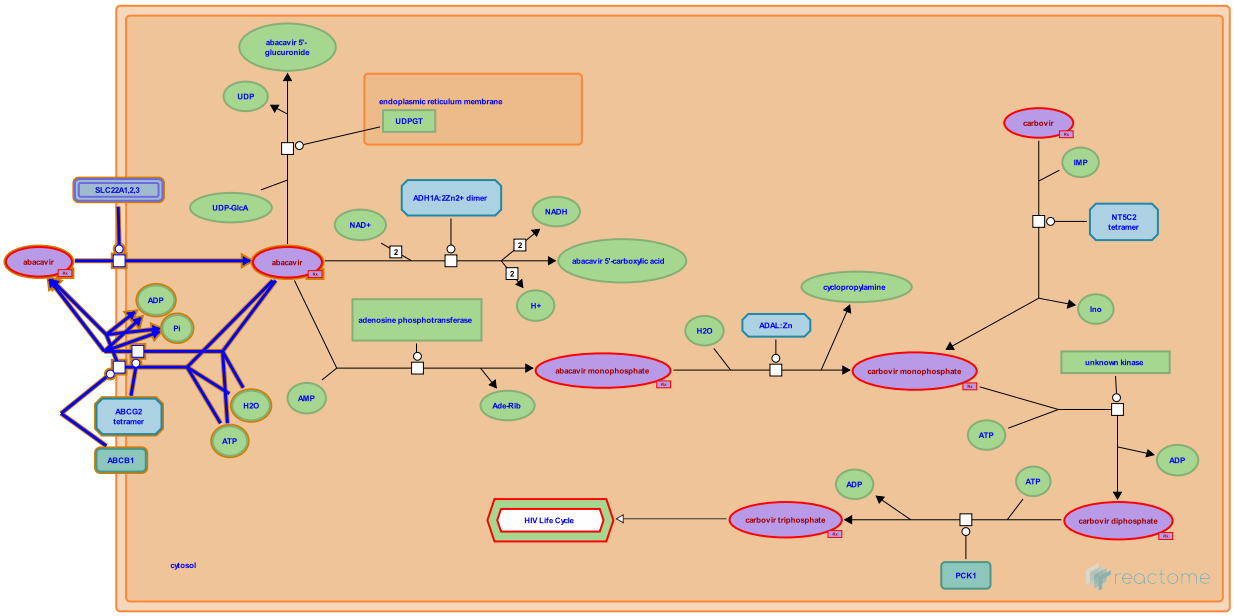
Abacavir transmembrane transport



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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.
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. ↗

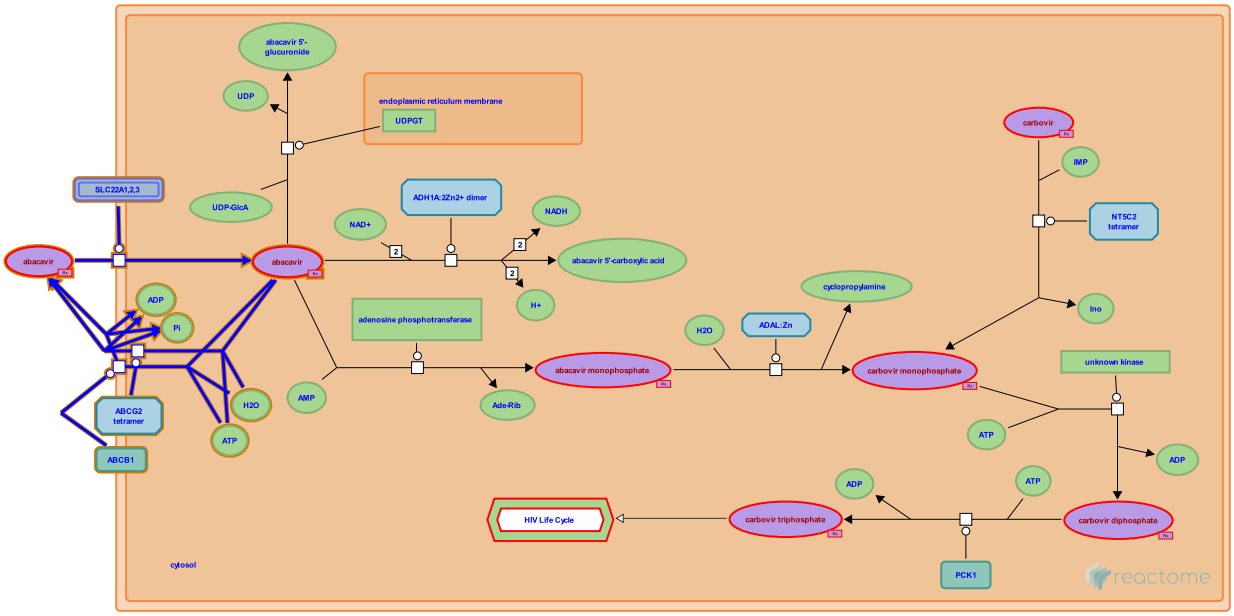
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Abacavir transmembrane transport ↗

Stable identifier: R-HSA-2161517



Cytosolic levels of abacavir are determined by the balance of its facilitated diffusion into the cell mediated by organic cation transporters SLC22A1, 2, and 3, and its ATP-dependent efflux from cells mediated by ABCG2 and ABCB1 (Klaasen and Aleksunes 2010; Pan et al. 2007; Shaik et al. 2007).

Literature references

Aleksunes, LM., Klaassen, CD. (2010). Xenobiotic, bile acid, and cholesterol transporters: function and regulation. *Pharmacol Rev, 62*, 1-96. ↗

Giri, N., Elmquist, WF., Pan, G., Shaik, N. (2007). P-glycoprotein-mediated active efflux of the anti-HIV1 nucleoside abacavir limits cellular accumulation and brain distribution. *Drug Metab Dispos, 35*, 2076-85. ↗

Giri, N., Elmquist, WF., Pan, G. (2007). Abcg2/Bcrp1 mediates the polarized transport of antiretroviral nucleosides abacavir and zidovudine. *Drug Metab Dispos, 35*, 1165-73. ↗

Editions

2012-03-14	Authored	D'Eustachio, P.
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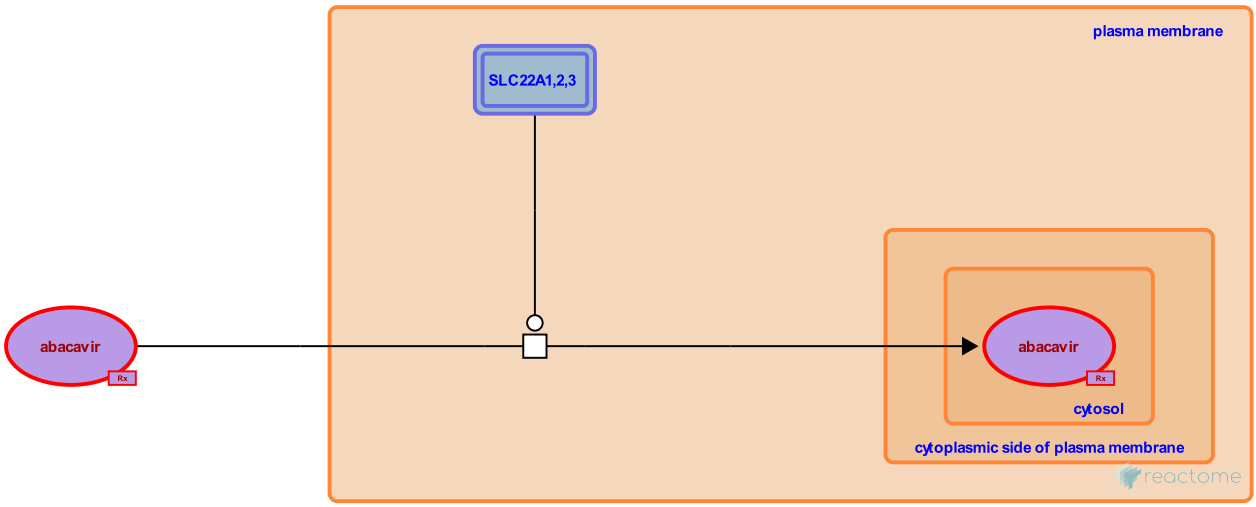
abacavir [extracellular] => abacavir [cytosol] ↗

Location: Abacavir transmembrane transport

Stable identifier: R-HSA-2161500

Type: transition

Compartments: plasma membrane, extracellular region, cytosol



Organic cation transporters 1 (OCT1, SLC22A1), 2 (OCT2, SLC22A2) and 3 (OCT3, SLC22A3) associated with the plasma membrane all mediate the influx of abacavir. The three transporters have similar affinities for abacavir (Minuesa et al. 2009) but differ in the tissues in which they are expressed and in their distributions on the surfaces of polarized cells (reviewed by Klaasen and Aleksunes 2010).

Followed by: abacavir [cytosol] + ATP + H2O => abacavir[extracellular] + ADP + phosphate, abacavir [cytosol] + ATP + H2O => abacavir[extracellular] + ADP + phosphate

Literature references

Aleksunes, LM., Klaassen, CD. (2010). Xenobiotic, bile acid, and cholesterol transporters: function and regulation. *Pharmacol Rev, 62*, 1-96. ↗

Volk, C., Pastor-Anglada, M., Koepsell, H., Arndt, P., Erkizia, I., Clotet, B. et al. (2009). Transport of lamivudine [(-)-beta-L-2',3'-dideoxy-3'-thiacytidine] and high-affinity interaction of nucleoside reverse transcriptase inhibitors with human organic cation transporters 1, 2, and 3. *J Pharmacol Exp Ther, 329*, 252-61. ↗

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abacavir [cytosol] + ATP + H2O => abacavir[extracellular] + ADP + phosphate ↗

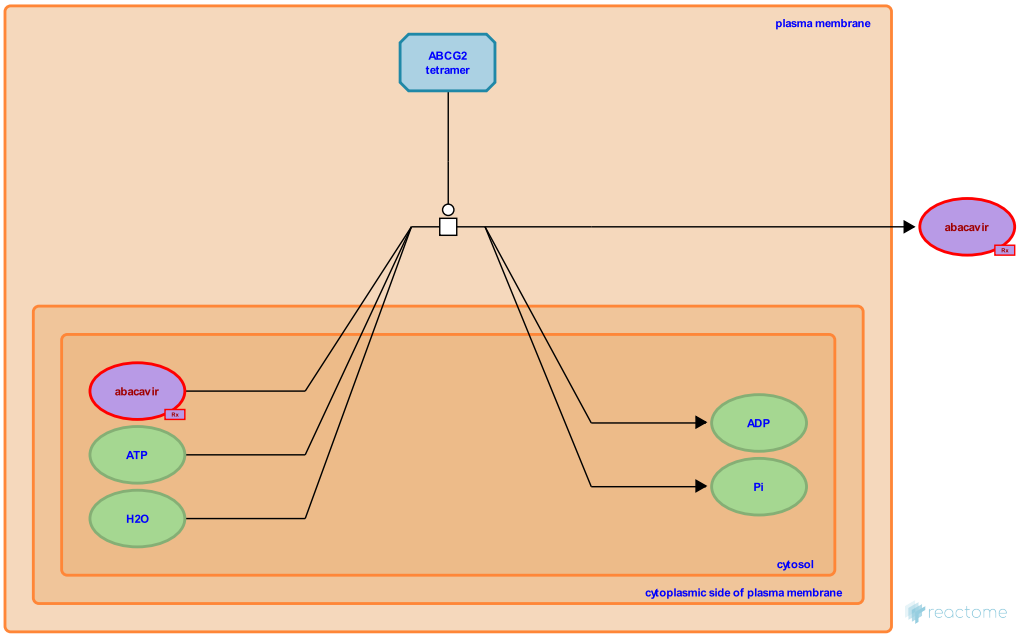
Location: Abacavir transmembrane transport

Stable identifier: R-HSA-2161506

Type: transition

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: abacavir [cytosol] + ATP + H2O => abacavir[extracellular] + ADP + phosphate (Mus musculus)



ATP-binding cassette sub-family G member 2 (ABCG2), associated with the plasma membrane, mediates the ATP-dependent efflux of abacavir (Doyle et al. 1998). The active form of ABCG2 is a homodimer stabilized by an interchain disulfide bond (Wakabayashi et al. 2007). The abacavir specificity of the human ABCG2 transporter is inferred from studies of the corresponding mouse protein (Pan et al. 2007).

Preceded by: abacavir [extracellular] => abacavir [cytosol]

Literature references

Nakagawa, H., Komada, M., Tamura, A., Ishikawa, T., Koshiba, S., Hoshijima, K. et al. (2007). Intramolecular disulfide bond is a critical check point determining degradative fates of ATP-binding cassette (ABC) transporter ABCG2 protein. *J Biol Chem, 282*, 27841-6. ↗

Giri, N., Elmquist, WF., Pan, G. (2007). Abcg2/Bcrp1 mediates the polarized transport of antiretroviral nucleosides abacavir and zidovudine. *Drug Metab Dispos, 35*, 1165-73. ↗

Yang, W., Ross, DD., Doyle, LA., Krogmann, T., Gao, Y., Rishi, AK. et al. (1998). A multidrug resistance transporter from human MCF-7 breast cancer cells. *Proc Natl Acad Sci U S A, 95*, 15665-70. ↗

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abacavir [cytosol] + ATP + H2O => abacavir[extracellular] + ADP + phosphate ↗

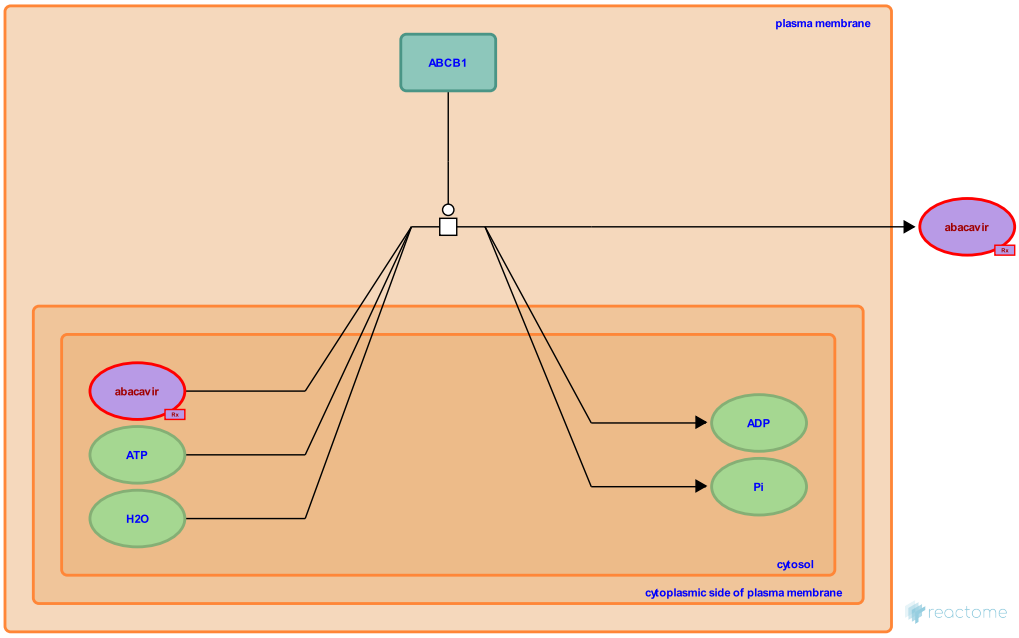
Location: Abacavir transmembrane transport

Stable identifier: R-HSA-2161538

Type: transition

Compartments: plasma membrane, extracellular region, cytosol

Inferred from: abacavir [cytosol] + ATP + H2O => abacavir[extracellular] + ADP + phosphate (Mus musculus)



The ABCB1 transporter associated with the plasma membrane mediates the ATP-dependent efflux of a variety of xenobiotic molecules. Its ability to transport abacavir is inferred from studies of the corresponding mouse protein (Shaik et al. 2007).

Preceded by: abacavir [extracellular] => abacavir [cytosol]

Literature references

Giri, N., Elmquist, WF., Pan, G., Shaik, N. (2007). P-glycoprotein-mediated active efflux of the anti-HIV1 nucleoside abacavir limits cellular accumulation and brain distribution. *Drug Metab Dispos, 35*, 2076-85. ↗

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