**Table S2. Template reactions list for *Saccharomyces cerevisiae* secretory machinery model.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **NO** | **Reaction Abbreviation** | **Reaction Name** | **Reaction Template** | **Directionality** | **Subsystem** | **Components** | **Comments** | **References** |
| 1 | SRPC | SRP complex formation | Srp14p[Cytoplasm] + Srp21p[Cytoplasm] + Srp68p[Cytoplasm] + Sec65p[Cytoplasm] + Srp72p[Cytoplasm] + scR1[Cytoplasm] + Srp54p[Cytoplasm] <=> **SRP**[Cytoplasm] | reversible | translocation from cytosol to ER | [***Srp14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp14)***,***[***Srp21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp21)***,*** [***Srp68p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp68)***,*** [***Srp72p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp72)***,*** [***Sec65p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec65)***,***[***ScR1***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=scr1)***,*** [***Srp54p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp54) | SRP is a cytosolic ribonucleoprotein which targets the SRP-dependent proteins to the ER membrane .Core components for SRP include: *SRP14p*, *SRP21p*, *SRP68p*, *SRP72p*,*SEC65*, and *SRP54*, and the RNA (termed scR1 and encoded by *SCR1*). Proteins and RNA assemble into a core complex in the nucleus (except Srp54p). It is use the NES pathway to export into the cytoplasm to bind to the Srp54p which is unique in yeast.  For simplicity we assumed that the SRP complex formation happens in cytoplasm (supplementary text S1). | **[**[**1**](#_ENREF_1)**]** |
| 2 | SRC | SRC complex formation | Srp101p[Cytoplasm] + Srp102p[Cytoplasm] <=> **SRC**[Cytoplasm] | Reversible | Co-translocation from cytosol to ER | [***Srp101p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp101)***,*** [***Srp102p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp102) | SRPC interacts with the signal peptide of the nascent proteins (to form RNC complex) then by interaction between SRP and a signal receptor complex (SR), encoded by SRP101 and SRP102 it attaches to the ER membrane. Finally, the RNC is transferred to the translocon, a protein-conducting membrane channel, and SRP and the SR dissociate. GTP bind to both SRP (via the Srp54p subunit) and the SR is critical for their interaction. | **[**[**1**](#_ENREF_1)**,** [**2**](#_ENREF_2)**]** |
| 3 | SEC61C1 | SEC61C1 complex formation | Sec61p[Endoplasmic Reticulum] + Sbh1p[Endoplasmic Reticulum] + Sss1p[Endoplasmic Reticulum] <=> **SEC61C1**[Endoplasmic Reticulum] | Reversible | Co-translocation translocation | [***Sec61p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec61)***,*** [***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)[***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1) | Sec61 complex or translocon comprised from 3 subunits including *Sec61p* (as major subunit), *Sbh1p* and *Sss1p*. SEC61C1 complex in yeast forms a channel for SRP-dependent protein import and retrograde transport of misfolded proteins out of the ER | **[**[**3**](#_ENREF_3)**,** [**4**](#_ENREF_4)**]** |
| 4 | SSH1C | **SSH1C** complex formation | Sbh1p[Endoplasmic Reticulum] + Sss1p[Endoplasmic Reticulum] + Ssh1p[Endoplasmic Reticulum] <= > **SSH1C**[Endoplasmic Reticulum] | Reversible | Post-translational translocation | [***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,*** [***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***,*** [***Ssh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ssh1) | *S. cerevisiae* contains a second Sec61-like complex involved in co-translational translocation called the Ssh1p complex | **[**[**5**](#_ENREF_5)**],[**[**4**](#_ENREF_4)**]** |
| 5 | SPC | SPC complex formation | Sec11p[Endoplasmic Reticulum] + Spc1p[Endoplasmic Reticulum] + Spc2p[Endoplasmic Reticulum] + Spc3p[Endoplasmic Reticulum] <=> **SPC**[Endoplasmic Reticulum] | Reversible | translocation from cytosol to ER | [***Sec11p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec11)***,*** [***Spc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spc1)[***Spc2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spc2)***,***[***Spc3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spc3) | The yeast SPC (signal peptidase complex) comprises four proteins, Spc1p Spc2p, Spc3p, and Sec11p. SEC11 is essential for viability and for signal peptidase activity. | **[**[**2**](#_ENREF_2)**,** [**6**](#_ENREF_6)**]** |
| 6 | SEC63C | SEC63C complex formation | Sec71p[Endoplasmic Reticulum] + sec62p[Endoplasmic Reticulum] + sec63p[Endoplasmic Reticulum] + sec72p[Endoplasmic Reticulum] <=> **SEC63C**[Endoplasmic Reticulum] | Reversible | Post-translational translocation | [***Sec63p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec63)***,***[***Sec62p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec62)***,*** [***Sec66p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec66)***,*** [***Sec72p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec72) | Sec63 complex (Sec63p, Sec62p, Sec66p and Sec72p); with Sec61 complex, Kar2p/BiP and Lhs1p forms a channel competent for SRP-dependent and post-translational SRP-independent protein targeting and import into the ER | **[**[**7**](#_ENREF_7)**,** [**8**](#_ENREF_8)**]** |
| 7 | OSTC | OSTC complex formation | Ost1p[Endoplasmic Reticulum] + Ost2p[Endoplasmic Reticulum] + Ost3p[Endoplasmic Reticulum] + Ost4p[Endoplasmic Reticulum] + Ost5p[Endoplasmic Reticulum] + Ost6p[Endoplasmic Reticulum] + Stt3p[Endoplasmic Reticulum] + Swp1p[Endoplasmic Reticulum] + Wbp1p[Endoplasmic Reticulum] <= > **OSTC**[Endoplasmic Reticulum] | Reversible | **Protein N-glycosylation** | [***Ost1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost1)***,*** [***Ost2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost2)***,*** [***Ost3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost3)***,*** [***Ost4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost4)***,*** [***Ost5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost5)***,*** [***Ost6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost6)***,*** [***Stt3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=stt3)***,*** [***Swp1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=swp1)***,*** [***Wbp1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=wbp1) | The OSTC complex contains nine protein subunits: Ost1p, Ost2p, Ost3p, Ost4p, Ost5p, Ost6p, Stt3p, Swp1p, and Wbp1p, all of which are integral membrane proteins of the ER. The OSTC interacts with the Sec61p pore complex involved in protein import into the ER.OSTC is responsible for N-linked glycosylation of the proteins. | **[**[**9**](#_ENREF_9)**]** |
| 8 | HRD1-HRD3C | HRD1-HRD3C  Complex formation | Hrd3p[Endoplasmic Reticulum] + Hrd1p[Endoplasmic Reticulum] + Usa1p[Endoplasmic Reticulum] + Der1p[Endoplasmic Reticulum] <=> **HRD1-HRD3C**  [Endoplasmic Reticulum] | Reversible | ERADL | [***Hrd3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd3)***,*** [***Hrd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd1)***,*** [***Usa1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=usa1)***,*** [***Der1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=der1) | Hrd1-Hrd3C is a core membrane complex,  Consisting of the ubiquitin ligase Hrd1p and its cofactors Hrd3p, Der1p, and Usa1p. These components form a near stoichiometric complex that is more loosely associated with the luminal Yos9p and the cytosolic Cdc48  ATPase complex, whose membrane recruitment is facilitated by Ubx2p and plays a central role in ER-associated protein degradation (ERAD). | [[10](#_ENREF_10)] |
| 9 | AAAC | AAAC complex formation | Ubx2p[Endoplasmic Reticulum]+ Cdc48p[Cytoplasm] + Ufd1p[Cytoplasm] + Npl4p[Cytoplasm] <=> AAAC[Cytoplasm] | Reversible | ERADL | [***Ubx2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ubx2)***,*** [***Cdc48p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cdc48)***,*** [***Ufd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hfd1)***,*** [***Npl4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=npl4) | AAAC involves in recognition of polyubiquitinated proteins and their presentation to the 26S proteasome for degradation; involved in transporting proteins from the ER to the cytosol. | [[10](#_ENREF_10), [11](#_ENREF_11)] |
| 10 | Sec23-Sec24C | Sec23-sec 24C  complex formation | Sec23p[COPII] + sec 24p[COPII] <=> Sec23-Sec 24C[COPII] | Reversible | COPII | [***Sec23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec23)***,***[***Sec 24p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec24) | Sec23p-Sec24pC heterodimer of the COPII vesicle coat, required for cargo selection during vesicle formation in ER to Golgi transport. Sar1p GTPase activity stimulated by Sec23p and Sec24 has cargo selection role. | [[12-14](#_ENREF_12)] |
| 11 | Sar1-GTPase-cycle | Sar 1 GDP GTP exchange | Sec12p[Endoplasmic Reticulum] + sar1p-GDP[Cytoplasm] + GTP[Cytoplasm] => Sar1p-GTP[Endoplasmic Reticulum] + GDP[Endoplasmic Reticulum] + sec12p[Endoplasmic Reticulum] | irreversible | COPII | [***Sec12p***](sec12)***,*** [***Sar1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sar1) | Assembly of the COPII coat is initiated through activation of the small Ras-like GTPase Sar1. Sec12 is an ER-bound transmembrane GEF (guanine exchange factor) for Sar1 and it is an ER membrane protein which activates Sar1p by exchanging GDP for GTP. | [[15](#_ENREF_15), [16](#_ENREF_16)] |
| 12 | TRAPPIC | TRAPPI complex formation | 2 Bet3p[Cytoplasm] + Bet5p[Cytoplasm] + Trs20p[Cytoplasm] + Trs23p[Cytoplasm] + Trs31p[Cytoplasm]+ Trs33p[Cytoplasm] <=> TRAPPIC[COPII] | Irreversible | COPII[[17](#_ENREF_17)] | [***Bet3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet3)***,***[***Bet5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet5)***,***[***Trs20p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs20)***,***[***Trs23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs23)***,***[***Trs31p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs31)[***Trs33p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs33) | In yeast, TRAPPI is a complex comprises seven small subunits (two  copies of Bet3p and one copy each of Bet5p, Trs20p, Trs23p,  Trs31p, and Trs33p) and mediates the tethering of endoplasmic reticulum (ER)-derived COPII-coated vesicles at the cis-Golgi. Except for Trs33p and Trs85p, all of the TRAPPI subunits are required for cell viability | [[18](#_ENREF_18), [19](#_ENREF_19)] |
| 13 | **AP1C** | AP1 coat formation and dissaciation | Apl4p[Cytoplasm] + Apl2p[Cytoplasm] +  Apm1p[Cytoplasm] + Aps1p[Cytoplasm] <=> **AP1C**[Cytoplasm] | Irreversible | CPY pathway, HDSV | [***Apl4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alp4)***,*** [***Apl2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alp2)  [***Apm1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apm1)***,***  [***Aps1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps1) | The roles of the yeast AP-1 and AP-2 complexes (not shown) have not been firmly established. | [[20](#_ENREF_20)] |
| 14 | **AP2C** | AP2 coat formation and dissaciation | Apl3p[Cytoplasm] + Apl1p[Cytoplasm] + Apm4p[Cytoplasm] + Apsp2[Cytoplasm] <=> **AP2C**[Cytoplasm] | irreversible |  | [***Apl3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl3)***,***  [***Apl1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl1) ***,***[***Apm4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apm4) ***,*** [***Aps2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps2) | The roles of the yeast AP-1 and AP-2 complexes (not shown) have not been firmly established. | [[20](#_ENREF_20)] |
| 15 | AP3C | AP3 coat formation and dissaciation | Apl6p[Cytoplasm] + Aps3p[Cytoplasm] + Apm3p[Cytoplasm] + Apl5p[Cytoplasm] + Vam3p[Vacuole] <=> **AP3C**[Cytoplasm] | Reversible | ALP pathway(AP-3 complex),  CPY Pathway | [***Apl6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl6)***,*** [***Aps3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps3)***,*** [***Apm3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apm3)***,***[***Apl5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl5)***,***[***Vam3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vam3) | The AP-3 adaptor complex is essential for cargo-selective transport (alkaline phosphatase) to the yeast vacuole (ALP pathway) rather than identified AP-1 and AP-2 complex which mediate protein sorting at the trans-Golgi network and plasma membrane. | [[21](#_ENREF_21), [22](#_ENREF_22)] |
| 16 | clathrinC | Clathrin Complex formation | 2 Chc1p[Cytoplasm] + Clc1p[Cytoplasm] <=> clathrinC[Cytoplasm] | Reversible | CPY Pathway, HDSV, LDSV | [***Chc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=chc1)***,***[***Clc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=clc1) | Two Chc1p (heavy chain) form the Clathrin triskelion structural which is the major coat protein involved in intracellular protein transport and endocytosis. The Clc1p (the light chain) have a regulatory role. | [[23](#_ENREF_23), [24](#_ENREF_24)] |
| 17 | Sec13-Sec31C | Sec13-sec31C complex formation | Sec13p[COPII] + sec31p[COPII] <=> Sec13-sec31C[COPII] | reversible | COPII | [***Sec13p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec13)***,***[***Sec31p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Sec31) | This complex is a subunits of the big complex called COPII vesicle coat complex needed for selection of the cargo and COPII vesicles to transport cargo from ER to Golgi. | [[25-27](#_ENREF_25)] |
| 18 | Arf1p-GTP | Arf1p-GTP formation | Arf1p-GDP[Cytoplasm] + Gea1p[Cytoplasm] + Gea2p[Cytoplasm] + 2 GTP[Cytoplasm] => Arf1p-GTP[Cytoplasm] + 2 GDP[Cytoplasm] + Gea1p[Cytoplasm] + Gea2p[Cytoplasm] | Irreversible | COPI | [***Arf1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Arf1)***,***[***Gea1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Gea1)***,***[***Gea2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Gea2) | Gea1p and Geap2p act as Arf1p ( ADP-ribosylation factor ) GEF( guanine nucleotide exchange factor ) and bound to the Golgi membrane and recruits the Arf1-GDP to bind and they convert it to the Arf1p-GTP which has essential role in COPI vesicle formation. | [[27-29](#_ENREF_27)] |
| 19 | COPIC | COPI coatomer | Cop1p[COPI] + Sec26p[COPI] + Sec27p[COPI] + Sec21p[COPI] + Ret2p[COPI] + Sec28p[COPI] + Ret3p[COPI] <=> COPIC[COPI] | reversible | COPI | [***Cop1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cop1)***,*** [***Sec26p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec26)***,*** [***Sec27p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec27)***,*** [***Sec21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec21)***,*** [***Ret2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ret2)***,***[***Sec28p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec28)***,***[***Ret3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ret3) | COPI coatomer is a complex of seven protein which they assembled tighter and provide a coat structure for the COPI vesicles .It has been shown that Ret2p has role in cargo detection. COPI vesicles have a vital role in maintenance of the ER function and morphology. | [[30-35](#_ENREF_30)] |
| 20 | CPYIC | CPYIC complex formation | Pep12p[endosome] + Vps45p[endosome] <=> CPYIC[endosome] | reversible | CPY pathway | [***Pep12p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pep12)***,*** [***Vps45p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vps45) | Golgi-to-endosome transport along the carboxypeptidase Y (CPY) pathway requires Pep12p  (t-SNARE) and Vps45p (Sec1p homologue) | [[36-39](#_ENREF_36)] |
| 21 | CPYIIC | CPYIIC complex formation | Vps4p[endosome] + Vps27p[endosome] <=> CPYIIC[endosome] | reversible | CPY pathway | [***Vps4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vps4) ***,***[***Vps27p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vps27) | endosome-to-vacuole transport along the CPY pathway requires Vps4p (AAA-type ATPase) and Vps27p(RING-finger protein) | [[40](#_ENREF_40), [41](#_ENREF_41)] |
| 22 | EXOC | LDSV exosytose | Sec3p[Cytoplasm]+ Sec5p[Cytoplasm]+ Sec6p[Cytoplasm]+ Sec8p[Cytoplasm]+ Sec10p[Cytoplasm]+ Sec15p[Cytoplasm]+ Exo70p[Cytoplasm]+ Exo84p[Cytoplasm]+ sec4p[Cytoplasm] <=> EXOC[Cytoplasm] | reversible | LDSV pathway | [***Sec3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec3)***,*** [***Sec5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec5)***,*** [***Sec6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec6)***,*** [***Sec8p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec8)***,*** [***Sec10p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec10)***,*** [***Sec15p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec15)***,*** [***Exo70p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=exo70)***,*** [***Exo84p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=exo84)***,***[***Sec4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Sec4) | The Exocyst complex involve in targeting of the post-golgi vesicles to the exocytosis pathway. | [[42-45](#_ENREF_42)] |
| 23 | XXX-TC1 | signal peptide recognition | XXX[Cytoplasm] + **SRPC**[Cytoplasm]=> XXX-**SRPC**[Cytoplasm] | irreversible | translocation from cytosol to ER (SRP-dependent) | ***SRPC(***[***Srp14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp14)***,***[***Srp21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp21)***,***[***Srp54p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp54)***,*** [***Srp65p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Srp65)***,***[***Srp68p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Srp68)***,***[***Srp72p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Srp72)***,*** [***ScR1***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=SCR1) ***RNA)*** | The SRPC (a ribonucleoprotein) is responsible to detect and bind to the signal peptide and target the protein to ER membrane. The formation of the SRPC and detecting of the SP is a sequential and complex stochastic process which starts in nucleus (by formation of core complex including the RNA subunit) and complete in cytoplasm by detecting the ribosome nascent chain complex (RNC) through the signal peptide. | [[46-48](#_ENREF_46)] |
| 24 | XXX-TC2 | ER receptor biding to XXX-SRPC | XXX-SRPC[Cytoplasm] + **SRC**[Endoplasmic Reticulum] => XXX-SRPC-SRC[Cytoplasm] | Irreversible | translocation from cytosol to ER (SRP-dependent) | ***SRPC(***[***Srp14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp14)***,***[***Srp21p***](srp21)***,***[***Srp54p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp54)***,*** [***Srp65p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp65)[***Srp68p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp68)***,***[***scR1***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=scr1)***RNA)***  ***SRC(***[***Srp101p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp101)***,*** [***Srp102p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp102)***)*** | The detected RNC (ribosome nascent chain) by SRPC binds to the to the SRP receptor (SR) on ER. | [[46-48](#_ENREF_46)] |
| 25 | XXX-TC3 | Biding of XXX-SRPC-SRC to the translocator(SEC61C) | XXX-SRPC-SRC[Cytoplasm] + 2 GTP[Cytoplasm] + **SEC61C**[Endoplasmic Reticulum] + **SSH1C**[Endoplasmic Reticulum] => XXX-SRPC-SRC-SEC61C[Cytoplasm] | Irreversible | translocation from cytosol to ER (SRP-dependent) | ***SRPC(***[***Srp14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp14)***,***[***Srp21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp21)***,***[***Srp54p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp54)***,*** [***Srp65p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp65)***,*** [***Srp68p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Srp68)***,*** [***scR1***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=scr1) ***RNA)***  ***SRC(***[***Srp101p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp101)***,***[***Srp102p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp102)***)***  ***SEC61C(***[***Sec61p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec61)***,***[***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,***[***Sss1p***](sss1)***)Alternative SEC61C(***[***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,***[***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***,***[***Ssh1p***](ssh1)***)*** | The Srp54p (subunits of SRP) and SR alpha (subunit of the SR) use a tightly coupled GTPase cycle to facilitates the signal sequence-dependent attachment of ribosomes to the SEC61C. This Cooperative binding stabilizes the SRP-SR complex and initiates the handing of signal sequence from Srp54p to Sec61 alpha. It has been shown that conformational change of the both SR alpha and Srp54p in binding to the GTP has distinct roles and SR alpha perform a predominant role in complex stabilization. | [[49-52](#_ENREF_49)] |
| 26 | XXX-TC4 | SRCPC and SRC dissociation | XXX-SRPC-SRC-SEC61C[Cytoplasm] **=>**  XXX-SEC61C[Cytoplasm] +Srp14p[Cytoplasm] + Srp21p[Cytoplasm] + Srp68p[Cytoplasm] + Sec65p[Cytoplasm] + Srp72p[Cytoplasm] + scR1[Cytoplasm] + Srp54p[Cytoplasm] + Srp51p[Cytoplasm] +  Srp52p[Cytoplasm] **+** 2GDP[Cytoplasm] + 2 pi[Cytoplasm] | Irreversible | translocation from cytosol to ER (SRP-dependent) | ***SRPC(***[***Srp14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp14)***,***[***Srp21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp21)***,***[***Srp54p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp54)***,*** [***Srp65p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp65)***,*** [***Srp68p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Srp68)***,*** [***scR1***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=scr1) ***RNA)***  ***SRC(***[***Srp101p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp101)***,***[***Srp102p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=srp102)***)*** | The dissociation of the SRP-SR complex cannot occur before the hydrolysis of bound GTP by both Srp54p and SR alpha.. | [[51](#_ENREF_51), [53](#_ENREF_53)] |
| 27 | XXX-TC5 | Signal peptidase | XXX-SEC61C[Cytoplasm] + **SPC**[Endoplasmic Reticulum] => XXX[Endoplasmic Reticulum] + Sec61p[Endoplasmic Reticulum] + Sbh1p[Endoplasmic Reticulum] + Sss1p[Endoplasmic Reticulum] + Sec11p[Endoplasmic Reticulum] + Spc1p[Endoplasmic Reticulum] + Spc2p[Endoplasmic Reticulum] + Spc3p[Endoplasmic Reticulum] + XXX**sp**[Cytoplasm] | Irreversible | translocation from cytosol to ER (SRP-dependent) | ***SEC61C(***[***Sec61p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec61)***,***[***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,***[***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***)***  ***SPC(***[***Sec11p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec11)***,*** [***Spc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spc1)***,*** [***Spc2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spc2)***,***[***Spc3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spc3)***)***  ***SSH1C (*** [***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,*** [***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***,*** [***Ssh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ssh1)***)*** | SPC (Signal peptidase complex) include the four subunits: Spc1p; Spc2p; Spc3p; Sec11p and is responsible for catalyzing the cleavage of signal peptides of proteins subjected to the secretory pathway. | [[2](#_ENREF_2)]; [[54-56](#_ENREF_54)] |
| 28 | SP-degradation | Signal peptide degradation | sp[Cytoplasm] => ac[Cytoplasm] | Irreversible | translocation from cytosol to ER |  | degradation of the signal peptide  **note:**(This reaction did not included in the model analysis and ignored due to its minor role) |  |
| 29 | XXX-PST1 | Post-translational translocation | XXX[Cytoplasm] + **SEC63C**[Endoplasmic Reticulum] + 5 Kar2p[Endoplasmic Reticulum] **+** 5 ATP[Endoplasmic Reticulum] + 5 Lhs1p[Endoplasmic Reticulum] <=> XXX-SEC63C-SEC61C-Kar2p-ATPcplx[Cytoplasm] | reversible | translocation from cytosol to ER (Post-translational translocation) | ***SEC63C (***[***Sec66p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec66)***,***[***Sec62p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec62)***,***[***Sec63p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec63)***,***[***Sec72p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec72) ***)SEC61C:(***[***Sec61***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec61)***p,***[***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,***[***Sss1p***](sss1)***)*** | SEC63C (Sec63p; Sec62p; Sec66p and Sec72p) with SEC61C, Kar2p/BiP and Lhs1p form two channel competent for SRP-dependent and post-translational SRP-independent protein targeting and import into the ER.  ATP and Kar2p are required for the insertion of precursor polypeptides into the Sec61C as well as for the completion of translocation into  the ER. Lhs1p only participates in post-translational import. | [[46](#_ENREF_46)]  [[57-59](#_ENREF_57)] |
| 30 | XXX-PSTII | Post-translational translocation | XXX-SEC63C-SEC61C-Kar2p-ATPcplx[Cytoplasm] => XXX[Endoplasmic Reticulum] + SSH1C[Endoplasmic Reticulum] + Sec61p[Endoplasmic Reticulum] + Sbh1p[Endoplasmic Reticulum] + Sss1p[Endoplasmic Reticulum] + 5 Kar2p[Endoplasmic Reticulum] +5 ADP[Endoplasmic Reticulum] + 5 Lhs1p[Endoplasmic Reticulum] | reversible | translocation from cytosol to ER (Post-translational translocation) | ***SEC63C(***[***Sec63p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec63)***,***[***Sec62p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec62)***,*** [***Sec66p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec66)***,*** [***Sec72p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec72) ***)SEC61C(***[***Sec61***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec61)***p,***[***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,***[***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***)*** | The SEC61C can interact  with the SEC63C which are involved in the BiP(Kar2p)-mediated  Post-translational translocation of preproteins across the ER membrane. |  |
| 31 | DOL-P-formation | Monophospho dolichol synthesis | Dol[Cytoplasm] + **CTP**[Cytoplasm] => Dol-p[Cytoplasm] + **CDP**[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Sec59p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec59) | Dolichol kinase catalyzes the last step in dolichol monophosphate (Dol-P) biosynthesis by phosphorylation of the Carrier lipid Dol (polyisoprenoid) consuming one CTP. This enzyme is essential for viability and for normal rates of lipid intermediate synthesis, protein *N*-glycosylation,*O*-glycosylation and GPI anchor synthesis. | [[60-62](#_ENREF_60)] |
| 32 | Dol-PP-GlcNAcI-formation | Dol-PP-GlcNAc formation I | Dol-p[Cytoplasm] + **UDP-GlcNAc**[Cytoplasm] => Dol-pp-GlcNAc[Cytoplasm] + **UMP**[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg7p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg7) | The biosynthesis of the oligosaccharide donor begins on the cytoplasmic face of the ER with Alg7; an N-acetylglucosamine-phosphate transferase that elaborates Dol-P to Dol-PP-GlcNAc. | [[63-65](#_ENREF_63)] |
| 33 | Dol-PP-GlcNAcII-formation | Dol-PP-GlcNAc formation II | Dol-pp-GlcNAc[Cytoplasm] + **UDP-GlcNAc**[Cytoplasm] => Dol-pp-GlcNAc(2)[Cytoplasm] + **UMP**[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg13p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg13)***/14p*** | The addition of the second α1;4-GlcNAc residue is catalyzed by a hetero-oligomeric protein classified as Alg13/14. | [[66-68](#_ENREF_66)] |
| 34 | Dol-pp-GlcNAc-man-formationI | Dol-pp-GlcNAc(2) manosylation I | Dol-pp-GlcNAc(2)[Cytoplasm] + GDP-man[Cytoplasm] => Dol-pp-GlcNAc(2) -man[Cytoplasm] + GDP[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg1) | Alg1p (beta 1;4 mannosyltransferase); catalyzes the addition of the first mannose moiety to the growing lipid-linked oligosaccharide (LLO).This reaction occurs on the cytosolic side of the endoplasmic reticulum. This enzyme is shown to form complex with Alg2p and Alg11p separately. The mutated strains are not able to add mannose to Dol-PP-GlcNAc2, but they can convert Man1-Dol-PP-GlcNAc2 to Man5-Dol-PP-GlcNAc2. | [[69-72](#_ENREF_69)] |
| 35 | Dol-pp- GlcNAc(2) -man-formationII | Dol-pp- GlcNAc(2) manosylation II | Dol-pp-GlcNAc(2) -man[Cytoplasm] + GDP-man[Cytoplasm] => Dol-pp-(GlcNAc)2(man)2[Cytoplasm] + UDP[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg2) | Alg2p (mannosyltransferase) catalyzes the addition of both the second (via an alpha-1;3 linkage) and third ( via an alpha-1;6 linkage ) mannose moieties to the growing oligosaccharide chain during LLO biosynthesis. The mutants show accumulation of oligosaccharide chains (with one or two mannose residues). Alg2p form complexes with Alg1p. | [[73-75](#_ENREF_73)] |
| 36 | Dol-pp- GlcNAc(2) -man-formationIII | Dol-pp- GlcNAc(2) manosylation III | Dol-pp-(GlcNAc)2(man)2[Cytoplasm] + GDP-man[Cytoplasm] => Dol-pp-(GlcNAc)2(man)3[Cytoplasm] + GDP[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg3) |  |  |
| 37 | Dol-pp- GlcNAc(2) -man-formationIV | Dol-pp- GlcNAc(2) manosylation IV | Dol-pp-(GlcNAc)2(man)3[Cytoplasm] + GDP-man[Cytoplasm] => Dol-pp-(GlcNAc)2(man)4[Cytoplasm] + GDP[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg11p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg11) | Alg11p is responsible to add the fourth and fifth mannose to LLO on cytoplasmic side of the ER. It forms complexes together with Alg2p | [[76](#_ENREF_76), [77](#_ENREF_77)] |
| 38 | Dol-pp- GlcNAc(2) -man-formationV | Dol-pp- GlcNAc(2) manosylation V | Dol-pp-(GlcNAc)2(man)4[Cytoplasm] + GDP-man[Cytoplasm] => Dol-pp-(GlcNAc)2(man)5[Cytoplasm] + GDP[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | ***Alg11p*** |  |  |
| 39 | Dol-pp- GlcNAc(2) -man(5)-filliping | Dol-pp- GlcNAc(2) -man(5) filliping to the ER | Dol-pp-(GlcNAc)2(man)5[Cytoplasm] => Dol-pp-(GlcNAc)2(man)5[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Rft1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rft1) | The completely assembled heptasaccharide is flipped to the lumenal face of the ER membrane.by Rft1p, a transmembrane ATP-independent and bi-directional flippase. | [[78](#_ENREF_78)] |
| 40 | Dol-p-er-manosylation | ER manosylation of Dol-p | Dol-p[Cytoplasm] + **GDP-man**[Cytoplasm] => Dol-p-man[Cytoplasm] + **GDP**[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Dpm1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=dpm1) | Dpm1p (dolichyl phosphate mannose synthase, Dol-P-Man) (EC 2.4.1.83) adds a mannose moiety to dolichyl phosphate on the cytosolic side of the ER. Dol-P-Man flips into the lumen of the ER; where it serves as a source of mannose for three types of protein modifications: *N*-linked glycosylation; *O*-linked glycosylation; and synthesis of glycosyl phosphatidylinositol (GPI) anchors. Deletion of DPM1 is lethal. | [[79](#_ENREF_79), [80](#_ENREF_80)] |
| 41 | Dol-p-er-glycosylation | ER glycosylation of Dol-p | Dol-p[Cytoplasm] + **UDP-Clc**[Cytoplasm] => Dol-p-Glc[Cytoplasm] + **UDP**[Cytoplasm] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg5) | Alg5p, a transmembrane dolichyl-phosphate beta-glucosyltransferase , adds glucose to dolichyl-phosphate (Dol-P) on the cytoplasmic side of the ER. By flipping Dol-P glucose enters into the lumen of the ER; where it serves as a source of glucose for growing lipid-linked oligosaccharides (LLO's). Mutation in ALG5 result in accumulation of LLO's (Man9) with no apparent growth defect. | [[81](#_ENREF_81)] |
| 42 | Dol-pp-GlcNAc(2)man(5)-er-manI | Dol-pp-GlcNAc(2)man(5) ER manosylation I | Dol-pp-GlcNAc(2)man(5)[Endoplasmic Reticulum] + **Dol-p-man**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(6)[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg3) | Alg3p(alpha 1;3 mannosyltransferase) that adds the the sixth mannose moiety to the growing lipid-linked oligosaccharide (LLO),the first sugar added in the lumen of the ER.. Disruption of ALG3 causes accumulation of lipid-linked oligosaccharides with five mannose residues. | [[82](#_ENREF_82)] |
| 43 | Dol-pp-GlcNAc(2)man(5)-er-manII | Dol-pp-GlcNAc(2)man(5) ER manosylation II | Dol-pp-GlcNAc(2)man(6)[Endoplasmic Reticulum] + **Dol-p-man**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(7)[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg9p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg9) | Alg9p (alpha 1;2 mannosyltransferase) catalyzes two steps: the addition of the seventh and ninth mannose moieties to the growing oligosaccharide in the lumen of the ER.. Disruption of ALG9 causes accumulation of lipid-linked oligosaccharides with six mannose residues and hypoglycosylation of secreted proteins. | [[83](#_ENREF_83)] |
| 44 | Dol-pp-GlcNAc(2)man(5)-er-manIII | Dol-pp-GlcNAc(2)man(5) ER manosylation III | Dol-pp-GlcNAc(2)man(7)[Endoplasmic Reticulum] + **Dol-p-man**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(8)[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg12p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg12) | Alg12p (Alpha-1,6-mannosyltransferase) is an ER enzyme which adds the eighth mannose moieties .Mutation in ALG12 result in the accumulation of the lipid-linked oligosaccharides (LLO's) with seven mannose moieties. | [[84](#_ENREF_84)] |
| 45 | Dol-pp-GlcNAc(2)man(5)-er-manI | Dol-pp-GlcNAc(2)man(5) ER manosylation IV | Dol-pp-GlcNAc(2)man(8)[Endoplasmic Reticulum] + **Dol-p-man**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(9)[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg9p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg9) | Alg9p (alpha 1,2 mannosyltransferase) shown to have a bi-functional nature. It catalyzes the addition of both the seventh and the ninth mannose residues (both α1;2-mannosyl linkages). | [[83](#_ENREF_83)] |
| 46 | Dol-pp-GlcNAc(2)man(9) - glcI | Dol-pp-GlcNAc(2)man(9) glycosylation I | Dol-pp-GlcNAc(2)man(9)[Endoplasmic Reticulum] + **Dol-p-Glc**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(9)-Glc[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] |  | synthesis of lipid linked precursor oligosaccharide | [***Alg6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg6) | Alg6p( alpha 1;3 glucosyltransferase; catalyzes the addition of the first glucose to the growing lipid-linked oligosaccharide (LLO) in the lumen of the endoplasmic reticulum. | [[85](#_ENREF_85)] |
| 47 | Dol-pp-GlcNAc(2)man(9) - glcII | Dol-pp-GlcNAc(2)man(9) glycosylation II | Dol-pp-GlcNAc(2)man(9)-Glc[Endoplasmic Reticulum] + **Dol-p-Glc**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(9)-Glc(2)[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Alg8p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=alg8) | Alg8p (alpha 1;3 glucosyltransferase ) an ER-membrane-bound adds of the second of three glucose moieties to growing LLO's in the lumen of ER. Mutants lacking ALG8 produce truncated LLO's with only one glucose residue that are able to be transferred to proteins with reduced efficiency. | [[86](#_ENREF_86)] |
| 48 | Dol-pp-GlcNAc(2)man(9) - glcIII | Dol-pp-GlcNAc(2)man(9) glycosylation III | Dol-pp-GlcNAc(2)man(9)-Glc(2)[Endoplasmic Reticulum] + **Dol-p-Glc**[Endoplasmic Reticulum] => Dol-pp-GlcNAc(2)man(9)-Glc(3)[Endoplasmic Reticulum] + **Dol-p**[Endoplasmic Reticulum] | Irreversible | synthesis of lipid linked precursor oligosaccharide | [***Die2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=die2) | Die2p (alpha-1;2 glucosyltransferase) catalyzes the addition of the third(The final sugar to add to LLO). | [[87](#_ENREF_87)] |
| 49 | GPIS1C |  | Gpi1p[Cytoplasm] + Gpi2p[Cytoplasm] + Spt14p[Cytoplasm] + Gpi15p[Cytoplasm] + Gpi19p[Cytoplasm] + Eri1p[Cytoplasm] <=> GPIS1C[Cytoplasm] | reversible | GPI biosynthesis | [***Gpi1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi1)***,*** [***Gpi2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi2)***,*** [***Spt14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spt14)***,***[***Gpi15p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi15)***,***[***Gpi19p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi19)***,***[***Eri1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=eri1) | The complex enzyme N-Acetyle-Glucoseamine-transferase comprised of 6 ER integrated membrane proteins. | [[88](#_ENREF_88), [89](#_ENREF_89)] |
| 50 | GPIB1 |  | PI[Cytoplasm] + UDP-GlcNAc[Cytoplasm] => PI-GlcNAc[Cytoplasm] + UDP[Cytoplasm] + Gpi1p[Cytoplasm] + Gpi2p[Cytoplasm] + Spt14p[Cytoplasm] + Gpi15p[Cytoplasm] + Gpi19p[Cytoplasm] + Eri1p[Cytoplasm] | Irreversible | GPI biosynthesis | [***Gpi1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi1)***,*** [***Gpi2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi2)***,*** [***Spt14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=spt14)***,***[***Gpi15p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi15)***,***[***Gpi19p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi19)***,***[***Eri1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=eri1) | N-Acetyle-Glucoseamine-transferase transfers GlcNAc consuming UDP-GlcNAc( donor) to the PI(phosphatidyle inositol) as the first step of the GPI biosynthesis. This reaction occurs in the cytoplasmic side of the ER. | [[88](#_ENREF_88), [89](#_ENREF_89)] |
| 51 | GPIB2 |  | PI-GlcNAc[Cytoplasm] => PI-GlcN[Cytoplasm] + Acetate[Cytoplasm] | Irreversible | GPI biosynthesis | [***Gpi12p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi12) | Gpi12p de-*N*-acetylated the Glc-NAc-PI in the first step. | [[89](#_ENREF_89), [90](#_ENREF_90)] |
| 52 | GPIB3 |  | PI-GlcN[Cytoplasm]=> PI-GlcN[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis |  | In second step Glc-N is flipped to the ER side for passing through future reaction |  |
| 53 | GPIB4 |  | PI-GlcN[Endoplasmic Reticulum] + Palmitoyl-CoA[Endoplasmic Reticulum] => Acyl-PI-GlcN[Endoplasmic Reticulum] + CoA[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Gwt1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gwt1) | In the fourth step in ER, PI-Glc-N IS inositol-acylated by Gw1p as enzyme. | [[89](#_ENREF_89), [91](#_ENREF_91)] |
| 54 | GPIB5 |  | Acyl-PI-GlcN[Endoplasmic Reticulum] + Dol-p-man[Endoplasmic Reticulum] => Acyl-PI-GlcN-man[Endoplasmic Reticulum] + Dol-p[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Gpi14p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi14) | In the fifth step,the first mannose is added to the Acyl-PI-GlcN. | [[89](#_ENREF_89), [92](#_ENREF_92)] |
| 55 | GPIB6 |  | Acyl-PI-GlcN-man[Endoplasmic Reticulum] + EtNP[Endoplasmic Reticulum] => Acyl-PI-GlcN-man-EtNP[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Mcd4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mcd4) | In the sixth step the phosphorylethanolamine is added to Man1 | [[89](#_ENREF_89), [93](#_ENREF_93)] |
| 56 | GPIB7 |  | Acyl-PI-GlcN-man-EtNP[Endoplasmic Reticulum] + Dol-p-man[Endoplasmic Reticulum] => Acyl-PI-GlcN-(man)2-EtNP[Endoplasmic Reticulum] + Dol-p[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Gpi5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi5) | In the seventh step the second mannose is added to the Acyl-PI-GlcN. | [[89](#_ENREF_89), [94](#_ENREF_94)] |
| 57 | GPIB8 |  | Acyl-PI-GlcN-(man)2-EtNP[Endoplasmic Reticulum] + Dol-p-man[Endoplasmic Reticulum] => Acyl-PI-GlcN-(man)3-EtNP[Endoplasmic Reticulum] + Dol-p[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Gpi10p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi10) | In eighth step the third mannose is added to the Acyl-PI-GlcN. | [[89](#_ENREF_89), [95](#_ENREF_95)] |
| 58 | GPIB9 |  | Acyl-PI-GlcN-(man)3-EtNP[Endoplasmic Reticulum] + Dol-p-man[Endoplasmic Reticulum] => Acyl-PI-GlcN-(man)4-EtNP[Endoplasmic Reticulum] + Dol-p[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Smp3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=smp3) | In ninth step, the forth mannose is added to the Acyl-PI-GlcN. | [[89](#_ENREF_89), [96](#_ENREF_96)] |
| 59 | GPIB10 |  | Acyl-PI-GlcN-(man)4-EtNP[Endoplasmic Reticulum] + EtNP[Endoplasmic Reticulum] => Acyl-PI-GlcN-(man)4-(EtNP)2[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Gpi13p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi13) | In tenth step, second phosphophorylethanolamine is added to Man3 | [[89](#_ENREF_89), [97](#_ENREF_97)] |
| 60 | GPIB11 |  | Acyl-PI-GlcN-(man)4-(EtNP)2[Endoplasmic Reticulum]+ EtNP[Endoplasmic Reticulum] => Acyl-PI-GlcN-(man)4-(EtNP)3[Endoplasmic Reticulum] | Irreversible | GPI biosynthesis | [***Gpi17p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi17) | In eleventh step, second phosphophorylethanolamine is added to Man2 | [[89](#_ENREF_89), [98](#_ENREF_98)] |
| 61 | XXX-GPIR1 |  | XXX-G5[Endoplasmic Reticulum] + Acyl-PI-GlcN-(man)4-(EtNP)3[Endoplasmic Reticulum] => XXX-G6[Endoplasmic Reticulum] | Irreversible | GPI transfer | [***Gaa1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gaa1)***,***[***Gpi8p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi8)***,***[***Gpi16p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi16)***,***[***Gpi17p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gpi17)***,***[***Gab1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gab1) | GPI-Transaminase (complex enzyme) transfers the GPI to the GPI site on the proteins. | [[89](#_ENREF_89), [99](#_ENREF_99)] |
| 62 | XXX-GPIR2 |  | XXX-G6[Endoplasmic Reticulum] => XXX-G6[Endoplasmic Reticulum] + acyl[Endoplasmic Reticulum] | Irreversible | GPI transfer | [***Bst1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bst1) | In this reaction the acyle is removed from the inositol after the GPI has been added to protein. | [[89](#_ENREF_89), [100](#_ENREF_100)] |
| 63 | XXX -ERNG | N-linked glycosylation | XXX-SEC61C[Endoplasmic Reticulum] + ?Dol-pp-GlcNAc(2)man(9)-Glc(3)[Endoplasmic Reticulum] + OSTC[[Endoplasmic Reticulum]] => XXX-G1-SEC61C[Endoplasmic Reticulum] + ?Dol-pp[Endoplasmic Reticulum] + Ost1p[Endoplasmic Reticulum] + Ost2p[Endoplasmic Reticulum] + st3p[Endoplasmic Reticulum] + Ost4p[Endoplasmic Reticulum] + Ost5p[Endoplasmic Reticulum] + Ost6p[Endoplasmic Reticulum] + Stt3p[Endoplasmic Reticulum] + Swp1p[Endoplasmic Reticulum] + Wbp1p[Endoplasmic Reticulum] | Irreversible | **Protein N-glycosylation** | ***OSTC(***[***Stt3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=stt3)***,***[***Ost1***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost1)***p,***[***Wbp1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=wbp1)***,***[***Ost3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost3)***,***[***Ost6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost6)***,***[***Swp1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=swp1)***,***[***Ost2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost2)***,***[***Ost5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost5)***,***[***Ost4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ost4)***)*** | The oligosaccharyl transferase complex (OST complex) (EC 2.4.1.119) transfers 14-sugar branched oligosaccharides from dolichyl pyrophosphate to asparagine residues. The complex contains nine protein subunits: Ost1p( alpha subunit); Ost2p( epsilon subunit); Ost3p; Ost4p; Ost5p; Ost6p; Stt3p; Swp1p( delta subunit); and Wbp1p; all of which are integral membrane proteins of the. Genetic-knockout experiments have revealed that five of these subunits (Ost2p; Ost1p; Stt3p; Swp1p; and Wbp1p) are absolutely essential for yeast viability | [[101-106](#_ENREF_101)] |
| 64 | XXX -EROG | Er O-linked glycosylation | XXX-SEC61C[Endoplasmic Reticulum] + Dol-pp-Man[Endoplasmic Reticulum] => XXX-G1-SEC61C[Endoplasmic Reticulum] + Dol-pp[Endoplasmic Reticulum] |  | **O-Glycosylation** | ***PMTC(***[***Pmt2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pmt2)***,***[***Pmt5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pmt5)***,***[***Pmt1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pmt1)***,***[***Pmt6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pmt6)***,***[***Pmt4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pmt4)***,*** [***Pmt3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pmt3)***)*** | PMTC, protein *O*-mannosyltransferase, transfers mannose residues from dolichyl phosphate-D-mannose to protein Ser/Thr residues; it has been shown it also involved in ER quality control. | [[107-109](#_ENREF_107)] |
| 65 | XXX-ERGB |  | XXX\_SEC61C[Endoplasmic Reticulum] + ?Dol-pp\_Man[Endoplasmic Reticulum] + ?Dol-pp\_GlcNAc(2)man(9)\_Glc(3)[Endoplasmic Reticulum] => XXX\_G1\_SEC61C[Endoplasmic Reticulum] + ?Dol-pp[Endoplasmic Reticulum] |  | **O and N-Glycosylation** |  | This reaction stands fort he protiens which they have both *N* and *O*-linked glycosylation sites to get gylcan chain. |  |
| 66 | XXX-FL1 | SEC61C dissociation | XXX-G1-SEC61C[Endoplasmic Reticulum] => XXX-G1[Endoplasmic Reticulum] + SEC61C[Endoplasmic Reticulum] | Irreversible | protein folding |  | After getting the glycan chain and cleavage of the signal peptide the protein disassociated from SEC61C. |  |
| 67 | XXX-FL2 | ER Glycan trimming I | XXX-G1[Endoplasmic Reticulum] => XXX-G2[Endoplasmic Reticulum] + Glc[Endoplasmic Reticulum] | Irreversible | protein folding | [***Cwh41p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cwh41) | Cwh41p (glucosidase I, Gls1) removes the most distal glucose from N-linked oligosaccharides ( Glc3-Man9-GlcNAc2).It is a type II ER transmembrane protein. | [[110](#_ENREF_110)] |
| 68 | XXX-FL3 | ER Glycan trimming II | XXX-G2[Endoplasmic Reticulum] => XXX-G3[Endoplasmic Reticulum] + Glc[Endoplasmic Reticulum] | Irreversible | protein folding | [***Rot2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rot2) | Rot2p ( glucosidase II ,GLS2) is a lumenal enzyme of the ER. It trims the two remaining glucose moieties previously added by Alg8p and Alg6p.  While Mutants lacking Rot2p do not have growth defect but cell wall biosynthesis and degradation of misfolded proteins have shown to be affected. | [[111](#_ENREF_111)] |
| 69 | XXX- FL3.1 | ER Glycan trimming III | XXX-G3[Endoplasmic Reticulum] => XXX-G4[Endoplasmic Reticulum] + Glc[Endoplasmic Reticulum] | irreversible | protein folding | [***Rot2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rot2) | Elemination of the last glucose from the glycan chain. | [[111](#_ENREF_111)] |
| 70 | XXX- FL3.2 | ER demanosylation I | XXX-G4[Endoplasmic Reticulum] => XXX-G5[Endoplasmic Reticulum] + man[Endoplasmic Reticulum] | irreversible | protein folding | [***Mns1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mns1) | Mns1p, type II ER membrane protein ,removes one of the mannose residues added by Alg9p from N-linked core oligosaccharides. This is the last trimming reaction that occurs in the ER before maturing proteins migrate to the Golgi apparatus. | [[112](#_ENREF_112), [113](#_ENREF_113)] |
| 71 | XXX- FL4 | Formation of folding complex with Kar2ATP and disulfide bond formation | XXX-G5[Endoplasmic Reticulum] + 5 Kar2p-ATP[Endoplasmic Reticulum]+ 5 Scj1p[Endoplasmic Reticulum] + 5 Jem1p[Endoplasmic Reticulum] + 5 Sec63p[Endoplasmic Reticulum] => XXX-G5-Kar2ATPcplx[Endoplasmic Reticulum] | reversible | protein folding | [***Kar2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kar2)***,***[***Scj1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=scj1)***,***[***Jem1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=jem1)***,*** [***Sec63p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec63) | Kar2p in the lumen of the ER is an essential protein that is a member of the HSP70 family of molecular chaperones which has the main role in secretory protein folding and translocation. Sec63p; Scj1p; and Jem1p ( DnaJ/HSP40 protein chaperone family) are cochaperones that enhance the ATPase activity of Kar2p. | [[114-120](#_ENREF_114)] |
| 72 | XXX - FL5 | XXX -Sulfation | XXX-G5-Kar2ATPcplx[Endoplasmic Reticulum] + Pdi1p[Endoplasmic Reticulum] + Ero1p[Endoplasmic Reticulum] + O2[Endoplasmic Reticulum] + FADH[Endoplasmic Reticulum] + Erv2p[Endoplasmic Reticulum] => XXX-S-G5-Kar2ATPcplx[Endoplasmic Reticulum] + H2O[Endoplasmic Reticulum] + FAD[Endoplasmic Reticulum] + h[Endoplasmic Reticulum] | irreversible | protein folding | [***Pdi1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pdi1)***,*** [***Ero1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ero1)***,***[***Erv2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=erv2) | Pdi1p is a well characterized enzyme in ER lumen responsible for disulfide bound formation. It is a member of protein disulfide isomerase (PDI family).Both Ero1p and Erv2p have shown to have disulfide isomerase activity with supportive role for Pdi1p activity. | [[116](#_ENREF_116), [121-123](#_ENREF_121)] |
| 73 | XXX – FL6 |  | XXX-G5-Kar2ATPcplx-[Endoplasmic Reticulum] => XXX-F-G5-Kar2ADPcplx[Endoplasmic Reticulum] + 5 Scj1p[Endoplasmic Reticulum] + 5 Jem1p[Endoplasmic Reticulum] + 5 pi[Endoplasmic Reticulum] + Sec63p[Endoplasmic Reticulum] | irreversible | protein folding |  |  |  |
| 74 | XXX- FL7 | Kar2-ADP complex ATP exchange | XXX-S-G5-Kar2ATPcplx-[Endoplasmic Reticulum] => XXX-F-G5-Kar2ADPcplx[Endoplasmic Reticulum] + 5 Scj1p[Endoplasmic Reticulum] + 5 Jem1p[Endoplasmic Reticulum] + 5 pi[Endoplasmic Reticulum] + Sec63p[Endoplasmic Reticulum] + Pdi1p[Endoplasmic Reticulum] + Ero1p[Endoplasmic Reticulum] + Erv2p[Endoplasmic Reticulum] | irreversible | protein folding | [***Scj1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=scj1)***,*** [***Jem1p***](jem1)***,*** [***Sec63p***](sec63) |  |  |
| 75 | XXX-FL8 | Folding complex dissociation | XXX-F-G5-Kar2-ADPcplx[Endoplasmic Reticulum] + 5 Sil1p[Endoplasmic Reticulum] + 5 Lhs1p[Endoplasmic Reticulum] + 5 ATP[Endoplasmic Reticulum] => XXX-F-G5[Endoplasmic Reticulum] + 5 Sil1p[Endoplasmic Reticulum] + 5 Lhs1p[Endoplasmic Reticulum] + 5 ADP[Endoplasmic Reticulum] + 5 Kar2p-ATP[Endoplasmic Reticulum] | irreversible | protein folding | [***Kar2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kar2p)***,***[***Lhs1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=lhs1)***,***[***Sil1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sil1) | Sil1p and Lhs1p promote the subsequent ADP-ATP exchange of the Kar2p. Lhs1p activity affects the refolding and stability of heat-denatured proteins.Sil1p is the main NEFs for Kar2p. | [[116](#_ENREF_116)] |
| 76 | XXX-ERGL1 | Pre budding complex forming for soluble proteins | XXX-F-G5[Endoplasmic Reticulum] + Sar1-GTP[Endoplasmic Reticulum] + sec23-sec24C[Cytoplasm] + Bet1p[Endoplasmic Reticulum] + Bos1p[Endoplasmic Reticulum]=> XXX-F-G5-COPII-pbud-cplx[Endoplasmic Reticulum] | irreversible | COPII (for transmembrane cargo) | [***Sar1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sar1),[***Sec23p***](sec23),[***Sec24p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec24),[***Bet1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet1),[***Bos1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bos1) | The COPII coated formation and cargo detection component for transmembrane cargo which has been shown to use some different component from the soluble or GPI-anchored proteins.  Sar1p,Sec23p and Sec24p are the common protein among the different cargo selection and coat formation mechanism. | [[69](#_ENREF_69)-72] |
| 77 | XXX-ERGL2 | Pre budding complex forming for soluble proteins | XXX-F-G5[Endoplasmic Reticulum] + Sar1-GTP[Endoplasmic Reticulum] + sec23-sec24C[Cytoplasm] + Erv29p[Endoplasmic Reticulum] + Bet1p[Endoplasmic Reticulum] + Bos1p[Endoplasmic Reticulum]=> XXX-F-G5-COPII-pbud-cplx[Endoplasmic Reticulum] | irreversible | COPII(for soluble cargo) | [***Sar1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sar1)***,***[***Sec23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec23)***,***[***Sec24p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=Sec24)***,***[***Erv29p***](Erv29) | selective export of soluble luminal cargo would require specific transmembrane cargo receptors.Yeast Erv29p has been shown to be required for efficient packaging of the glycosylated alpha factor pheromone precursor (gpaf) into COPII vesicles and for efficient secretion of arboxypeptidase Y (CPY) | [[69](#_ENREF_69)-72] |
| 78 | XXX-ERGL3 | Pre budding complex forming for GPI-anchored proteins | XXX-7-G5[Endoplasmic Reticulum] + Sar1-GTP[Endoplasmic Reticulum] + Sec23-Sec24C[Cytoplasm] + Emp24p[Endoplasmic Reticulum] + Bet1p[Endoplasmic Reticulum] + Bos1p[Endoplasmic Reticulum] => XXX-F-G7-COPII-pbud-cplx[Endoplasmic Reticulum] | irreversible | COPII(for GPI-anchored cargo) | [***Sar1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sar1)***,***[***Sec23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec23)***,***[***Sec24p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec24)***,*** [***Emp24p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=emp24) | GPI-anchored proteins also need adaptor for cargo selection like soluble proteins (as they do not have cytoplasmic tail).But according to the experimental evidence they use different kind of transmembrane adaptors than soluble proteins. Emp24 which is from yeast p24 family proteins is one of these studied proteins which have shown to work as adaptor for efficient transport of GPI-anchored cargo. | [[69](#_ENREF_69)-[[124](#_ENREF_124)]72] |
| 79 | XXX- ERGL4 | COPII formation | XXX-F-G7orG5-COPII-pbud-cplx[Endoplasmic Reticulum] + sec13-sec31C[Cytoplasm] + sec16p[Endoplasmic Reticulum] + sed4p[Endoplasmic Reticulum] + Sec5p[Endoplasmic Reticulum] + Sec17p[Endoplasmic Reticulum] => XXX-F-G5orG7-COPII[COPII] | Irreversible | COPII | [***Sec13p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec13)***,***[***Sec31p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec31)***,***[***Sec16p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec16)***,***[***Sed4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sed4)***,*** [***Sec5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec5)***,*** [***Sec17p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec17) | prebudding complex  recruits Sec13-Sec31C heterotetramer providing the outer layer of the coat.Although Sar1p; Sec23p; Sec24p; Sec13p; and Sec31p are necessary and sufficient for vesicle formation; additional factors such as Sec16p and Sed4p are also involved in this process. Through interactions with other COPII proteins; Sec16p is thought to facilitate the assembly of the vesicle coat by stabilizing the pre-budding complex while Sed4p may regulate the vesicle budding process by inhibiting the GAP activity of Sec23p. | [[125-127](#_ENREF_125)] |
| 80 | XXX- ERGL5 | COPII fusion | XXX-F-G5-COPII[COPII] + TRAPPIC[COPII] + Ypt1p[COPII] + GTP[COPII] => XXX-F-G5[Golgi] + sar1-GDP[Cytoplasm] + pi[Cytoplasm] + sec13-sec31C[Cytoplasm] + sec16p[Cytoplasm] + sec12-sed24C[Cytoplasm] + Bet3p[Cytoplasm] + Bet5p[Cytoplasm] + Trs20p[Cytoplasm] + Trs23p[Cytoplasm] + Trs31p[Cytoplasm]+ Trs33p[Cytoplasm] + Bet1p[Endoplasmic Reticulum] + Bos1p[Endoplasmic Reticulum] | Irreversible | COPII (for transmembrane cargo) | ***[Ypt1p](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ypt1),***[***Uso1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=uso1)***,***[***bug1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bug1)***, |TRAPPIC (*** [***Bet3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet3)***,*** [***Bet5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet5)***,***[***Trs20p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs20)***,***[***Trs23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs23)***,***[***Trs31p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs31)***,***[***Trs33p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs33)***)*** | This proteins involve in this reaction summarize the docking and tethering step of the COPII vesicles to the Golgi membrane.Ypt1p is a rab family protein and TRAPPIC acts as NEFs of the Ypt1. Uso1p is an essential protein involved in the vesicle-mediated ER to Golgi transport along with Ypt1p and it is required for assembly of the ER-to-Golgi SNARE complex | [[125](#_ENREF_125)]. [[23](#_ENREF_23), [128-133](#_ENREF_128)] |
| 81 | XXX- ERGL6 | COPII fusion | XXX-5-G5-COPII[COPII] + TRAPPIC[COPII] + Ypt1p[COPII] + GTP[COPII] => XXX-F-G5[Golgi] + sar1-GDP[Cytoplasm] + pi[Cytoplasm] + sec13-sec31C[Cytoplasm] + sec16p[Cytoplasm] + sec12-sed24C[Cytoplasm] + Erv29p[Endoplasmic Reticulum] + 2 Bet3p[Cytoplasm] + Bet5p[Cytoplasm] + Trs20p[Cytoplasm] + Trs23p[Cytoplasm] + Trs31p[Cytoplasm]+ Trs33p[Cytoplasm] + Bet1p[Endoplasmic Reticulum] + Bos1p[Endoplasmic Reticulum] | Irreversible | COPII(for soluble cargo) | [***Ypt1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ypt1)***,***[***Uso1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=uso1)***,***[***bug1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bug1)***, |TRAPPIC (*** [***Bet3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet3)***,*** [***Bet5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet5)***,***[***Trs20p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs20)***,***[***Trs23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs23)***,***[***Trs31p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs31)***,***[***Trs33p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs33)***)*** |  | [[125](#_ENREF_125)]. [[23](#_ENREF_23), [128-130](#_ENREF_128)] |
| 82 | XXX- ERGL7 | COPII fusion | XXX-F-G7-COPII[COPII] + TRAPPIC[COPII] + Ypt1p[COPII] + GTP[COPII] => XXX-F-G7[Golgi] + sar1-GDP[Cytoplasm] + pi[Cytoplasm] + sec13-sec31C[Cytoplasm] + sec16p[Cytoplasm] + Sec23p[COPII] + Sec 24p[COPII] + Emp24p[Endoplasmic Reticulum] + Bet3p[Cytoplasm] + Bet5p[Cytoplasm] + Trs20p[Cytoplasm] + Trs23p[Cytoplasm] + Trs31p[Cytoplasm]+ Trs33p[Cytoplasm] + Bet1p[Endoplasmic Reticulum] + Bos1p[Endoplasmic Reticulum] | Irreversible | COPII(for GPI-anchored cargo) | [***Ypt1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ypt1)***,***[***Uso1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=uso1)***,***[***bug1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bug1)***, |TRAPPIC (*** [***Bet3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet3)***,*** [***Bet5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet5)***,***[***Trs20p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs20)***,***[***Trs23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs23)***,***[***Trs31p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs31)***,***[***Trs33p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=trs33)***)*** |  | [[125](#_ENREF_125)]. [[23](#_ENREF_23), [128-130](#_ENREF_128)] |
| 83 | XXX-GLER1 | COPI formation | XXX-F-G5orG7[Golgi] + Rer1p[Golgi] + Arf1p-GTP[Cytoplasm] + COPIC[Cytoplasm] + Erd2p[Golgi] + COPIV-SNARE[Cytoplasm] <=> XXX-F-G7orG5-COPI[COPI] | Irreversible | COPI | [***Arf1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ARF1),[***Rer1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rer1)***,*** [***Erd2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=erd2)  ***COPIC(*** [***Cop1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cop1)***,*** [***Sec26p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec26)***,*** [***Sec27p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec27)***,*** [***Sec21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec21)***,***[***Ret2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ret2)***,***[***Sec28p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec28)***,***[***Ret3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ret3)***)| COPIV-SNARE*** | Arf1p (member of GTPase Ras superfamily) has a key role in regulating the formation of COPIC (coat complex).Arf1p activity regulation in controlled by guanine nucleotide exchange factors (GEF) such as Gea1p,Gea2p,Sec7p etc. The coat assembly starts and the coatamer complex and cargo selection protein (Rer1p) recruit. | [[134-137](#_ENREF_134)] |
| 84 | XXX- GLER2 | COPI uncoating and fission | XXX-F-G5orG7-COPI[COPI] + Glo3p[Cytoplasm] => XXX-F-G7orG5[Endoplasmic Reticulum] + Arf1p-GDP[Cytoplasm] + Rer1p[Golgi] + Sec27p[Cytoplasm] + Sec21p[Cytoplasm] + Erd2p[Cytoplasm]+ Ret1p[Cytoplasm] + Sec26p[Cytoplasm] + Sec27p[Cytoplasm] + Sec21p[Cytoplasm] + Ret2p[Cytoplasm] + Sec28p[Cytoplasm] + Ret3p[Cytoplasm] + GDP[Cytoplasm] + 2 pi[Cytoplasm] + COPIv-SNARE[Cytoplasm] | Irreversible | COPI | [***Rer1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rer1)***,***[***Ret2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rer2)***,***[***Cop1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cop1)***,***[***Sec27p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec27)***,***[***Sec21p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec21)***,***[***Bet1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=bet1) | The uncoating and fusion are two separate step in ER-Golgi vesicle transport, but for simplicity these processes lumped in one reaction .By hydolysing of the ARF1-GTP the uncoating starts and then the uncoated vesicle bind to the golgi membrane by the t-SNARE s. | [[134](#_ENREF_134), [135](#_ENREF_135)] |
| 85 | XXX- ERADL1 | ER demanosylation II; ERAD check point | XXX-misf-G5[Endoplasmic Reticulum] + 4 Kar2p[Endoplasmic Reticulum] + 2 Pdi1pEndoplasmic Reticulum] + Mnl1p[Endoplasmic Reticulum] + 2 FADH2[Endoplasmic Reticulum] => XXX-misf-G8-cplx[Endoplasmic Reticulum] + man[Endoplasmic Reticulum] + 2 FAD[Endoplasmic Reticulum] | Irreversible | ERADL | [***Mnl1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mnl1)***,*** [***Kar2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kar2)***,***[***Pdi1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pdi1) | Mnl1p/Htm1p (α1;2-specific exomannosidase) generates the Man7GlcNAc2 oligosaccharide with a terminal α1;6-linked mannosyl residue on misfolding proteins. Processing of the N-glycan by glucosidase I; glucosidase II; and mannosidase I is perquisite for Mnl1p exomannosidase activity which result in a sequential order of specific N-glycan structures that reflect the folding status of the glycoprotein.Mnl1p works in complex with Pdi1p and Kar2p. | [[138-140](#_ENREF_138)] |
| 86 | XXX - ERADL2 | Survaliancecplx formation of misfoled protein | XXX-misf-G8-cplx[Endoplasmic Reticulum] + Yos9p[Endoplasmic Reticulum] + Hrd1-Hrd3C[Endoplasmic Reticulum] => XXX-misf-G8-surC[Endoplasmic Reticulum] + 2 Pdi1p[Endoplasmic Reticulum] + 2 Mnl1p[Endoplasmic Reticulum] ERADL] | Irreversible | ERADL | [***Yos9p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=yos9)***,*** [***Hrd3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd3)***,*** [***Hrd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd1)***,*** [***Usa1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=usa1)***,*** [***Der1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=der1) | Yos9p (ER quality-control lectin) is an integral subunit of the HRD ligase and binds to glycans with terminal alpha-1;6 linked mannose on misfolded N-glycosylated proteins and participates in targeting proteins to ERAD. Yos9p in conjunction with Hrd3p triggers the ubiquitin-proteasome–dependent hydrolysis of these glycoproteins. The proteins such as Usa1p and Der1p provide a scaffold for the assembly of degradation machinery. | [[141](#_ENREF_141), [142](#_ENREF_142)] |
| 87 | XXX - ERADL3 | Co retrotranslocation ubiquitin addition to the misfold prtotein | XXX-misf-G8-surC[Endoplasmic Reticulum] + Ubc7p[Cytoplasm] + Cue1p[Cytoplasm] + AAAC[Cytoplasm] => XXX-misf-G8-UBcplx[Endoplasmic Reticulum] + 4 kar2p[Endoplasmic Reticulum] + 2 Pdi1p[Endoplasmic Reticulum] + Yos9p[Endoplasmic Reticulum | Irreversible | ERADL | [***Usa1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=usa1)***, ,***[***Der1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=der1)***,***[***Ubx2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ubx2)***,***  [***Hrd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd1)***,SSH1C(***[***Ssh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ssh1)***,*** [***Sbh2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh2)***,*** [***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***)*** | Hrd3p interacts with Kar2p and Yos9p to specifically target misfolded cytosolic proteins.  Sec61p, the largest and major subunit of the SEC61C( translocon) facilitates backward transport of mis-folded proteins to the cytoplasm for degradation. The other subunits of the Sec61 complex (Sss1p and Sbh1p) stabilize the complex. | [[143](#_ENREF_143), [144](#_ENREF_144)], |
| 88 |  |  | XXX -misf-(G)-UBcplx[Endoplasmic Reticulum] ?ATP[Cytoplasm] + ub => XXX -misf-(G)-UB[Cytoplasm] + Ubc7p[Cytoplasm] + Cue1p[Cytoplasm] + Ubx2p[Endoplasmic Reticulum]+ Cdc48p[Cytoplasm] + Ufd1p[Cytoplasm] + Npl4p[Cytoplasm]+ Hrd3p[Endoplasmic Reticulum] + Hrd1p[Endoplasmic Reticulum] + Usa1p[Endoplasmic Reticulum] + Der1p[Endoplasmic Reticulum] | Irreversible | ERADL | ***SSH1C(*** [***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,*** [***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***,*** [***Ssh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***),*** [***Ubc7p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ubc7)***,*** [***Cue1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cue1)***, AAAC(*** [***Ubx2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ubx2)***,*** [***Cdc48p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cdc48)***,*** [***Ufd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ufd1)***,*** [***Npl4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=npl4)***), Hrd1-Hrd3C(*** [***Hrd3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd3)***,*** [***Hrd1p***](hrd1)***,*** [***Usa1p***](usa1)***,*** [***Der1p***](der1)***)*** | Misfolded luminal and membrane proteins are ubiquitinated by Hrd1p  (ER membrane) . Each ubiquitin ligase complex interacts with the Cdc48p-Npl4p-Ufd1p AAA ATPase complex via Ubx2p in order to extract ubiquitinated substrates from the ER. Hrd1p-Hrd3pC interacts with Kar2p (by Hrd3p) and Yos9p and specifically target misfolded cytosolic proteins. Ubc7p or Ubc1p can act as the ubiquitin-conjugating enzyme (E2) for Hrd1p. Ubc7p interacts with Hrd1p(RING-H2 domain). |  |
| 89 | XXX - ERADL4 |  | XXX-misf-G8-UBcplx[Endoplasmic Reticulum] + 50 ATP[Cytoplasm] + 50 ub[Cytoplasm] + Uba1p[Cytoplasm] => XXX-misf-G8-UB[Cytoplasm] + Ubc7p[Cytoplasm] + Cue1p[Cytoplasm] + Ubx2p[Endoplasmic Reticulum]+ Cdc48p[Cytoplasm] + Ufd1p[Cytoplasm] + Npl4p[Cytoplasm]+ Hrd3p[Endoplasmic Reticulum] + Hrd1p[Endoplasmic Reticulum] + Usa1p[Endoplasmic Reticulum] + Der1p[Endoplasmic Reticulum] | Irreversible | ERADL | [***Dsk2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=dsk2)***,***[***Rad23p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=rad23)***,***[***Png1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=png1)***,*** [***Uba1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=uba1) |  |  |
| 90 | XXX-ERADL5 |  | XXX-misf-G8-UB[Cytoplasm] + Png1[Cytoplasm] + 50 ATP[Cytoplasm] + 26sproteosome[Cytoplasm] + 50 H2O[Cytoplasm] => G8[Cytoplasm] + 50 Uniquitin[Cytoplasm] + 50 ADP[Cytoplasm] + 50 pi[Cytoplasm] + aminoacid[Cytoplasm] | Irreversible | ERADL |  |  |  |
| 91 | XXX-ERADM1 |  | XXX-misf-G8-cplx[Endoplasmic Reticulum] + Yos9p[Endoplasmic Reticulum] + Hrd1p-Hrd3pC[Endoplasmic Reticulum] => XXX-misf-G8-HRDcplx[Endoplasmic Reticulum] | Irreversible | ERADM | [***Yos9p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=yos9)***, HRD[***[***Hrd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd1)***,*** [***Hrd3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hrd3)***]*** | Substrates with misfolded intramembrane domains define a use ERAD-M pathway whicht differs from ERAD-L and ERAD-C its independence of Usa1p and Der1p.  Substrates of the ERAD-M pathway may be targeted to the ubiquitin ligase Hrd1p by Yos9p, as is the case for the glycosylated substrate Pdr5\*, or by other factors that are too loosely associated to be detected by pull-down experiments. | [[10](#_ENREF_10), [145](#_ENREF_145)] |
| 92 | XXX-ERADM2 |  | XXX-misf-G8-HRDcplx[Endoplasmic Reticulum] + Ubc7p[Cytoplasm] + Cue1p[Cytoplasm] + AAAC[Cytoplasm] => XXX-misf-G8-UBcplx[Endoplasmic Reticulum] + Hrd3p[Endoplasmic Reticulum] + Hrd1p[Endoplasmic Reticulum] + Usa1p[Endoplasmic Reticulum] + Der1p[Endoplasmic Reticulum] + Yos9p[Endoplasmic Reticulum] | Irreversible | ERADM | ***AAAC(***[***Ubx2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ubx2)***,*** [***Cdc48p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cdc48)***,***[***Ufd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ufd1)***,*** [***Npl4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=npl4)***)*** | The rest of the ERAD-M pathway would be similar to that of ERAD-L substrates, employing the  Cdc48p ATPase complex and the adaptor Ubx2p. However,ERAD-M might either use a smaller channel consisting of Hrd1p alone or directly be extracted from the membrane, as what it has been shown to happen for bacterial FtsH protein . | [[10](#_ENREF_10), [146](#_ENREF_146)] |
| 93 | XXX-ERADM3 |  | XXX-misf-G8-UBcplx[Endoplasmic Reticulum] + 50 ATP[Cytoplasm] + 50 ub[Cytoplasm] => XXX-misf-G8-UB[Cytoplasm] + Ubc7p[Cytoplasm] + Cue1p[Cytoplasm] + Ubx2p[Endoplasmic Reticulum]+ Cdc48p[Cytoplasm] + Ufd1p[Cytoplasm] + Npl4p[Cytoplasm] Hrd3p[Endoplasmic Reticulum] + Hrd1p[Endoplasmic Reticulum] + Usa1p[Endoplasmic Reticulum] + Der1p[Endoplasmic Reticulum] | Irreversible | ERADM |  |  |  |
| 94 | XXX-ERADM4 |  | XXX-misf-G8-UB[Cytoplasm] + Dsk2pp[Cytoplasm] + Rad23pp[Cytoplasm] + Png1p[Cytoplasm] + 50 ATP[Cytoplasm] + 26sproteosome[Cytoplasm] + 50 H2O[Cytoplasm] => G8[Cytoplasm] + 50 Uniquitin[Cytoplasm] + 50 ADP[Cytoplasm] + 50 pi[Cytoplasm] + aminoacid[Cytoplasm] | Irreversible | ERADM |  |  |  |
| 95 | XXX-ERADC1 |  | XXX-misf-G6[Cytoplasm] + Doa10p[Endoplasmic Reticulum] + SSH1C[Endoplasmic Reticulum] + AAAC[Cytoplasm] => XXX-misf-G6-UBcplx[Cytoplasm] | Irreversible | ERADC | [***Sbh1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sbh1)***,*** [***Sss1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sss1)***, Ssh1p|AAAC(*** [***Ubx2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ubx2)***,*** [***Cdc48p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=cdc48)***,*** [***Ufd1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ufd1)***,*** [***Npl4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=npl4)***)*** | ERAD-C pathway is potential to degrade the membrane proteins with cytoplasmic misfolded domain. While the core proteins are the same, it is shown that the deletion of USA1 does not affect the degradation of ERAD-C substrate. Also, Usa1p is functionally required for the ERAD-L but not the ERAD-C pathway. Similar to the other ERAD pathways the for the degradation part ERAD-C use also use the common protein machinery AAAC and proteasome. | [[145](#_ENREF_145), [147](#_ENREF_147)] |
| 96 | XXX-ERADC2 |  | XXX-misf-G6-UBcplx[Endoplasmic Reticulum] + 50 ATP[Cytoplasm] + 50 ub[Cytoplasm] => XXX-misf-G6-UB + 50 ADP[Cytoplasm] + Doa10p[Endoplasmic Reticulum] Sbh1p[Endoplasmic Reticulum] + Sss1p[Endoplasmic Reticulum] + Ssh1p[Endoplasmic Reticulum] + Ubx2p[Endoplasmic Reticulum]+ Cdc48p[Cytoplasm] + Ufd1p[Cytoplasm] + Npl4p[Cytoplasm] + 50 pi[Cytoplasm] | Irreversible | ERADC |  |  |  |
| 97 | XXX-ERADC3 |  | XXX-misf-G6-UB[Cytoplasm] + Dsk2p[Cytoplasm] + Rad23p[Cytoplasm] + Png1[Cytoplasm] + 50 ATP[Cytoplasm] + 26s proteosome[Cytoplasm] + 50 H2O[Cytoplasm] => G6[Cytoplasm] + 50 Uniquitin[Cytoplasm] + 50 ADP[Cytoplasm] + 50 pi[Cytoplasm] + aminoacid[Cytoplasm] | Irreversible | ERADC |  |  |  |
| 98 | XXX- GLNMAN1 | Golgi N-linked glycosylation I | XXX-G5orG7[Golgi] + GDP-man[Golgi] => XXX-G9[Golgi] + GDP[Golgi] | Irreversible | Golgi processing | [***Och1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=och1) | Och1p( *cis*-Golgi membrane-bound alpha-1;6-mannosyltransferase ) adds a mannose moiety to core N-linked oligosaccharides upon their arrival in the Golgi apparatus. This is the last modification before the N-linked glycosylation pathway forks to produce either large mannan outer chains or small core-type oligosaccharides. | [[148](#_ENREF_148), [149](#_ENREF_149)]. |
| 99 | XXX- GLNMAN2 | Golgi N-linked glycosylation II | XXX-G9[Golgi] + 5 GDP-man[Golgi] => XXX-G10[Golgi] + 5 GDP[Golgi] | Irreversible | Golgi processing | ***M POL I(***[***Mnn9p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mnn9)***,*** [***Van1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=van1)***)*** | M-Pol I is a heterodimeric complex consisting of one copy of Van1p and one copy of Mnn9p.Mnn9p Acts as Both an α-1;2- and an α-1;6-Mannosyltransferase. Both proteins contribute to mannose olymerization in The Golgi.Mnn9p also take part in M Pol II complex. | [[150](#_ENREF_150)] |
| 100 | XXX- GLNMAN3 | Golgi N-linked glycosylation III | XXX-G10[Golgi] + 40 GDP-man[Golgi] => XXX-G11[Golgi] + 40 GDP[Golgi] | Irreversible | Golgi processing | ***M Pol II complex (***[***Anp1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=anp1)***,*** [***Mnn9p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mnn9)***,*** [***Mnn10p***](mnn10)***,*** [***Mnn11p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mnn11)***,*** [***Hoc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=hoc1)***)*** | M-Pol II, Golgi mannosyltransferase complex, involves five subunits (at least two of which are present in multiple copies). It contains Mnn9p Anp1p, Mnn10p, Mnn11p, and Hoc1p and elongate the polysaccharide mannan chain | [[150](#_ENREF_150)] |
| 101 | XXX GLOMAN1 | Golgi N-linked pro-peptide hydrolase | XXX-G12[Golgi] + GDP-man[Golgi] => XXX-G13[Golgi] + GDP[Golgi] | Irreversible | Golgi processing | [***Kre2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kre2)***,***[***Ktr1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ktr1)***,***[***Ktr3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ktr3) | Ktr1p and Ktr3p along with the Kre2p/Mnt1p α1,2-mannosyltransferase participate in the addition of the second mannose residue onto O-linked chains. Kre2p has been known to be the main enzyme responsible for the addition of the third mannose on O-glycans. Ktr1p and Ktr3p are also able to add this particular mannose, although to a lesser extent than Kre2p. | [[151-153](#_ENREF_151)] |
| 102 | XXX- GLOMAN3 | First golgi N-linked O –linked manosylation | XXX-G13[Golgi] + GDP-man[Golgi] => XXX-G14[Golgi] + GDP[Golgi] | Irreversible | Golgi processing | [***Kre2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kre2) | Kre2, alpha-1,2-mannosyltransferase which together with Ktr1p and Ktr3p is responsible for the second and the third α1,2-linked mannose residues on O-linked carbohydrate chains and that also participate in N-linked outer chain elaboration. , | [[151](#_ENREF_151)] |
| 103 | XXX- GLOMAN3 | Second golgi N-linked O –linked manosylation | XXX-G14[Golgi] + GDP-man[Golgi] => XXX-15[Golgi] + GDP[Golgi] | Irreversible | Golgi processing | [***Mnn1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=mnn1) | The Mnn1p α1,3- annosyltransferase attaches the fourth mannose residue in the linear chain of up to five mannose residues | [[151](#_ENREF_151)] |
| 104 | XXX- GP | golgi N-linked O –linked pro-peptide hydrolization | XXX-G15[Golgi] => XXX-G16[Golgi] + aminoacid[Golgi] | Irreversible | Golgi processing | [***Kex1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kex1)***,***[***Kex2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=kex2)***,***[***Ste13p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=ste13) | Maturation of the proteins in The Golgi needs cleavage of the polypeptide chain. There are three known protease (Kex1p, Kex2p and Ste13p) in yeast Golgi which are specific to sequence motifs and provide the proteins to be catalytically active or be able to bind to specific receptor. | [[154](#_ENREF_154)] |
| 105 | XXX- ALP | Direct vacuol transit pathway | XXX-M1[Golgi] + 4 GTP[Cytoplasm] + clathrinC[Cytoplasm] + Arf1p[Cytoplasm] + AP3C[Cytoplasm] + Vps1p[Cytoplasm] + Swa2p[Cytoplasm] => XXX-M1[vacuole] + 4 GDP[Cytoplasm] + + Arf1p[Cytoplasm] + Apl6p[Cytoplasm] + Aps3p[Cytoplasm] + Apm3p[Cytoplasm] + Apl5p[Cytoplasm] + Vam3p[Vacuole] + Vps1p[Cytoplasm] + Swa2p[Cytoplasm] | Irreversible | ALP pathway(AP-3 complex) | ***AP3C(*** [***Apl6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl6)***,*** [***Aps3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps3)***,*** [***Apm3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apm3)***,*** [***Apl5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl5)***,***[***Vam3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vam3) ***)|t-SNARE|*** [***Arf1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=arf1)***| clathrinC(***[***Chc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=chc1)***,***[***Clc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=clc1)***)***  ***Vps1p,Swa2p*** | After Golgi processing the mature protein can transport to many destination depended on final localization. ALP pathway is one of the known trafficking routes from Golgi to vacuole. Many key proteins involved as detecting ( ***Vps1p,Swa2p)***, tethering(,ClathrinC,Arf1p) and docking(t-SNAREC) of the vesicles ALP pathway are characterized. Apm3:Mu3-like subunit of the clathrin associated protein complex (AP-3); Apl6: Beta3-like subunit of the AP-3 complex;Aps3p: Small subunit of the clathrin-associated adaptor complex AP-3; Apl5p: Delta adaptin-like subunit of the clathrin associated protein complex (AP-3) are among these proteins which are involved in this transport route. | [[21](#_ENREF_21), [155](#_ENREF_155)] |
| 106 | XXX- CPY1 | CPYI | XXX-M1[Golgi] + 4 GTP[Cytoplasm] + Pep12p[endosome] + Vps45p[endosome] + Vps5p[Golgi] + clathrinC[Cytoplasm] + Arf1p[Cytoplasm] + Gga1p[Cytoplasm] + Gga2p[Cytoplasm] + AP1C[Cytoplasm] + Swa2p[Cytoplasm] => XXX-M1[endosome] + 4 GDP[Cytoplasm] + Pi[Cytoplasm] + Apl6p[Cytoplasm] + Aps3p[Cytoplasm] + Apm3p[Cytoplasm] + Apl5p[Cytoplasm] + Vam3p[Vacuole] + 2 Chc1p[Cytoplasm] + Clc1p[Cytoplasm] | Irreversible | CPY pathway | ***CPYIC,*** [***Gga1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gga1)***,*** [***Gga2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=gga2)***,*** [***Arf1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=arf1);***AP1C(*** [***Apl4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl4)***,*** [***Apl2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl2)  [***Apm1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apm1)***,***  [***Aps1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps1)***;clathrinC(***[***Chc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=chc1)***,***[***Clc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=clc1)***);***  [***Pep12p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pep12)***,*** [***Vps45p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vps45) | CPY pathway is the defult route to the vacuole from Golgi apparatus.A two step process using AP complexes. The pathway is named because it has mainly been  studied in the for trafficking of carboxypeptidase Y (CPY) to the vacuole. AP-1C complex vesicles can transfer proteins from the trans-Golgi to the early or late  endosome. After this, the AP-3C complex vesicle moves proteins from the Golgi/endosome to vacuole. | [[20](#_ENREF_20), [37](#_ENREF_37), [156](#_ENREF_156)] |
| 107 | XXX- CPY2 | CPYII | XXX-M1[endosome] + ATP[Cytoplasm] + CPYIIC[Cytoplasm] + AP3C[Cytoplasm] => XXX-M1[vacuole] + ADP[Cytoplasm] + pi[Cytoplasm] + Vps5p[Golgi] + 2 Chc1p[Cytoplasm] + Clc1p[Cytoplasm] + Gga1p[Cytoplasm] + Gga2p[Cytoplasm] + Apl4p[Cytoplasm] + Apl2p[Cytoplasm] + Apm1p[Cytoplasm] + Aps1p[Cytoplasm + Swa2p[Cytoplasm] + Arf1p[Cytoplasm] + Vps4p[endosome] + Vps27p[endosome] + Pep12p[endosome] + Vps45p[endosome] | Irreversible | CPY pathway | ***CPYIIC |AP3C(*** [***Apl6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl6)***,*** [***Aps3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps3)***,*** [***Apm3p***](apm3)***,***[***Apl5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl5)***,***[***Vam3p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vam3) ***)*** |  | [[157](#_ENREF_157)] |
| 108 | XXX-LDSV | LDSV secretion | XXX-M1[Golgi] + GTP[Cytoplasm] + clathrinC[Cytoplasm] + Arf1p[Cytoplasm] + EXOC[Cytoplasm] => XXX-M1[cell membrane] + GDP[Golgi] + 2 Chc1p[Cytoplasm] + Clc1p[Cytoplasm] + Arf1p[Cytoplasm] + Sec3p[Cytoplasm]+ Sec5p[Cytoplasm]+ Sec6p[Cytoplasm]+ Sec8p[Cytoplasm]+ Sec10p[Cytoplasm]+ Sec15p[Cytoplasm]+ Exo70p[Cytoplasm]+ Exo84p[Cytoplasm]+ sec4p[Cytoplasm] | Irreversible | LDSV(low density secretory vesicle) | [***Arf1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=arf1); ***LDSV([Sec3p](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec3),*** [***Sec5p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec5)***,*** [***Sec6p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec6)***,*** [***Sec8p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec8)***,*** [***Sec10p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec10)***,*** [***Sec15p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec15)***,*** [***Exo70p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec70)***,*** [***Exo84p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=exo84)***,***[***Sec4p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=sec4)***)| ;clathrinC(*** [***Chc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=chc1)***,*** [***Clc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=clc1)***)*** | There are two types of vesicle( pathway) for proteins that will follow the exocytotic pathway from the trans-Golgi called light density secretory vesicles (LDSV) and heavy density secretory vesicles (HDSV)(upon density-based separation experiments). LDSV are known to carry  constitutively expressed cell membrane proteins, such as Bgl2p, Pma1p, and Gas1p and believed to emerge from the trans-Golgi and transit directly to the cell  membrane.  : | [[42-45](#_ENREF_42)] |
| 109 | XXX- HDSV1 | HDSV secretion | XXX-M1[Golgi] + GTP[Cytoplasm] + clathrin[Cytoplasm] + Arf1p[Cytoplasm] + Pep12p[endosome] + AP1C[Cytoplasm] + Swa2p[Cytoplasm] => XXX-M1[endosome] + GDP[Cytoplasm] + Pi[Cytoplasm] + 2 Chc1p[Cytoplasm] + Clc1p[Cytoplasm] | Irreversible | HDSV(high density secretory vesicle) | [***Arf1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=arf1)***,*** [***Pep12p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=pep12)***,*** [***Swa2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=swa2)***| clathrinC( [Chc1p](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=chc1),*** [***Clc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=clc1)***)| APC1( [Apl4p](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl4),*** [***Apl2p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apl2)  [***Apm1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=apm1)***,***  [***Aps1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=aps1)***)|*** |  | [[45](#_ENREF_45), [158](#_ENREF_158)] |
| 110 | XXX- HDSV2 | HDSV secretion | XXX-M1[endosome] + GTP[Cytoplasm] + clathrin[Cytoplasm] => XXX-M1[extracellular] + GDP[Cytoplasm] + Arf1p[Cytoplasm] + Pep12p[endosome] + Apl4p[Cytoplasm] + Apl2p[Cytoplasm] + Apm1p[Cytoplasm] + Aps1p[Cytoplasm] + 2 Chc1p[Cytoplasm] + Clc1p[Cytoplasm] | Irreversible | HDSV(high density secretory vesicle) | [***Vps1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=vps1) ***|clathrinC(*** [***Chc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=chc1)***,*** [***Clc1p***](http://www.yeastgenome.org/cgi-bin/locus.fpl?locus=clc1)***)*** | HDSV vesicles package soluble, secreted proteins, such as invertase  (Suc2p) and acid phosphates (Pho11p, Pho12p, Pho5p) that are transcriptionally regulated and induced under certain conditions. HDSV move from the endosome to the cell membrane, and are thus subject to many of the mutations that block movement to and through the early/late endosome . These mutants, that block the HDSV pathway, were shown to use the LDSV pathway for secretion of proteins normally bound for HDSV pathway. | [[45](#_ENREF_45)] |
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