in health and disease. J Intern Med, 261, 32-43.

Bergeron MJ, Simonin A, Bürzle M & Hediger MA (2008). Inherited epithelial transporter disorders--an overview. J. Inherit. Metab. Dis., 31, 178-87.

Wright EM (2013). Glucose transport families SLC5 and SLC50. Mol. Aspects Med., 34, 183-96.

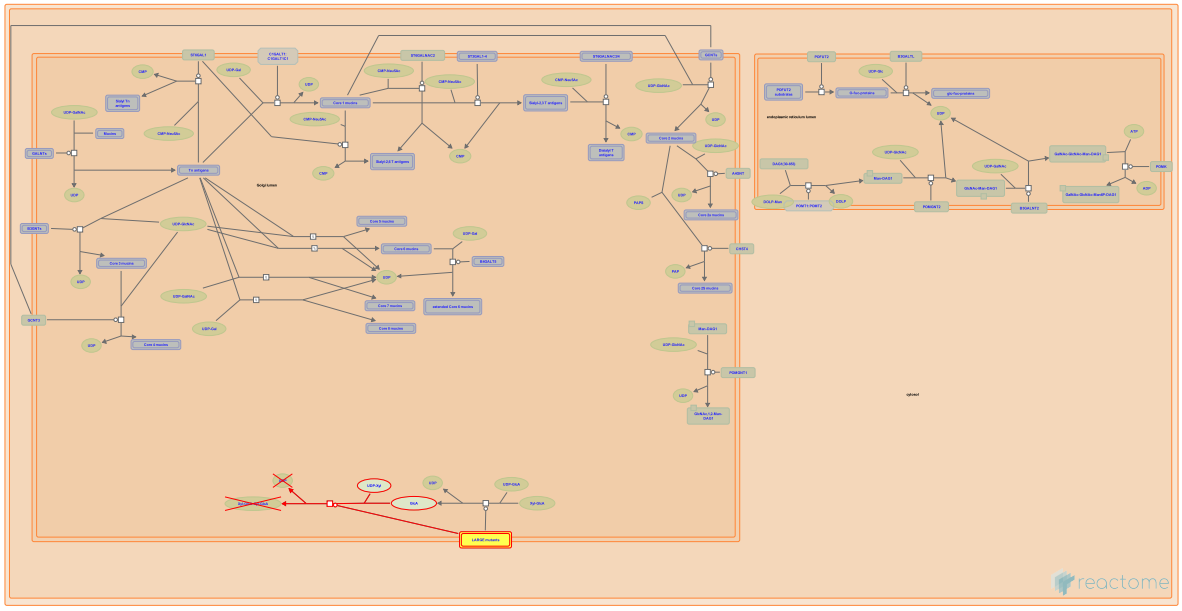
Edit history

Date	Action	Author
2014-08-22	Edited	Jassal B
2014-08-22	Authored	Jassal B
2014-12-12	Created	Jassal B
2015-08-04	Reviewed	Broer S
2018-12-05	Modified	Croft D

Entities found in this pathway (1)

Input	UniProt Id
SLC5A1	P13866

3. Defective LARGE causes MDDGA6 and MDDGB6 (R-HSA-5083627)



Diseases: congenital muscular dystrophy.

Glycosyltransferase-like protein LARGE (MIM:603590) is a bifunctional glycosyltransferase with both xylosyltransferase and beta-1,3-glucuronyltransferase activities involved in the biosynthesis of a phosphorylated O-mannosyl trisaccharide, a structure present in alpha-dystroglycan (DAG1; MIM:128239) which plays a key role in skeletal muscle function and regeneration. LARGE contains two substrate-specific GT-domains and belongs to the CAZy glycosyltransferase families GT8 and GT49. Defects in LARGE result in hypoglycosylation of DAG1 and cause several congenital muscular dystrophies (CMDs). Muscular dystrophy-dystroglycanopathy congenital with brain and eye anomalies A6 (MDDGA6; MIM:613154) is associated with brain anomalies, eye malformations, profound mental retardation, and death usually in the first years of life (Clement et al. 2008, Mercuri et al. 2009). Muscular dystrophy-dystroglycanopathy congenital with mental retardation B6 (MDDGB6; MIM:608840) is associated with profound mental retardation, white matter changes and structural brain abnormalities (Longman et al. 2003).

References

Longman C, Brockington M, Torelli S, Jimenez-Mallebrera C, Kennedy C, Khalil N, ... Muntoni F (2003). Mutations in the human LARGE gene cause MDC1D, a novel form of congenital muscular dystrophy with severe mental retardation and abnormal glycosylation of alpha-dystroglycan. Hum. Mol. Genet., 12, 2853-61.

Clement E, Mercuri E, Godfrey C, Smith J, Robb S, Kinali M, ... Muntoni F (2008). Brain involvement in muscular dystrophies with defective dystroglycan glycosylation. Ann. Neurol., 64, 573-82.

Mercuri E, Messina S, Bruno C, Mora M, Pegoraro E, Comi GP, ... Bertini E (2009). Congenital muscular dystrophies with defective glycosylation of dystroglycan: a population study. Neurology, 72, 1802-9.

Edit history

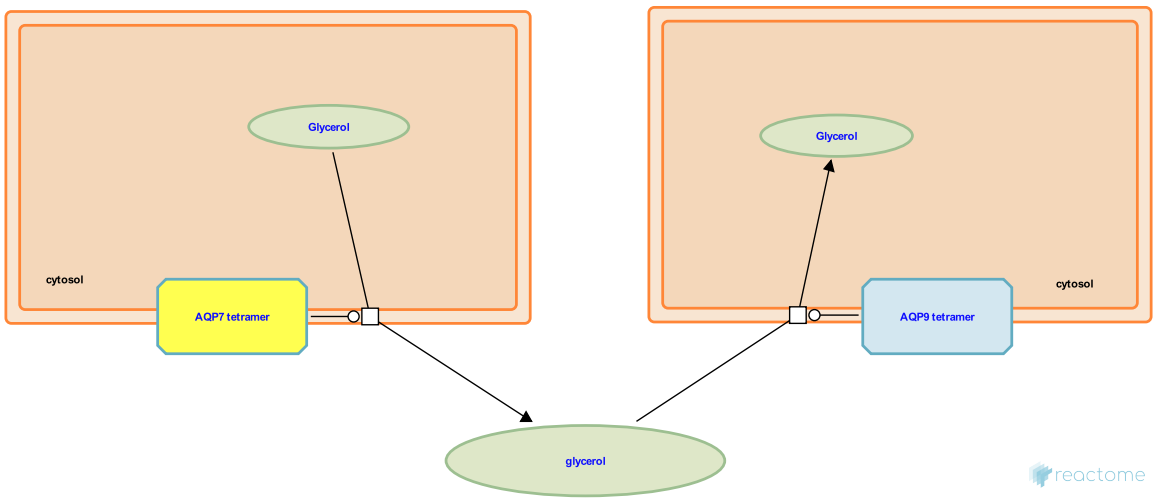
Date	Action	Author
2013-11-07	Edited	Jassal B

Date	Action	Author
2013-11-07	Authored	Jassal B
2013-11-07	Created	Jassal B
2015-12-18	Modified	Jassal B
2015-12-18	Reviewed	Hansen L, Joshi HJ

Entities found in this pathway (1)

Input	UniProt Id
LARGE	O95461

4. Transport of glycerol from adipocytes to the liver by Aquaporins (R-HSA-432030)



Cellular compartments: extracellular region, plasma membrane.

Triglycerides stored in adipocytes are hydrolyzed to yield fatty acids and glycerol. The glycerol is passively transported out of the adipocyte and into the bloodstream by Aquaporin-7 (AQP7) located in the plasma membrane of adipocytes. Glycerol in the bloodstream is passively transported into liver cells by AQP9 located in the plasma membrane of hepatocytes. Once inside the liver cell the glycerol is a substrate for gluconeogenesis.

References

Maeda N, Hibuse T & Funahashi T (2009). Role of aquaporin-7 and aquaporin-9 in glycerol metabolism; involvement in obesity. Handb Exp Pharmacol, 233-49.

Frühbeck G, Catalán V, Gómez-Ambrosi J & Rodriguez A (2006). Aquaporin-7 and glycerol permeability as novel obesity drug-target pathways. Trends Pharmacol Sci, 27, 345-7.

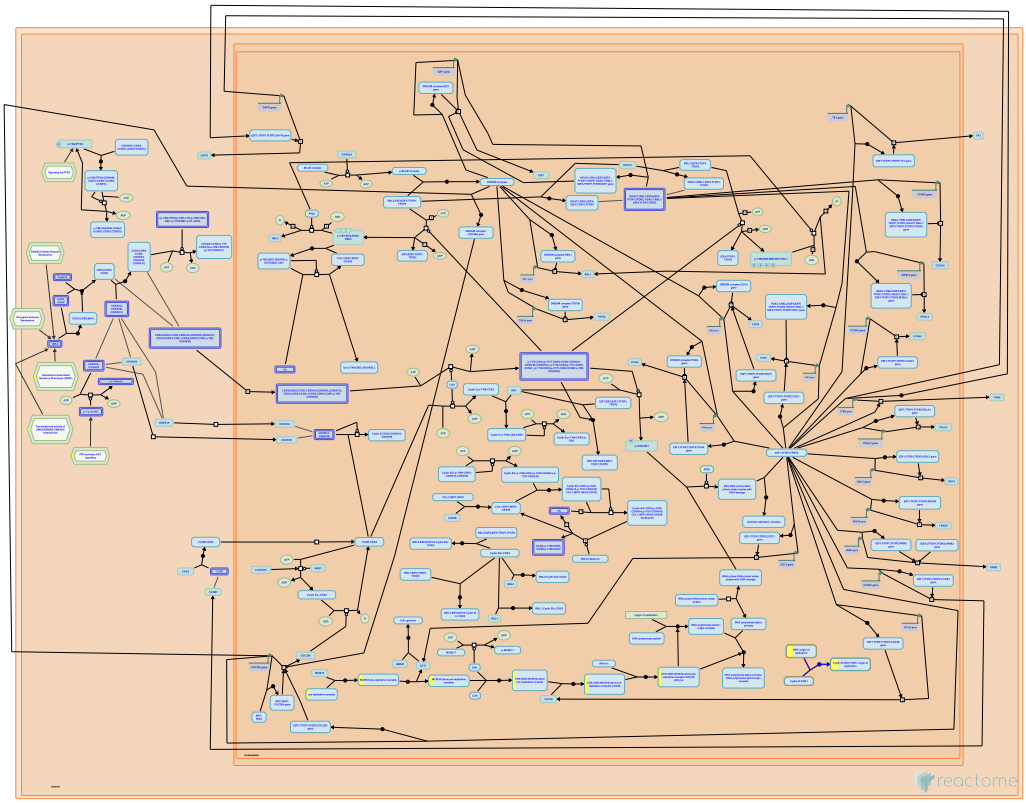
Edit history

Date	Action	Author
2009-08-07	Edited	May B
2009-08-07	Authored	May B
2009-08-09	Created	May B
2010-06-24	Reviewed	Beitz E
2010-07-15	Reviewed	Calamita G
2010-07-31	Reviewed	Mathai JC, MacIver B
2018-11-29	Modified	Weiser D

Entities found in this pathway (1)

Input	UniProt Id
AQP7	O14520

5. E2F-enabled inhibition of pre-replication complex formation (R-HSA-113507)



Cellular compartments: nucleoplasm.

Under specific conditions, Cyclin B, a mitotic cyclin, can inhibit the functions of pre-replicative complex. E2F1 activates Cdc25A protein which regulates Cyclin B in a positive manner. Cyclin B/Cdk1 function is restored which leads to the disruption of pre-replicative complex. This phenomenon has been demonstrated by Bosco et al (2001) in Drosophila.

References

Kennedy BK, Barbie DA, Classon M, Harlow E & Dyson NJ (2000). Nuclear organization of DNA replication in primary mammalian cells. Genes Dev, 14, 2855-68.

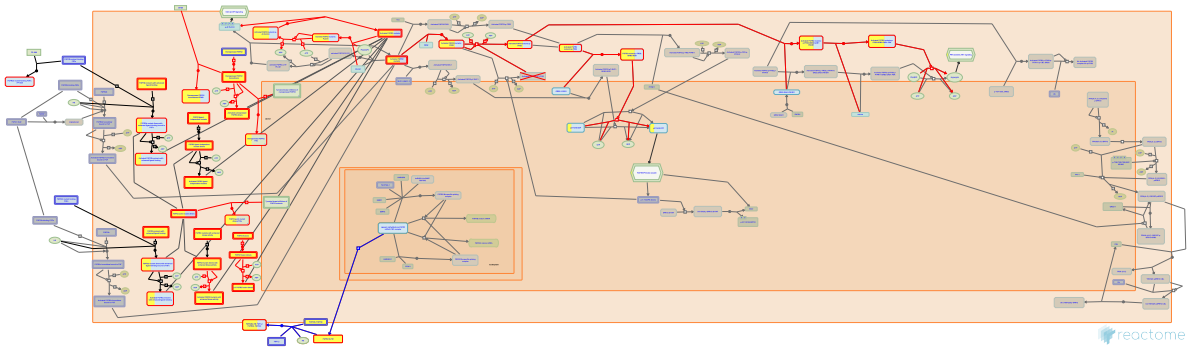
Edit history

Date	Action	Author
2004-05-26	Authored	Gopinathrao G
2004-06-17	Created	Bosco G
2017-02-07	Modified	Orlic-Milacic M

Entities found in this pathway (2)

Input	UniProt Id	Input	UniProt Id
MCM8	Q9UJA3	ORC3L	Q9UBD5

6. Signaling by FGFR2 IIIa TM (R-HSA-8851708)



Diseases: acrocephalosyndactylia.

A soluble truncated form of FGFR2 is aberrantly expressed in an Apert Syndrome mouse model and inhibits FGFR signaling in vitro and in vivo. This variant, termed FGFR IIIa TM, arises from an mis-spliced transcript that fuses exon 7 to exon 10 and that escapes nonsense-mediated decay. FGFR2 IIIa TM may inhibit signaling by sequestering FGF ligand and/or by forming nonfunctional heterodimers with full-length receptors at the cell surface (Wheldon et al, 2011).

References

Wheldon LM, Khodabukus N, Patey SJ, Smith TG, Heath JK & Hajihosseini MK (2011). Identification and characterization of an inhibitory fibroblast growth factor receptor 2 (FGFR2) molecule, up-regulated in an Apert Syndrome mouse model. Biochem. J., 436, 71-81.

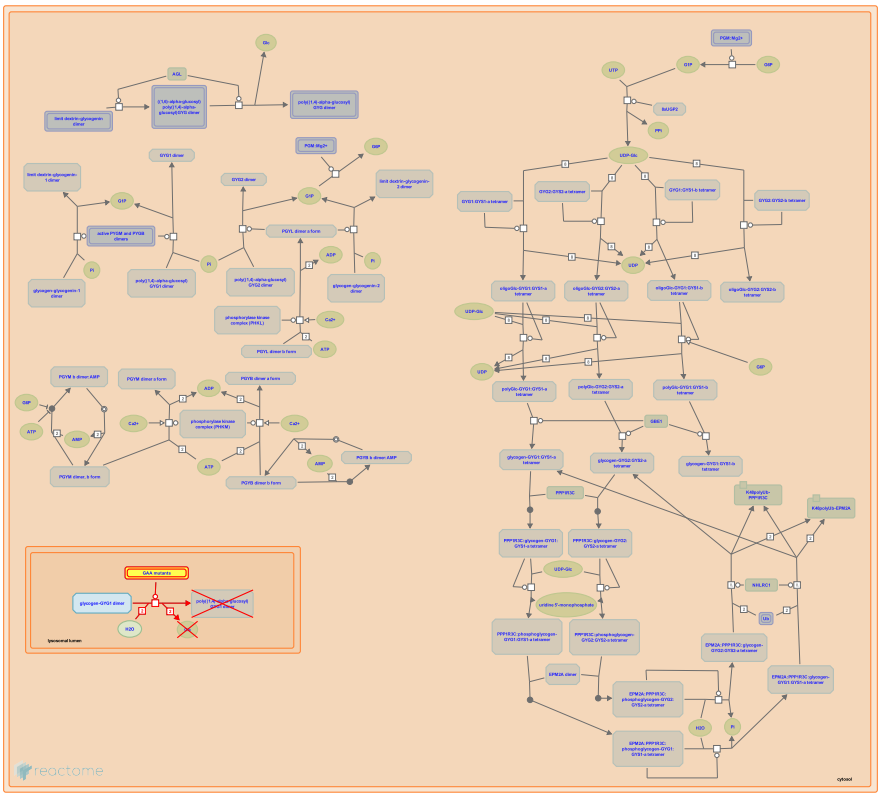
Edit history

Date	Action	Author
2016-01-09	Edited	Rothfels K
2016-01-09	Authored	Rothfels K
2016-01-09	Created	Rothfels K
2016-01-25	Modified	Rothfels K
2016-01-25	Reviewed	Grose RP

Entities found in this pathway (1)

Input	UniProt Id
FGFR2	P21802, P21802-1, P21802-18, P21802-3, P21802-5

7. Glycogen storage disease type II (GAA) (R-HSA-5357609)



Diseases: glycogen storage disease II.

Glycogen storage disease type II (GSD II - Pompe's disease) is caused by mutations that reduce or eliminate the activity of lysosomal alpha-glucosidase (GAA) (Hers 1963). The presentation of GSD II varies with the severity of the mutation: patients with little or no GAA activity are affected shortly after birth and multiple tissues are severely affected. Patients with higher levels of GAA activity present later in life, often with symptoms restricted tocardiac and skeletal muscle (Leslie & Tinkle). At a cellular level, symptoms of the disease are due to accumulation of structurally normal glycogen in lysosomes. Glycogen, thought to enter lysosomes via autophagy, is fully degraded by GAA (Brown et al. 1970), but accumulates if the enzyme is absent or reduced in activity.

The two mutant alleles annotated here are associated with near-complete loss of enzyme activity and early onset of disease (Hermans et al. 1991; Zhong et al. 1991). Many other mutant alleles have been described and their residual activities correlated with disease presentation (e.g., Kroos et al. 2012).

References

Brown BI, Brown DH & Jeffrey PL (1970). Simultaneous absence of alpha-1,4-glucosidase and alpha-1,6-glucosidase activities (pH 4) in tissues of children with type II glycogen storage disease. Biochemistry, 9, 1423-8.

Hermans MM, de Graaff E, Kroos MA, Wisselaar HA, Oostra BA & Reuser AJ (1991). Identification of a point mutation in the human lysosomal alpha-glucosidase gene causing infantile glycogenosis type II. Biochem. Biophys. Res. Commun., 179, 919-26.

Hers HG (1963). alpha-Glucosidase deficiency in generalized glycogen-storage disease (Pompe's disease). Biochem. J., 86, 11-6.

Kroos MA, Hoogeveen-Westerveld M, Michelakakis H, Pomponio RJ, Van der Ploeg AT, Halley DJ & Reuser AJ (2012). Update of the pompe disease mutation database with 60 novel GAA sequence variants and additional studies on the functional effect of 34 previously reported variants. Hum. Mutat., 33, 1161-5.

Glycogen Storage Disease Type II (Pompe Disease). Retrieved from http://www.ncbi.nlm.nih.gov/books/NBK1261/

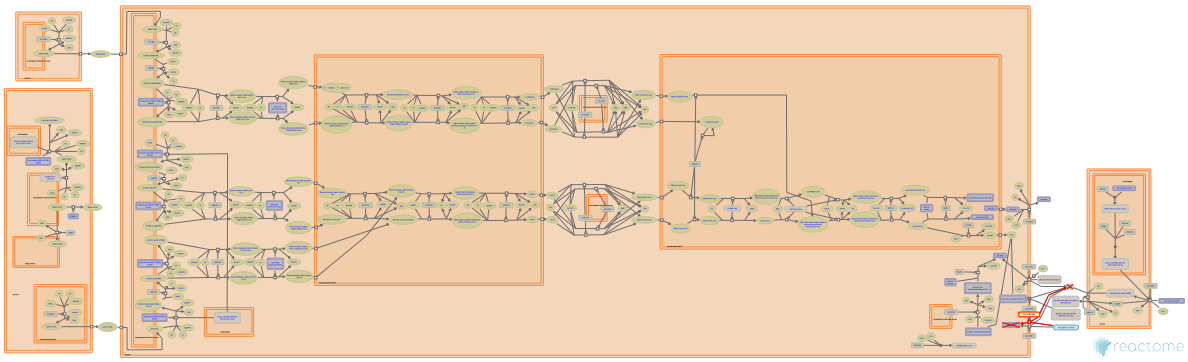
Edit history

Date	Action	Author
2014-03-25	Edited	D'Eustachio P
2014-03-25	Authored	D'Eustachio P
2014-03-25	Created	D'Eustachio P
2015-08-17	Reviewed	Jassal B
2018-02-08	Modified	D'Eustachio P

Entities found in this pathway (1)

Input	UniProt Id
GAA	P10253

8. Defective SLCO1B3 causes hyperbilirubinemia, Rotor type (HBLRR) (R-HSA-5619058)



Diseases: bilirubin metabolic disorder.

The bile acids glycocholate (GCCA) or taurocholate (TCCA) can be transported into the cytosol by SLCO1B3, which encodes the solute carrier organic anion transporter family member 1B3 (OATP1B3 aka OATP8, SLC21A8). GCCA and TCCA exist in the blood as complexes with serum albumin (ALB), and its uptake by SLCO1B1 must involve disruption of this complex, but the molecular mechanism coupling disruption and uptake is unknown. In the body, SLCO1B1 is expressed on the basolateral surfaces of hepatocytes and may play a role in the uptake of GCCA and TCCA by the liver under physiological conditions. Defects in SLCO1B3 can cause hyperbilirubinemia, Rotor type (HBLRR; MIM:237450), an autosomal recessive form of primary conjugated hyperbilirubinemia. Mild jaundice, not associated with hemolysis, develops shortly after birth or in childhood (van de Steeg et al. 2012, Sticova & Jirsa 2013, Keppler 2014).

References

van de Steeg E, Stranecký V, Hartmannová H, Nosková L, Hebíek M, Wagenaar E, ... Schinkel AH (2012). Complete OATP1B1 and OATP1B3 deficiency causes human Rotor syndrome by interrupting conjugated bilirubin reuptake into the liver. J. Clin. Invest., 122, 519-28.

Sticová E & Jirsa M (2013). New insights in bilirubin metabolism and their clinical implications. World J. Gastroenterol., 19, 6398-407.

Keppler D (2014). The roles of MRP2, MRP3, OATP1B1, and OATP1B3 in conjugated hyperbilirubinemia. Drug Metab. Dispos., 42, 561-5.

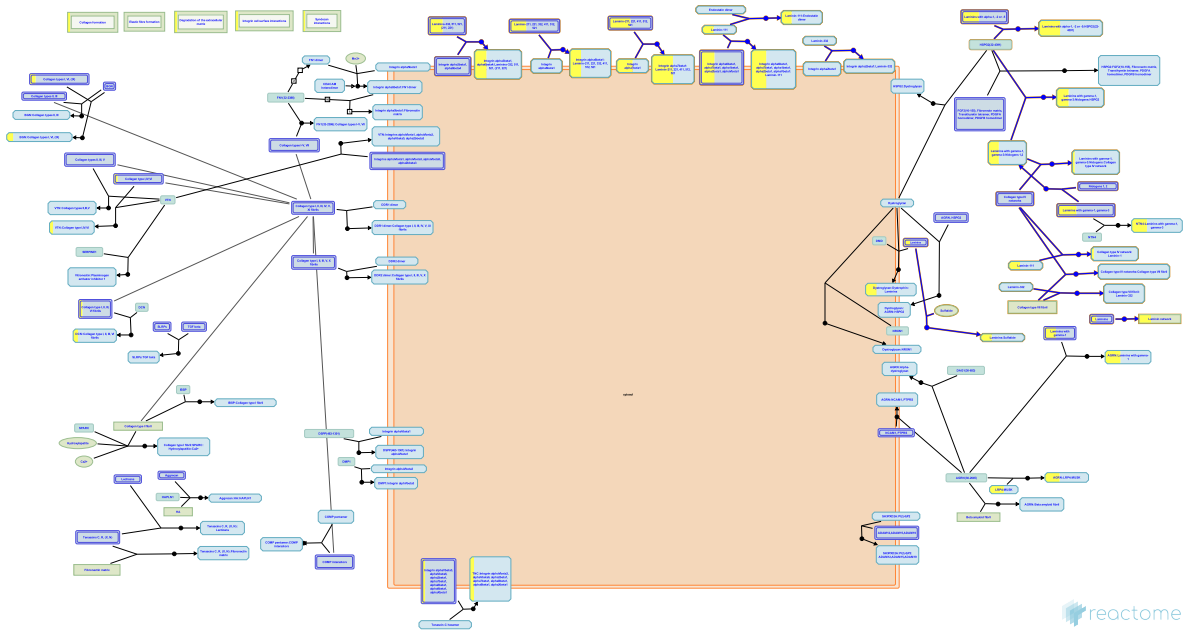
Edit history

Date	Action	Author
2014-08-22	Edited	Jassal B
2014-08-22	Authored	Jassal B
2014-08-22	Created	Jassal B
2015-08-04	Modified	Jassal B
2015-08-04	Reviewed	Broer S

Entities found in this pathway (1)

Input	UniProt Id
SLCO1B3	Q9NPD5

9. Laminin interactions (R-HSA-3000157)



Laminins are a large family of conserved, multidomain trimeric basement membrane proteins. There are many theoretical trimer combinations but only 18 have been described (Domogatskaya et al. 2012, Miner 2008, Macdonald et al. 2010) and the existence of isoforms laminin-212 and/or laminin-222 (Durbeej et al. 2010) awaits further confirmation. The chains assemble through coiled-coil domains at their C-terminal end. Alpha chains additionally have a large C-terminal globular domain containing five LG subdomains (LG1-5). The N termini are often referred to as the short arms. These have varying numbers of laminin-type epidermal growth factor-like (LE) repeats. Trimer assembly is controlled by highly specific coiled-coil interactions (Domogatskaya et al. 2012). Some laminin isoforms are modified extracellularly by proteolytic processing at the N- or C-terminal ends prior to their binding to cellular receptors or other matrix molecules (Tzu & Marinkovitch 2008).

The cell adhesion properties of laminins are mediated primarily through the alpha chain G domain to integrins, dystroglycan, Lutheran glycoprotein, or sulfated glycolipids. The N-terminal globular domains of the alpha-1 (Colognato-Pyke et al. 1995) and alpha-2 chains (Colognato et al. 1997) and globular domains VI (Nielsen & Yamada 2001) and IVa (Sasaki & Timpl 2001) of the alpha-5 chain can bind to several integrin isoforms (alpha1beta1, alpha2beta1, alpha3beta1, and alphaVbeta3), which enables cell binding at both ends of laminins with these alpha chains.

References

Domogatskaya A, Rodin S & Tryggvason K (2012). Functional diversity of laminins. Annu. Rev. Cell Dev. Biol., 28, 523-53.

Edit history

Date	Action	Author
2008-05-07	Reviewed	Hynes R, Humphries MJ, Yamada KM
2012-08-08	Authored	Jupe S
2013-01-24	Created	Jupe S
2013-08-13	Edited	Jupe S

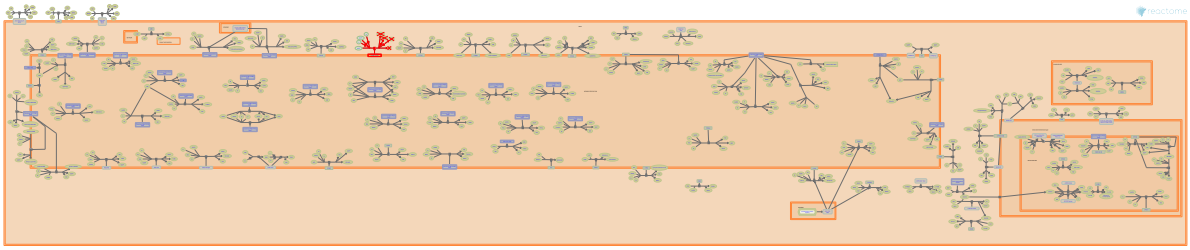
Date	Action	Author
2013-08-13	Reviewed	Ricard-Blum S
2018-11-29	Modified	Weiser D

Entities found in this pathway (4)

Input	UniProt Id
ITGA1	P56199
LAMA5	O15230

Input	UniProt Id
ITGA7	Q13683
LAMB2	P11047, P55268

10. Defective CYP19A1 causes Aromatase excess syndrome (AEXS) (R-HSA-5579030)



Diseases: pseudohermaphroditism.

Aromatase (CYP19A1) catalyses the conversion of androstenedione (ANDST) to estrone (E1). Defects in CYP19A1 can cause aromatase excess syndrome (AEXS; MIM:139300) and aromatase deficiency (AROD; MIM:613546). Affected individuals cannot synthesise endogenous estrogens. In females the lack of estrogen leads to pseudohermaphroditism and progressive virilization at puberty, whereas in males pubertal development is normal (Bulun 2014).

References

Bulun SE (2014). Aromatase and estrogen receptor ? deficiency. Fertil. Steril., 101, 323-9.

Edit history

Date	Action	Author
2014-06-06	Edited	Jassal B
2014-06-06	Authored	Jassal B
2014-06-06	Created	Jassal B
2014-11-03	Reviewed	Nakaki T
2015-02-09	Modified	Wu G

Entities found in this pathway (1)

Input	UniProt Id
CYP19A1	P11511

6. Identifiers found

Below is a list of the input identifiers that have been found or mapped to an equivalent element in Reactome, classified by resource.

Entities (178)

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
A2M	F1SLX2, K7GQ48	ABCB4	P21439	ABCB8	Q9NUT2
ABCB9	A0A0A0MY39	ABCC2	Q92887	ABLIM3	O94929
ACAA2	A0A286ZPP6, D0G0B3, F6PZX4	ACACA	A0A286ZW28, A0A287AU59, D2D0D8	ACADSB	A0A287B1V1, F1SED0
ACOT12	A0A286ZN15, A0A287AYT0	ACVRL1	A0A287BHN5, F1SGK0, K7GKU4	ALAS2	F1RUD4, K7GKX6, K7GR18
ALDH4A1	F1PRD6, F1PT06, J9P0M6, J9P2L3	ALOXE3	Q9BYJ1	ANO6	Q4KMQ2
AQP7	A0A287BBQ1, A9Y007	ARHGAP26	Q9UNA1	ARHGAP8	P85298
BCR	P11274	C1S	F1MJ12	CACNA1I	Q9P0X4
CALD1	D3Z6I7, E9Q0M9, E9Q9F3, E9QA15, E9QA16, F6QLP8, F6RGN9, F6T2Z7, F6ZAW1, Q8VCQ8, S4R1T7	CCL16	E2RA70, J9NV49	CD46	F1N4W4, F1N4W5, G3MWX4
CDC14A	A0A286ZMN0, A0A287AH86, A0A287BDL8, F1S565	CDK19	Q9BWU1	CES3	F1MI11
CHEK2	A0A286ZMG9, A0A286ZND4, A0A287A7U1, A0A287B5S2	CHID1	Q9BWS9	COL6A3	A0A286ZLV2, A0A286ZMC0, A0A286ZPQ1, A0A286ZVG7, A0A287B163, A0A287BL81, A0A287BLM4, A0A287BPF4, I3LUR7
CYP19A1	P11511	CYP3A43	Q9HB55	CYP3A5	G3X6Z4, Q3T047
DBNL	F6VCZ7	DGKD	A0A286ZPS1, A0A287A7P0, F1RJ92, F1SM29	DUSP10	F1S9I4
DUSP9	A0A287B227	ECHS1	A0A287AA21, A0A287BF56	EGFR	A0A286ZV23, I3LMY0
EGR2	P11161	ELL2	A0A287A147, A0A287A2R2, F1RNV6	ESR1	A0A0G2JXN1, A0A0G2JZG2, A0A0G2K0D4, A0A0G2K1T9, D0FYH4
ETNK2	F1S6B0	F7	A0A1D5PES2, A0A1D5PU41, F1P2T9	FAM20C	Q8IXL6
FGFR2	D3Z5M8, D6RJK5, E9PVU6, E9PX60, E9PX67, E9PX88, E9PX90, E9PXV8, E9Q5C2, E9Q5C3, E9Q700, E9Q708, E9Q7C7, E9Q7E6, E9Q7E8, E9Q7T0, E9QK53, F2Z480, F7BDU9	FH	A0A286ZIY0, A0A287AR55, I3LPP1	FLAD1	A0A286ZN22, A0A287BDR1, A0A287BT25, F1RGP6, I3L6M9
FUT3	P21217	GAA	P10253	GBA2	E7F5W0, F8W4V9, F8W624
GGCX	A0A0G2K0A3, B5DEF3, Q497C4	GJB1	F1RSW9	GLRX5	Q6DJ11

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
GNAI2	A0A287B697, I3LA61, Q06AS6	GNB2	P62879	GNB3	P16520
GPNMB	A0A286ZJF6, A0A287AKW4, A0A287AME8, A5A766	GRB10	A0A1D5P405, F1NT13	GRHPR	A0A287A1W5, F1ST73
HMGCS2	P54868	HSD17B4	A0A287A3B5, I3LEF8	HSP90AB1	A0A1D5PHC5, A0A1L1RL18, A0A1L1RLE5, F1NC33
IGF2R	B1H0W0, F1PWR1	IL1R1	A0A1D5PPV9, F1P4T7	IRAK1	F1QSH4, F6NJE2
ISYNA1	A0A287ADQ1, A0A287AXJ7, A0A287BDF8	ITGA1	Q3V3R4	ITGA7	A0A286ZY33, A0A287AHE4
ITIH1	A0A0R4IL78, E7FCH6	ITIH3	Q06033	ITIH4	Q14624
ITPR1	A0A0A0MY31, A0A0G2KAH9, C7E1V2, F1LNT1, F1LQX8	ITSN1	Q15811	JAK1	F1S818, K7GME4, Q9TTJ1
KALRN	O60229	KCNJ8	Q15842	KCNQ2	A0A0G2JFQ2, A0A0G2JGA6, B7ZBV3, B7ZBV4, B7ZBV5, B7ZBV6, B7ZBV7, B7ZBV8, B7ZBV9, B7ZBW1, B7ZBW2, F6UC55
KCNQ4	Q9JK97	KDM3A	A0A0G2K220, D3ZLJ9	KMO	I3LAL5
KRAS	P32883	KSR1	A0A1D5NVM9, A0A1D5PD92, A0A1D5PR70, A0A1D5PYC6, E1C7R3	LAMA5	A0A287AEH1
LAMB2	A0A286ZM22, A0A286ZTY3, A0A287A858, A0A287AJ64, A0A287AMT2, A0A287AWV5, F1SPT5	LARGE	O95461	LCN2	P80188
MAP2K7	A0A286YA49, D6RRB7, F6P5Q1	MAPK13	A0A287A819, A0A287AND8	MARCO	Q60754
MAT1A	Q00266	MCM8	Q9UJA3	MGAT5	A0A287BBT7, A0A287BF42, F1RY31
MTMR10	Q9NXD2	MUSK	O15146	MYO9B	A0A286ZZ30, A0A287A148, A0A287BDH3, A0A287BJA3, F1S959, F1S9U2
NBAS	H0ZS89	NCOA6	A0A1D5P7P0, A0A1D5PID6, A0A1D5PXP4, E1BUS5	NCSTN	Q8CGU6
NDUFA4	O00483	NPR2	A0A0G2KGK2	NUDT2	R4GJX0
NUP210	F1PSK9, J9JHT5, J9P6V8	ORC3L	Q9UBD5	P2RX1	P47824
PAOX	F1MG46, F1MG47, F1MQP7, G3MWK2	PEMT	Q9UBM1	PEX14	A0A286ZLS4, F1RHS6
PFKL	P17858	PHKA2	A0A286ZQP9, A0A287B6P0, F1SQP0	PIGU	A0A0G2KAR3, A0A140TAE9, F1LPK9
PIGV	F1PQ81, J9NWG9, J9P185, J9P6Y3	PIM1	P11309	PLXND1	H0ZJX0
PMM1	A0A1D5PJ31, A0A1D5PQW2	PON3	A9XLQ9, F6KQD9	POR	P16435
PPARG	A0A0N4SV67, A0A0N4SVF8, M1VPI1, Q6GU14	PPARGC1B	Q86YN6	PPP2R1A	Q76MZ3

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
PRKCE	A0A287ADC9, A0A287AHR4, F1S5K7	PTK2B	A0A287AFD2, A0A287AR80, A0A287ARL0, A0A287BHX4, A0A287BQ84, F1RJS6	PTPN23	Q9H3S7
PTPRF	A0A1D5NWI8, A0A1D5P2D6, A0A1D5P2W7, A0A1D5PTH8, A0A1D5PX53, F1N897	PTPRK	A0A286ZLL2, A0A286ZUS2, A0A287A519, A0A287AEP8, A0A287AN74, A0A287AP07, A0A287B937, F1S2Z2	RARA	A0A0G2JW78, Q499N1
RNF14	Q3ZAU6	ROCK2	A0A1Y7VLD1, A0A1Y7VMN0, F8VPK5	SAMD8	F1S2F8
SCN1A	P35498	SDC1	P18827	SERPINA1	Q5SPJ4, X1WF94
SERPINA10	Q9UK55	SIRPA	A0A287AKY3, K7GP73, Q5K4Q3	SLC12A7	A0A287B5R1, A0A287BE45, A0A287BQE2, I3L7H3
SLC13A3	A0A286ZXQ1, A0A287A374, A0A287ADP3, A0A287AXW9	SLC16A2	A0A287BBN6, I3LJG4	SLC17A7	F1RHZ7
SLC23A2	I3LRM4, I3LV44	SLC25A11	A0A287AN76, F1RFX9	SLC38A3	F1SPP6
SLC45A3	I3L8D4	SLC4A5	A0A286ZZZ0, A0A287B192, I3L7Z1	SLC5A1	A0A286ZNZ2, A0A286ZRN2, A0A287B9U9, F1RLV1
SLC7A2	A0A287B453, A0A287BGS3, F1SET3, I3LME2	SLC8A3	A0A287ANZ5, A0A287BCG8, F1S4A9	SLC9A6	A0A140LJ55, A1L3P4, B0QZV3, D3Z0Q9
SLCO1A2	A0A287AM41, A0A287AYE5, F1SQZ6	SLCO1B3	Q9NPD5	SMARCA2	A0A140LHE2, A0A140LHF4, A0A140LHJ8, A0A140LHL7, A0A140LHP6, A0A140LHZ8, A0A140LI08, A0A140LI12, A0A140LI14, A0A140LID0, A0A140LIK7, A0A140LIM0, A0A140LIQ9, A0A140LIV3, A0A140LJD7, A0A140LJK1, E9QAB8, F2Z4A9, H3BJI1, H3BJK2, H3BJM2, H3BK47, H3BKD2, H3BKJ3, H3BKN5, H3BLH0, H3BLI4, Q9D007
SORBS1	A0A286YCI8, A0A286YCN8, A0A286YCQ0, A0A286YD34, A0A286YDJ3, A0A286YDN0, D3Z5J3, E9PYX6, E9Q6A3, E9QNA7	SPR	E1C4L3	SRF	P11831
ST8SIA5	A0A286ZQF4, A0A287ACS3, A0A287BE15, I3LNL0	STAB1	A0A286ZIL8, A0A287ALB0, A0A287AM33, A0A287AR45, A0A287AS75, A0A287BJE5, F1SIW0	STARD3	A0A1D5PID8, H9L0L3
STAT1	A0A287A5C9, A0A287AB86, A0A287AVD2, A0A287BKW1, A0A287BNK4, G9BFU0, G9BFU1, K7GST8	SUCLG2	A0A286ZWJ9, A0A287ABW8, A0A287BA45, F1SFR6	SULT1B1	O43704

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
SULT1E1	P49888	TAF2	A0A287AM99, A0A287B693, F1S282, K7GLS4, K7GP24	TGFBI	Q15582
TGOLN2	O43493	THPO	P40225	TIMM13	Q9Y5L4
TNFSF14	A0A287A9X9, F1SBS6	TPI1	A0A286ZRV2, A0A288CFT0, D0G7F6	TRIB3	Q8K4K2
TRMT11	Q7Z4G4	TTYH3	Q9C0H2	TXN2	A0A1D5PWT4, F1NCD5
UBE2J2	Q8N2K1, Q8N2K1-1	UBR4	Q5T4S7	UGT2B4	P06133
UTP18	A0A1D5NXC2, A0A1L1RVK6, E1C7Z0	VNN3	Q9NY84	YWHAE	Q5ZMT0
ZNF230	Q9UIE0				

Input	Ensembl Id	Input	Ensembl Id	Input	Ensembl Id
ABCB4	ENSG00000005471	ACACA	ENSG00000132142	DGKD	ENSDARP00000148770
EGFR	ENSG00000146648	ESR1	ENSG00000091831	F7	ENSG00000057593
FH	ENSGALP00000021472	GAA	ENSDARP00000152693	GJB1	ENST00000361726.6
HMGCS2	ENSG00000134240	IL1R1	ENSG00000115594	IRAK1	ENSG00000184216
LAMA5	ENSG00000130702	LCN2	ENSG00000148346	MAPK13	ENSGALP00000001204
PIM1	ENSG00000137193	PLXND1	ENSG00000004399	PPARG	ENSG00000132170
PTPN23	ENSG00000076201	STAT1	ENSG00000115415	SUCLG2	ENSGALP00000012380
TRIB3	ENSG00000101255				

Interactors (112)

Input	ChEBI Id	Interacts with	Input	ChEBI Id	Interacts with
CD46	P15529	16851	FAM20C	Q8IXL6	15422
KRAS	P01116	16618	PFKL	P17858	18348

Input	UniProt Id	Interacts with	Input	UniProt Id	Interacts with
ABCC2	Q92887	P19838	ABLIM3	O94929	Q53FT3
ACACA	Q13085	P02654	ACOT12	Q8WYK0	Q02548
ALAS2	P22557	Q8N9N5	AQP7	Q6P5T0	P21964
ARHGAP8	P85298	Q63932	BCR	P11274	P18031
CCL16	O15467	P13501	CD46	P15529	P78504
CDK18	Q07002	Q9Y6D9	CDK19	Q9BWU1	Q15648
CHEK2	O96017	Q9Y248	DGKD	Q16760	O75923
DUSP10	Q9Y6W6	P49639	DUSP9	Q99956	Q16539
ECHS1	P30084	P42227	EGFR	P00533	P22682
EGR2	P08152	P63280	ELL2	O00472	P42568, Q9UHB7, Q96JC9, Q03111
ERMP1	Q7Z2K6	Q9UBD6	ESR1	P03372	Q12778
ETNK2	Q9NVF9	Q16623	F7	P08709	P08709
FAM20C	Q8IXL6	P10451	FGFR2	P21802	O15520
FH	P07954	P21673	FLAD1	Q8NFF5	Q8NFF5
GJB1	P08034	P21964	GLRX5	Q86SX6	Q8IWL3
GNAI2	P04899	P32302	GPNMB	Q14956	P00533
GRB10	Q13322	Q16613	HSP90AB1	P08238	P35916
IER3IP1	Q9Y5U9	P08034	IGF2R	P11717	Q9NZ52
IL1R1	P14778	Q9Y4K3	IRAK1	P51617	Q9NWZ3
ISYNA1	Q9NPH2	Q9NUX5	ITGA7	Q13683	Q14192
ITPR1	Q14643	P21796	ITSN1	Q15811	Q07889

Input	UniProt Id	Interacts with	Input	UniProt Id	Interacts with
JAK1	P23458	O60674	KDM3A	Q9Y4C1	O75582
KIAA0090	Q8N766	P27824	KRAS	P32883	Q01279
KSR1	Q8IVT5	P36507	LARGE	O95461	Q6VN20
LCN2	P80188	Q969S2	MAP2K7	O14733	P45983
MAP4K2	Q12851	Q9NUX5	MAP4K3	Q924I2	Q99962
MAPK13	O15264	P21462	MAST2	Q60592	P60484
MATR3	P43243	P09651	MUSK	Q61006	P46460
NBAS	A2RRP1	Q9NZ43, Q9P2W9	NCOA6	Q14686	P06400
NCSTN	Q92542	Q15363	NEK4	P51957	P35221
ORC3L	Q9UBD5	O43929, Q13415, Q9Y5N6, O43913	PEMT	P15941	Q96AA3
PEX14	O75381	P40855	PFKL	P17858	Q969Y2
PIM1	P11309	Q8N9N5	PLXND1	Q9Y4D7	P70275
PMM1	Q92871	P20340	PPARG	P37231	P37231
PPP2R1A	P30153	Q86XL3	PRKCE	Q02156	P08238
PTK2B	Q14289	P06241	PTP4A1	Q93096	P50747
PTPN23	Q9H3S7	Q99962	PTPRF	P10586	Q03135
PTPRK	Q15262	P04183	RARA	P10276	P37231
RNF14	Q9UBS8	P20823	RNF165	Q6ZSG1	P12755
ROCK2	Q28021	Q22038	RRBP1	Q9P2E9	P27824
RREB1	Q92766	O15379	SDC1	P18827	Q13009
SEPHS1	P49903	Q6GPH4	SERPINA1	P01009	P43307
SFXN5	Q8TD22	Q8N661	SIRPA	P97710	P41499
SLC12A7	Q9Y666	P08034	SLC13A3	Q8WWT9	Q3SXY8
SLC16A2	EBI-12816227	Q9H1C4	SLC22A23	A1A5C7	P27352
SLC25A11	Q02978	Q7KZN9	SLC5A1	P13866	P00533
SMARCA2	P51531	Q07666	SORBS1	Q9BX66	P39052
SPEN	Q96T58	Q06330	SRF	P11831	Q969V6
STAT1	P42224	Q01094	SUCLG2	Q96I99	Q8IWL3
SULT1B1	O43704	Q9NUX5	TCHP	Q9BT92	P14373
TGOLN2	O43493	Q9NZ52	TIE1	P35590	Q9UGI0
TLK2	Q86UE8	Q92985	TNFSF14	O43557	P36941
TNK2	Q07912	Q8WXH5	TPI1	P60174	P12004
TRIB3	Q96RU7	P18848	TXN2	Q99757	P49247
UBE2J2	Q8N2K1	A1L3X0	UBR4	Q5T4S7	Q08379
YWHAE	P62259	P51003	ZNF230	Q8WVD5	Q9H4B4

7. Identifiers not found

These 31 identifiers were not found neither mapped to any entity in Reactome.

ACVR1	AFM	ANLN	ATF6B	C11orf58	C1QTNF3	C20orf3	C21orf33
C5orf13	CAMK1G	CAMK2N1	CAMSAP1	CCL15	CCNL2	CCT8P1	CPVL
FAM171A1	INF2	KIAA1161	MFSD10	RNF10	SHROOM1	SIL1	SLC22A9
SLC25A25	SNRK	SNX4	TBC1D2B	TMEM62	TNS1	ZDHHC11	