Organelle biogenesis and maintenance

Goncalves, J., Jassal, B., Lezza, AM., Lorentzen, E., Matthews, L., May, B., Rothfels, K.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

18/11/2022

https://reactome.org
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: 82

This document contains 3 pathways (see Table of Contents)
This module describes the biogenesis of organelles. Organelles are subcellular structures of distinctive morphology and function. The organelles of human cells include: mitochondria, endoplasmic reticulum, Golgi apparatus, vacuoles, nucleus, (auto)phagosome, centriole, lysosome, melanosome, myofibril, nucleolus, peroxisome, cilia (in some cell types), proteasome, ribosome, and transport vesicles.

**Literature references**


**Editions**

2011-10-28

Authored, Edited, Reviewed

Matthews, L.
Mitochondrial biogenesis and remodeling occur in response to exercise and redox state (reviewed in Scarpulla et al. 2012, Handy and Loscalzo 2012, Plantadosi and Suliman 2012, Scarpulla 2011, Wenz et al. 2011, Bo et al. 2010, Jornayvaz and Shulman 2010, Ljubicic et al. 2010, Hock and Kralli 2009, Canto and Auwerx 2009, Lin 2009, Scarpulla 2008, Ventura-Clapier et al. 2008). It is hypothesized that calcium influx and energy depletion are the signals that initiate changes in gene expression leading to new mitochondrial proteins. Energy depletion causes a reduction in ATP and an increase in AMP which activates AMPK. AMPK in turn phosphorylates the coactivator PGC-1alpha (PPARGC1A), one of the master regulators of mitochondrial biosynthesis. Likewise, p38 MAPK is activated by muscle contraction (possibly via calcium and CaMKII) and phosphorylates PGC-1alpha. CaMKIV responds to intracellular calcium by phosphorylating CREB, which activates expression of PGC-1alpha.

Deacetylation of PGC-1alpha by SIRT1 may also play a role in activation (Canto et al. 2009, Gurd et al. 2011), however Sirt11 deacetylation of Ppargc1a in mouse impacted genes related to glucose metabolism rather than mitochondrial biogenesis (Rodgers et al. 2005) and mice lacking SIRT1 in muscle had normal levels of mitochondrial biogenesis in response to exercise (Philp et al. 2011) so the role of deacetylation is not fully defined. PGC-1beta and PPRC appear to act similarly to PGC-1alpha but they have not been as well studied.

Phosphorylated PGC-1alpha does not bind DNA directly but instead interacts with other transcription factors, notably NRF1 and NRF2 (via HCF1). NRF1 and NRF2 together with PGC-1alpha activate the transcription of nuclear-encoded, mitochondrially targeted proteins such as TFB2M, TFB1M, and TFAM.
Literature references


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011-08-20</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2013-12-07</td>
<td>Reviewed</td>
<td>Lezza, AM.</td>
</tr>
</tbody>
</table>

https://reactome.org
Cilia are membrane-covered organelles that extend from the surface of eukaryotic cells. Cilia may be motile, such as respiratory cilia, or non-motile (such as the primary cilium) and are distinguished by the structure of their microtubule-based axonemes. The axoneme consists of nine peripheral doublet microtubules, and in the case of many motile cilia, may also contain a pair of central single microtubules. These are referred to as 9+0 or 9+2 axonemes, respectively. Relative to their non-motile counterparts, motile cilia also contain additional structures that contribute to motion, including inner and outer dynein arms, radial spokes, and nexin links. Four main types of cilia have been identified in humans: 9+2 motile (such as respiratory cilia), 9+0 motile (nodal cilia), 9+2 non-motile (kinocilium of hair cells) and 9+0 non-motile (primary cilium and photoreceptor cells) (reviewed in Fliegauf et al., 2007).

This pathway describes cilia formation, with an emphasis on the primary cilium. The primary cilium is a sensory organelle that is required for the transduction of numerous external signals such as growth factors, hormones, and morphogens, and an intact primary cilium is needed for signaling pathways mediated by Hh, WNT, calcium, G-protein coupled receptors and receptor tyrosine kinases, among others (reviewed in Goetz and Anderson, 2010; Berbari et al., 2009; Nachury, 2014). Unlike the motile cilia, which are generally present in large numbers on epithelial cells and are responsible for sensory function as well as wave-like beating motions, the primary cilium is a non-motile sensory organelle that is present in a single copy at the apical surface of most quiescent cells (reviewed in Hsiao et al., 2012).

Cilium biogenesis involves the anchoring of the basal body, a centriole-derived organelle, near the plasma membrane and the subsequent polymerization of the microtubule-based axoneme and extension of the plasma membrane (reviewed in Ishikawa and Marshall, 2011; Reiter et al., 2012). Although the ciliary membrane is continuous with the plasma membrane, the protein and lipid content of the cilium and the ciliary membrane are distinct from those of the bulk cytoplasm and plasma membrane (reviewed in Emmer et al., 2010; Rohatgi and Snell, 2010). This specialized compartment is established and maintained during cilium biogenesis by the formation of a ciliary transition zone, a proteinaceous structure that, with the transition fibres, anchors the basal body to the plasma membrane and acts as a ciliary pore to limit free diffusion from the cytosol to the cilium (reviewed in Nachury et al., 2010; Reiter et al., 2012). Ciliary components are targeted from the secretory system to the ciliary base and subsequently transported to the ciliary tip, where extension of the axoneme occurs, by a motor-driven process called intraflagellar transport (IFT). Anterograde transport of cargo from the ciliary base to the tip of the cilium requires kin-
esin-2 type motors, while the dynein-2 motor is required for retrograde transport back to the ciliary base. In addition, both anterograde and retrograde transport depend on the IFT complex, a multiprotein assembly consisting of two subcomplexes, IFT A and IFT B. The primary cilium is a dynamic structure that undergoes continuous steady-state turnover of tubulin at the tip; as a consequence, the IFT machinery is required for cilium maintenance as well as biogenesis (reviewed in Bhogaraju et al, 2013; Hsiao et al, 2012; Li et al, 2012; Taschner et al, 2012; Sung and Leroux, 2013).

The importance of the cilium in signaling and cell biology is highlighted by the wide range of defects and disorders, collectively known as ciliopathies, that arise as the result of mutations in genes encoding components of the ciliary machinery (reviewed in Goetz and Anderson, 2010; Madhivanan and Aguilar, 2014).

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014-08-07</td>
<td>Authored</td>
<td>Rothfels, K.</td>
</tr>
<tr>
<td>2014-10-13</td>
<td>Edited</td>
<td>Jassal, B.</td>
</tr>
<tr>
<td>2014-11-10</td>
<td>Reviewed</td>
<td>Lorentzen, E.</td>
</tr>
<tr>
<td>2014-11-14</td>
<td>Reviewed</td>
<td>Goncalves, J.</td>
</tr>
</tbody>
</table>

https://reactome.org
## Table of Contents

Introduction 1

- Organelle biogenesis and maintenance 2
  - Mitochondrial biogenesis 3
  - Cilium Assembly 5

Table of Contents 7