Loss of function of MECP2 in Rett syndrome

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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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Literature references


Reactome database release: 79

This document contains 5 pathways (see Table of Contents)

https://reactome.org
Loss of function mutations in methyl-CpG-binding protein 2 (MECP2), an epigenetic regulator of transcription, are the major cause of Rett syndrome, a neurodevelopmental disorder that affects 1 in 10,000-15,000 female births. The symptoms of Rett syndrome appear after 6-18 months of apparently normal postnatal development and include regression of acquired language and motor skills, stereotypic hand movements, intellectual disability, epileptic seizures and respiratory disturbances. Besides Rett syndrome, aberrant MECP2 expression is implicated as an underlying cause of other neuropsychiatric disorders (reviewed by Banerjee et al. 2012, Ebert and Greenberg 2013, Lyst and Bird 2015). Only functionally characterized MECP2 mutations are annotated. For a comprehensive list of MECP2 mutations reported in Rett syndrome, please refer to the RettBASE (http://mecp2.chw.edu.au), a database dedicated to curation of disease variants of MECP2, CDKL5 and FOXG1 in Rett syndrome (Krishnaraj et al. 2017).

**Literature references**


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Editions
Loss of MECP2 binding ability to the NCoR/SMRT complex

Location: Loss of function of MECP2 in Rett syndrome

Stable identifier: R-HSA-9022537

Compartments: nucleoplasm

Diseases: Rett syndrome

Missense mutations in the transcriptional repression domain of methyl-CpG-binding protein 2 (MECP2) can negatively affect binding of MECP2 to the nuclear receptor co-repressor (NCoR/SMRT) complex (Lyst et al. 2013, Ebert et al. 2013).

Literature references


Editions

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Loss of phosphorylation of MECP2 at T308

Location: Loss of function of MECP2 in Rett syndrome

Stable identifier: R-HSA-9022535

Compartments: nucleoplasm

Diseases: Rett syndrome

Missense mutations of methyl-CpG-binding protein 2 (MECP2) in the vicinity of its threonine T308 phosphorylation site can negatively affect the ability of MECP2 to be phosphorylated at T308 in response to neuronal membrane depolarization (neuronal activity) (Ebert et al. 2013).

Literature references

Loss of MECP2 binding ability to 5hmC-DNA

Location: Loss of function of MECP2 in Rett syndrome

Stable identifier: R-HSA-9022534

Compartments: nucleoplasm

Diseases: Rett syndrome

Missense mutations in the methyl-CpG binding domain (MBD) of MECP2, spanning amino acids 90 to 162, negatively affect the binding ability of MECP2 to hydroxymethylated DNA (Mellen et al. 2012).

Literature references


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Loss of MECP2 binding ability to 5mC-DNA

Location: Loss of function of MECP2 in Rett syndrome

Stable identifier: R-HSA-9022538

Compartments: nucleoplasm

Diseases: Rett syndrome

Missense mutations in the methyl-CpG binding domain (MBD) of methyl-CpG-binding protein 2 (MECP2), spanning amino acids 90 to 162, negatively affect the binding ability of MECP2 to methylated DNA (Ghosh et al. 2008, Ho et al. 2008, Goffin et al. 2012, Mellen et al. 2012).

Literature references


Editions

2017-10-03 Authored Orlic-Milacic, M.
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2018-08-08 Edited Orlic-Milacic, M.
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