Defective ABCC8 does not form functional KATP channels, causing hyperinsulinemic hypoglycemia

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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. ↗

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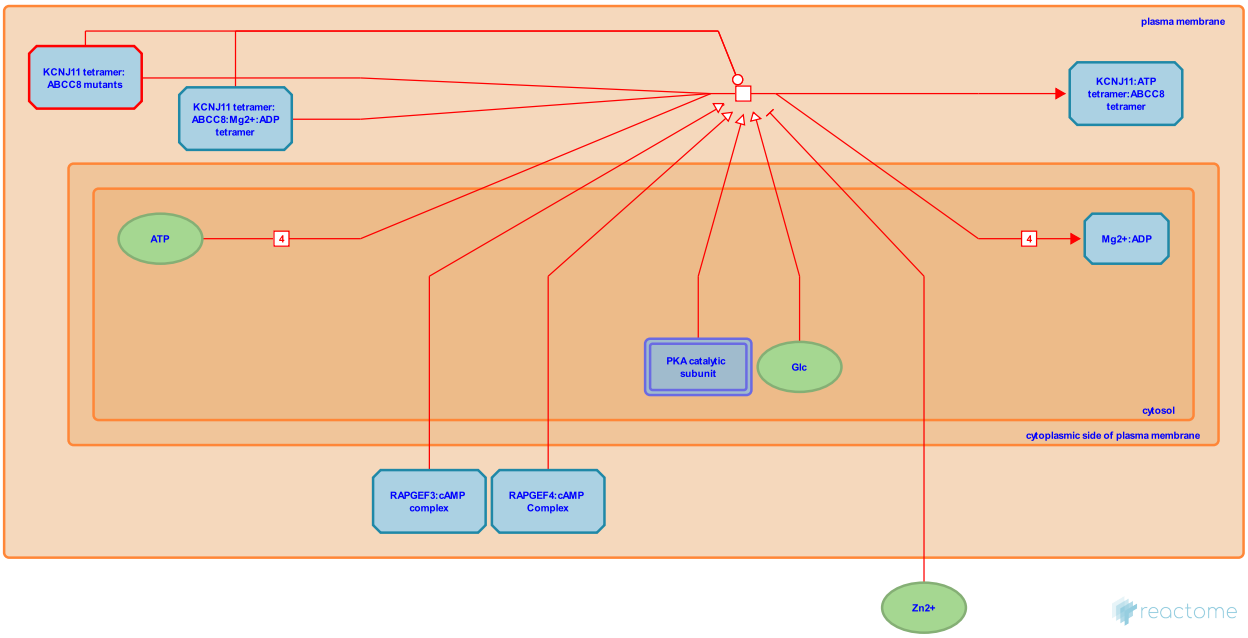
Stable identifier: R-HSA-5683113

Type: transition

Compartments: plasma membrane

Diseases: hyperinsulinemic hypoglycemia



ATP-binding cassette sub-family C member 8 (ABCC8) is a subunit of the beta-cell ATP-sensitive potassium channel (KATP). KATP channels play an important role in the control of insulin release. Elevation of the ATP:ADP ratio closes KATP channels leading to cellular depolarisation, calcium influx and exocytosis of insulin from its storage granules. Defects in ABCC8 can cause dysregulation of insulin secretion resulting in hyperglycemias or hypoglycemias.

Familial hyperinsulinemic hypoglycemia (see HHF1; MIM:256450) is a disorder caused by defective negative feedback regulation of insulin secretion (persistent hyperinsulinism) leading to severe hypoglycemia. The most commom ABCC8 mutations causing HHF1 include F1388del, A1330Gfs*35, V187D and E1507K (Thomas et al. 1995, Nestorowicz et al. 1996, Otonkoshi et al. 1999).

Literature references

Bryan, J., Landau, H., Wilson, BA., Nestorowicz, A., Aguilar-Bryan, L., Inoue, H. et al. (1996). Mutations in the sulonylurea receptor gene are associated with familial hyperinsulinism in Ashkenazi Jews. *Hum. Mol. Genet., 5*, 1813-22. ↗

Thomas, PM., Mathew, PM., Hallman, DM., Cote, GJ. (1995). Homozygosity mapping, to chromosome 11p, of the gene for familial persistent hyperinsulinemic hypoglycemia of infancy. *Am. J. Hum. Genet., 56*, 416-21. ↗

Otonkoski, T., Huang, E., Ammälä, C., Kere, J., Cote, GJ., Thomas, PM. et al. (1999). A point mutation inactivating the sulfonylurea receptor causes the severe form of persistent hyperinsulinemic hypoglycemia of infancy in Finland. *Diabetes, 48*, 408-15. ↗

Editions

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