MET channel transports cations from the extracellular region into the cytosol of stereocilia of cochlear outer hair cell

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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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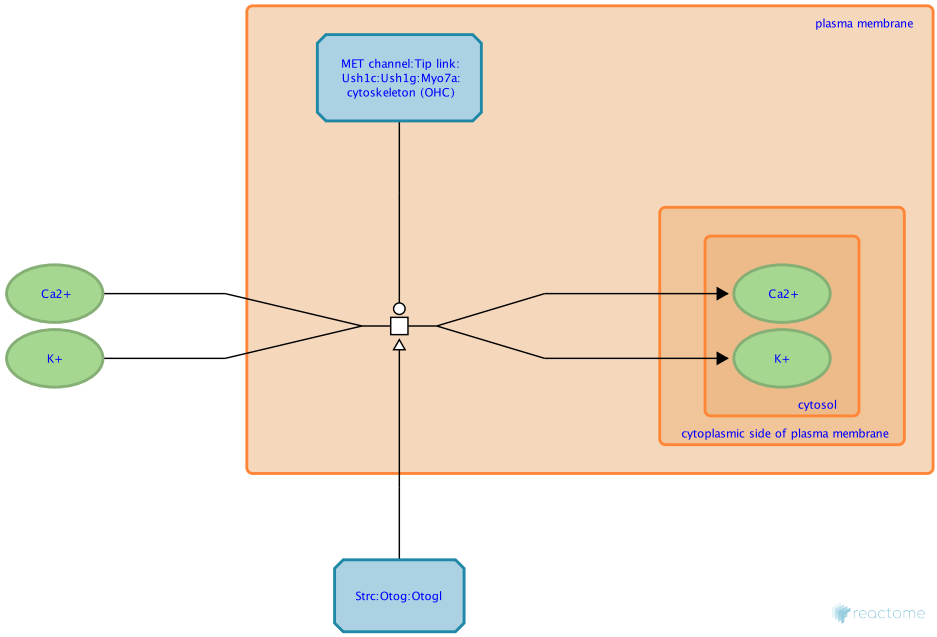
Stable identifier: R-MMU-9663360

Type: transition

Compartments: plasma membrane



The mechanoelectrical transduction (MET) channels (also called mechanotransducer channels) located at the tips of stereocilia on the apical surface of outer hair cells (OHCs) are opened by mechanical force exerted on the channels by Cdh23:Pcdh15 tip links that traverse the tips of stereocilia (Siemens et al. 2004, Ahmed et al. 2006, Kazmierczak et al. 2007, Narui and Sotomayor 2018, Oroz et al. 2019). A Cdh23 dimer is connected to the cytoskeleton of a taller stereocilium via Ush1c (Harmonin), Ush1g (SANS), and Myo7a (MyoVIIa) (Boeda et al. 2002, Adato et al. 2005, Bahloul et al. 2010, Grati and Kachar 2011, Bahloul et al. 2017). By a calcium-dependent interaction, a Cdh23 dimer on a taller stereocilium is bound to a Pcdh15 dimer (Elledge et al. 2010, Schwander et al. 2009, Sotomayor et al. 2010) that is connected to a MET channel on a shorter stereocilium. The MET channel comprises at least Tmc1 and Tmc2 (Kawashima et al. 2011, Pan et al. 2013, Beurg et al. 2015, Kurima et al. 2015, Corns et al. 2016, Beurg et al. 2018, Pan et al. 2018, Beurg et al. 2019, Goldring et al. 2019), Tmie (Zhao et al. 2014), and the auxiliary subunits Cib2 (Michel et al. 2017, Wang et al. 2017) and Lhfpl5 (also called Tmhs), which interacts with Pcdh15 (Xiong et al. 2012, Geng et al. 2013, Beurg et al. 2015, Ge et al. 2018). In mice, Tmc2 expression is highest during the first week after birth and decreases in adulthood; Tmc1 expression is low in the first week after birth and increases in adulthood (Kawashima et al. 2011, Kurima et al. 2015). The MET channel may also contain additional, unidentified proteins (Beurg et al. 2014).

Deflection of the stereocilia by sound causes increased tension on Cdh23:Pcdh15, resulting in an increased probability of the open state of the MET channel (Beurg et al. 2006, Pan et al. 2013, Beurg et al. 2018, Pan et al. 2018). The MET channel is relatively non-specific for cations (inferred from rat homologs) and allows calcium ions (Kim and Fettiplace 2013, Pan et al. 2013, Beurg et al. 2015, Corns et al. 2016, Corns et al. 2017) and potassium ions to pass from the extracellular scala media to the cytosol of the OHC. Depolarization of the OHC results in shortening of the OHC due to a change in conformation of Slc26a5 (prestin) located in the membrane of the OHC. The composition of the cytoskeleton of OHCs differs from that of inner hair cells (IHCs): MPP1 (Mburu et al. 2006) and GSN (Mbruru et al. 2010, Olt et al. 2014) are

present in OHCs but absent from IHCs.

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