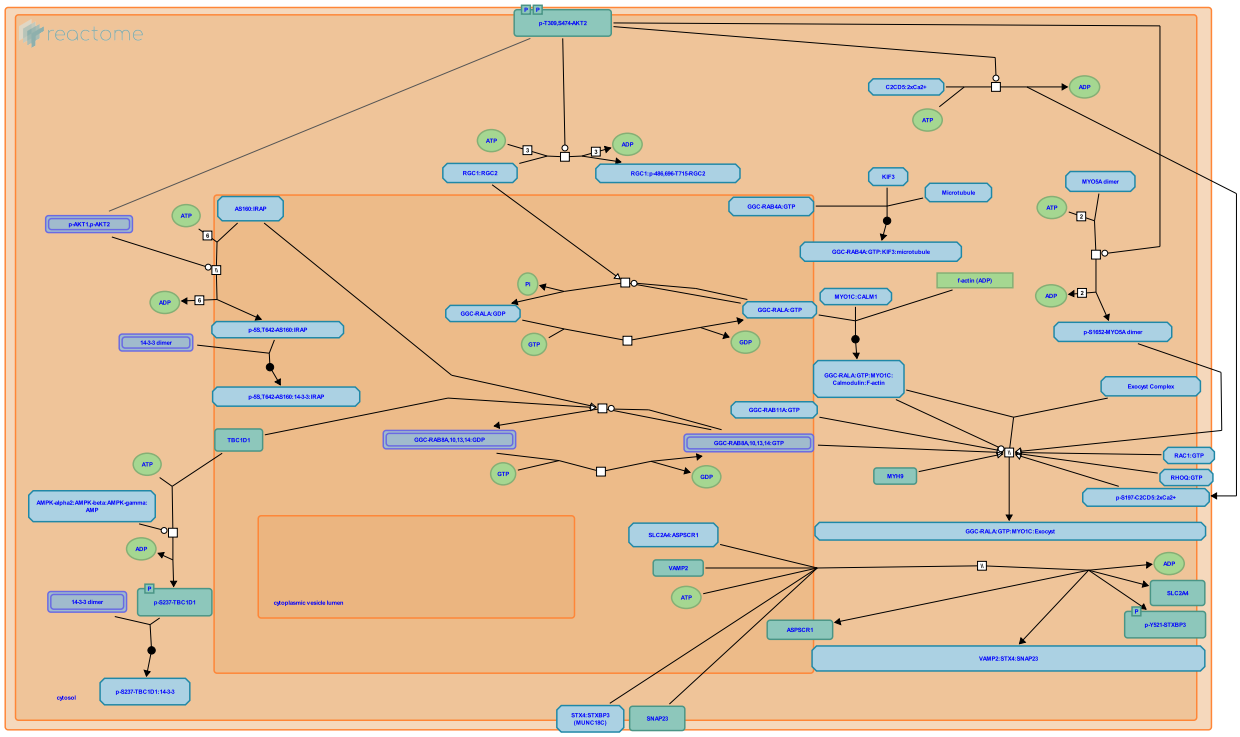
Translocation of SLC2A4 (GLUT4) to the plasma membrane



D'Eustachio, P., Jassal, B., Klip, A., May, B.

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

07/02/2023

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.

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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. ↗

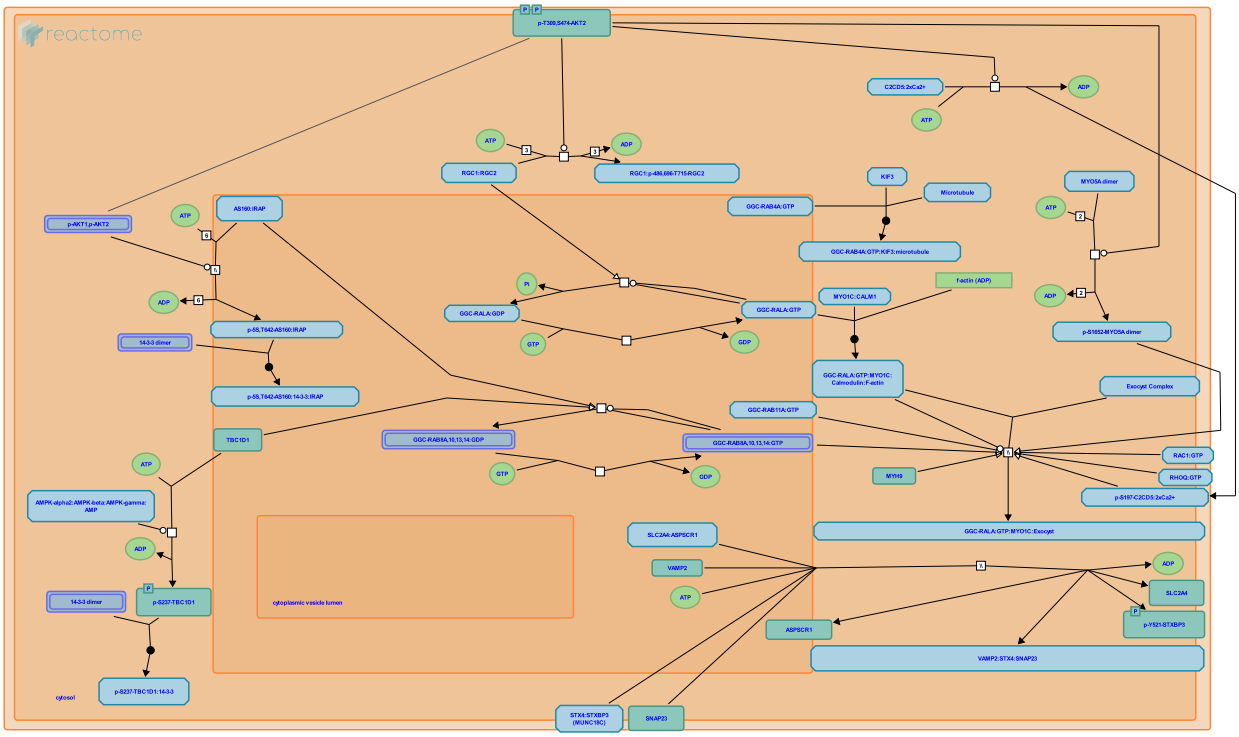
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Translocation of SLC2A4 (GLUT4) to the plasma membrane ↗

Stable identifier: R-HSA-1445148

Compartments: cytoplasmic vesicle membrane, cytosol



In adipocytes and myocytes insulin signaling causes intracellular vesicles carrying the GLUT4 (SLC2A4) glucose transporter to translocate to the plasma membrane, allowing the cells to take up glucose from the bloodstream (reviewed in Zaid et al. 2008, Leney and Tavare 2009, Bogan and Kandror 2010, Foley et al. 2011, Hoffman and Elmendorf 2011, Kandror and Pilch 2011, Jaldin-Fincati et al. 2017). In myocytes muscle contraction alone can also cause translocation of GLUT4.

Though the entire pathway leading to GLUT4 translocation has not been elucidated, several steps are known. Insulin activates the kinases AKT1 and AKT2. Muscle contraction activates the kinase AMPK-alpha2 and possibly also AKT. AKT2 and, to a lesser extent, AKT1 phosphorylate the RAB GTPase activators TBC1D1 and TBC1D4, causing them to bind 14-3-3 proteins and lose GTPase activation activity. As a result RAB proteins (probably RAB8A, RAB10, RAB14 and possibly RAB13) accumulate GTP. The connection between RAB:GTP and vesicle translocation is unknown but may involve recruitment and activation of myosins.

Myosins 1C, 2A, 2B, 5A, 5B have all been shown to play a role in translocating GLUT4 vesicles near the periphery of the cell. Following docking at the plasma membrane the vesicles fuse with the plasma membrane in a process that depends on interaction between VAMP2 on the vesicle and SNAP23 and SYNTAXIN-4 at the plasma membrane.

Literature references

Kandror, KV., Bogan, JS. (2010). Biogenesis and regulation of insulin-responsive vesicles containing GLUT4. *Curr Opin Cell Biol, 22*, 506-12. ↗

Bilan, PJ., Klip, A., Frendo-Cumbo, S., Pavarotti, M., Jaldin-Fincati, JR. (2017). Update on GLUT4 Vesicle Traffic: A Cornerstone of Insulin Action. *Trends Endocrinol. Metab., 28*, 597-611. ↗

Klip, A., Boguslavsky, S., Foley, K. (2011). Endocytosis, recycling, and regulated exocytosis of glucose transporter 4. *Biochemistry, 50*, 3048-61. ↗

Leney, SE., Tavaré, JM. (2009). The molecular basis of insulin-stimulated glucose uptake: signalling, trafficking and potential drug targets. *J Endocrinol, 203*, 1-18. ↗

Elmendorf, JS., Hoffman, NJ. (2011). Signaling, cytoskeletal and membrane mechanisms regulating GLUT4 exocytosis. *Trends Endocrinol Metab, 22*, 110-6. ↗

Editions

2011-07-07	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

RAB4A:GTP binds KIF3 and activates KIF3 ↗

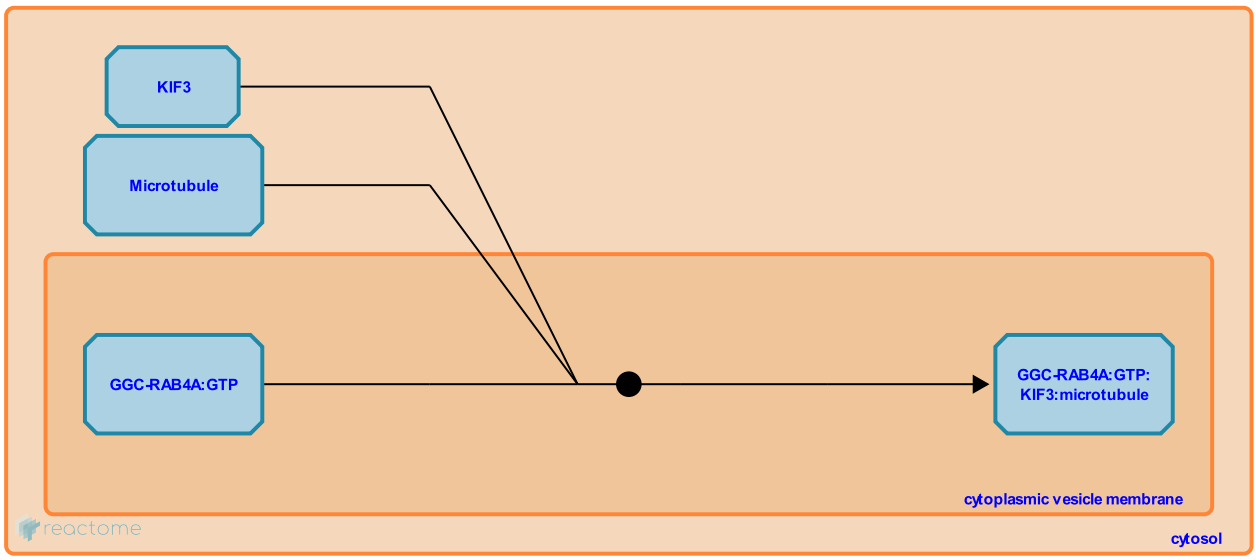
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-2316347

Type: binding

Compartments: cytoplasmic vesicle membrane, cytosol

Inferred from: Rab4a:GTP Activates Kif3 (Mus musculus)



As inferred from mouse adipocytes, insulin signals via PKC-lambda to cause Rab4 to load GTP and associate with Kif3, which then has higher affinity for microtubules. Motor activity of Kif3 along microtubules is believed to transport vesicles containing Glut4 (Slc2a4) across the cytosol to the cortical actin network.

Followed by: RALA:GTP binds MYO1C:CALM1 and activates MYO1C

Editions

2012-05-27	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

p-AKT1,p-AKT2 phosphorylates AS160 (TBC1D4) ↗

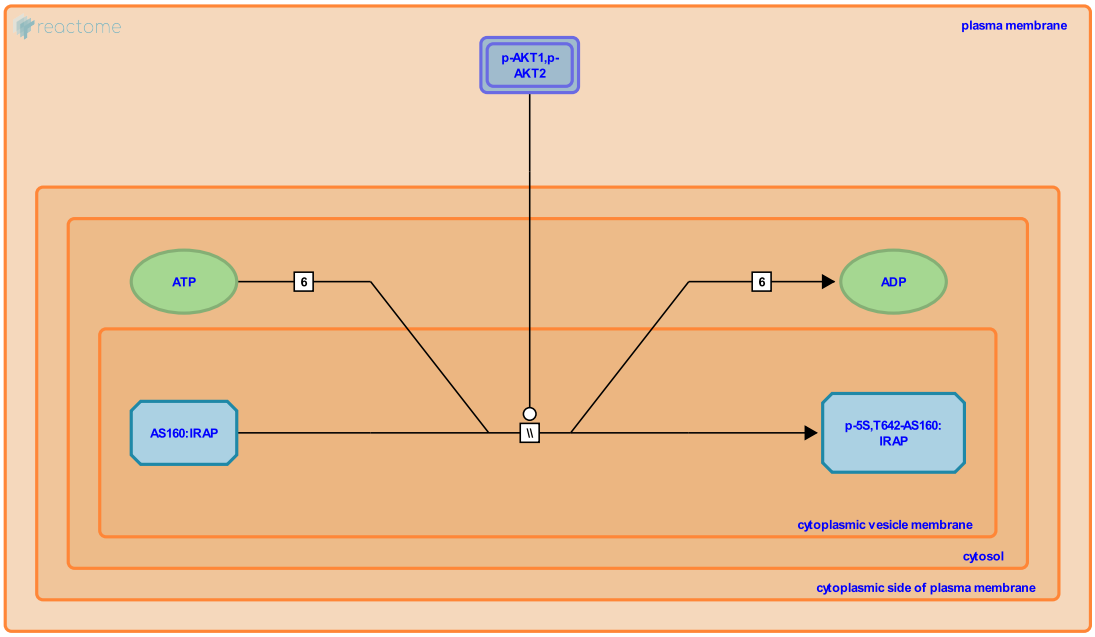
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1445144

Type: omitted

Compartments: cytoplasmic vesicle membrane, cytosol

Inferred from: Akt Phosphorylates As160 (Tbc1d4) (Mus musculus)



As inferred from mouse, AKT2 and, to a lesser extent, AKT1 phosphorylate AS160 (TBC1D4) in response to insulin signaling (Howlett et al. 2007, Karlsson et al 2005). AS160, a RAB GTPase activating protein, interacts with IRAP (LNPEP) and is associated with cytoplasmic vesicles containing GLUT4 (SLC2A4).

Followed by: 14-3-3 binds p-5S,T642-AS160 (TBC1D4)

Literature references

Lienhard, GE., Zierath, JR., Kane, S., Krook, A., Wallberg-Henriksson, H., Karlsson, HK. (2005). Insulin-stimulated phosphorylation of the Akt substrate AS160 is impaired in skeletal muscle of type 2 diabetic subjects. *Diabetes, 54*, 1692-7. ↗

Hargreaves, M., Sakamoto, K., Howlett, KF., Garnham, A., Cameron-Smith, D. (2007). Resistance exercise and insulin regulate AS160 and interaction with 14-3-3 in human skeletal muscle. *Diabetes, 56*, 1608-14. ↗

Editions

2011-07-07	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

14-3-3 binds p-5S,T642-AS160 (TBC1D4) ↗

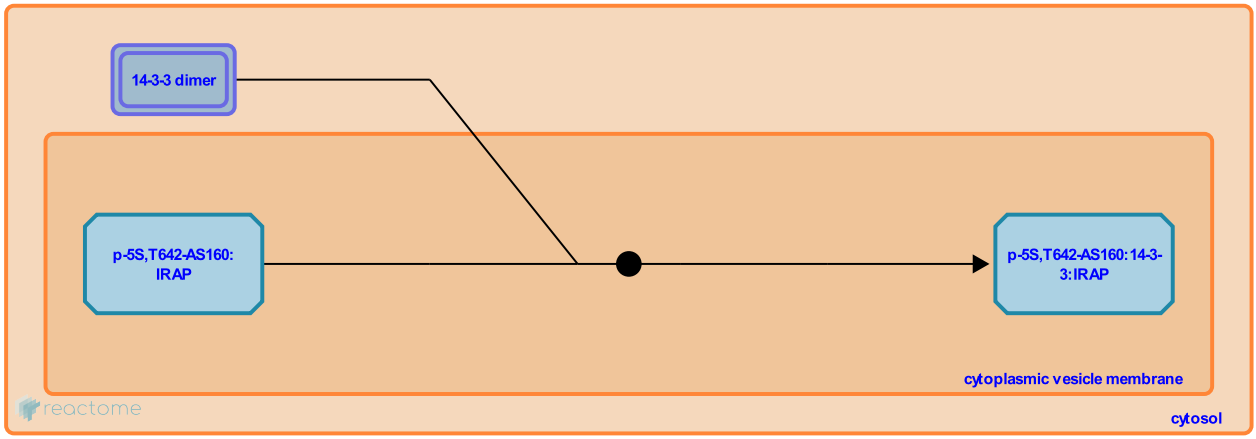
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1445149

Type: binding

Compartments: cytoplasmic vesicle membrane, cytosol

Inferred from: 14-3-3 Binds Phosphorylated Tbc1d4 (AS160) (Mus musculus)



AS160 (TBC1D4) phosphorylated on serines 318, 341, 570, 588, and 751 and threonine 642 binds to all 14-3-3 proteins, although binding to 14-3-3 delta (YWHAZ) is comparatively low (Ramm et al. 2006, Howlett et al. 2007, Ngo et al. 2009, Treebak et al. 2009, Koumanov et al. 2011). As inferred from mouse, binding to 14-3-3 does not interfere with the interaction between AS160 and IRAP (LNPEP).

Preceded by: p-AKT1,p-AKT2 phosphorylates AS160 (TBC1D4)

Followed by: RAB8A,10,13,14 exchange GDP for GTP

Literature references

Holman, GD., Koumanov, F., Richardson, JD., Murrow, BA. (2011). AS160 phosphotyrosine-binding domain constructs inhibit insulin-stimulated GLUT4 vesicle fusion with the plasma membrane. *J Biol Chem, 286*, 16574-82. ↗

Brandt, N., Richter, EA., Maarbjerg, SJ., Kiens, B., Mackintosh, C., Treebak, JT. et al. (2009). Potential role of TBC1D4 in enhanced post-exercise insulin action in human skeletal muscle. *Diabetologia, 52*, 891-900. ↗

Barry, JB., Ngo, S., Prins, JB., Whitehead, JP., Nisbet, JC. (2009). Reduced phosphorylation of AS160 contributes to glucocorticoid-mediated inhibition of glucose uptake in human and murine adipocytes. *Mol Cell Endocrinol, 302*, 33-40. ↗

James, DE., Guilhaus, M., Larance, M., Ramm, G. (2006). A role for 14-3-3 in insulin-stimulated GLUT4 translocation through its interaction with the RabGAP AS160. *J Biol Chem, 281*, 29174-80. ↗

Hargreaves, M., Sakamoto, K., Howlett, KF., Garnham, A., Cameron-Smith, D. (2007). Resistance exercise and insulin regulate AS160 and interaction with 14-3-3 in human skeletal muscle. *Diabetes, 56*, 1608-14. ↗

Editions

2011-07-07	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

AMPK-alpha2 phosphorylates TBC1D1 ↗

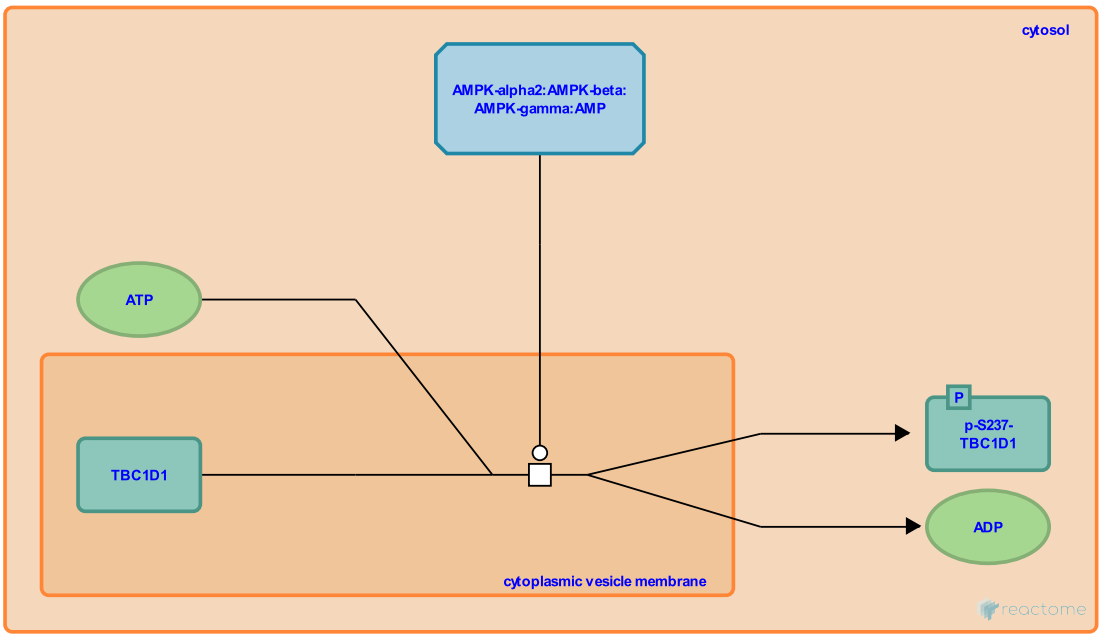
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1454699

Type: transition

Compartments: cytoplasmic vesicle membrane, cytosol

Inferred from: Ampk-alpha2 Phosphorylates Tbc1d1 (Mus musculus)



In response to muscle contraction and insulin signaling, AMPK-alpha2 phosphorylates TBC1D1 on serine 237 and probably other residues (Frosig et al. 2010, Vichaiwong et al. 2010). As inferred from rat L6 muscle cells TBC1D1 colocalizes with perinuclear vesicles bearing GLUT4 (SLC2A4) and may be involved in an early step that mobilizes them (Chen et al. 2008). Human TBC1D1 appears cytosolic and is believed to be concentrated near vesicle membranes (Park et al. 2011).

Followed by: 14-3-3 Binds p-S237-TBC1D1

Literature references

Campbell, DG., Murphy, J., Toth, R., Chen, S., Morrice, NA., Mackintosh, C. (2008). Complementary regulation of TBC1D1 and AS160 by growth factors, insulin and AMPK activators. *Biochem J, 409*, 449-59. ↗

An, D., Hirshman, MF., Goodyear, LJ., Vichaiwong, K., Jessen, N., Purohit, S. et al. (2010). Contraction regulates site-specific phosphorylation of TBC1D1 in skeletal muscle. *Biochem J, 431*, 311-20. ↗

Shoelson, SE., Jin, W., Park, SY., Woo, JR. (2011). Crystal structures of human TBC1D1 and TBC1D4 (AS160) RabGTPase-activating protein (RabGAP) domains reveal critical elements for GLUT4 translocation. *J. Biol. Chem., 286*, 18130-8. ↗

Wojtaszewski, JF., Frøsig, C., Richter, EA., Pehmøller, C., Birk, JB. (2010). Exercise-induced TBC1D1 Ser237 phosphorylation and 14-3-3 protein binding capacity in human skeletal muscle. *J Physiol, 588*, 4539-48. ↗

Editions

2011-07-15	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

14-3-3 Binds p-S237-TBC1D1 ↗

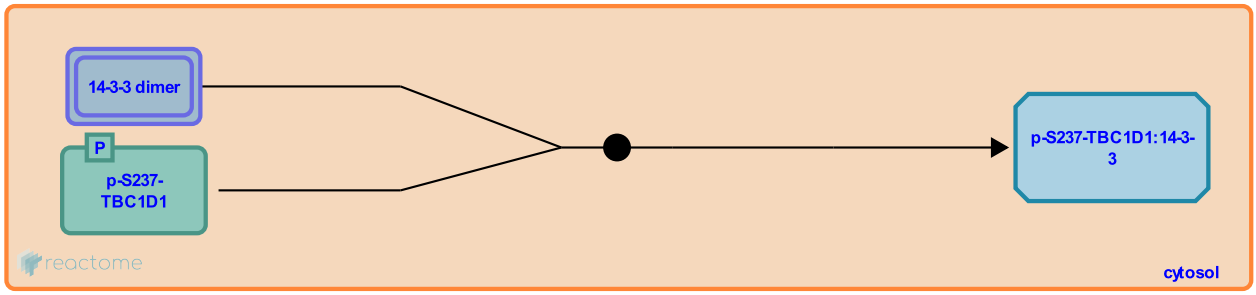
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1454689

Type: binding

Compartments: cytosol

Inferred from: 14-3-3 Binds Phosphorylated Tbc1d1 (Mus musculus)



TBC1D1 phosphorylated on serine-237 binds 14-3-3 proteins in assays with yeast 14-3-3 proteins BMH1 and BMH2 (Chen et al. 2008, Frosig et al. 2010). Binding with human 14-3-3 proteins is inferred.

Preceded by: AMPK-alpha2 phosphorylates TBC1D1

Followed by: RAB8A,10,13,14 exchange GDP for GTP

Literature references

Campbell, DG., Murphy, J., Toth, R., Chen, S., Morrice, NA., Mackintosh, C. (2008). Complementary regulation of TBC1D1 and AS160 by growth factors, insulin and AMPK activators. *Biochem J, 409*, 449-59. ↗

Wojtaszewski, JF., Frøsig, C., Richter, EA., Pehmøller, C., Birk, JB. (2010). Exercise-induced TBC1D1 Ser237 phosphorylation and 14-3-3 protein binding capacity in human skeletal muscle. *J Physiol, 588*, 4539-48. ↗

Editions

2011-07-15	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

RAB8A,10,13,14 exchange GDP for GTP ↗

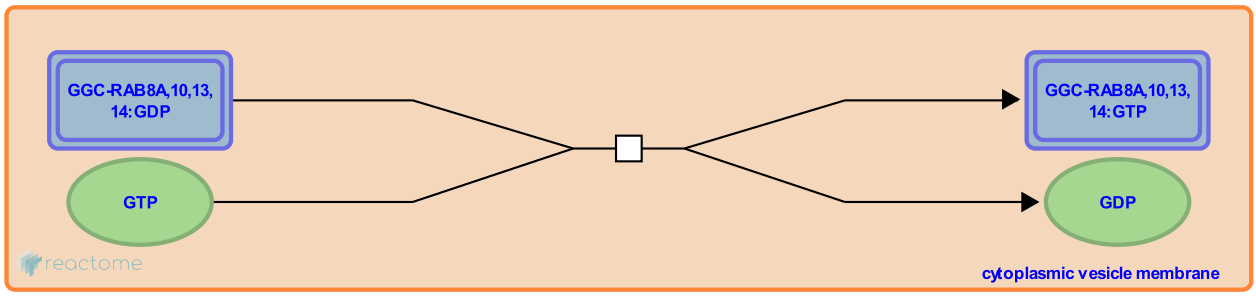
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-2255343

Type: transition

Compartments: cytoplasmic vesicle membrane

Inferred from: Rab8A/13/14 Exchange GDP for GTP (Rattus norvegicus), Rab8A/10/13/14 Exchange GDP for GTP (Mus musculus)



RAB8A/10/13/14 release GDP and bind GTP to yield the active complex. Guanine nucleotide exchange factors (GEFs) stimulate the reaction. GTPase-activating proteins (GAPs) oppose the reaction by stimulating the intrinsic GTPase activity of the RAB proteins.

Preceded by: 14-3-3 binds p-5S,T642-AS160 (TBC1D4), 14-3-3 Binds p-S237-TBC1D1, RAB8A,10,13,14 hydrolyze GTP

Followed by: SLC2A4 (GLUT4) vesicle translocates and docks at the plasma membrane, RAB8A,10,13,14 hydrolyze GTP

Literature references

Linford, A., Rigden, DJ., Barr, FA., Gerondopoulos, A., Yoshimura, S. (2010). Family-wide characterization of the DENN domain Rab GDP-GTP exchange factors. *J. Cell Biol., 191*, 367-81. ↗

Peranen, J., Murga-Zamalloa, CA., Khanna, H., Swaroop, A., Atkins, SJ. (2010). Interaction of retinitis pigmentosa GTPase regulator (RPGR) with RAB8A GTPase: implications for cilia dysfunction and photoreceptor degeneration . *Hum. Mol. Genet., 19*, 3591-8. ↗

Editions

2012-05-16	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

RAB8A,10,13,14 hydrolyze GTP ↗

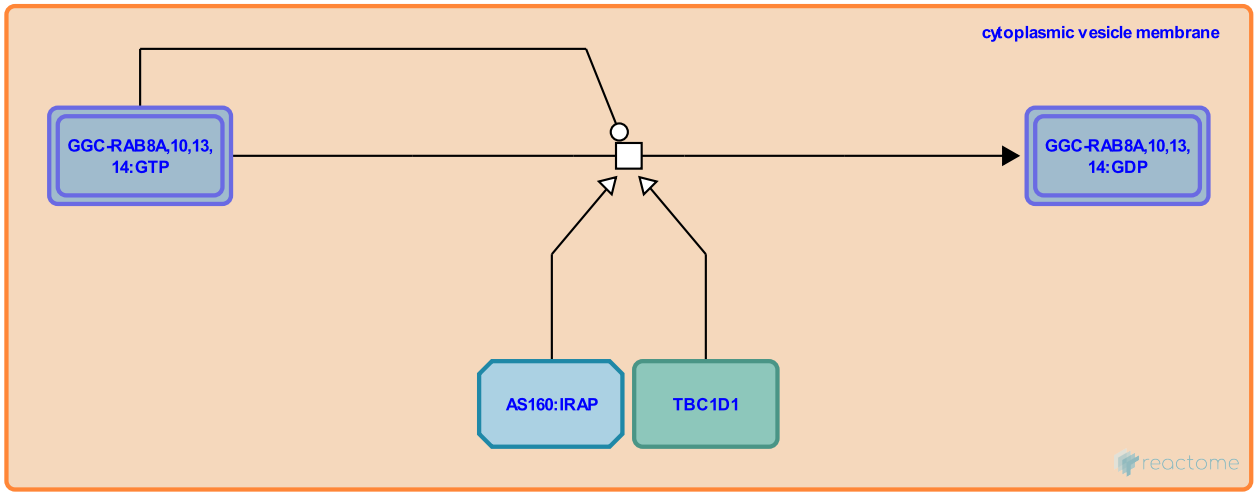
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1445143

Type: transition

Compartments: cytoplasmic vesicle membrane

Inferred from: Rab8a/10/13/14 Hydrolyze GTP (Mus musculus)



RAB proteins have intrinsic weak GTPase activity that is enhanced by RAB-GTPase activating proteins (RAB-GAPs, Sano et al. 2007). The GTPase activity of RAB13 is inferred from other RAB proteins. AS160 (TBC1D4) and TBC1D1 are GAPs that activate the GTPase activity of RAB8A/10/13. Insulin signaling activates AKT, which phosphorylates and inactivates AS160 and TBC1D1, allowing GTP-bound (active) RABs to accumulate.

The GAP domain of TBC1D4 (AS160) activates the GTPase activity of RAB proteins (Sano et al. 2007). The effect of TBC1D4 on RAB13 is inferred from rat muscle cells (Sun et al. 2010).

As inferred from mouse, TBC1D1 activates GTPase activity of RAB2A, 8A, 8B, 10, and 14 (Roach et al. 2007).

Preceded by: RAB8A,10,13,14 exchange GDP for GTP

Followed by: RAB8A,10,13,14 exchange GDP for GTP

Literature references

Fukuda, M., Lienhard, GE., Lane, WS., Sano, H., Kane, S., Sano, E. et al. (2005). AS160, the Akt substrate regulating GLUT4 translocation, has a functional Rab GTPase-activating protein domain. *Biochem J, 391*, 87-93. ↗

Editions

2011-07-07	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

p-AKT2 phosphorylates Myosin 5A ↗

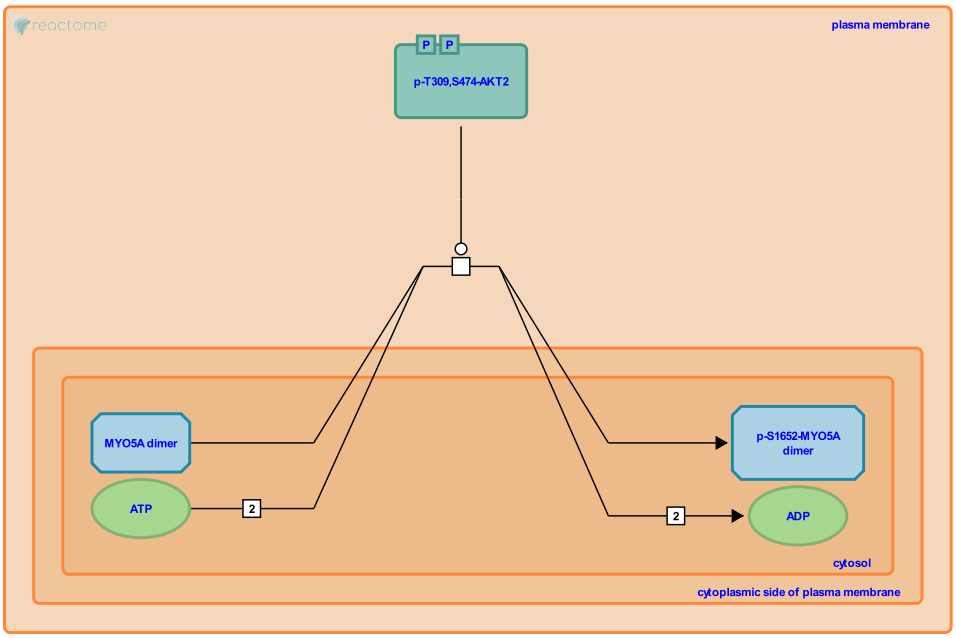
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1449597

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Akt2 Phosphorylates Myosin 5a (Mus musculus)



As inferred from mouse, AKT2 phosphorylates Myosin 5A on serine-1652. The phosphorylation promotes association of Myosin 5A with actin and ATPase activity of Myosin 5A.

Followed by: SLC2A4 (GLUT4) vesicle translocates and docks at the plasma membrane

Editions

2011-07-13	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

p-AKT2 phosphorylates RGC2 ↗

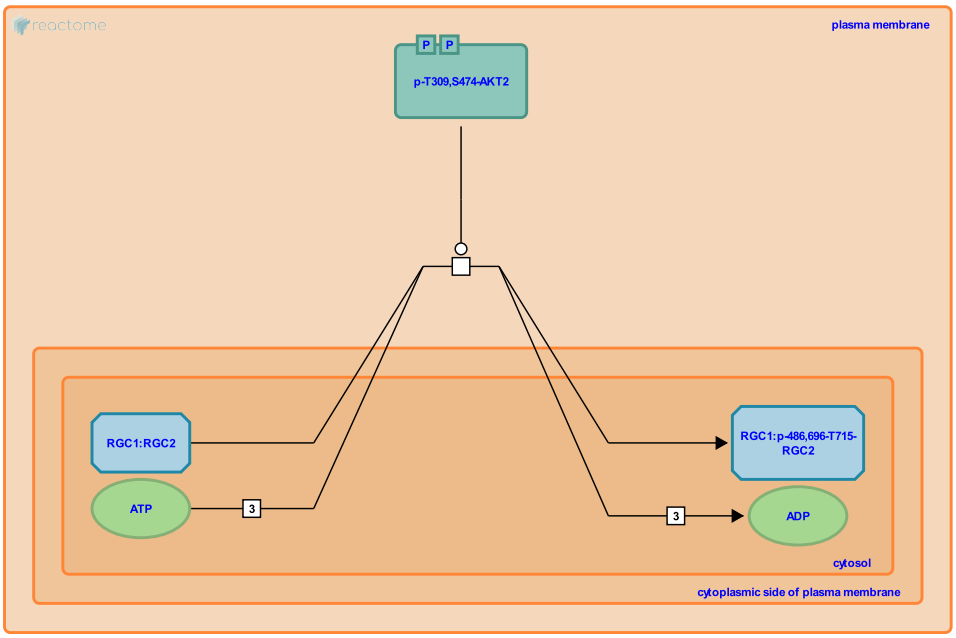
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1458463

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: Akt2 Phosphorylates Rgc2 (Mus musculus)



As inferred from mouse, AKT2 (PKB-beta) phosphorylates RBC2 (RALGAPA2) on serine-486, serine-696, and threonine-715 in response to insulin. The phosphorylation prevents RBC1:RBC2 from activating RALA GTPase and allows RALA:GTP to accumulate.

Followed by: RALA exchanges GDP for GTP

Editions

2011-07-17	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

RALA exchanges GDP for GTP ↗

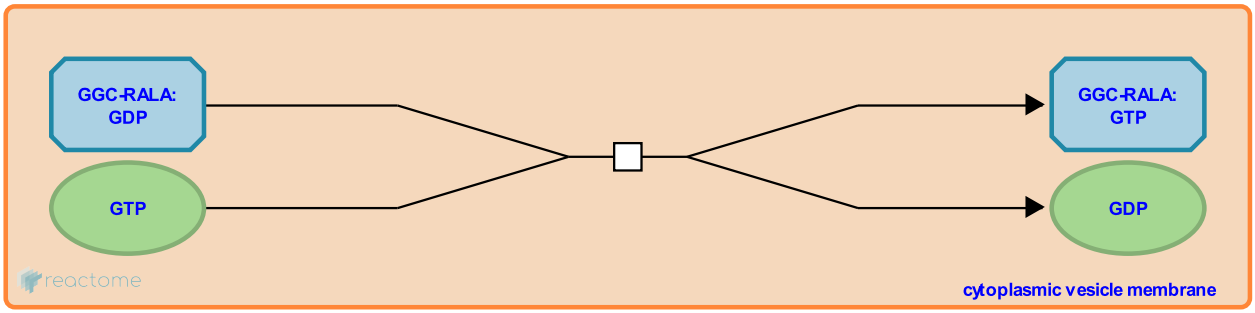
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-2255342

Type: transition

Compartments: cytoplasmic vesicle membrane

Inferred from: RalA Exchanges GDP for GTP (Mus musculus)



RALA releases GDP and binds GTP, producing the active form of RALA. The reaction is accelerated by guanine nucleotide exchange factors (GEFs) and opposed by GTPase-activating proteins (GAPs) which enhance the conversion of RALA:GTP back to RALA:GDP by activating the GTPase activity of RALA.

Preceded by: p-AKT2 phosphorylates RGC2, RALA hydrolyzes GTP

Followed by: RALA:GTP binds MYO1C:CALM1 and activates MYO1C, RALA hydrolyzes GTP

Literature references

Weber, RF., Snyderman, R., Evans, T., Didsbury, JR., Polakis, PG., Nevins, B. (1989). Identification of the ral and rac1 gene products, low molecular mass GTP-binding proteins from human platelets. *J. Biol. Chem., 264*, 16383-9. ↗

Weinberg, RA., Liu, J., Albright, CF., Giddings, BW., Vito, M. (1993). Characterization of a guanine nucleotide dissociation stimulator for a ras-related GTPase. *EMBO J., 12*, 339-47. ↗

Editions

2012-05-16	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

RALA:GTP binds MYO1C:CALM1 and activates MYO1C ↗

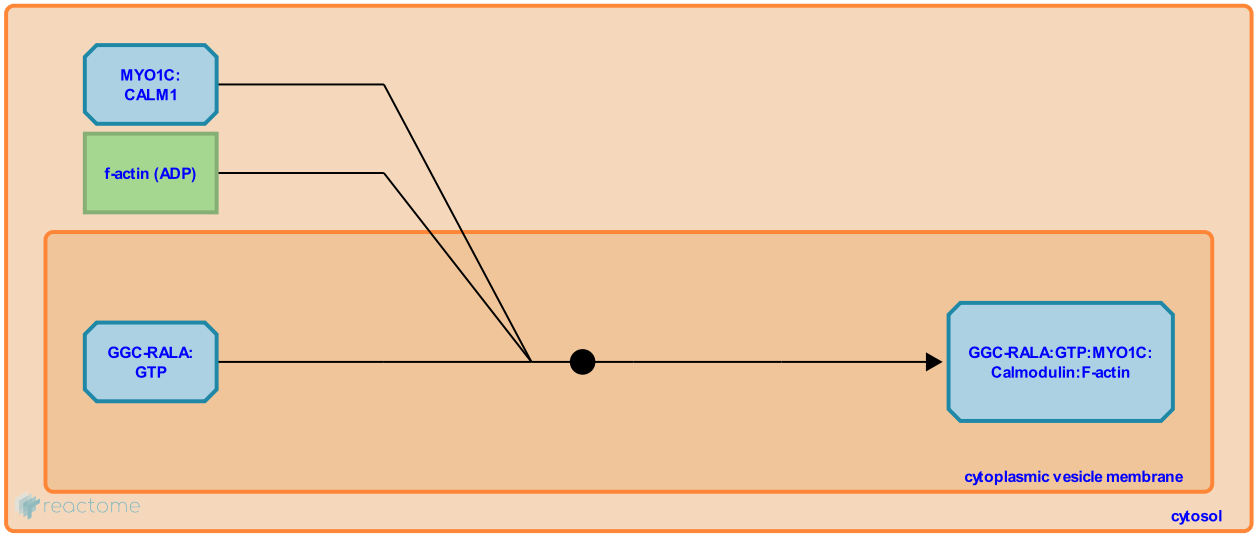
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-2316349

Type: binding

Compartments: cytoplasmic vesicle membrane, cytosol

Inferred from: RalA:GTP binds Myo1c:Calm1 and F-actin (Mus musculus)



As inferred from mouse, insulin causes phosphorylation and inactivation of the Ral GTPase activating complex RGC, causing RALA:GTP to accumulate and associate with the unconventional myosin MYO1C. MYO1C, with calmodulin as a light chain, motors across cortical actin and interacts with the exocyst complex to tether vesicles at the plasma membrane (Chen et al. 2007).

Preceded by: RALA exchanges GDP for GTP, RAB4A:GTP binds KIF3 and activates KIF3

Followed by: SLC2A4 (GLUT4) vesicle translocates and docks at the plasma membrane

Editions

2012-05-27	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

RALA hydrolyzes GTP ↗

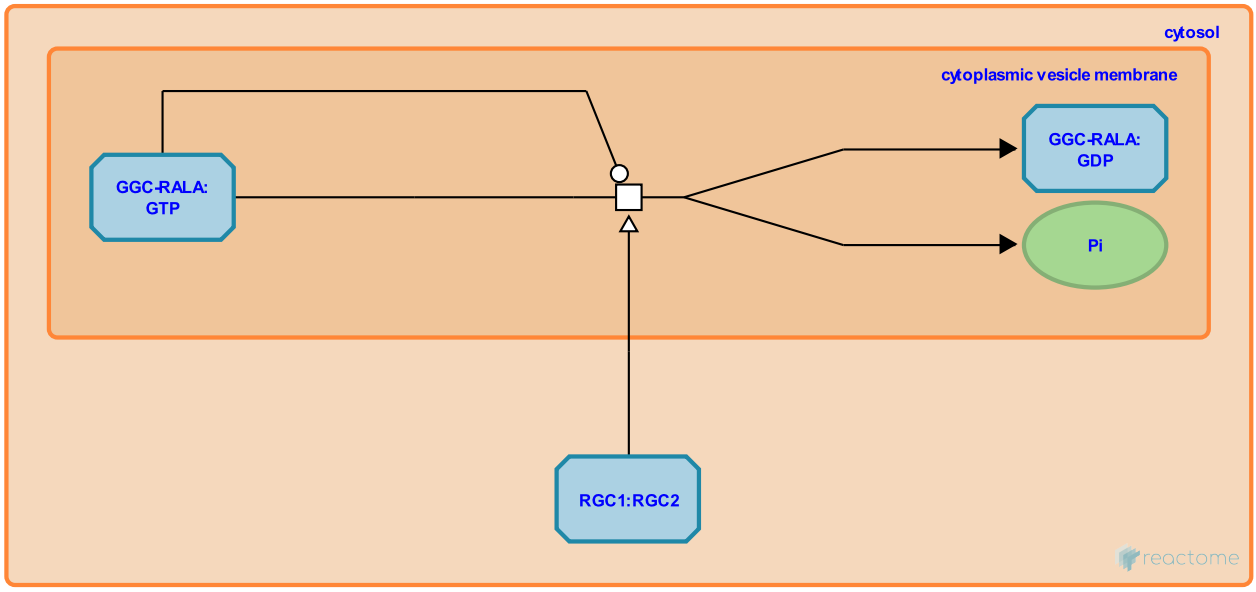
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1458485

Type: transition

Compartments: cytoplasmic vesicle membrane

Inferred from: RalA Hydrolyzes GTP (Mus musculus)



As inferred from mouse, RGC1:RGC2 (RALGAPB:RALGAPA2) activate the GTPase activity of RALA (Chen et al. 2011).

RALA is a guanine nucleotide binding protein that hydrolyzes bound GTP to yield GDP and phosphate. RGC1 and RGC2 are GAPs (GTPase-activating proteins) that activate the GTPase activity of RALA. Insulin activates AKT, which phosphorylates RGC2, inactivating the GAP activity of RGC1:RGC2 and allowing RALA:GTP to accumulate.

Preceded by: RALA exchanges GDP for GTP

Followed by: RALA exchanges GDP for GTP

Literature references

Bhullar, RP., Seneviratne, HD. (1996). Characterization of human platelet GTPase activating protein for the Ral GTP-binding protein. *Biochim Biophys Acta, 1311*, 181-8. ↗

Editions

2011-07-17	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

p-AKT2 phosphorylates C2CD5 ↗

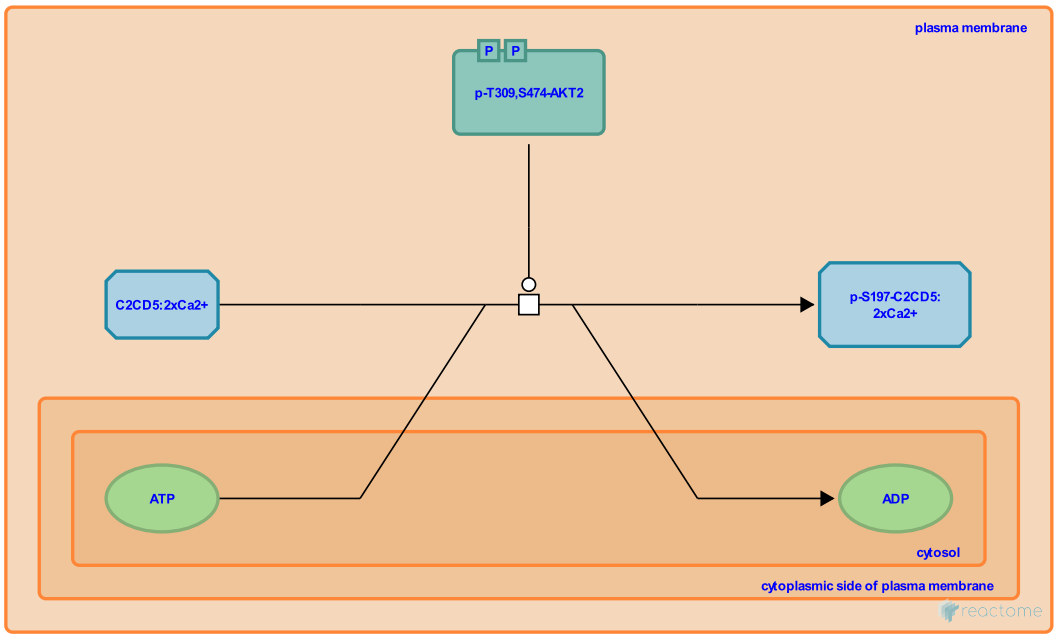
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-5260201

Type: transition

Compartments: plasma membrane, cytosol

Inferred from: p-Akt2 phosphorylates C2cd5 (Mus musculus)



The protein kinase B beta (AKT) pathway mediates insulin-stimulated glucose transport by increasing glucose transporter GLUT4 translocation from intracellular stores to the plasma membrane. C2 domain-containing protein 5 (C2CD5 aka C2 domain-containing phosphoprotein 138kDa) has been shown to be required for optimal insulin-stimulated GLUT4 translocation and fusion of GLUT4 vesicles with the plasma membrane in adipocytes. It is also able to bind Ca2+ and lipid membranes in its C2 domain. C2CD5 is a substrate for RAC-beta serine/threonine-protein kinase (AKT2), which phosphorylates C2CD5 at serine 197. Phosphorylated C2CD5 optimises GLUT4 translocation to the plasma membrane. The role of human C2CD5 is inferred from the role of the orthologous mouse protein (Xie et al. 2011).

Literature references

Xie, X., Mansuy-Aubert, V., Tatulian, SA., Jiang, ZY., Zhou, QL., Gong, Z. et al. (2011). C2 domain-containing phosphoprotein CDP138 regulates GLUT4 insertion into the plasma membrane. *Cell Metab., 14*, 378-89. ↗

Editions

2014-02-07	Authored, Edited	Jassal, B.
2015-02-11	Reviewed	D'Eustachio, P.

SLC2A4 (GLUT4) vesicle translocates and docks at the plasma membrane ↗

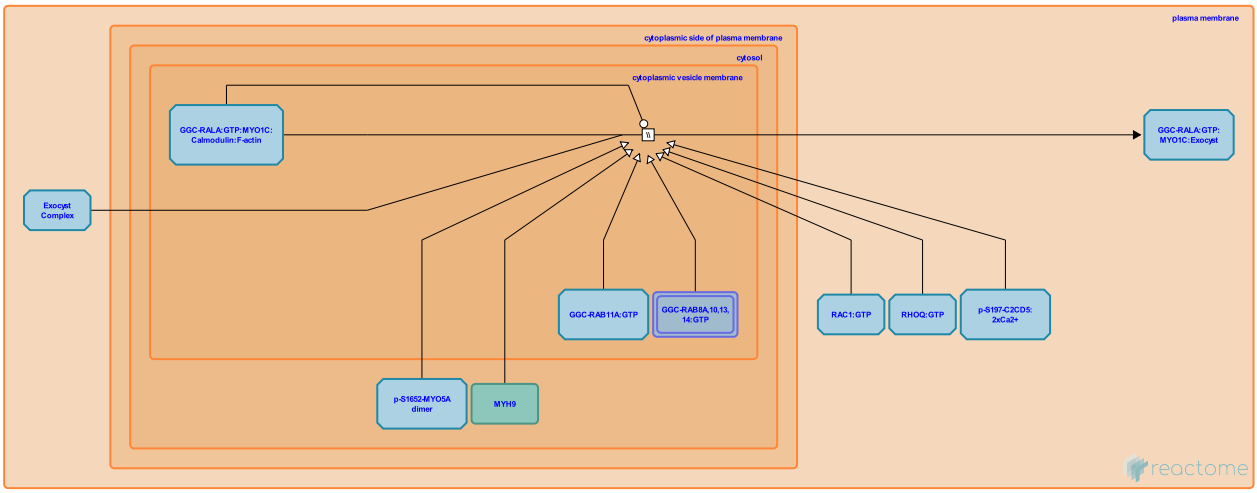
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-2316352

Type: omitted

Compartments: cytoplasmic vesicle membrane, plasma membrane

Inferred from: Translocation of Glut4 Vesicle and Docking at the Plasma Membrane (Mus musculus)



As inferred from mouse, GLUT4 (SLC2A4) initially translocates from endosomes to insulin-responsive vesicles (IRVs, GSVs). RAB11 appears to play a role in this process. IRVs bearing GLUT4 are then translocated across the cortical actin network to the plasma membrane. Unconventional myosin 5A (MYO5A) interacts with RAB10 or RAB8A on the vesicle and participates in transport of the IRV. Myosin 1C appears to act close to the plasma membrane and may facilitate fusion of the vesicle with the plasma membrane. RAB:GTP complexes coupled to the vesicles may interact with myosins to regulate their activity. Non-muscle myosin IIA (MYH9) appears to interact with the SNAP23 complex to dock the IRV at the inner membrane face.

As inferred from mouse (Zeigerer et al. 2002) and rat (Uhlig et al. 2005), RAB11A enhances translocation of GLUT4 to the plasma membrane by mobilizing GLUT4 (SLC2A4) from endosomes to insulin responsive vesicles.

As inferred from mouse (Sano et al. 2007) and rat (Ishikura et al. 2007, Ishikura and Klip 2008, Sun et al. 2010), RAB:GTP activates translocation of GLUT4 (SLC2A4) to the plasma membrane, possibly by interacting with myosins. RAB8A, RAB10, and RAB14 predominate in 3T3-L1 adipocytes; RAB13 predominates in L6 muscle cells.

As inferred from mouse, TC10 participates in the translocation and docking of GLUT4 (SLC2A4) vesicles at the plasma membrane (Chang et al. 2007).

As inferred from mouse (Ueda et al. 2008, Ueda et al. 2010) and rat (Chiu et al. 2010), RAC1:GTP enhances translocation of GLUT4 (SLC2A4) to the plasma membrane by causing actin remodeling that requires ARP2/3. The exact mechanism of RAC1 action is unknown.

Preceded by: RALA:GTP binds MYO1C:CALM1 and activates MYO1C, RAB8A,10,13,14 exchange GDP for GTP, p-AKT2 phosphorylates Myosin 5A

Followed by: SLC2A4 (GLUT4) vesicle fuses with the plasma membrane

Editions

2012-05-27	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

SLC2A4 (GLUT4) vesicle fuses with the plasma membrane ↗

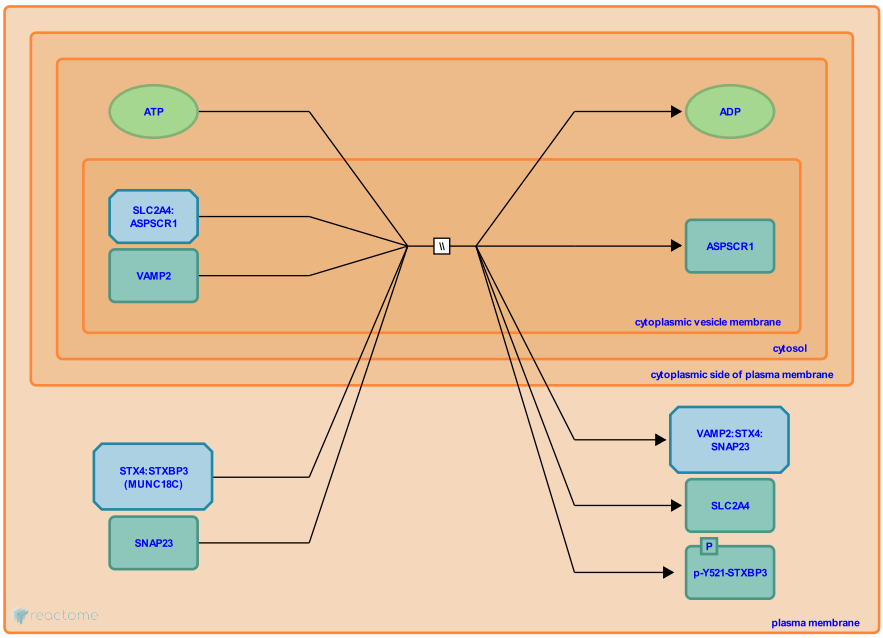
Location: Translocation of SLC2A4 (GLUT4) to the plasma membrane

Stable identifier: R-HSA-1449574

Type: omitted

Compartments: cytoplasmic vesicle membrane, plasma membrane

Inferred from: Fusion of Glut4 Vesicle with the Plasma Membrane (Mus musculus)



After docking at the membrane VAMP2 on the vesicle interacts with SYNTAXIN-4 and SNAP23 on the plasma membrane to catalyze fusion of the vesicle with the plasma membrane. STXBP3 (MUNC18C) bound to STX4 prevents fusion until STXBP3 is phosphorylated.

Preceded by: SLC2A4 (GLUT4) vesicle translocates and docks at the plasma membrane

Editions

2011-07-13	Authored, Edited	May, B.
2012-08-21	Reviewed	Klip, A.

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