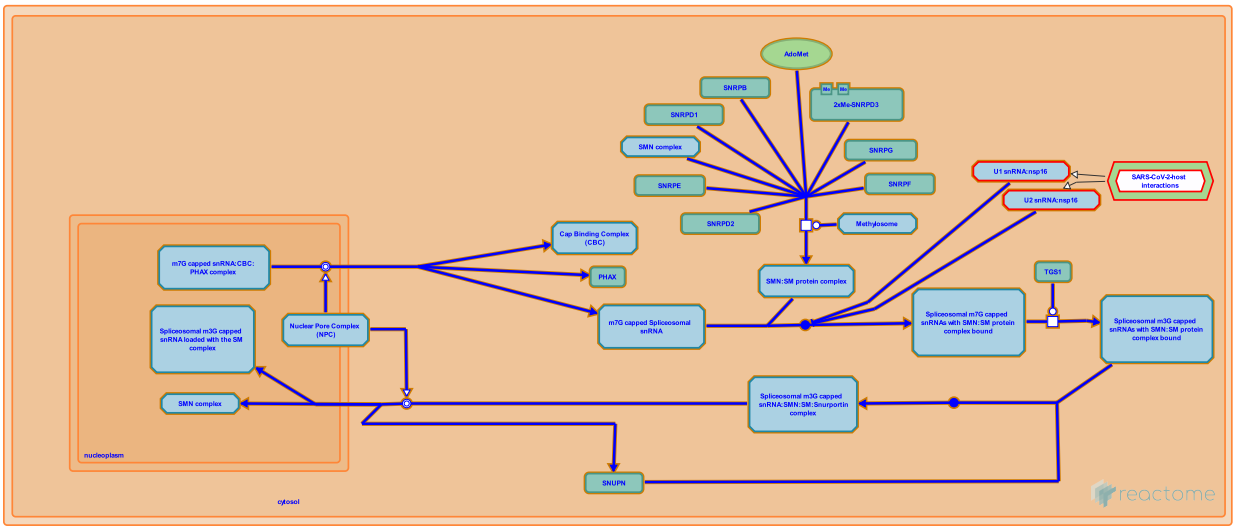
snRNP Assembly



Gillespie, ME., Luhrmann, R., Messina, F.

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

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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.
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

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

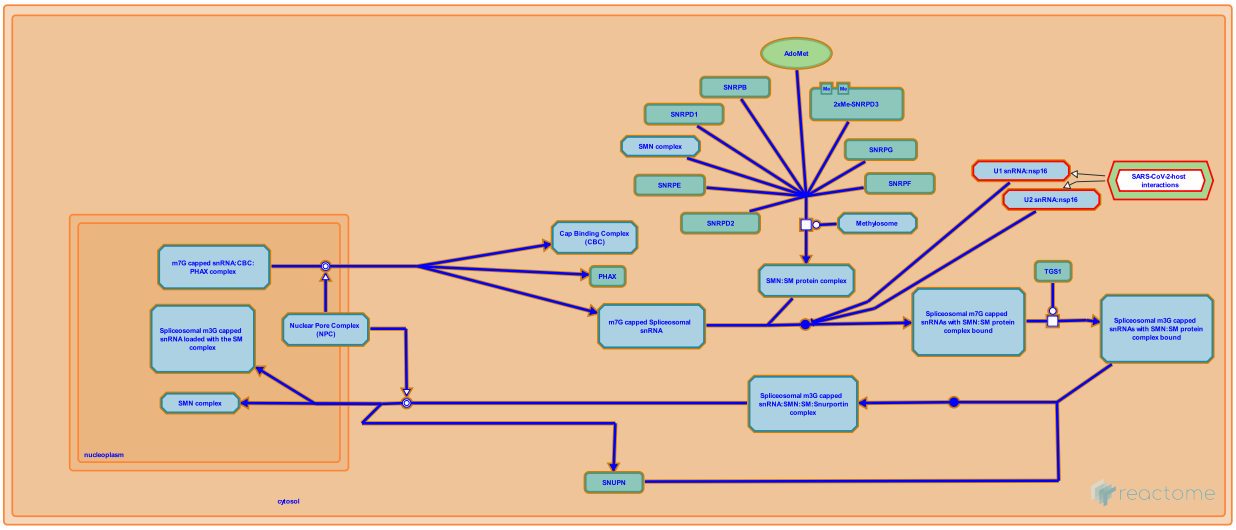
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

snRNP Assembly ↗

Stable identifier: R-HSA-191859



Small nuclear ribonucleoproteins (snRNPs) are crucial for pre-mRNA processing to mRNAs. Each snRNP contains a small nuclear RNA (snRNA) and an extremely stable core of seven Sm proteins. The U6 snRNA differs from the other snRNAs; it binds seven Sm-like proteins and its assembly does not involve a cytoplasmic phase. The snRNP biogenesis pathway for all of the other snRNAs is complex, involving nuclear export of snRNA, Sm-core assembly in the cytoplasm and re-import of the mature snRNP. The assembly of the snRNA:Sm-core is carried out by the survival of motor neurons (SMN) complex. The SMN complex stringently scrutinizes RNAs for specific features that define them as snRNAs and binds the RNA-binding Sm proteins.

Literature references

Wan, L., Dreyfuss, G., Yong, J. (2004). Why do cells need an assembly machine for RNA-protein complexes?. *Trends Cell Biol, 14*, 226-32. ↗

Editions

2007-01-30	Authored	Gillespie, ME.
2007-04-30	Reviewed	Luhrmann, R.

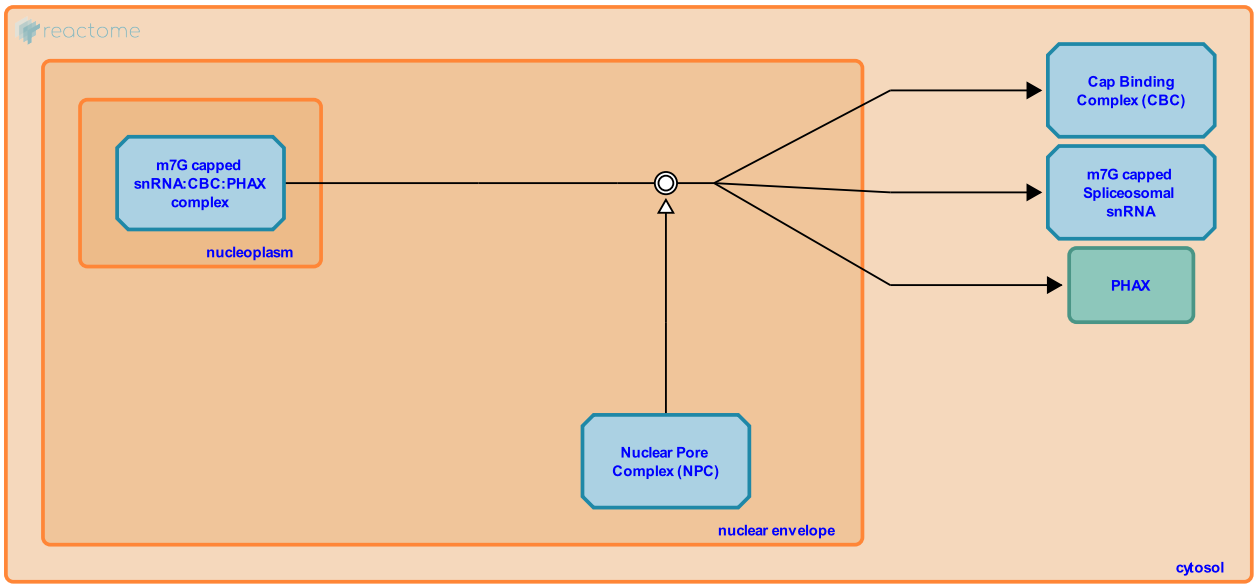
Nuclear export of snRNA transcripts ↗

Location: snRNP Assembly

Stable identifier: R-HSA-191825

Type: dissociation

Compartments: nuclear envelope



The snRNAs, except U6 snRNA, are transcribed by RNA polymerase II, co-transcriptionally capped and exported rapidly to the cytoplasm in association with a cap-binding complex and the export factor PHAX.

Followed by: snRNP complex assembly

Literature references

Segref, A., Ohno, M., Mattaj, IW. (2001). The evolutionarily conserved region of the U snRNA export mediator PHAX is a novel RNA-binding domain that is essential for U snRNA export. *RNA, 7*, 351-60. ↗

Editions

2007-01-30	Authored	Gillespie, ME.
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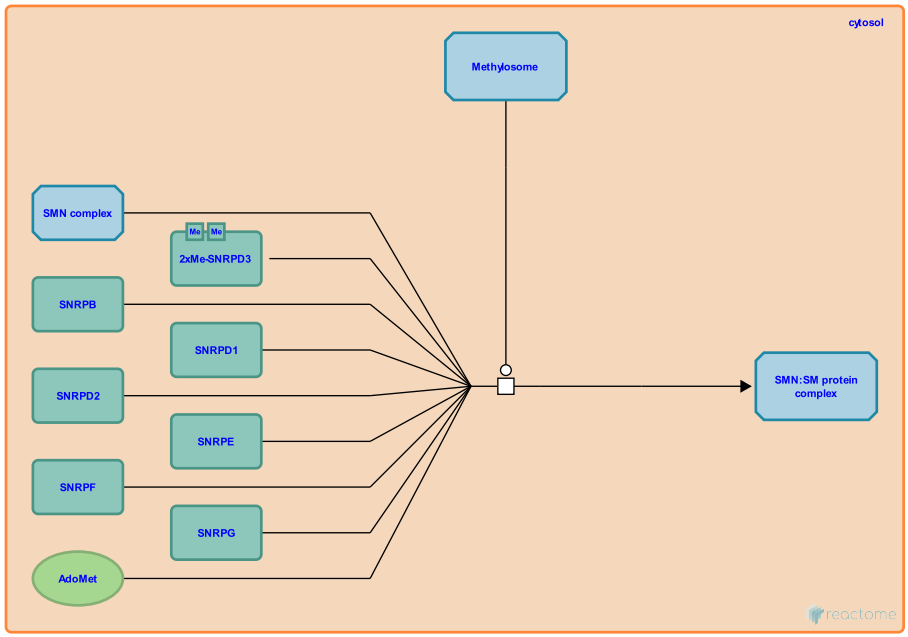
Loading and methylation of Sm proteins onto SMN Complexes ↗

Location: snRNP Assembly

Stable identifier: R-HSA-191790

Type: transition

Compartments: cytosol



The survival of motor neurons (SMN) complex binds to Sm proteins and small nuclear RNAs (snRNAs) in the cytoplasm. Sm is part the SMN multiprotein complex that contains Gemins 2 – 7, including the DEAD-box RNA helicase Gemin3. The binding of the SMN complex to the snRNAs depends on the presence of specific, high-affinity (nanomolar) binding domains in the snRNAs. The SMN complex binds the Sm proteins through the Sm domains interaction with the Gemins, the TUDOR domain, and through unique arginine- and glycine-rich (RG) domains found in three of these, SmB, SmD1 and SmD3. The association with RG domains is strongly enhanced by the post-translational symmetric dimethylation of specific arginines in these domains, a process that is carried out by the methylosome (JBP1 or PRMT5) complex.

Followed by: snRNP complex assembly

Literature references

Dreyfuss, G., Friesen, WJ. (2000). Specific sequences of the Sm and Sm-like (Lsm) proteins mediate their interaction with the spinal muscular atrophy disease gene product (SMN). *J Biol Chem, 275*, 26370-5. ↗

Dreyfuss, G., Charroux, B., Shevchenko, A., Mann, M., Pellizzoni, L., Perkinson, RA. (1999). Gemin3: A novel DEAD box protein that interacts with SMN, the spinal muscular atrophy gene product, and is a component of gems. *J Cell Biol, 147*, 1181-94. ↗

Dreyfuss, G., Rappsilber, J., Baccon, J., Mann, M., Pellizzoni, L. (2002). Identification and characterization of Gemin7, a novel component of the survival of motor neuron complex. *J Biol Chem, 277*, 31957-62. ↗

Dreyfuss, G., Rappsilber, J., Baccon, J., Mann, M., Pellizzoni, L. (2002). Purification of native survival of motor neurons complexes and identification of Gemin6 as a novel component. *J Biol Chem, 277*, 7540-5. ↗

Dreyfuss, G., Charroux, B., Shevchenko, A., Mann, M., Pellizzoni, L., Perkinson, RA. et al. (2000). Gemin4. A novel component of the SMN complex that is found in both gems and nucleoli. *J Cell Biol, 148*, 1177-86. ↗

Editions

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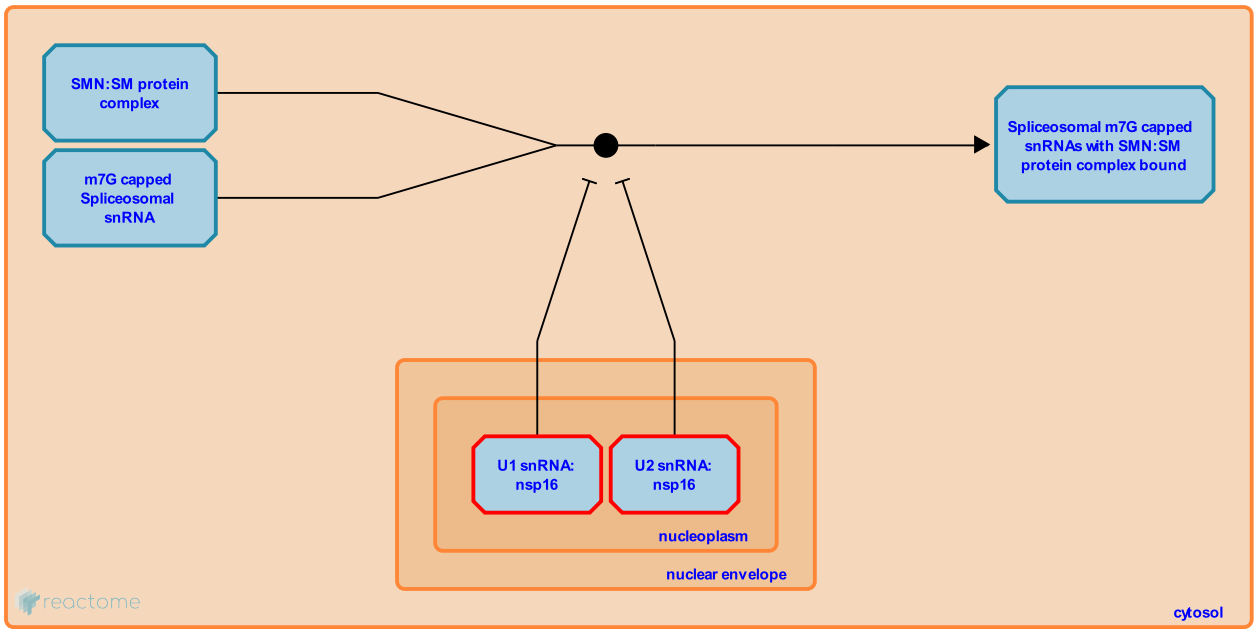
snRNP complex assembly ↗

Location: snRNP Assembly

Stable identifier: R-HSA-191786

Type: binding

Compartments: cytosol



To facilitate snRNP assembly, the SMN complex must bring together the Sm proteins and a Sm-site-containing snRNA. The SMN:Sm protein complex binds to the m7G capped snRNAs in the cytoplasm.

SARS-CoV-2 nonstructural protein 16 (nsp16) binds to the 5′ splice site recognition sequence of U1 snRNA and the branchpoint recognition site of U2 snRNA, both parts of the spliceosome, disrupting global mRNA splicing (Banerjee et al, 2020).

Preceded by: Loading and methylation of Sm proteins onto SMN Complexes, Nuclear export of snRNA transcripts

Followed by: snRNA Cap hypermethylation

Literature references

Kataoka, N., Dreyfuss, G., Charroux, B., Pellizzoni, L. (1998). A novel function for SMN, the spinal muscular atrophy disease gene product, in pre-mRNA splicing. *Cell, 95*, 615-24. ↗

Eggert, C., Fischer, U., Meister, G. (2002). SMN-mediated assembly of RNPs: a complex story. *Trends Cell Biol, 12*, 472-8. ↗

Luhrmann, R., Buhler, D., Raker, V., Fischer, U. (1999). Essential role for the tudor domain of SMN in spliceosomal U snRNP assembly: implications for spinal muscular atrophy. *Hum Mol Genet, 8*, 2351-7. ↗

Editions

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2007-04-30	Reviewed	Luhrmann, R.
2022-02-18	Reviewed	Messina, F.

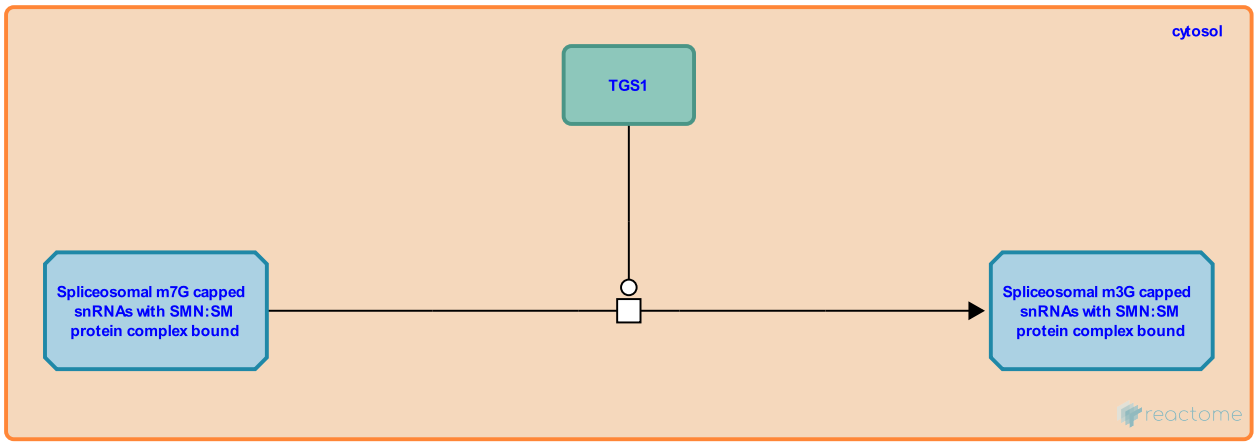
snRNA Cap hypermethylation ↗

Location: snRNP Assembly

Stable identifier: R-HSA-191784

Type: transition

Compartments: cytosol



The snRNA:SMN:SM protein complex is engaged by a hypermethylase that hypermethylates the snRNA cap from m7G (7-methylguanosine) to m3G (2,2,7-trimethylguanosine).

Preceded by: snRNP complex assembly

Followed by: snRNP:Snurportin complex formation

Literature references

Luhrmann, R., Plessel, G., Fischer, U. (1994). m3G cap hypermethylation of U1 small nuclear ribonucleoprotein (snRNP) in vitro: evidence that the U1 small nuclear RNA-(guanosine-N2)-methyltransferase is a non-snRNP cytoplasmic protein that requires a binding site on the Sm core domain. *Mol Cell Biol, 14*, 4160-72. ↗

Bertrand, E., Tazi, J., Narayanan, U., Matera, AG., Verheggen, C., Bordonne, R. et al. (2003). Interaction between the small-nuclear-RNA cap hypermethylase and the spinal muscular atrophy protein, survival of motor neuron. *EMBO Rep, 4*, 616-22. ↗

Editions

2007-01-30	Authored	Gillespie, ME.
2007-04-30	Reviewed	Luhrmann, R.

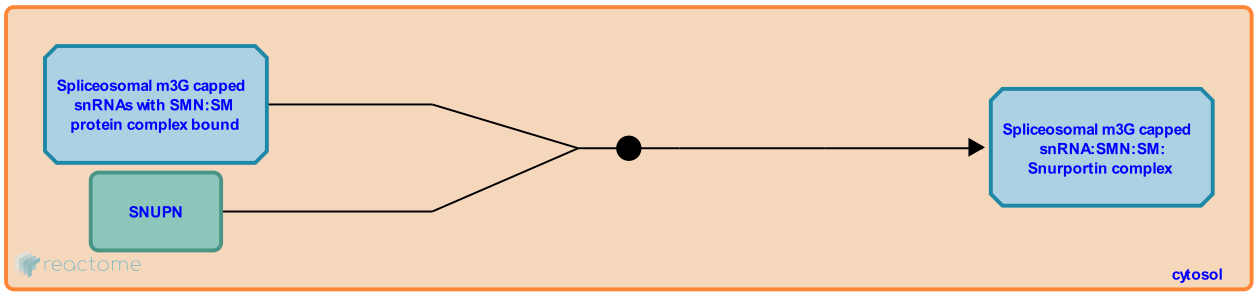
snRNP:Snurportin complex formation ↗

Location: snRNP Assembly

Stable identifier: R-HSA-191763

Type: binding

Compartments: cytosol



The nuclear import signal has two parts; Cap hypermethylation triggers nuclear import via snurportin1 binding and by receptor recognition of the Sm proteins. Snurportin1 (SPN) is an adaptor that links the assembled snRNP to the nuclear transport machinery, recruiting importin beta for nuclear import. The import receptor that recognizes the Sm proteins is not yet known.

Preceded by: snRNA Cap hypermethylation

Followed by: snRNP nuclear import and release

Literature references

Bertrand, E., Tazi, J., Narayanan, U., Matera, AG., Verheggen, C., Bordonne, R. et al. (2003). Interaction between the small-nuclear-RNA cap hypermethylase and the spinal muscular atrophy protein, survival of motor neuron. *EMBO Rep, 4*, 616-22. ↗

Narayanan, U., Matera, AG., Ospina, JK., Hebert, MD., Frey, MR. (2002). SMN, the spinal muscular atrophy protein, forms a pre-import snRNP complex with snurportin1 and importin beta. *Hum Mol Genet, 11*, 1785-95. ↗

Editions

2007-01-30	Authored	Gillespie, ME.
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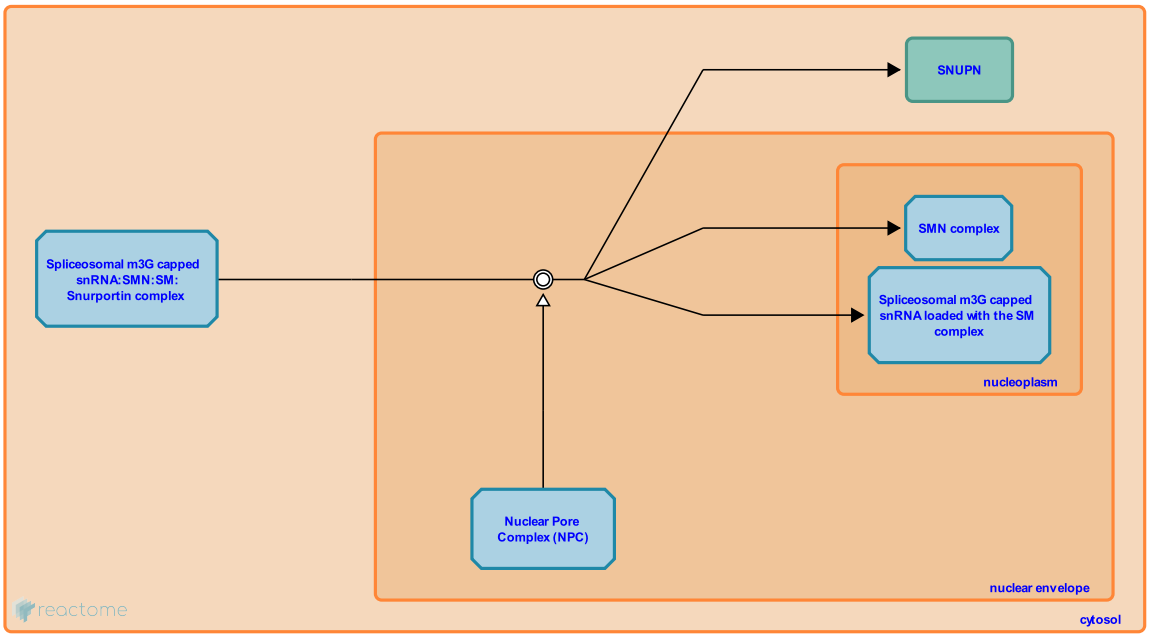
snRNP nuclear import and release ↗

Location: snRNP Assembly

Stable identifier: R-HSA-191830

Type: dissociation

Compartments: nuclear envelope



A properly assembled Sm core and the m3G cap structure are prerequisites for small nuclear ribonucleoprotein (snRNP) import into the nucleus. Once imported into the nucleus, the snRNPs are initially concentrated in Cajal bodies (CBs), where there is further processing of the snRNAs plus binding of additional proteins, from CRBs they transit to "speckles", from where they are engaged for pre-mRNA splicing. The SMN complexes in the nucleus are found throughout the nucleoplasm but are particularly concentrated in Gems, the "twins" of the snRNP-rich CBs.

Preceded by: snRNP:Snurportin complex formation

Literature references

Sleeman, JE., Lamond, AI. (1999). Newly assembled snRNPs associate with coiled bodies before speckles, suggesting a nuclear snRNP maturation pathway. *Curr Biol, 9*, 1065-74. ↗

Editions

2007-01-30	Authored	Gillespie, ME.
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