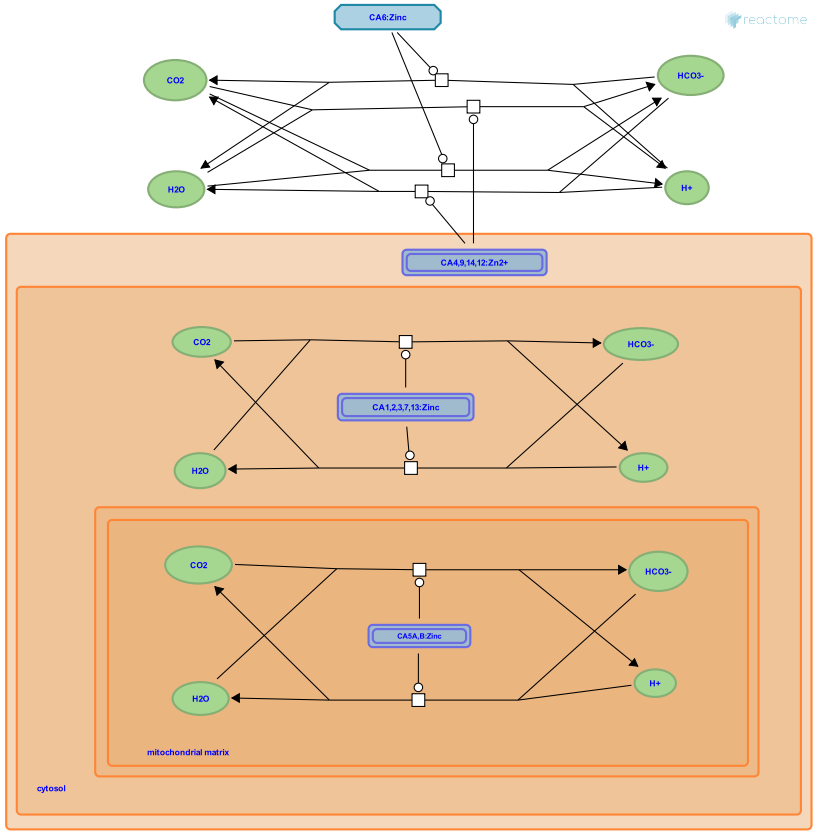
Reversible hydration of carbon dioxide



Jassal, B., May, B., Silverman, DN.

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

16/01/2021

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. ↗

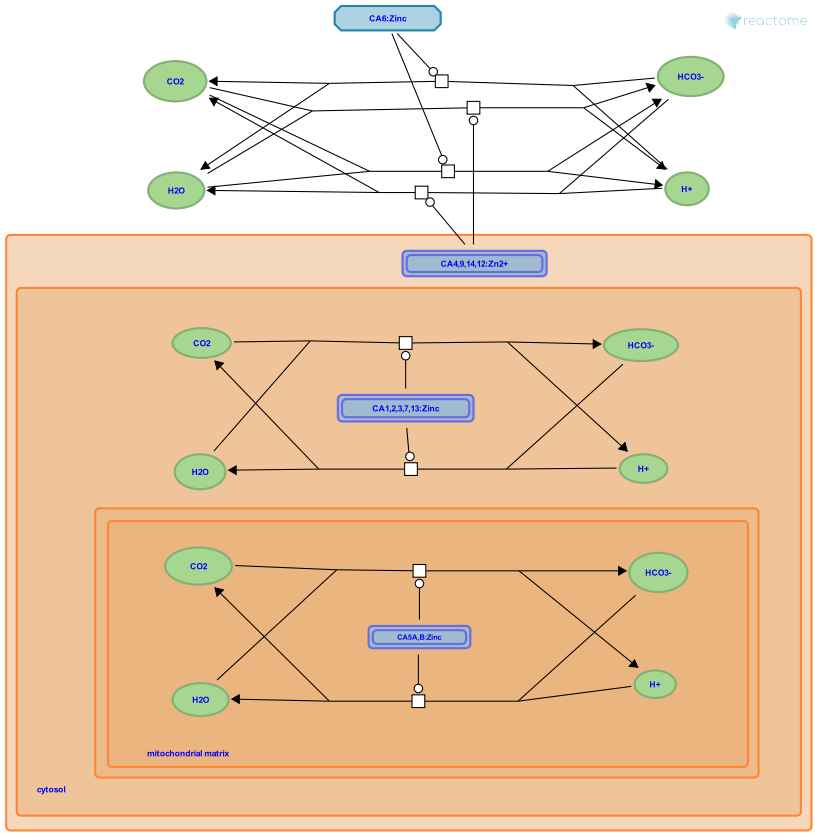
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Reversible hydration of carbon dioxide ↗

Stable identifier: R-HSA-1475029

Compartments: cytosol, extracellular region, mitochondrial matrix, plasma membrane



Carbonic anhydrases reversibly catalyze the hydration of carbon dioxide and directly produce bicarbonate and protons, bypassing the formation of carbonic acid (reviewed in Lindskog 1997, Breton 2001, Esbaugh and Tufts 2006, Boron 2010, Gilmour 2010). Carbonic anhydrase deprotonates water to yield a zinc-hydroxyl group and a proton which is transferred to external buffer molecules via histidine or glutamate residues in carbonic anhydrase. The hydroxyl group reacts with carbon dioxide in the active site to yield bicarbonate. A water molecule displaces the bicarbonate and the reaction cycle begins again. There are currently 12 known active carbonic anhydrases in humans.

Literature references

Breton, S. (2001). The cellular physiology of carbonic anhydrases. *JOP, 2*, 159-64. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Esbaugh, AJ., Tufts, BL. (2006). The structure and function of carbonic anhydrase isozymes in the respiratory system of vertebrates. *Respir Physiol Neurobiol, 154*, 185-98. ↗

Boron, WF. (2010). Evaluating the role of carbonic anhydrases in the transport of HCO3--related species. *Biochim Biophys Acta, 1804*, 410-21. ↗

Gilmour, KM. (2010). Perspectives on carbonic anhydrase. *Comp Biochem Physiol A Mol Integr Physiol, 157*, 193-7. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

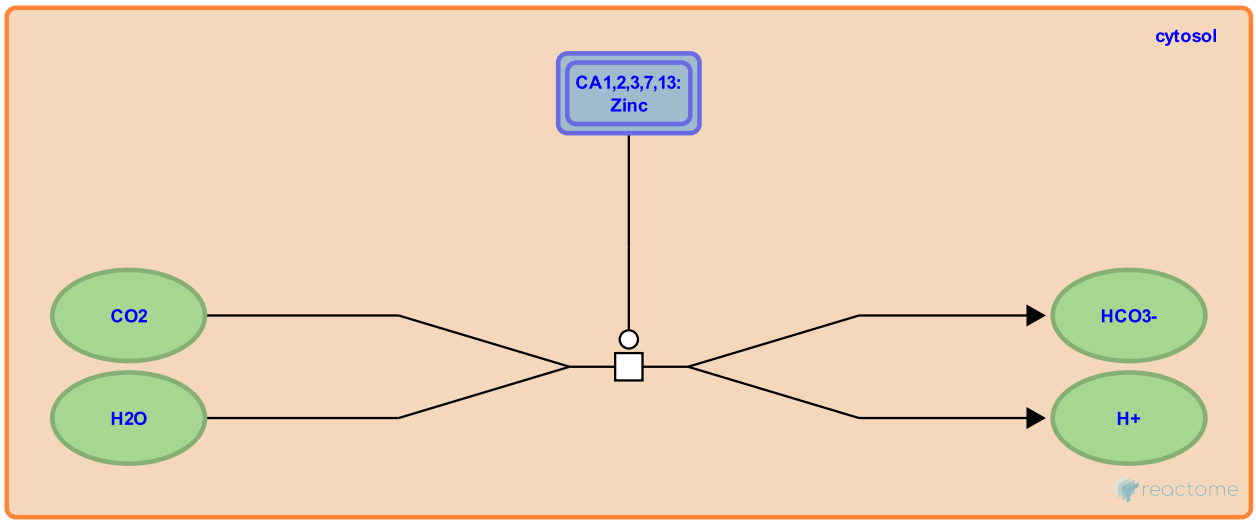
Carbonic anhydrase hydrates carbon dioxide (cytosol) ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1475026

Type: transition

Compartments: cytosol



Carbonic anhydrase I (CA1, Khalifah 1971, Simonsson et al. 1982, Ren and Lindskog 1992), carbonic anhydrase II (CA2, Tibell et al. 1984, Jones and Shaw 1983, Pesando 1975, Ghannam et al. 1986), carbonic anhydrase III (CA3, Carter et al. 1979, Tu et al. 1990, Tu et al. 1994, Tu et al. 1998, Silverman et al. 1993), carbonic anhydrase VII (CA7, Bootorabi et al. 2010, Gitto et al. 2010) hydrate carbon dioxide to yield bicarbonate and a proton. Carbonic anhydrase deprotonates water to yield a zinc-hydroxyl group and a proton which is transferred to external buffer molecules via histidine or glutamate residues in carbonic anhydrase. The hydroxyl group reacts with carbon dioxide in the active site to yield bicarbonate. A water molecule displaces the bicarbonate and the reaction cycle begins again (reviewed in Lindskog 1997). Depending on the concentrations of reactants the reaction is reversible.

CA2 and CA7 have high catalytic activity, CA1 has low activity (10% of the activity of CA2), and CA3 has very low activity (1% of the activity of CA2). CA1 and CA2 are found in erythrocytes. CA2 is also found in kidney, lung, and white muscle where it facilitates diffusion of carbon dioxide. CA3 is found in red muscle where it participates in resistance against oxidative stress.

Literature references

Khalifah, RG. (1971). The carbon dioxide hydration activity of carbonic anhydrase. I. Stop-flow kinetic studies on the native human isoenzymes B and C. *J Biol Chem, 246*, 2561-73. ↗

Simonsson, I., Jonsson, BH., Lindskog, S. (1982). A 13C nuclear magnetic resonance study of CO2/HCO-3 exchange catalyzed by human carbonic anhydrase I. *Eur J Biochem, 129*, 165-9. ↗

Ren, X., Lindskog, S. (1992). Buffer dependence of CO2 hydration catalyzed by human carbonic anhydrase I. *Biochim Biophys Acta, 1120*, 81-6. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Tibell, L., Forsman, C., Simonsson, I., Lindskog, S. (1984). Anion inhibition of CO2 hydration catalyzed by human carbonic anhydrase II. Mechanistic implications. *Biochim Biophys Acta, 789*, 302-10. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

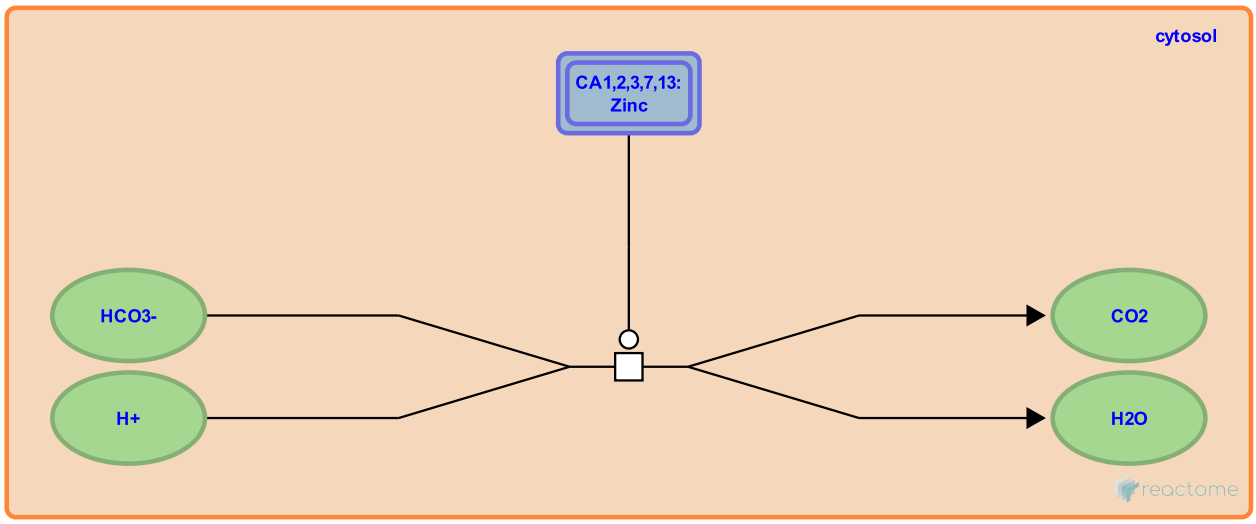
Carbonic anhydrase dehydrates bicarbonate (cytosol) ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1475022

Type: transition

Compartments: cytosol



Carbonic anhydrase I (CA1, Khalifah 1971, Simonsson et al. 1982, Ren and Lindskog 1992), carbonic anhydrase II (CA2, Tibell et al. 1984, Jones and Shaw 1983, Pesando 1975, Ghannam et al. 1986), carbonic anhydrase III (CA3, Carter et al. 1979, Tu et al. 1990, Tu et al. 1994, Tu et al. 1998, Silverman et al. 1993), carbonic anhydrase VII (CA7, Bootorabi et al. 2010, Gitto et al. 2010) dehydrate cytosolic bicarbonate to yield water and carbon dioxide (reviewed in Lindskog 1997). Depending on the concentrations of reactants the reaction is reversible.

CA2 and CA7 have high catalytic activity, CA1 has low activity (10% of the activity of CA2), and CA3 has very low activity (1% of the activity of CA2). CA1 and CA2 are found in erythrocytes. CA2 is also found in kidney, lung, and white muscle where it facilitates diffusion of carbon dioxide. CA3 is found in red muscle where it participates in resistance against oxidative stress.

Literature references

Khalifah, RG. (1971). The carbon dioxide hydration activity of carbonic anhydrase. I. Stop-flow kinetic studies on the native human isoenzymes B and C. *J Biol Chem, 246*, 2561-73. ↗

Simonsson, I., Jonsson, BH., Lindskog, S. (1982). A 13C nuclear magnetic resonance study of CO2/HCO-3 exchange catalyzed by human carbonic anhydrase I. *Eur J Biochem, 129*, 165-9. ↗

Ren, X., Lindskog, S. (1992). Buffer dependence of CO2 hydration catalyzed by human carbonic anhydrase I. *Biochim Biophys Acta, 1120*, 81-6. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Tibell, L., Forsman, C., Simonsson, I., Lindskog, S. (1984). Anion inhibition of CO2 hydration catalyzed by human carbonic anhydrase II. Mechanistic implications. *Biochim Biophys Acta, 789*, 302-10. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

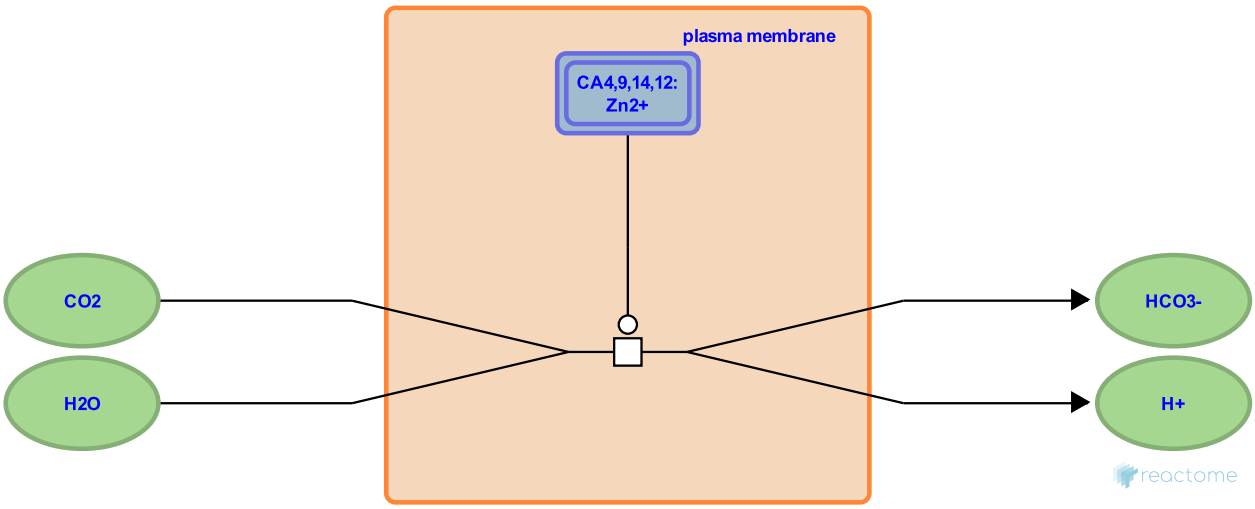
Carbonic anhydrase hydrates carbon dioxide (plasma membrane) ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1475025

Type: transition

Compartments: plasma membrane, extracellular region



Carbonic anhydrase IV (CA4, Zhu and Sly 1990, Okuyama et al. 1992, Baird et al. 1997, Innocenti et al. 2004), carbonic anhydrase IX (CA9, Wingo et al. 2001, Hilvo et al. 2008), carbonic anhydrase XII (CA12, Ulmasov et al. 2000, Pastorekova et al. 2008), and carbonic anhydrase XIV (CA14Ozensoy et al. 2005, Temperini et al. 2008) are membrane-bound enzymes that hydrate extracellular carbon dioxide to yield bicarbonate and a proton.Carbonic anhydrase deprotonates water to yield a zinc-hydroxyl group and a proton which is transferred to external buffer molecules via histidine or glutamate residues in carbonic anhydrase. The hydroxyl group reacts with carbon dioxide in the active site to yield bicarbonate. A water molecule displaces the bicarbonate and the reaction cycle begins again (reviewed in Lindskog 1997). Depending on the concentrations of reactants the reaction is reversible.

CA4 has high catalytic activity. CA9, CA12, and CA14 have moderate activity. CA4 is anchored to the extracellular face of the plasma membrane by glycosylphosphatidylinositol. CA9, CA12, and CA14 are single-pass transmembrane proteins. CA4 is found on the extracellular face of capillaries in kidney, lung, and muscle where it maintains the gradient of carbon dioxide between tissue and blood. CA9 and CA12 are found on basolateral membranes of epithelia. CA9 is inducible by Hypoxia-inducible factor 1 alpha (HIF1alpha) and acidifies the extracellular environment of tumors. In rodents CA15 is membrane anchored and has low activity; in primates CA15 is a pseudogene.

Literature references

Zhu, XL., Sly, WS. (1990). Carbonic anhydrase IV from human lung. Purification, characterization, and comparison with membrane carbonic anhydrase from human kidney. *J Biol Chem, 265*, 8795-801. ↗

Okuyama, T., Waheed, A., Kusumoto, W., Zhu, XL., Sly, WS. (1995). Carbonic anhydrase IV: role of removal of C-terminal domain in glycosylphosphatidylinositol anchoring and realization of enzyme activity. *Arch Biochem Biophys , 320*, 315-22. ↗

Innocenti, A., Firnges, MA., Antel, J., Wurl, M., Scozzafava, A., Supuran, CT. (2004). Carbonic anhydrase inhibitors: inhibition of the membrane-bound human isozyme IV with anions. *Bioorg Med Chem Lett, 14*, 5769-73. ↗

Baird TT, Jr., Waheed, A., Okuyama, T., Sly, WS., Fierke, CA. (1997). Catalysis and inhibition of human carbonic anhydrase IV. *Biochemistry, 36*, 2669-78. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

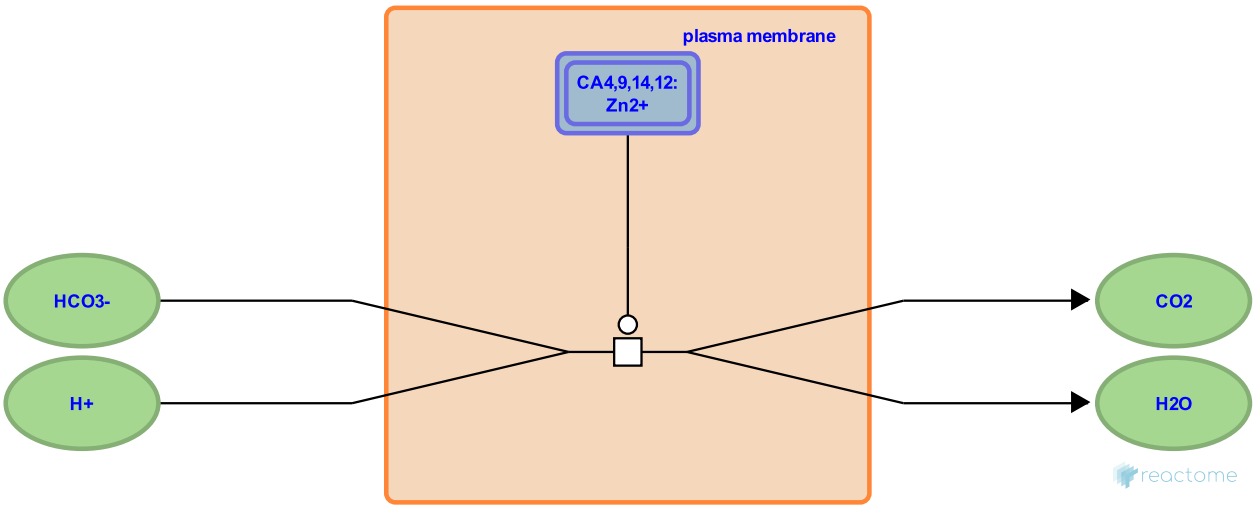
Carbonic anhydrase dehydrates bicarbonate (plasma membrane) ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1475017

Type: transition

Compartments: plasma membrane, extracellular region



Carbonic anhydrase IV (CA4, Zhu and Sly 1990, Okuyama et al. 1992, Baird et al. 1997, Innocenti et al. 2004), carbonic anhydrase IX (CA9, Wingo et al. 2001, Hilvo et al. 2008), carbonic anhydrase XII (CA12, Ulmasov et al. 2000, Pastorekova et al. 2008), and carbonic anhydrase XIV (CA14, Ozensoy et al. 2005, Temperini et al. 2008) are membrane-bound enzymes that dehydrate bicarbonate to yield water and carbon dioxide. Depending on the concentrations of reactants the reaction is reversible.

CA4 has high catalytic activity. CA9, CA12, and CA14 have moderate activity. CA4 is anchored to the extracellular face of the plasma membrane by glycosylphosphatidylinositol. CA9, CA12, and CA14 are single-pass transmembrane proteins. CA4 is found on the extracellular face of capillaries in kidney, lung, and muscle where it maintains the gradient of carbon dioxide between tissue and blood. CA9 and CA12 are found on basolateral membranes of epithelia. CA9 is inducible by Hypoxia-inducible factor 1 alpha (HIF1alpha) and acidifies the extracellular environment of tumors. In rodents CA15 is membrane anchored and has low activity; in primates CA15 is a pseudogene.

Literature references

Zhu, XL., Sly, WS. (1990). Carbonic anhydrase IV from human lung. Purification, characterization, and comparison with membrane carbonic anhydrase from human kidney. *J Biol Chem, 265*, 8795-801. ↗

Okuyama, T., Waheed, A., Kusumoto, W., Zhu, XL., Sly, WS. (1995). Carbonic anhydrase IV: role of removal of C-terminal domain in glycosylphosphatidylinositol anchoring and realization of enzyme activity. *Arch Biochem Biophys , 320*, 315-22. ↗

Innocenti, A., Firnges, MA., Antel, J., Wurl, M., Scozzafava, A., Supuran, CT. (2004). Carbonic anhydrase inhibitors: inhibition of the membrane-bound human isozyme IV with anions. *Bioorg Med Chem Lett, 14*, 5769-73. ↗

Baird TT, Jr., Waheed, A., Okuyama, T., Sly, WS., Fierke, CA. (1997). Catalysis and inhibition of human carbonic anhydrase IV. *Biochemistry, 36*, 2669-78. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

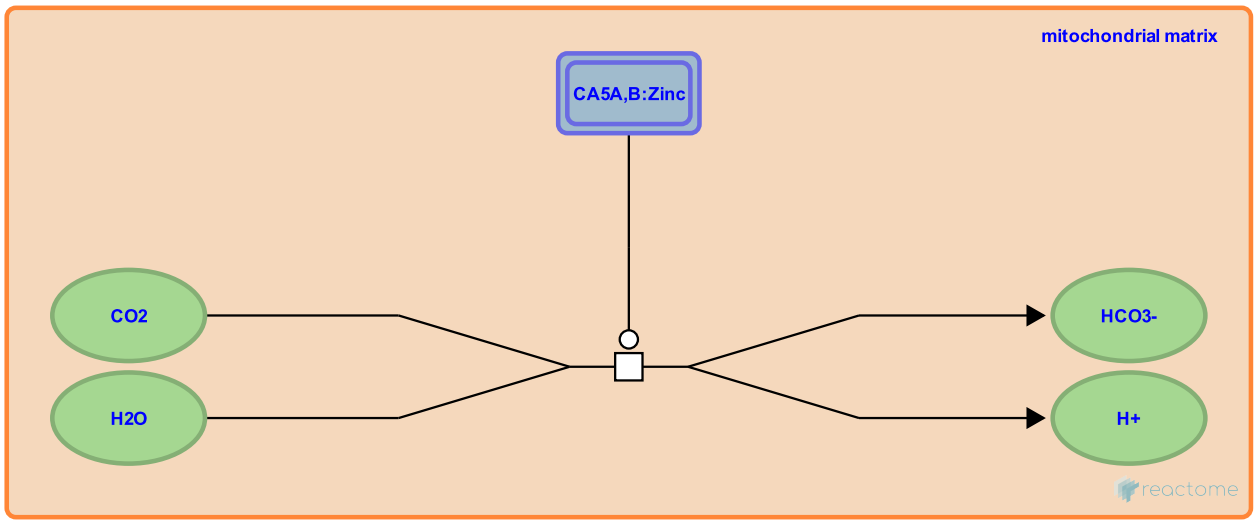
Carbonic anhydrase hydrates carbon dioxide (mitochondria) ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1475032

Type: transition

Compartments: mitochondrial matrix



Carbonic anhydrase VA (CA5A, Nagao et al. 1993, Franchi et al. 2003, Nishimori et al. 2007) and carbonic anhydrase VB (CA5B, Fujikawa-Adachi et al. 1999, Nishimori et al. 2005, Nishimori et al. 2007) hydrate carbon dioxide in mitochondria to yield bicarbonate and a proton. Carbonic anhydrase deprotonates water to yield a zinc-hydroxyl group and a proton which is transferred to external buffer molecules via histidine or glutamate residues in carbonic anhydrase. The hydroxyl group reacts with carbon dioxide in the active site to yield bicarbonate. A water molecule displaces the bicarbonate and the reaction cycle begins again (reviewed in Lindskog 1997). Depending on the concentrations of reactants the reaction is reversible.

Literature references

Nishimori, I., Vullo, D., Innocenti, A., Scozzafava, A., Mastrolorenzo, A., Supuran, CT. (2005). Carbonic anhydrase inhibitors. The mitochondrial isozyme VB as a new target for sulfonamide and sulfamate inhibitors. *J Med Chem, 48*, 7860-6. ↗

Franchi, M., Vullo, D., Gallori, E., Antel, J., Wurl, M., Scozzafava, A. et al. (2003). Carbonic anhydrase inhibitors: inhibition of human and murine mitochondrial isozymes V with anions. *Bioorg Med Chem Lett, 13*, 2857-61. ↗

Nishimori, I., Innocenti, A., Vullo, D., Scozzafava, A., Supuran, CT. (2007). Carbonic anhydrase inhibitors: the inhibition profiles of the human mitochondrial isoforms VA and VB with anions are very different. *Bioorg Med Chem, 15*, 6742-7. ↗

Fujikawa-Adachi, K., Nishimori, I., Taguchi, T., Onishi, S. (1999). Human mitochondrial carbonic anhydrase VB. cDNA cloning, mRNA expression, subcellular localization, and mapping to chromosome x. *J Biol Chem, 274*, 21228-33. ↗

Nagao, Y., Platero, JS., Waheed, A., Sly, WS. (1993). Human mitochondrial carbonic anhydrase: cDNA cloning, expression, subcellular localization, and mapping to chromosome 16. *Proc Natl Acad Sci U S A, 90*, 7623-7. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

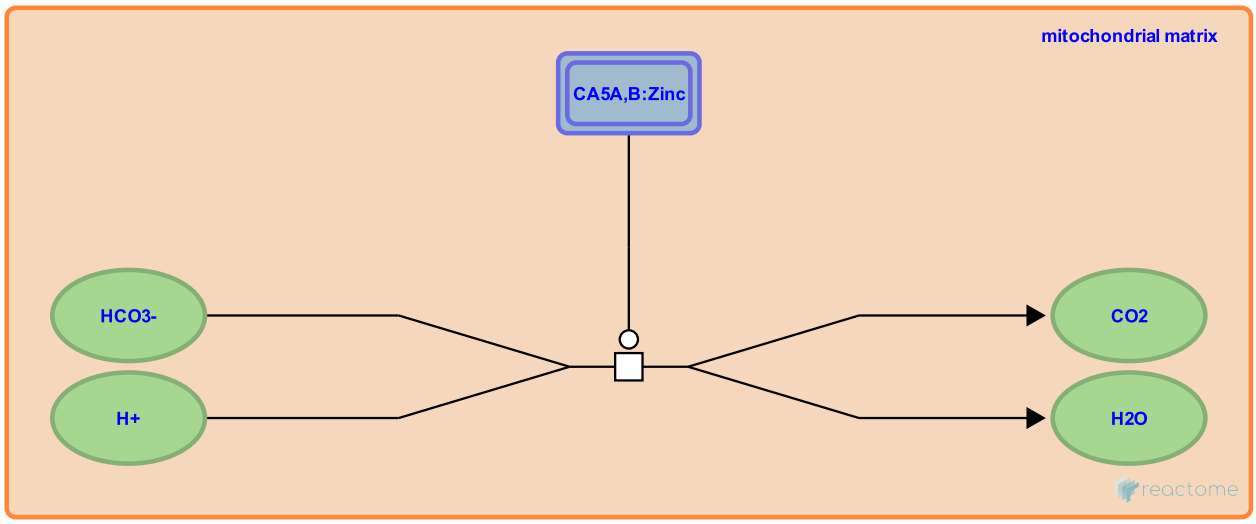
Carbonic anhydrase dehydrates bicarbonate (mitochondria) ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1475028

Type: transition

Compartments: mitochondrial matrix



Carbonic anhydrase VA (CA5A, Nagao et al. 1993, Franchi et al. 2003, Nishimori et al. 2007) and carbonic anhydrase VB (CA5B, Fujikawa-Adachi et al. 1999, Nishimori et al. 2005, Nishimori et al. 2007) dehydrate bicarbonate in mitochondria to yield water and carbon dioxide (reviewed in Lindskog 1997). Depending on the concentrations of reactants the reaction is reversible.

Literature references

Nishimori, I., Vullo, D., Innocenti, A., Scozzafava, A., Mastrolorenzo, A., Supuran, CT. (2005). Carbonic anhydrase inhibitors. The mitochondrial isozyme VB as a new target for sulfonamide and sulfamate inhibitors. *J Med Chem, 48*, 7860-6. ↗

Franchi, M., Vullo, D., Gallori, E., Antel, J., Wurl, M., Scozzafava, A. et al. (2003). Carbonic anhydrase inhibitors: inhibition of human and murine mitochondrial isozymes V with anions. *Bioorg Med Chem Lett, 13*, 2857-61. ↗

Nishimori, I., Innocenti, A., Vullo, D., Scozzafava, A., Supuran, CT. (2007). Carbonic anhydrase inhibitors: the inhibition profiles of the human mitochondrial isoforms VA and VB with anions are very different. *Bioorg Med Chem, 15*, 6742-7. ↗

Fujikawa-Adachi, K., Nishimori, I., Taguchi, T., Onishi, S. (1999). Human mitochondrial carbonic anhydrase VB. cDNA cloning, mRNA expression, subcellular localization, and mapping to chromosome x. *J Biol Chem, 274*, 21228-33. ↗

Nagao, Y., Platero, JS., Waheed, A., Sly, WS. (1993). Human mitochondrial carbonic anhydrase: cDNA cloning, expression, subcellular localization, and mapping to chromosome 16. *Proc Natl Acad Sci U S A, 90*, 7623-7. ↗

Editions

2011-08-06	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

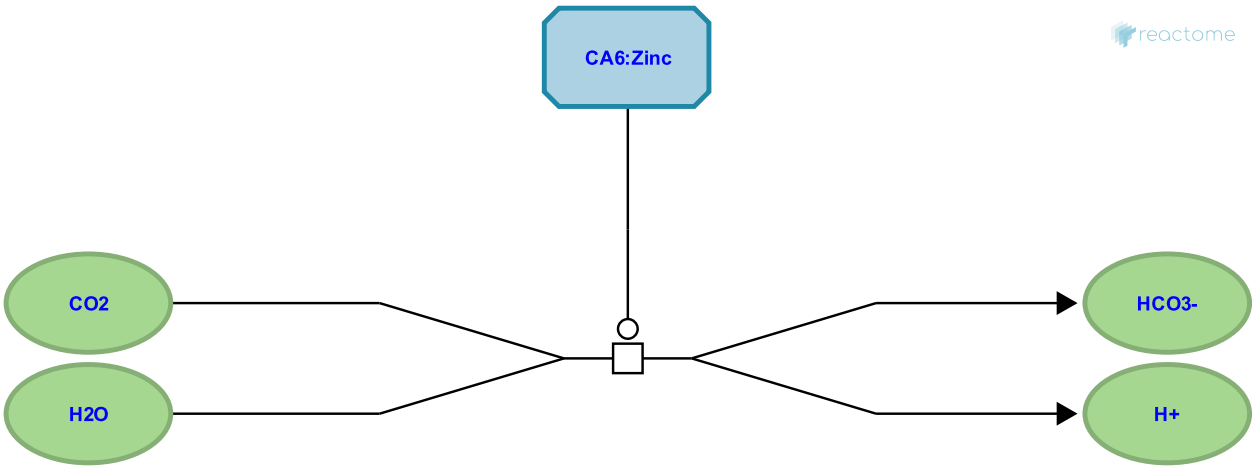
Carbonic Anhydrase VI hydrates carbon dioxide to bicarbonate and a proton ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1237045

Type: transition

Compartments: extracellular region



Carbonic anhydrase VI (CA6) hydrates carbon dioxide to yield bicarbonate and a proton (Thatcher et al. 1998, Nishimori et al. 2007).Carbonic anhydrase deprotonates water to yield a zinc-hydroxyl group and a proton which is transferred to external buffer molecules via histidine or glutamate residues in carbonic anhydrase. The hydroxyl group reacts with carbon dioxide in the active site to yield bicarbonate. A water molecule displaces the bicarbonate and the reaction cycle begins again (reviewed in Lindskog 1997). Depending on the concentrations of reactants the reaction is reversible. CA6 is a major protein of saliva and is also known as gustin.

Literature references

Thatcher, BJ., Doherty, AE., Orvisky, E., Martin, BM., Henkin, RI. (1998). Gustin from human parotid saliva is carbonic anhydrase VI. *Biochem Biophys Res Commun, 250*, 635-41. ↗

Nishimori, I., Onishi, S., Vullo, D., Innocenti, A., Scozzafava, A., Supuran, CT. (2007). Carbonic anhydrase activators: the first activation study of the human secretory isoform VI with amino acids and amines. *Bioorg Med Chem, 15*, 5351-7. ↗

Nishimori, I., Minakuchi, T., Onishi, S., Vullo, D., Scozzafava, A., Supuran, CT. (2007). Carbonic anhydrase inhibitors. DNA cloning, characterization, and inhibition studies of the human secretory isoform VI, a new target for sulfonamide and sulfamate inhibitors. *J Med Chem, 50*, 381-8. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Editions

2011-03-24	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

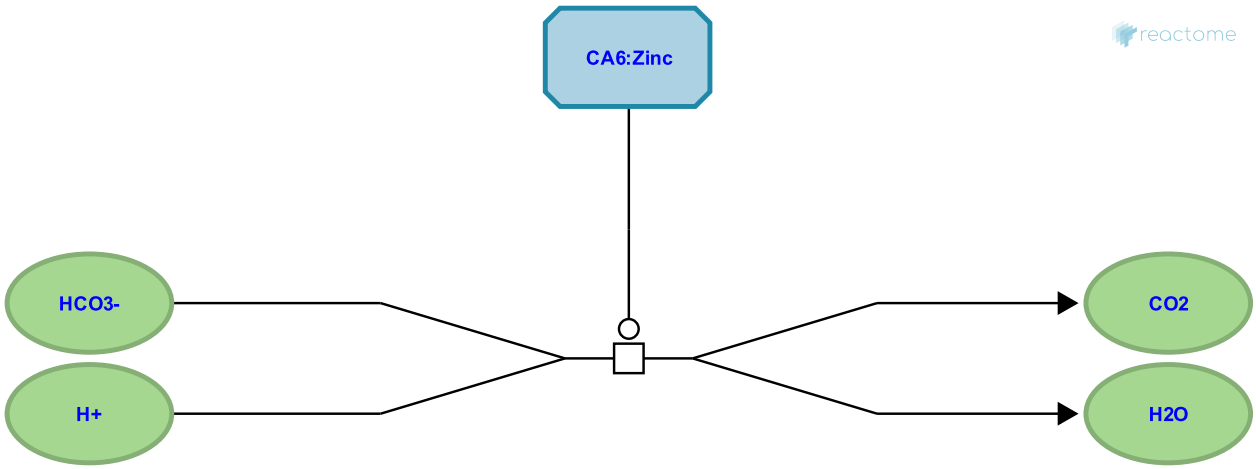
Carbonic anhydrase VI dehydrates bicarbonate to water and carbon dioxide ↗

Location: Reversible hydration of carbon dioxide

Stable identifier: R-HSA-1237081

Type: transition

Compartments: extracellular region



Carbonic anhydrase VI (CA6) dehydrates bicarbonate to yield water and carbon dioxide (Thatcher et al. 1998, Nishimori et al. 2007). Depending on the concentrations of reactants the reaction is reversible. CA6 is a major protein of saliva and is also known as gustin.

Literature references

Thatcher, BJ., Doherty, AE., Orvisky, E., Martin, BM., Henkin, RI. (1998). Gustin from human parotid saliva is carbonic anhydrase VI. *Biochem Biophys Res Commun, 250*, 635-41. ↗

Nishimori, I., Onishi, S., Vullo, D., Innocenti, A., Scozzafava, A., Supuran, CT. (2007). Carbonic anhydrase activators: the first activation study of the human secretory isoform VI with amino acids and amines. *Bioorg Med Chem, 15*, 5351-7. ↗

Nishimori, I., Minakuchi, T., Onishi, S., Vullo, D., Scozzafava, A., Supuran, CT. (2007). Carbonic anhydrase inhibitors. DNA cloning, characterization, and inhibition studies of the human secretory isoform VI, a new target for sulfonamide and sulfamate inhibitors. *J Med Chem, 50*, 381-8. ↗

Lindskog, S. (1997). Structure and mechanism of carbonic anhydrase. *Pharmacol Ther, 74*, 1-20. ↗

Editions

2011-03-24	Authored, Edited	May, B.
2012-05-16	Reviewed	Jassal, B., Silverman, DN.

Table of Contents