

## Supplemental Data

### **The Sec61/SecY complex is inherently deficient in translocating intrinsically disordered proteins**

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**TABLE S1. Primary and secondary structure of constructs.**

Primary and secondary structure of proteins used in this study in FASTA-like format.  $\alpha$ -helix: framed;  $\beta$ -strand: bold and labeled in grey; epitope tag: italic and light grey, asterisk: secondary structure based on Jpred 4 prediction.

**Signal peptides:**

**PrP:** MANLGYWLLALFVTMWTDVGLC

**pelB:** MKYLLPTAAAGLLLLAAQPAM

**dsbA:** MKKIWLALAGLVLAFSASA

**kre5p:** MRLALVLLLLCAPLRA

**Shadoo:** MNWAPATCWALLLAAAFLCDSGAA

**Primary and secondary structures of the constructs without signal peptide:**

**$\alpha$ :**

GGLGGYMLGSAMSRPMIHFGND  $\alpha$  WEDRYRENMYRYPNQVYRYPVDQYSNQNFVHDCVNITIKQHTVTTTTK  $\alpha$  GENFTE  $\alpha$  TDVKM  
MERVVEQMCVTQYQKES  $\alpha^*$  QAYYDGRSSSTVLFSSPP  $\alpha^*$  VILLISFLIFLI  $\alpha^*$  IVG

**$\alpha$  (PB):**

KKRPKPGGWNTGGGLGGYMLGSAMSRPMIHFGND  $\alpha$  WEDRYRENMYRYPNQVYRYPVDQYSNQNFVHDCVNITIKQHTVTTTTK  $\alpha$   
 $\alpha$  K GENFTE  $\alpha$  TDVKMERVVEQMCVTQYQKES  $\alpha^*$  QAYYDGRSSSTVLFSSPP  $\alpha^*$  VILLISFLIFLI  $\alpha^*$  IVG

**IDD114:**

PGGNFTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPKTNMKH  
MAGA

**IDD133:**

KKRPK/AAAPA-PGGNFTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQW  
NKPSKPKTNMKHMAGAAAAGAVVGGGLGGYMLGSAM

**IDD209:**

KKRPK/AAAPA-PGGNFTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQW  
NKPSKPKTNMKHMAGAAPRKKRPKPGGWNTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGG  
GWQGGGTHNQWNKPSKPKTNMKHMAGA

**IDD $\cdot\alpha$ :**

KKRPK/AAAPA-PGGWNTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQW  
NKPSKPKTNMKHMAGAQNFVHDCVNITIKQHTVTTTTK  $\alpha$  GENFTE  $\alpha$  TDVKMERVVEQMCVTQYQKES

**$\alpha$ •IDD:**

QNFVHDCVNITIKQHTVTTTTK  $\alpha$  GENFTE  $\alpha$  TDVKMERVVEQMCVTQYQKES KKRPK/AAAPA-PGGWNTGGSRYPGQSPGGN  
RYPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPKTNMKHMAGA

**$\alpha$ •IDD•IDD:**

QNFVHDCVNITIKQHTVTTTTK  $\alpha$  GENFTE  $\alpha$  TDVKMERVVEQMCVTQYQKES KKRPKPGGWNTGGSRYPGQSPGGNRYPPQGG  
TWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPKTNMKHMAGAAPRKKRPKPGGWNTGGSRYPGQ  
SPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGGWQPHGGGWQGGGTHNQWNKPSKPKTNMKHMAGA

**IDD• $\alpha$ •IDD:**

KKRPKPGGWNTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPK  
TNMKHMAGAQN <sup>$\alpha$</sup> NFVHDCVNITIKQHTVTTTTKGENFTE <sup>$\alpha$</sup> TDVKMMERVVEQMCVTQYQKESKKRPKPGGWNTGGSRYPGQSPG  
GNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPKTNMKHMAGA

**IDD•IDD• $\alpha$ :**

KKRPKPGGWNTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPK  
TNMKHMAGAAPRKKRPPGGWNTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGG  
THNQWNKPSKPKTNMKHMAGAQN <sup>$\alpha$</sup> NFVHDCVNITIKQHTVTTTTKGENFTE <sup>$\alpha$</sup> TDVKMMERVVEQMCVTQYQKES

**IDD• $\beta$ :**

KKRPKPGNFTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPK  
TNMKHMAGA <sup>$\beta$</sup> YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNILGHKLEYNYNSHNVYIMADKQKNGIKVNF  
KIRHNIEDGSVQLADHYQQNTPIGDGPVLLPDNHYLSTQSALS KDPNEKRDMVLEFVTAAGITLGMDELYK

**$\alpha$ • $\beta$  (HA):**

QN <sup>$\alpha$</sup> NFVHDCVNITIKQHTVTTTTKGENFTE <sup>$\alpha$</sup> TDVKMMERVVEQMCVTQYQKES <sup>$\beta$</sup> YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRI  
ELKGIDFKEDGNILGHKLEYNYNSHNVYIMADKQKNGIKVNFKIRHNIEDGSVQLADHYQQNTPIGDGPVLLPDNHYLSTQSA  
LSKDPNEKRDMVLEFVTAAGITLGMDELYK<sup>HA</sup>AAAYPYDVPDYA

**$\beta$  (HA):**

KKRPK/AAAPA-PGGNFTGGSRYG <sup>$\beta$</sup> YVQERTIFFKDDGNYKTRAEVKFEGDTLVNRIELKGIDFKEDGNILGHKLEY NYNSHN  
VYIMADKQKNGIKVNFKIRHNIEDGSVQLADHYQQNTPIGDGPVLLPDNHYLSTQSALS KDPNEKRDMVLEFVTAAGITLGM  
DELYK<sup>HA</sup>AAAYPYDVPDYA

**Prion protein:**

KKRPK/AAAPA-PGGWNTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQW  
NKPSKPKTNMKHMAGAAAAGAVVGLGGYMLGSAMS RPMIHFND <sup>$\alpha$</sup> WEDRYRENMYRYPNQVYRQYVYRPNQNFVHDCVNIT  
 <sup>$\alpha$</sup> TIKQHTVTTTTKGENFTE <sup>$\alpha$</sup> TDVKMMERVVEQMCVTQYQKESQAYYDGRSSSTVLFSSPP <sup>$\alpha^*$</sup> VILLISFLIFLIIVG

**Shadoo (V5):**

MKGGRGARGSARGGVRGARGASRVVRPAQRYGAPGSSLRVAAAGAAAGAAAGAAAGLAAGSGWRRRAAGPGERGLEDEEDG  
VPGNGTGPGIYSYRAWT<sup>V5</sup>GKPIPNPLLGLDSTSGAGPTRGPRCLV <sup>$\alpha$</sup> LGGALGALGLLRP

**IDD114•Syn:**

KKRPKPGNFTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPK  
TNMKHMAGADVFMKGLSKAKEGVVAAA EKTQGVAAEAGKTKEGVLYVGSKTKEGVVHGVATVAEKTKEQVTNVGGAVVTGVT  
AVAQKTVEGAGSIAAATGFVKKDQLGKNEEGAPQEGILEDMPVDPDNEAYEMPSEEGYQDYEPEA

**IDD114•Tau:**

KKRPKPGNFTGGSRYPGQSPGGNRYPPQGGTWGQPHGGGWQPHGGSWGQPHGGSWGQPHGGGWQGGGTHNQWNKPSKPK  
TNMKHMAGAAEEAGNGDTPSLEDEAAGHVTQARMVSKSKDGTGSDDKAKAGADGKTKIATPRGAAPPQKQGANATRIPAKTP  
PAPKTPPSSGEPKSGDRSGY