Acyl chain remodeling of CL

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19/02/2020


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


Reactome database release: 71

This document contains 1 pathway and 12 reactions (see Table of Contents)
Acyl chain remodeling of cardiolipin (CL)

Stable identifier: R-HSA-1482798


Literature references


Zachman, DK., Chicco, AJ., McCune, SA., Murphy, RC., Moore, RL., Sparagna, GC. (2010). The role of calcium-independent phospholipase A2 in cardiolipin remodeling in the spontaneously hypertensive heart failure rat heart. *J Lipid Res*, 51, 525-34.


Editions

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CL is hydrolyzed to MLCL by PLA2G6 (IM)

Location: Acyl chain remodeling of CL

Stable identifier: R-HSA-1482778

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: CL is hydrolyzed to MLCL by Pla2g6 (IM) (Rattus norvegicus)

At the inner mitochondrial membrane (IM), calcium-independent phospholipase A2 gamma (PLA2G6) hydrolyzes, removing one of the acyl chains, cardiolipin (CL) to form monolysocardiolipin (MLCL). This reaction is inferred from rats. PLA2G6 has also been characterized in humans (Larsson et al. 1998, Ma et al. 1999, Larsson Forsell et al. 1999).

Preceded by: MLCL and PC are converted to CL and 1-acyl LPC by TAZ (IM) (Reversible), MLCL and PE are converted to CL and 1-acyl LPE by TAZ (IM) (Reversible), MLCL is acylated to CL by HADH (IM), CL transports from the ER to the IM

Followed by: MLCL and PE are converted to CL and 1-acyl LPE by TAZ (IM) (Reversible), MLCL is acylated to CL by HADH (IM), MLCL transports from the IM to the ER, MLCL is hydrolyzed to DLCL by PLA2G4A (IM), MLCL and PC are converted to CL and 1-acyl LPC by TAZ (IM) (Reversible)

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MLCL and PC are converted to CL and 1-acyl LPC by TAZ (IM) (Reversible)

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482781

**Type:** transition

**Compartments:** mitochondrial inner membrane

At the inner mitochondrial membrane (IM), tafazzin (TAZ) converts monolysocardiolipin (MLCL) and phosphatidylcholine (PC) to cardiolipin (CL) and 1-acyl lysophosphatidylcholine (LPC) (Xu et al. 2003, Xu et al. 2006, Malhotra et al. 2009). Although this reaction is reversible, the net effect of the phospholipase A and acyltransferase reactions drives it towards the formation of LPC and CL.

**Preceded by:** CL is hydrolyzed to MLCL by PLA2G6 (IM)

**Followed by:** CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible), CL is hydrolyzed to MLCL by PLA2G6 (IM)

**Literature references**


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CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible)

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482794

**Type:** transition

**Compartments:** mitochondrial inner membrane

At the inner mitochondrial membrane (IM), tafazzin (TAZ) converts cardiolipin (CL) and 1-acyl lysophosphatidylcholine (LPC) to monolysocardiolipin (MLCL) and phosphatidylcholine (PC) (Xu et al. 2003, Xu et al. 2006, Malhotra et al. 2009).

**Preceded by:** MLCL and PC are converted to CL and 1-acyl LPC by TAZ (IM) (Reversible), MLCL and PE are converted to CL and 1-acyl LPE by TAZ (IM) (Reversible), MLCL is acylated to CL by HADH (IM), CL transports from the ER to the IM

**Followed by:** MLCL is acylated to CL by HADH (IM), MLCL transports from the IM to the ER, MLCL is hydrolyzed to DLCL by PLA2G4A (IM)

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MLCL and PE are converted to CL and 1-acyl LPE by TAZ (IM) (Reversible)

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482850

**Type:** transition

**Compartments:** mitochondrial inner membrane

At the inner mitochondrial membrane (IM), tafazzin (TAZ) converts monolysocardiolipin (MLCL) and phosphatidylethanolamine (PE) to cardiolipin (CL) and 1-acyl lysophosphatidylethanolamine (LPE) (Xu et al. 2003, Xu et al. 2006, Malhotra et al. 2009). Although this reaction is reversible, the net effect of the phospholipase A and acyltransferase reactions drives it towards the formation of LPE and CL.

**Preceded by:** CL is hydrolyzed to MLCL by PLA2G6 (IM)

**Followed by:** CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible), CL is hydrolyzed to MLCL by PLA2G6 (IM)

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CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible)

Location: Acyl chain remodeling of CL

Stable identifier: R-HSA-1482894

Type: transition

Compartments: mitochondrial inner membrane

At the inner mitochondrial membrane (IM), tafazzin (TAZ) converts cardiolipin (CL) and 1-acyl lysophosphatidylethanolamine (LPE) to monolysocardiolipin (MLCL) and phosphatidylethanolamine (PE) (Xu et al. 2003, Xu et al. 2006, Malhotra et al. 2009).

Preceded by: MLCL and PC are converted to CL and 1-acyl LPC by TAZ (IM) (Reversible), MLCL and PE are converted to CL and 1-acyl LPE by TAZ (IM) (Reversible), MLCL is acylated to CL by HADH (IM), CL transports from the ER to the IM

Followed by: MLCL is acylated to CL by HADH (IM), MLCL transports from the IM to the ER, MLCL is hydrolyzed to DLCL by PLA2G4A (IM)

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MLCL is acylated to CL by HADH (IM)

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482775

**Type:** transition

**Compartments:** mitochondrial inner membrane, mitochondrial matrix

At the inner mitochondrial membrane (IM), the trifunctional enzyme HADH (3-hydroxyacyl-CoA dehydrogenase), an octamer of four alpha (HADHA) and four beta (HADHB) subunits, acylates monolysocardiolipin (MLCL) to cardiolipin (CL) (Taylor & Hatch 2009).

**Preceded by:** CL is hydrolyzed to MLCL by PLA2G6 (IM), CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible)

**Followed by:** CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible), CL is hydrolyzed to MLCL by PLA2G6 (IM)

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MLCL transports from the IM to the ER

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482773

**Type:** transition

**Compartments:** mitochondrial inner membrane, endoplasmic reticulum membrane

Monolysocardiolipin (MLCL) transports via membrane contact sites between the endoplasmic reticulum (ER) and the inner mitochondria membranes (IM) (Cao et al. 2004, Zhao et al. 2009, Taylor & Hatch 2009).

**Preceded by:** CL is hydrolyzed to MLCL by PLA2G6 (IM), CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible)

**Followed by:** MLCL is acylated to CL by LCLAT1 (ER)

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MLCL is acylated to CL by LCLAT1 (ER)

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482861

**Type:** transition

**Compartments:** endoplasmic reticulum membrane, cytosol

At the endoplasmic reticulum (ER) membrane, lysocardiolipin acyltransferase 1 (LCLAT1) aka ALCAT1 acylates monolysocardiolipin (MLCL) to cardiolipin (CL) (Cao et al. 2004, Zhao et al. 2009).

**Preceded by:** MLCL transports from the IM to the ER, DLCL is acylated to MLCL by LCLAT1 (ER)

**Followed by:** CL transports from the ER to the IM

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CL transports from the ER to the IM

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482857

**Type:** transition

**Compartments:** endoplasmic reticulum membrane, mitochondrial inner membrane


**Preceded by:** MLCL is acylated to CL by LCLAT1 (ER)

**Followed by:** CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible), CL is hydrolyzed to MLCL by PLA2G6 (IM)

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https://www.reactome.org
**MLCL is hydrolyzed to DLCL by PLA2G4A (IM)**

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482759

**Type:** transition

**Compartments:** mitochondrial inner membrane, mitochondrial matrix

At the inner mitochondrial membrane (IM), the phospholipase A2 group IV alpha (PLA2G4A) protein hydrolyzes monolysocardiolipin (MLCL) and produces dilysocardiolipin (DLCL) (Buckland et al. 1998, Sharp et al. 1994).

**Preceded by:** CL is hydrolyzed to MLCL by PLA2G6 (IM), CL and 1-acyl LPC are converted to MLCL and PC by TAZ (IM) (Reversible), CL and 1-acyl LPE are converted to MLCL and PE by TAZ (IM) (Reversible)

**Followed by:** DLCL transports from the IM to the ER

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DLCL transports from the IM to the ER

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482860

**Type:** transition

**Compartments:** mitochondrial inner membrane, endoplasmic reticulum membrane

Dilysocardiolipin (DLCL) transports via membrane contact sites between the endoplasmic reticulum (ER) and the inner mitochondria membranes (IM) (Zhao et al. 2009, Buckland et al. 1998).

**Preceded by:** MLCL is hydrolyzed to DLCL by PLA2G4A (IM)

**Followed by:** DLCL is acylated to MLCL by LCLAT1 (ER)

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DLCL is acylated to MLCL by LCLAT1 (ER)

**Location:** Acyl chain remodeling of CL

**Stable identifier:** R-HSA-1482867

**Type:** transition

**Compartments:** endoplasmic reticulum membrane, cytosol

At the endoplasmic reticulum (ER) membrane, lysocardiolipin acyltransferase 1 (LCLAT1) aka ALCAT1 acylates dilyso cardiolipin (DLCL) to produce monolysocardiolipin (MLCL) (Zhao et al. 2009).

**Preceded by:** DLCL transports from the IM to the ER

**Followed by:** MLCL is acylated to CL by LCLAT1 (ER)

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   - MLCL and PC are converted to CL and 1-acyl LPC by TAZ (IM) (Reversible)
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