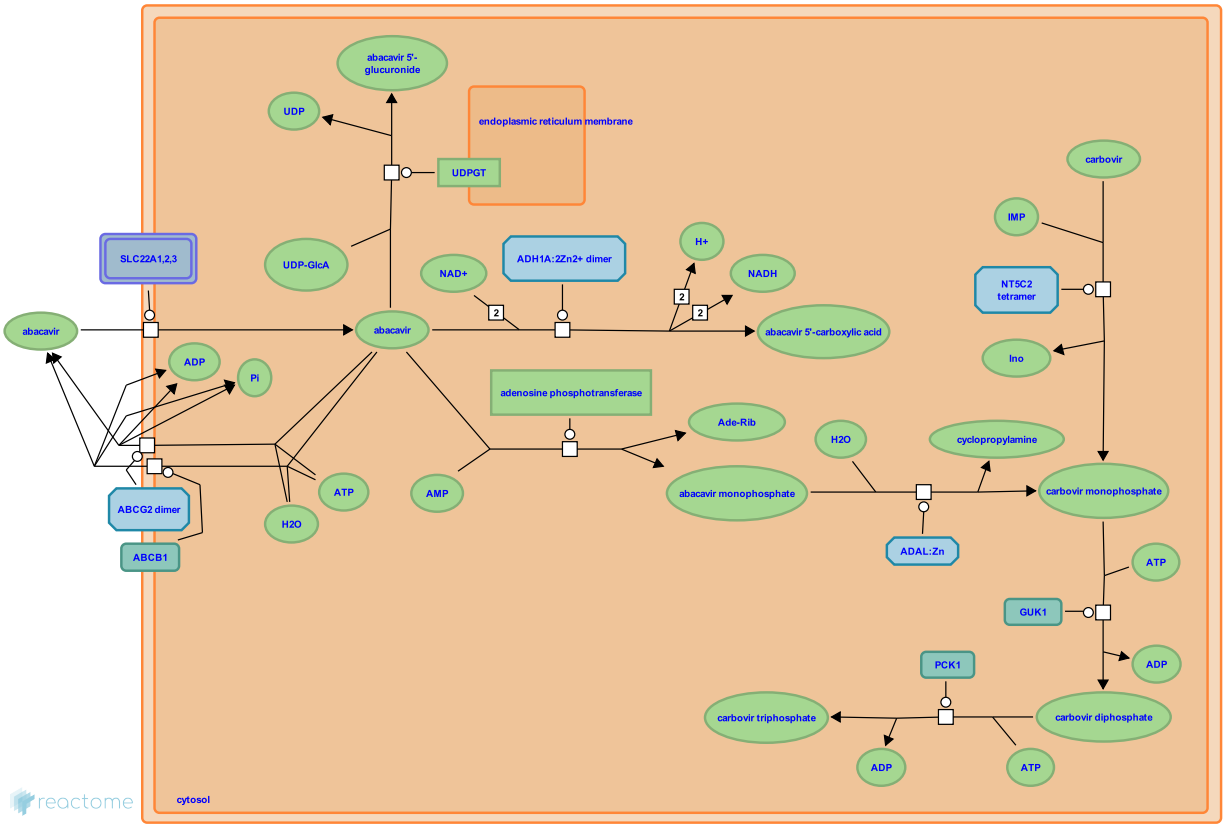
Abacavir transport and metabolism



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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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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. ↗

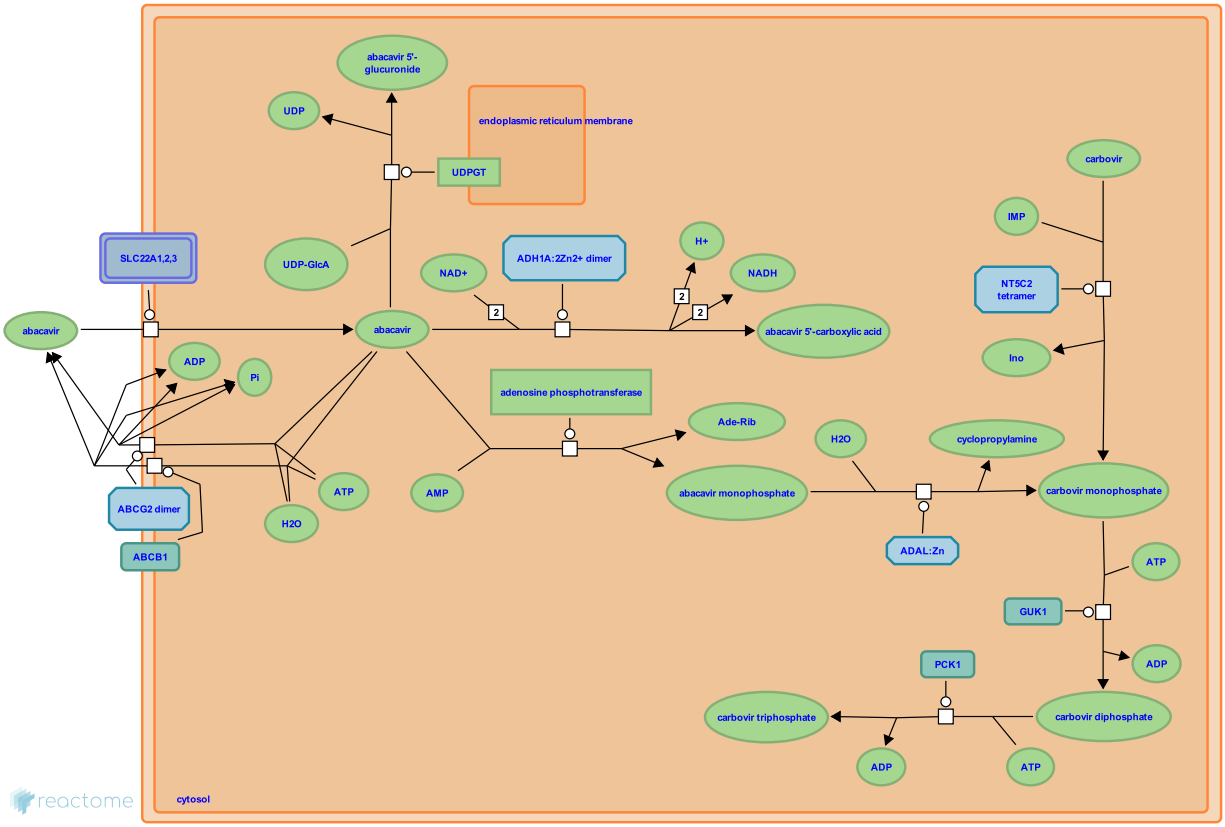
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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 transport and metabolism ↗

Stable identifier: R-HSA-2161522



Abacavir is a nucleoside analogue reverse transcriptase inhibitor with antiretroviral activity, widely used in combination with other drugs to treat HIV-1 infection (Yuen et al. 2008). Its uptake across the plasma membrane is mediated by organic cation transporters SLC22A1, 2, and 3; the transport proteins ABCB1 and ABCG2 mediate its efflux. Abacavir itself is a prodrug. Activation requires phosphorylation by a cytosolic adenosine phosphotransferase and deamination by ADAL deaminase to yield carbovir monophosphate. Cytosolic nucleotide kinases convert carbovir monophosphate to carbovir triphosphate, the active HIV reverse transcriptase inhibitor. Abacavir can be glucuronidated or oxidized to a 5'-carboxylate; these are the major forms in which it is excreted from the body.

Literature references

Yuen, GJ., Weller, S., Pakes, GE. (2008). A review of the pharmacokinetics of abacavir. *Clin Pharmacokinet, 47*, 351-71. ↗

Editions

2012-03-14	Authored	D'Eustachio, P.
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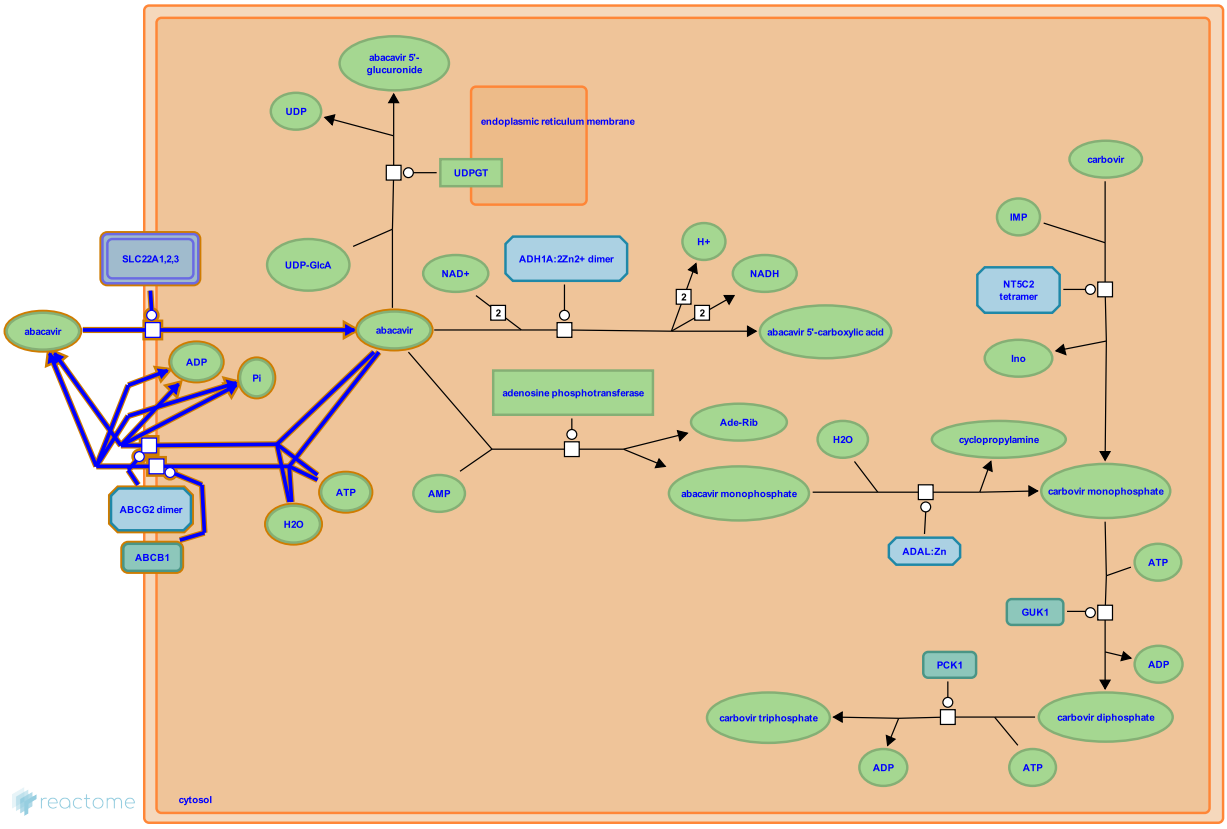
Abacavir transmembrane transport ↗

Location: Abacavir transport and metabolism

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

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

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

Shaik, N., Giri, N., Pan, G., Elmquist, WF. (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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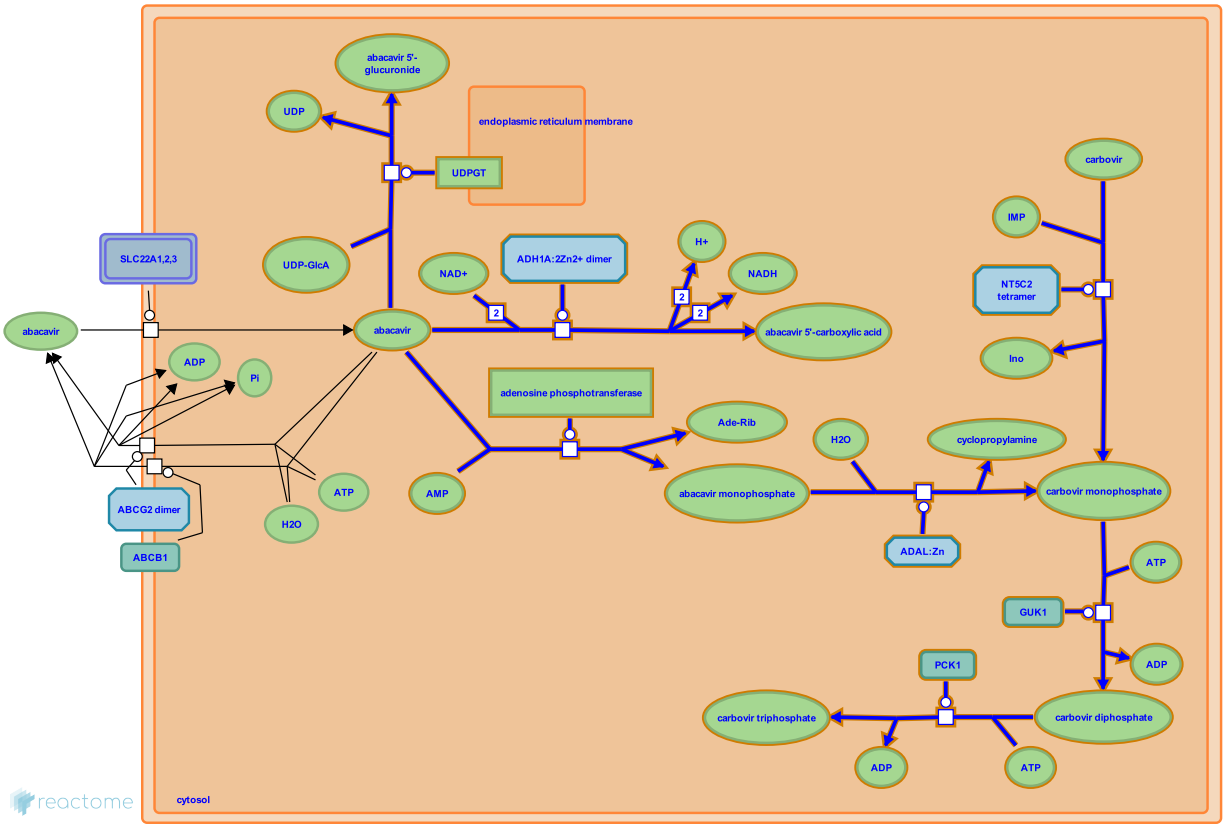
Abacavir metabolism ↗

Location: Abacavir transport and metabolism

Stable identifier: R-HSA-2161541



Abacavir activation proceeds steps of phosphorylation, deamination to yield carbovir monophosphate, and phosphorylation of the latter compound to yield the triphosphate. In addition, abacavir can be conjugated with glucuronide or oxidized to its 5'-carboxylate derivative, the two major forms in which it is excreted from the body (Yuen et al. 2008).

Literature references

Yuen, GJ., Weller, S., Pakes, GE. (2008). A review of the pharmacokinetics of abacavir. *Clin Pharmacokinet, 47*, 351-71. ↗

Editions

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