OCTN2 / SLC22A5 transports CAR from extracellular space to cytosol

D'Eustachio, P., Jassal, B.

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

02/05/2024

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. ↗

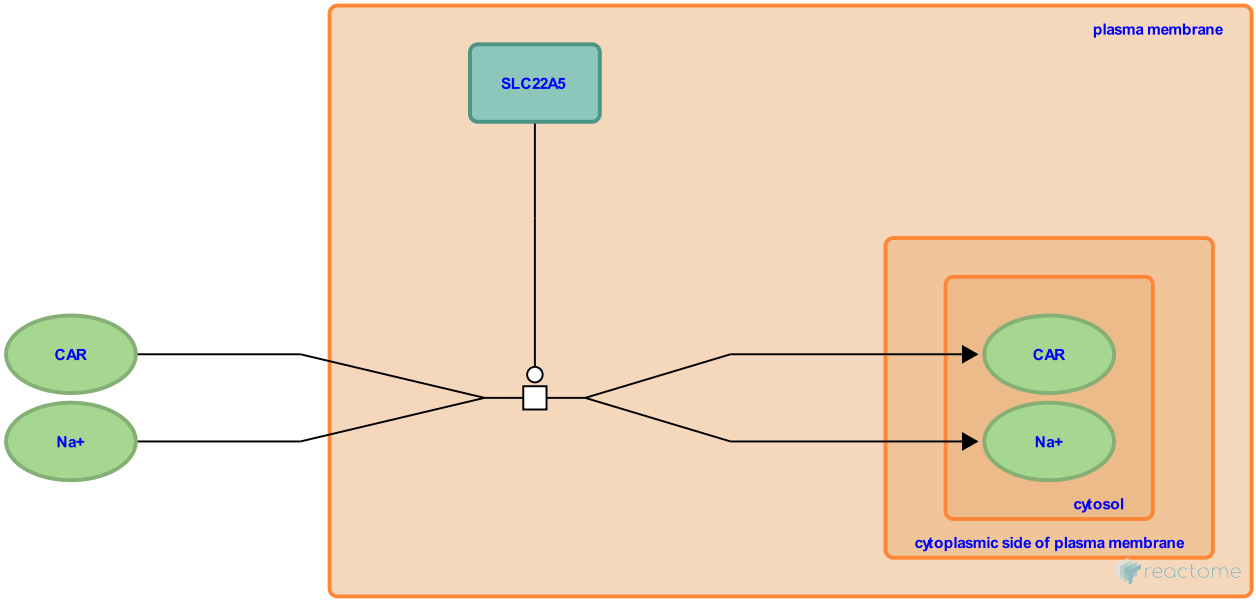
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

OCTN2 / SLC22A5 transports CAR from extracellular space to cytosol

Stable identifier: R-HSA-165026

Type: transition

Compartments: plasma membrane



OCTN2 (organic cation transporter novel 2, encoded by the SLC22A5 gene) mediates the sodium-dependent transport of CAR (carnitine) from the extracellular space into the cytosol.

While humans are capable of synthesizing carnitine de novo, the enzyme that catalyzes the last reaction of the biosynthetic pathway is found only in liver and kidney cells, and at very low levels in brain cells. Other tissues that require carnitine, such as muscle, are dependent on transport systems that mediate its export from the liver and uptake by other tissues (Kerner & Hoppel 1998). The specific transport systems responsible for liver export have been characterized biochemically in model organisms but specific transport proteins have not yet been identified. OCTN2 is the major transporter responsible for carnitine uptake in extrahepatic tissues, as demonstrated both by the biochemical characterization of overexpressed recombinant human protein (Tamai et al. 1998) and by the appearance of symptoms of carnitine deficiency in humans lacking a functional SLC22A5 gene (Seth et al. 1999; reviewed by Longo et al. 2016).

Literature references

Leibach, FH., Seth, P., Ganapathy, V., Huang, W., Wu, X. (1999). Mutations in novel cation transporter (OCTN2), an organic cation/carnitine transporter,with differential effects on the organic cation transport function and the carnitine transport function. *J Biol Chem, 274*, 33388-33392.

Oku, A., Shimane, M., Nezu, J., Tamai, I., Yabuuchi, H., Tsuji, A. et al. (1998). Molecular and functional identification of sodium ion-dependent, high-affinity human carnitine transporter OCTN2. *J Biol Chem, 273*, 20378-20382.

Pasquali, M., Frigeni, M., Longo, N. (2016). Carnitine transport and fatty acid oxidation. *Biochim. Biophys. Acta, 1863*, 2422-35.

Hoppel, C., Kerner, J. (1998). Genetic disorders of carnitine metabolism and their nutritional management. *Annu Rev Nutr, 18*, 179-206.

Editions

2005-07-26	Authored	D'Eustachio, P.
2016-12-23	Reviewed	Jassal, B.
2024-03-06	Edited	D'Eustachio, P.