CD isomers transform to BT, BTCA, BZ, ODHBT

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05/05/2024

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

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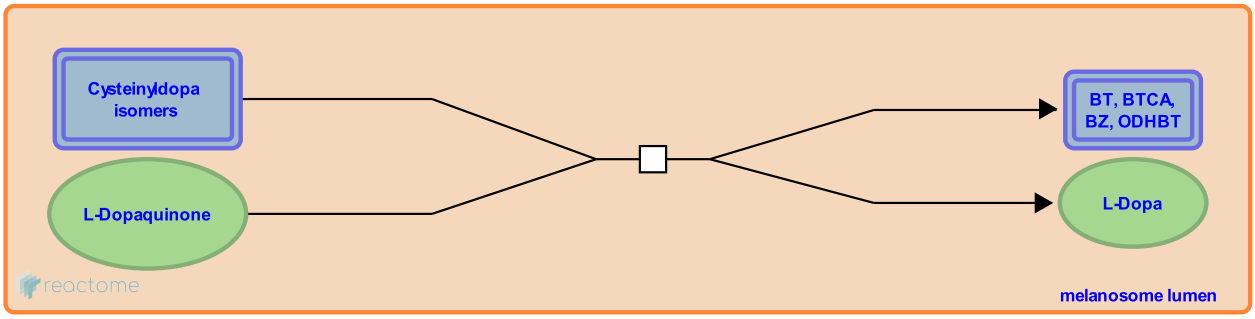
Stable identifier: R-HSA-5662904

Type: transition

Compartments: melanosome lumen



Following the formation of cysteinyldopa (CD) isomers, pheomelanogenesis continues with the redox exchange of CD isomers with dopaquinone (DQ), generating cysteinyldopaquinone (CDQ). Once formed, CDQ rapidly cyclizes via attack of the cysteinyl side-chain amino group on the carbonyl group to produce a cyclic ortho-quinonimine intermediate (QI) (Napolitano et al. 1994, Land & Riley 2000). Redox exchange between CD and QI leads to the production of a reduced form of QI, 3,4-dihydro-1,4-benzothiazine-3-carboxylic acid (DHBTCA) and CDQ (Napolitano et al. 2000, Wakamatsu et al. 2009). QI rapidly undergoes rearrangement, with or without decarboxylation, leading to 2H-1,4-benzothiazine (BT) and its 3-carboxy derivative, 2H-1,4-benzothiazine-3-carboxylic acid (BTCA) (Napolitano et al. 1994, 2008). The ratio of BT to BTCA depends on many factors including the pH of the medium and the presence or absence of metal ions (Di Donato et al. 2002, Napolitano et al. 2000). BT and BTCA are unstable, decaying in seconds. Modifications of the benzothiazine moiety of BT and BTCA lead to the formation of 3-oxo-3,4-dihydro-1,4-benzothiazine (ODHBT) and benzothiazole (BZ) (Napolitano et al. 1999, 2008).

The reactions beyond BT and BTCA which ultimately lead to the production of pheomelanin appear to be very complex (Di Donato & Napolitano 2003). Zn2+ promotes retention of the carboxyl group in BTCA while Fe3+ accelerates the ring contraction of BT to BZ (Di Donato et al. 2002). Production of ODHBT is increased by the presence of hydrogen peroxide (Di Donato et al. 2002).

Literature references

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Editions

2015-01-13	Authored	Jupe, S.
2015-02-10	Edited	Jupe, S.
2015-02-13	Reviewed	Ito, S., d'Ischia, M.