Neuronal System

Garapati, P V., Gillespie, ME., Jassal, B., Joshi-Tope, G., Kavalali, E., Mahajan, SS., Restituito, S., Rush, MG., Washbourne, P., Wen, H.

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.

02/03/2022
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: 79

This document contains 5 pathways (see Table of Contents)
Neuronal System

Stable identifier: R-HSA-112316

The human brain contains at least 100 billion neurons, each with the ability to influence many other cells. Clearly, highly sophisticated and efficient mechanisms are needed to enable communication among this astronomical number of elements. This communication occurs across synapses, the functional connection between neurons. Synapses can be divided into two general classes: electrical synapses and chemical synapses. Electrical synapses permit direct, passive flow of electrical current from one neuron to another. The current flows through gap junctions, specialized membrane channels that connect the two cells. Chemical synapses enable cell-to-cell communication using neurotransmitter release. Neurotransmitters are chemical agents released by presynaptic neurons that trigger a secondary current flow in postsynaptic neurons by activating specific receptor molecules. Neurotransmitter secretion is triggered by the influx of Ca2+ through voltage-gated channels, which gives rise to a transient increase in Ca2+ concentration within the presynaptic terminal. The rise in Ca2+ concentration causes synaptic vesicles (the presynaptic organelles that store neurotransmitters) to fuse with the presynaptic plasma membrane and release their contents into the space between the pre- and postsynaptic cells.

Literature references


Editions

2005-11-10 Authored, Edited Gillespie, ME.
Transmission across Electrical Synapses

**Location:** Neuronal System

**Stable identifier:** R-HSA-112307

Electrical transmission across nerve cells is accomplished when the current generated in the upstream neuron spreads to the downstream neuron through a path of low electrical resistance. In neurons this is accomplished at gap junctions. Electrical synapses are found in neuronal tissue where the activity of neurons must be highly synchronized. The neurons responsible for hormone secretion from the mammalian hypothalamus are a class of highly synchronized electric neurons. Gap junctions connecting the presynaptic cell with the postsynaptic cell allow current generated in the presynaptic cell to flow directly into the postsynaptic cell. Transmission speed is dramatically increased in such a system. The junction itself is composed of two hemichannels, one each on the pre- and postsynaptic cells. These channels are composed of members of the connexin family of proteins.

**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004-04-22</td>
<td>Authored</td>
<td>Joshi-Tope, G.</td>
</tr>
<tr>
<td>2008-01-11</td>
<td>Reviewed</td>
<td>Rush, MG.</td>
</tr>
<tr>
<td>2008-01-14</td>
<td>Edited</td>
<td>Mahajan, SS.</td>
</tr>
</tbody>
</table>
Transmission across Chemical Synapses

Location: Neuronal System

Stable identifier: R-HSA-112315

Chemical synapses are specialized junctions that are used for communication between neurons, neurons and muscle or gland cells. The synapse involves a presynaptic neuron and a postsynaptic neuron, muscle cell or glad cell. The pre and the postsynaptic cell are separated by a gap (space) of 20 to 40 nm called the synaptic cleft. The signals pass in a single direction from the presynaptic to postsynaptic neuron (cell). The presynaptic neuron communicates via the release of neurotransmitter which bind the receptors on the postsynaptic cell. The process is initiated when an action potential invades the terminal membrane of the presynaptic neuron.

Action potentials occur in electrically excitable cells such as neurons and muscles and endocrine cells. They are initiated by the transient opening of voltage dependent sodium channels, causing a rapid, large depolarization of membrane potentials that spread along the axon membrane.

When action potentials arrive at the synaptic terminals, depolarization in membrane potential leads to the opening of voltage gated calcium channels located on the presynaptic membrane. The external Ca2+ concentration is approximately 10-3 M while the internal Ca2+ concentration is approximately 10-7 M. Opening of calcium channels causes a rapid influx of Ca2+ into the presynaptic terminal. The elevated presynaptic Ca2+ concentration allows synaptic vesicles to fuse with the plasma membrane of the presynaptic neuron and release their contents, neurotransmitters, into the synaptic cleft. These diffuse across the synaptic cleft and bind to specific receptors on the membrane of the postsynaptic cells. Activation of postsynaptic receptors upon neurotransmitter binding can lead to a multitude of effects in the postsynaptic cell, such as changing the membrane potential and excitability, and triggering intracellular signaling cascades.

Literature references

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author/Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008-01-14</td>
<td>Authored, Edited</td>
<td>Mahajan, SS.</td>
</tr>
<tr>
<td>2008-12-02</td>
<td>Reviewed</td>
<td>Kavalali, E., Restituito, S.</td>
</tr>
<tr>
<td>2020-01-24</td>
<td>Reviewed</td>
<td>Wen, H.</td>
</tr>
</tbody>
</table>
Potassium channels are tetrameric ion channels that are widely distributed and are found in all cell types. Potassium channels control resting membrane potential in neurons, contribute to regulation of action potentials in cardiac muscle and help release of insulin from pancreatic beta cells.

Broadly K+ channels are classified into voltage gated K+ channels, Hyperpolarization activated cyclic nucleotide gated K+ channels (HCN), Tandem pore domain K+ channels, Ca2+ activated K+ channels and inwardly rectifying K+ channels.

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010-09-23</td>
<td>Reviewed</td>
<td>Jassal, B.</td>
</tr>
<tr>
<td>2011-05-19</td>
<td>Authored</td>
<td>Mahajan, SS.</td>
</tr>
<tr>
<td>2011-05-23</td>
<td>Edited</td>
<td>Mahajan, SS.</td>
</tr>
</tbody>
</table>

https://reactome.org
Protein-protein interactions at synapses

Location: Neuronal System

Stable identifier: R-HSA-6794362

Compartments: plasma membrane, cytosol

Synapses constitute highly specialized sites of asymmetric cell-cell adhesion and intercellular communication. Its formation involves the recruitment of presynaptic and postsynaptic molecules at newly formed contacts. Synapse assembly and maintenance invokes heterophilic presynaptic and postsynaptic transmembrane proteins that bind each other in the extracellular space and recruit additional proteins via their intracellular domains. Members of the cadherin and immunoglobulin (Ig) superfamilies are thought to mediate this function. Several molecules, including synaptic cell-adhesion molecule (SynCAM), N-cadherin, neural cell-adhesion molecule (NCAM), Eph receptor tyrosine kinases, and neuroligins and neurexins, have been implicated in synapse formation and maintenance (Dean & Dresbach 2006, Craig et al. 2006, Craig & Kang 2007, Sudhof 2008).

Literature references


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Activity</th>
<th>Author(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015-09-04</td>
<td>Authored, Edited</td>
<td>Garapati, P.V.</td>
</tr>
<tr>
<td>2015-11-09</td>
<td>Reviewed</td>
<td>Washbourne, P.</td>
</tr>
</tbody>
</table>
# Table of Contents

- Introduction  
- Neuronal System  
  - Transmission across Electrical Synapses  
  - Transmission across Chemical Synapses  
  - Potassium Channels  
  - Protein-protein interactions at synapses

Table of Contents