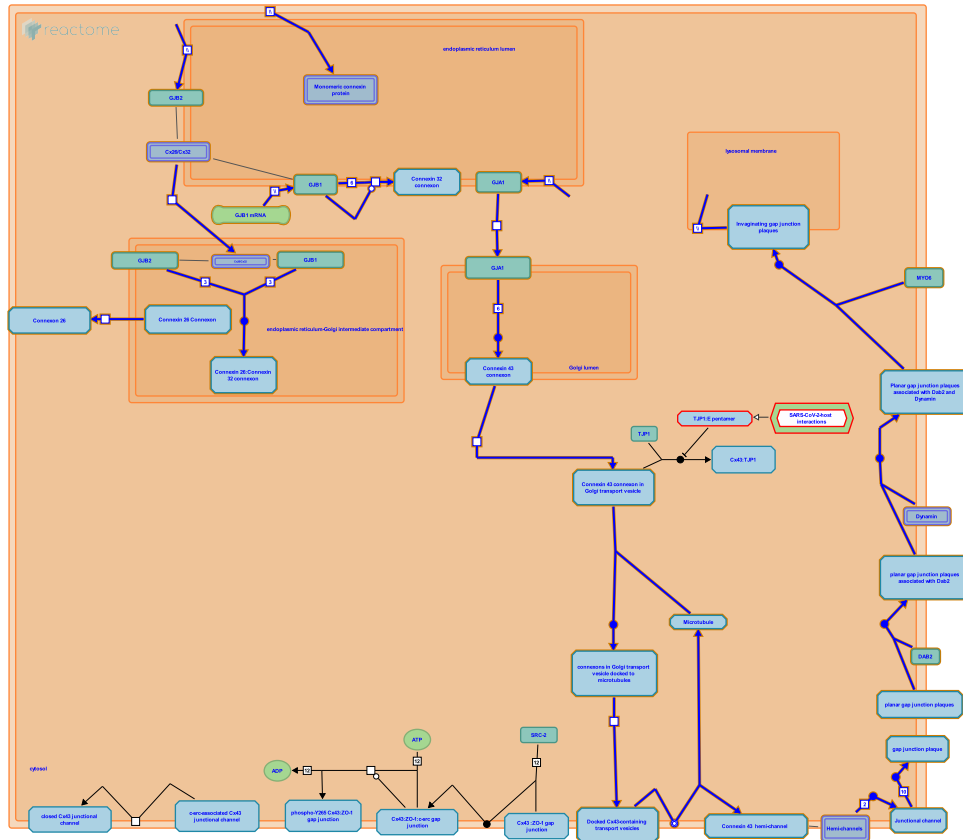


# Gap junction trafficking



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

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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](https://reactome.org/textbook/).

27/04/2024

## 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

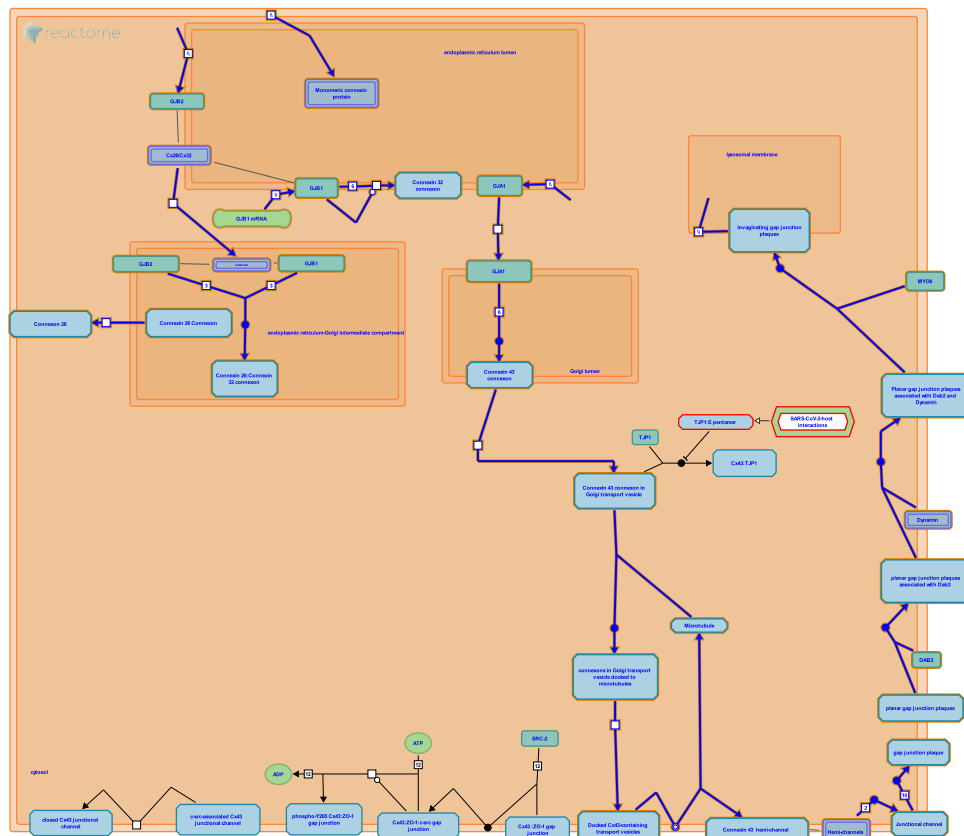
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- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
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Reactome database release: 88

This document contains 3 pathways ([see Table of Contents](#))

# Gap junction trafficking ↗

Stable identifier: R-HSA-190828



Gap junctions are intercellular communication channels formed from Cx (connexin) protein subunits (see Segretain and Falk 2004 and Evans et al. 2006 for comprehensive reviews). Connexins are transported to the plasma membrane after oligomerizing into hexameric assemblies called hemichannels (CxHcs) or connexons. Connexons dock head-to-head in the extracellular space with opposing hexameric channels located in the plasma membranes of neighbouring cells. The double membrane channel or gap junction generated directly links the cytoplasm of interacting cells and facilitates the integration and co-ordination of cellular signalling, metabolism, secretion and contraction. In addition to their role in intercellular communication, connexon hemichannels coordinate the release of ATP, glutamate, NAD<sup>+</sup> and prostaglandin E2 from the cells. CxHcs open in response to various types of external changes, including mechanical, shear, ionic and ischaemic stress.

The trafficking of gap junctions involves (1) synthesis of connexin polypeptides at endoplasmic reticulum membranes, (2) oligomerization into homomeric- and heteromeric gap junction connexons (hemi-channels), (3) passage through the Golgi stacks, (4) intracellular storage within Trans Golgi membranes, (5) trafficking along microtubules, (6) insertion of connexons into the plasma membrane, (7) lateral diffusion of connexons in the plasma membrane, (8) aggregation of individual gap junction channels into plaques, (9) stabilization of peripheral microtubule plus-ends by binding to Cx43-based gap junctions, (10) internalization of the channel plaque leading to cytoplasmic annular junctions, and (11) complete degradation via lysosomal and proteasomal pathways (see Segretain and Falk 2004). Aspects of gap assembly are described here.

## Literature references

Segretain, D., Falk, MM. (2004). Regulation of connexin biosynthesis, assembly, gap junction formation, and removal. *Biochim Biophys Acta*, 1662, 3-21. ↗

Kasprzak, L., Laird, DW., Castillo, M. (1995). Gap junction turnover, intracellular trafficking, and phosphorylation of connexin43 in brefeldin A-treated rat mammary tumor cells. *J Cell Biol*, 131, 1193-203. ↗

## Editions

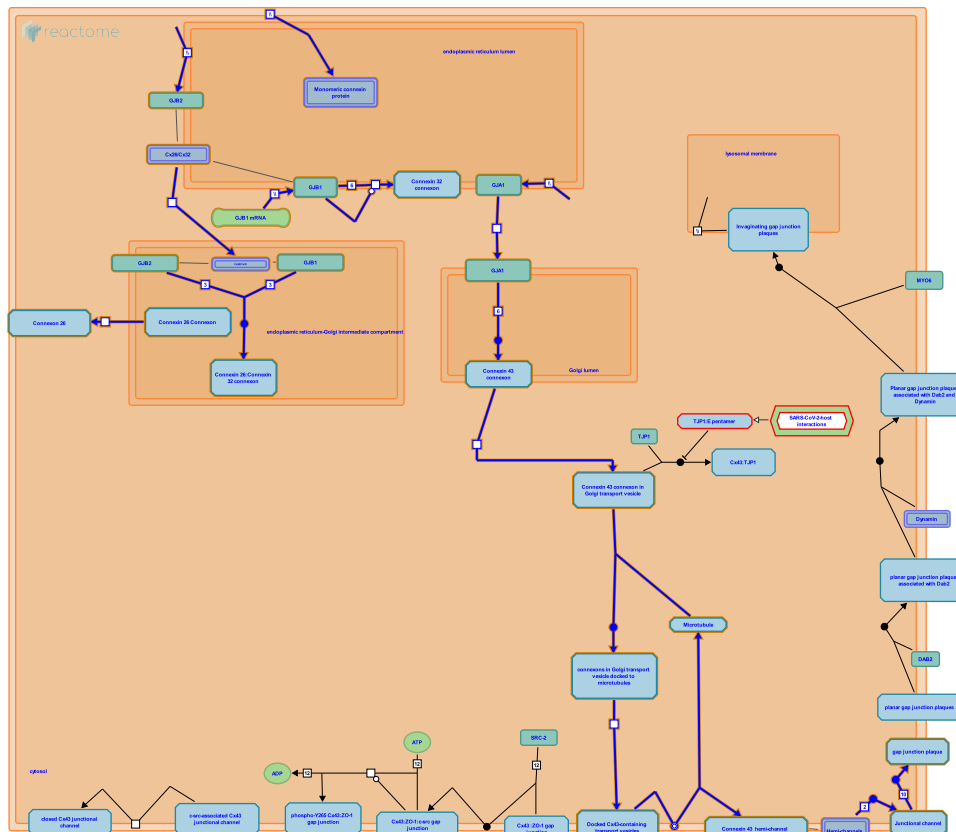
2007-01-03	Authored	Gilleron, J., Segretain, D., Falk, MM.
2007-01-07	Edited	Matthews, L.

# Gap junction assembly ↗

**Location:** Gap junction trafficking

**Stable identifier:** R-HSA-190861

**Compartments:** cytosol



The assembly of gap junctions involves (1) synthesis of connexin polypeptides at endoplasmic reticulum membranes, (2) oligomerization into homomeric- and heteromeric gap junction connexons (hemi-channels), (3) passage through the Golgi stacks, (4) intracellular storage within Trans Golgi membranes, (5) trafficking along microtubules, (6) insertion of connexons into the plasma membrane, (7) lateral diffusion of connexons in the plasma membrane, (8) aggregation of individual gap junction channels into plaques, and (9) stabilization of peripheral microtubule plus-ends by binding to Cx43-based gap junctions (see Segretain and Falk, 2004.)

## Literature references

Segretain, D., Falk, MM. (2004). Regulation of connexin biosynthesis, assembly, gap junction formation, and removal. *Biochim Biophys Acta*, 1662, 3-21. ↗

Bruzzone, R., White, TW., Paul, DL. (1996). Connections with connexins: the molecular basis of direct intercellular signaling. *Eur J Biochem*, 238, 1-27. ↗

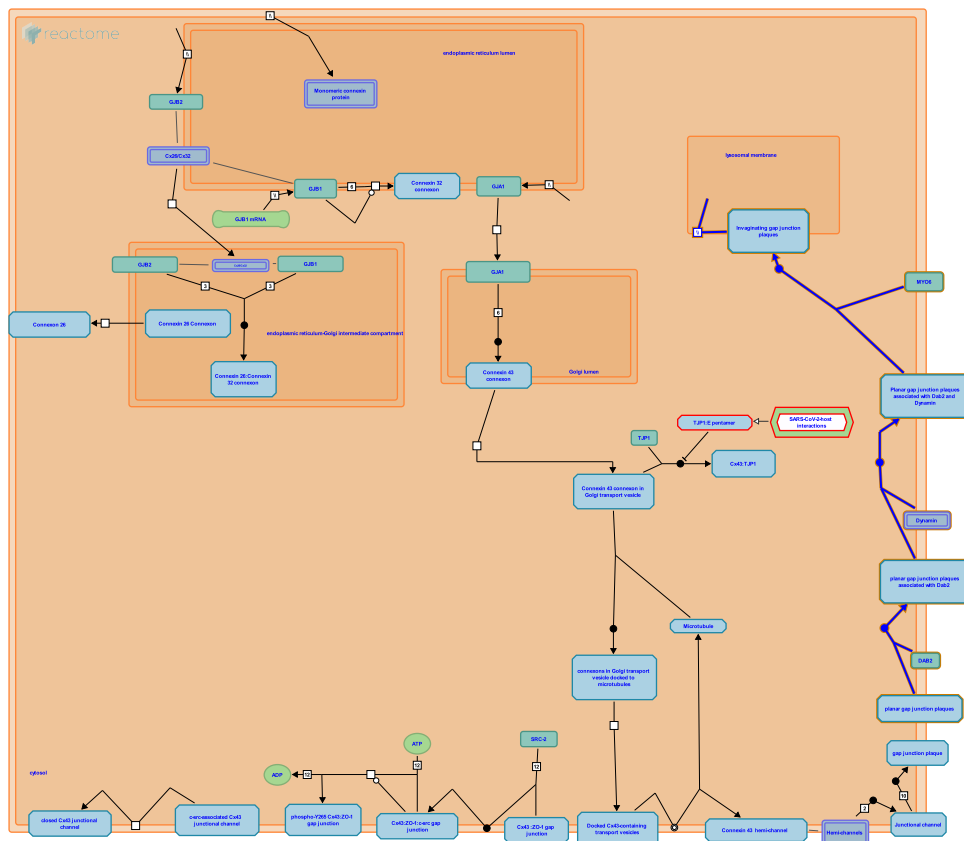
## Editions

2004-04-22	Edited	Joshi-Tope, G.
2007-01-03	Authored	Gilleron, J., Segretain, D., Falk, MM.
2007-01-26	Edited	Matthews, L.

# Gap junction degradation ↗

**Location:** Gap junction trafficking

**Stable identifier:** R-HSA-190873



The half-life of Cx is very short (1 to 5h) compared to other junctional proteins (Laird et al., 1995 ; Fallon and Goudenough, 1981). Connexins are targeted for degradation by the proteasome and the lysosome. Degradation appears to involve the phosphorylation of Connexins as well as their interactions with other proteins (Piehl et al., 2007).

## Literature references

Gumpert, A., Segretain, D., Falk, MM., Piehl, M., Denizot, JP., Lehmann, C. (2007). Internalization of Large Double-Membrane Intercellular Vesicles by a Clathrin-dependent Endocytic Process. *Mol Biol Cell.* ↗

Kasprzak, L., Laird, DW., Castillo, M. (1995). Gap junction turnover, intracellular trafficking, and phosphorylation of connexin43 in brefeldin A-treated rat mammary tumor cells. *J Cell Biol, 131*, 1193-203. ↗

## Editions

2007-01-03	Authored	Gilleron, J., Segretain, D., Falk, MM.
2007-03-27	Edited	Matthews, L.

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