Defective ABCC9 causes dilated cardiomyopathy 10, familial atrial fibrillation 12 and hypertrichotic osteochondrodysplasia

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10/05/2020
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: 72

This document contains 1 pathway and 1 reaction (see Table of Contents)

https://release.reactome.org
Defective ABCC9 causes dilated cardiomyopathy 10, familial atrial fibrillation 12 and hypertrichotic osteochondrodysplasia

Stable identifier: R-HSA-5678420

Diseases: osteochondrodysplasia, dilated cardiomyopathy, familial atrial fibrillation, hypertrichosis

ATP-binding cassette sub-family C member 9 (ABCC9) forms cardiac and smooth muscle-type KATP channels with ATP-sensitive inward rectifier potassium channel 11 (KCNJ11). KCNJ11 forms the channel pore while ABCC9 is required for activation and regulation (Babenko et al. 1998, Tammaro & Ashcroft 2007). Inward rectifier potassium channels favor the flow of potassium into the cell rather than out of it. KATP channels open and close in response to intracellular changes in the ADP/ATP ratio, thereby linking the metabolic state of the cell to its membrane potential. Inhibition of KATP channel activity causes membrane depolarization and thereby activation of voltage-dependent Ca2+ channels, leading to Ca2+ influx and a rise in intracellular Ca2+ concentration. Correct maintenance of calcium balance is essential for the normal functioning of the heart.

Defects in ABCC9 can cause dilated cardiomyopathy 10 (CMD10: MIM:608569), a disorder characterised by ventricular dilation and impaired systolic function, resulting in congestive heart failure and arrhythmia (Bienengraeber et al. 2004). Defects in ABCC9 can also cause familial atrial fibrillation 12 (ATFB12; MIM:614050), characterised by disorganized atrial electrical activity and ineffective atrial contraction resulting in blood stasis in the atria and reduces ventricular filling. It can result in palpitations, syncope, thromboembolic stroke, and congestive heart failure (Olson et al. 2007). Defects in ABCC9 can also cause hypertrichotic osteochondrodysplasia (Cantu syndrome; MIM:239850), a rare disorder characterised by congenital hypertrichosis, neonatal macrosomia, a distinct osteochondrodysplasia and cardiomegaly (van Bon et al. 2012, Harakalova et al. 2012).

Literature references


**Editions**

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<td>Authored, Edited</td>
<td>Jassal, B.</td>
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<td>2015-04-28</td>
<td>Reviewed</td>
<td>Moitra, K.</td>
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Defective ABCC9 (in KCNJ11:ABCC9) does not transport K+ from extracellular region to cytosol

Location: Defective ABCC9 causes dilated cardiomyopathy 10, familial atrial fibrillation 12 and hypertrichotic osteochondrodysplasia

Stable identifier: R-HSA-5678418