Spliceosome nanomachinery
is coded by more than **100 genes**

Every human **cell** contains
~ 100.000 spliceosomes

It takes **20-30 s to transcript
and excise** a short intron (1.3 - 1.4 Kb)

35 % of human **genetic disorders**
are caused by **splicing alterations**

Mutations in spliceosome have been linked to
retinitis pigmentosa and **cancers**

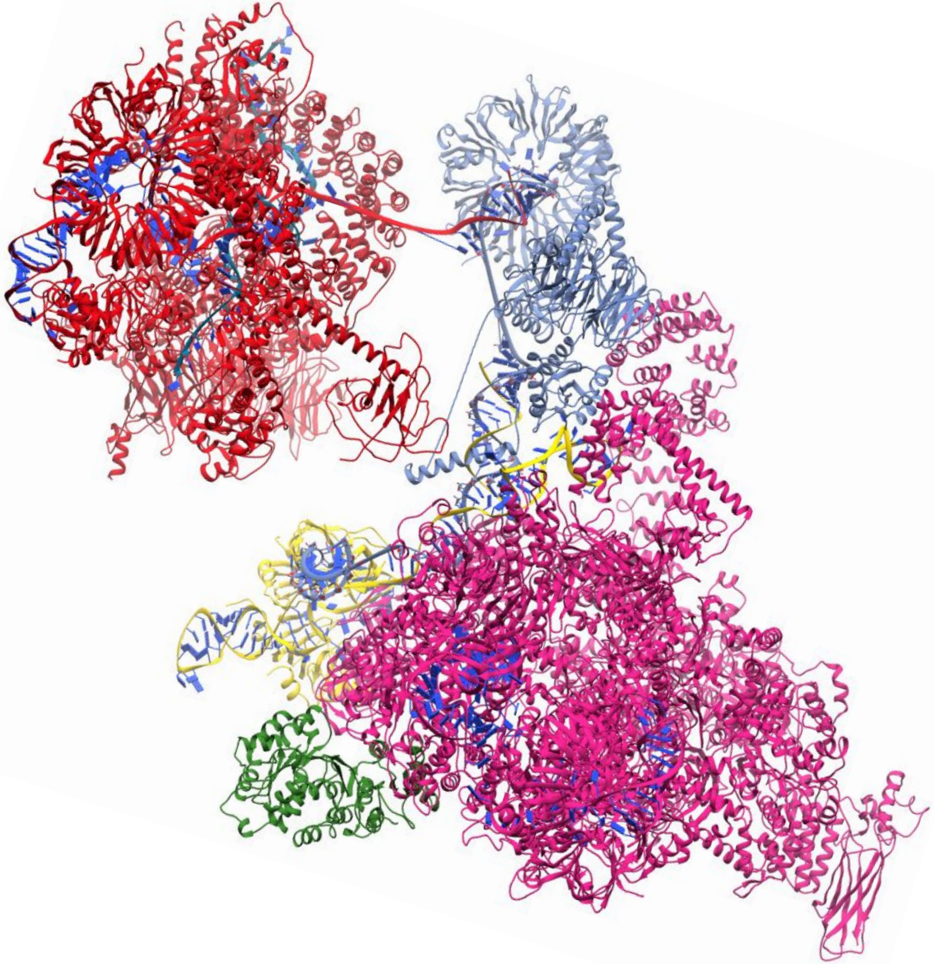
Discovered in 1977 by Philip Sharp and Richard J. Roberts **(Nobel 1993)**

The Spliceosome

U2 protein complex

and a closer look into

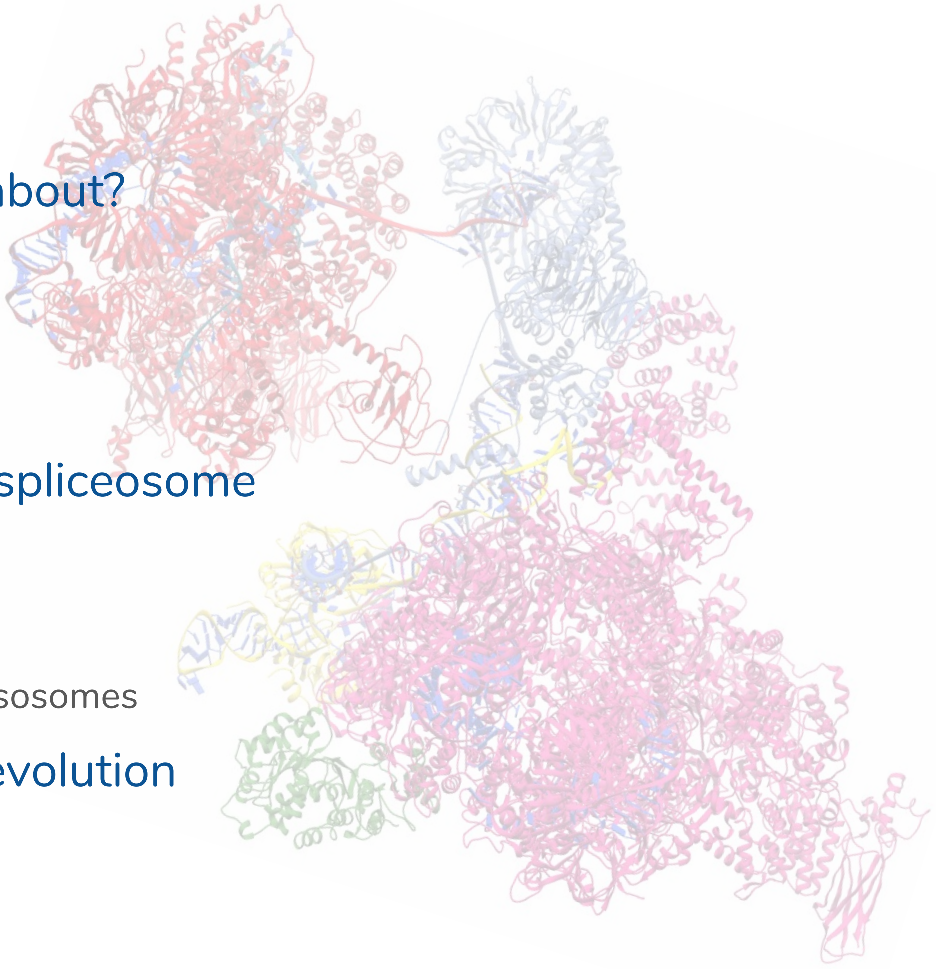
Splicing Factor 3a



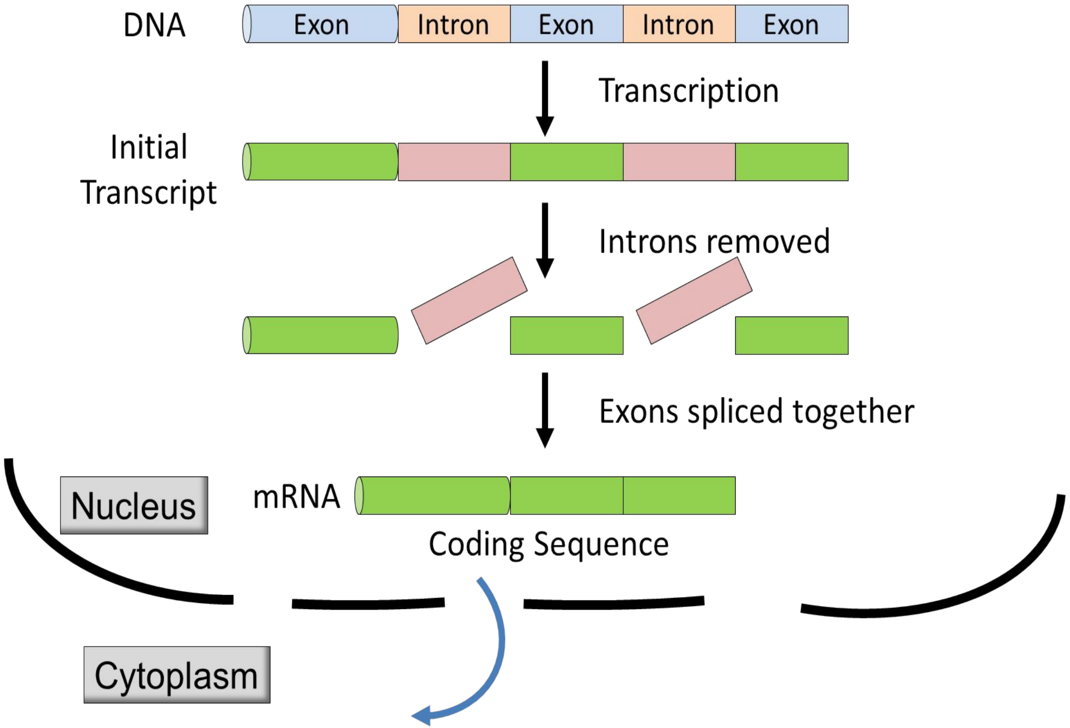
Universitat Pompeu Fabra Barcelona

Ona Baguer, Carlota Cerrillo,
Florian Conrad, Clara Escala

Contents



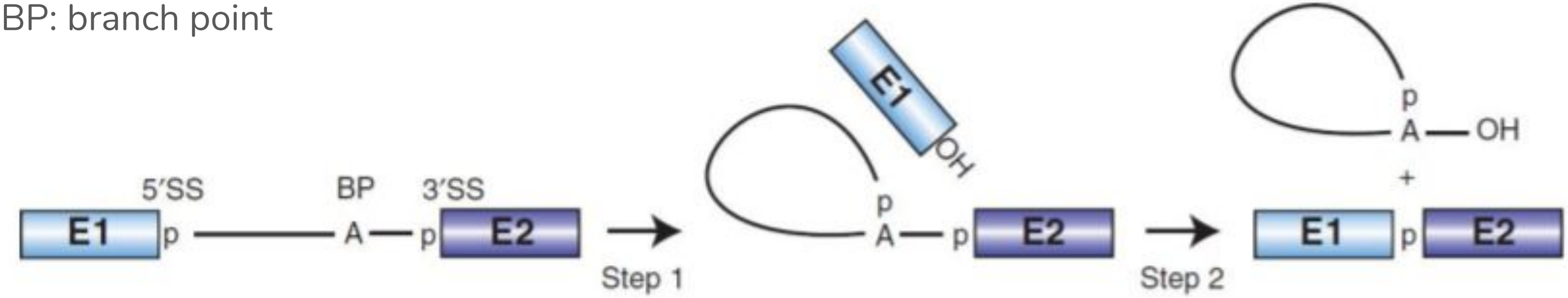
Splicing: what are we talking about?



Protein-coding genes in humans contain typically 9-10 introns, but some > 100

SS: splice site

BP: branch point

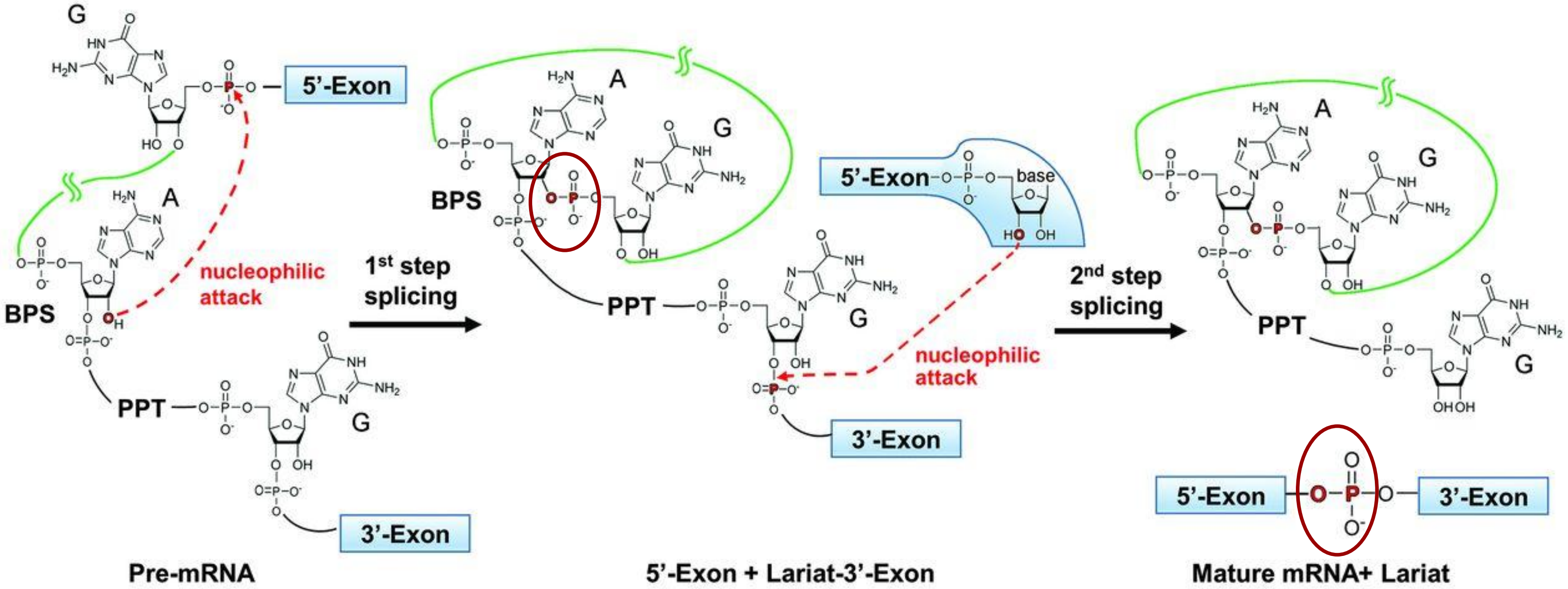


Step 1. 2’OH (branch-point adenosine) ➛ PO_4 (between 5’ **exon$_1$** and **intron**)

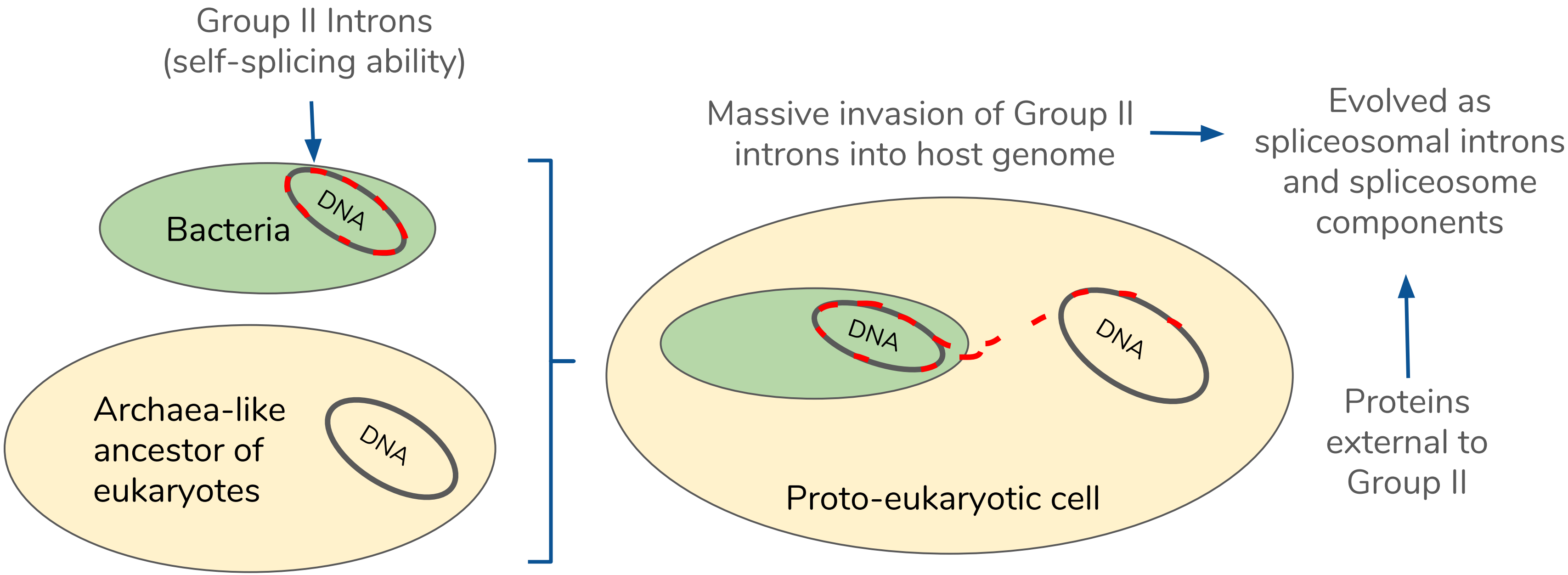
↬ *Formation of **lariat** harboring a 2’-5’ phosphodiester bond*

Step 2. 3’OH (5’ **exon$_1$**) ➛ PO_4 (between **intron** and 3’ **exon$_2$**)

Extracted from: Weaver R.F. Molecular Biology. Boston: McGraw-Hill, 1999.



Extracted from: Hang J, Wan R, Yan C, Shi Y. Structural basis of pre-mRNA splicing. Science. 2015;349(6253):1191-8.



Group II Introns
(self-splicing ability)

Bacteria

DNA

Archaea-like
ancestor of
eukaryotes

DNA

Massive invasion of Group II
introns into host genome

Evolved as
spliceosomal introns
and spliceosome
components

DNA

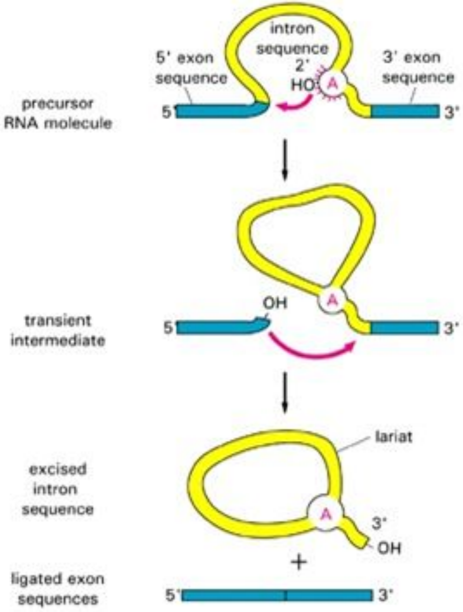
DNA

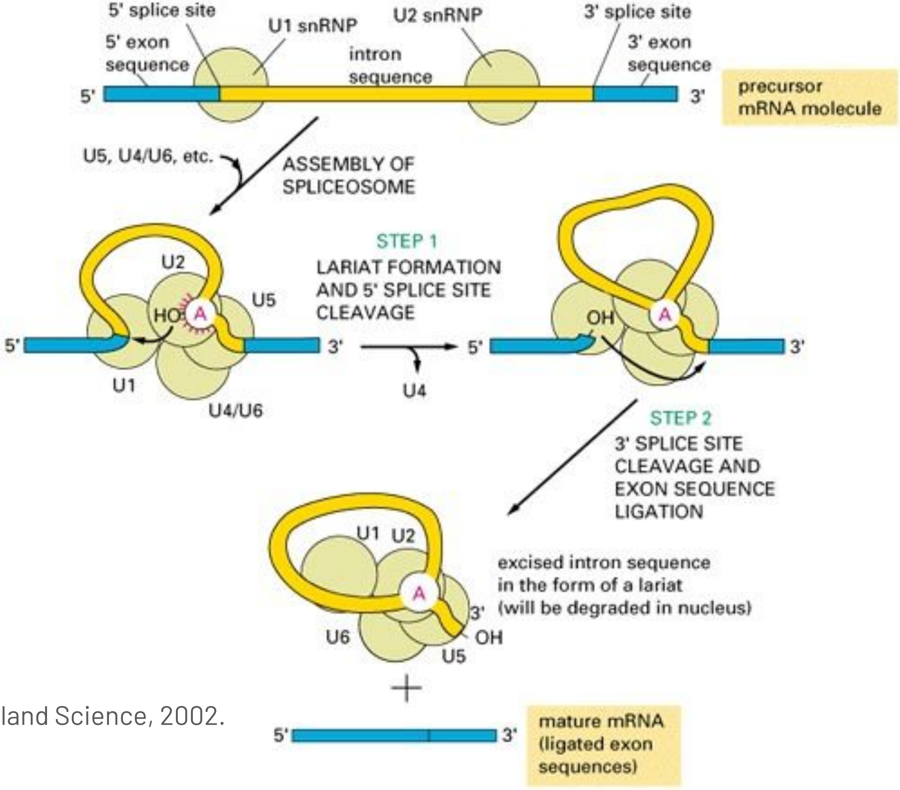
Proto-eukaryotic cell

Proteins
external to
Group II

Group II introns

Spliceosomal introns





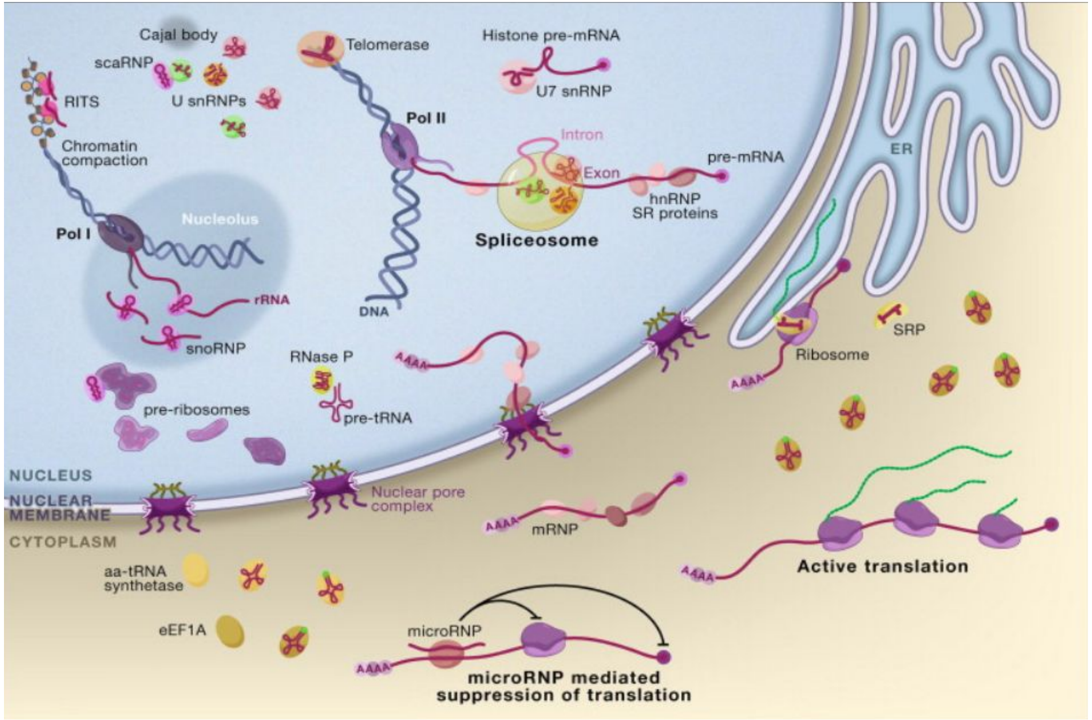
Extracted from: Alberts B. Molecular Biology of the Cell. New York: Garland Science, 2002.

Eukaryote-specific
RNA-protein complex

5 snRNPs* with
over **100 proteins**

Major and **minor**
spliceosome

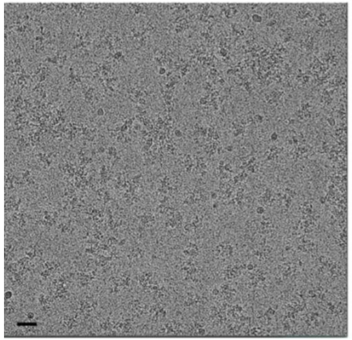
Major spliceosome: ~ **99.5%** of
human **intron removal**



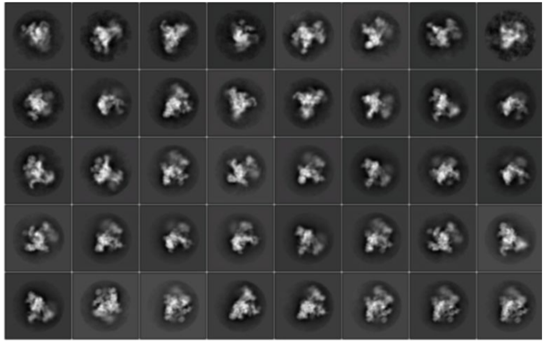
*snRNP: small nuclear ribonucleoprotein particles

Extracted from: Wahl M, Will C, Lührmann R. The Spliceosome: Design Principles of a Dynamic RNP Machine. Cell. 2009; 136(4): 701-718.

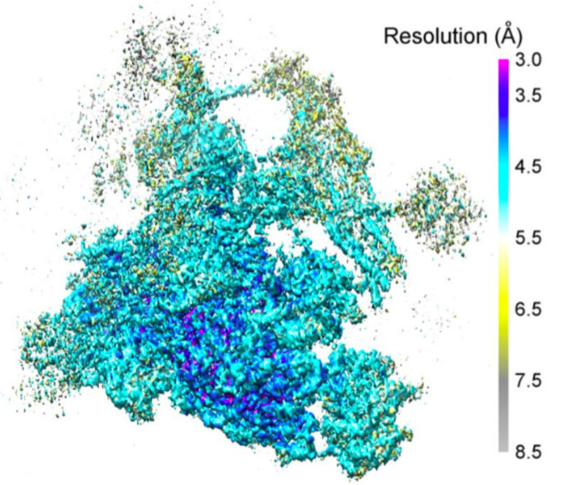
Cryo- Electron Microscopy



Cryo-EM micrograph of the yeast spliceosomal complex. Scale bar, 30 nm

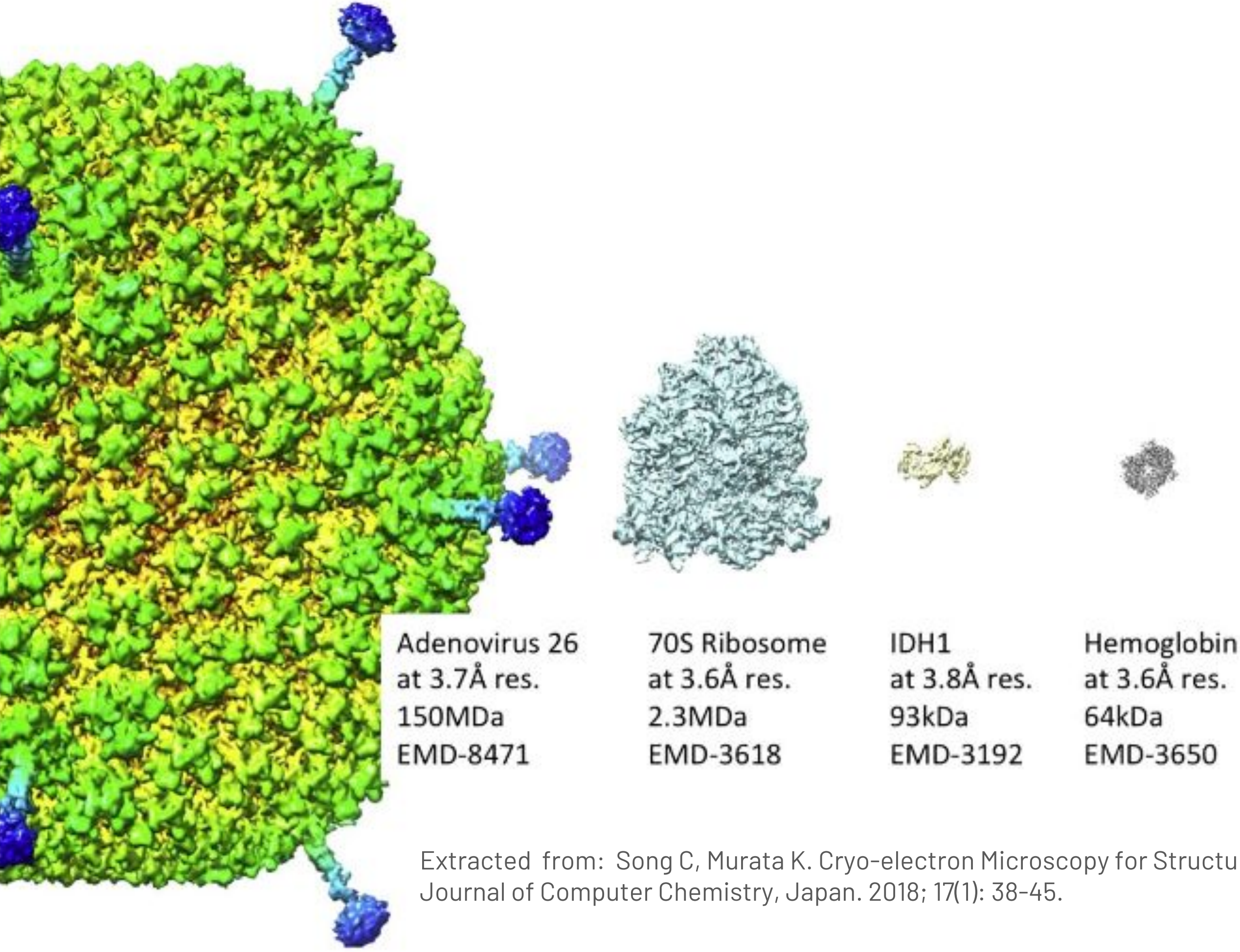


2D class averages of the yeast spliceosome

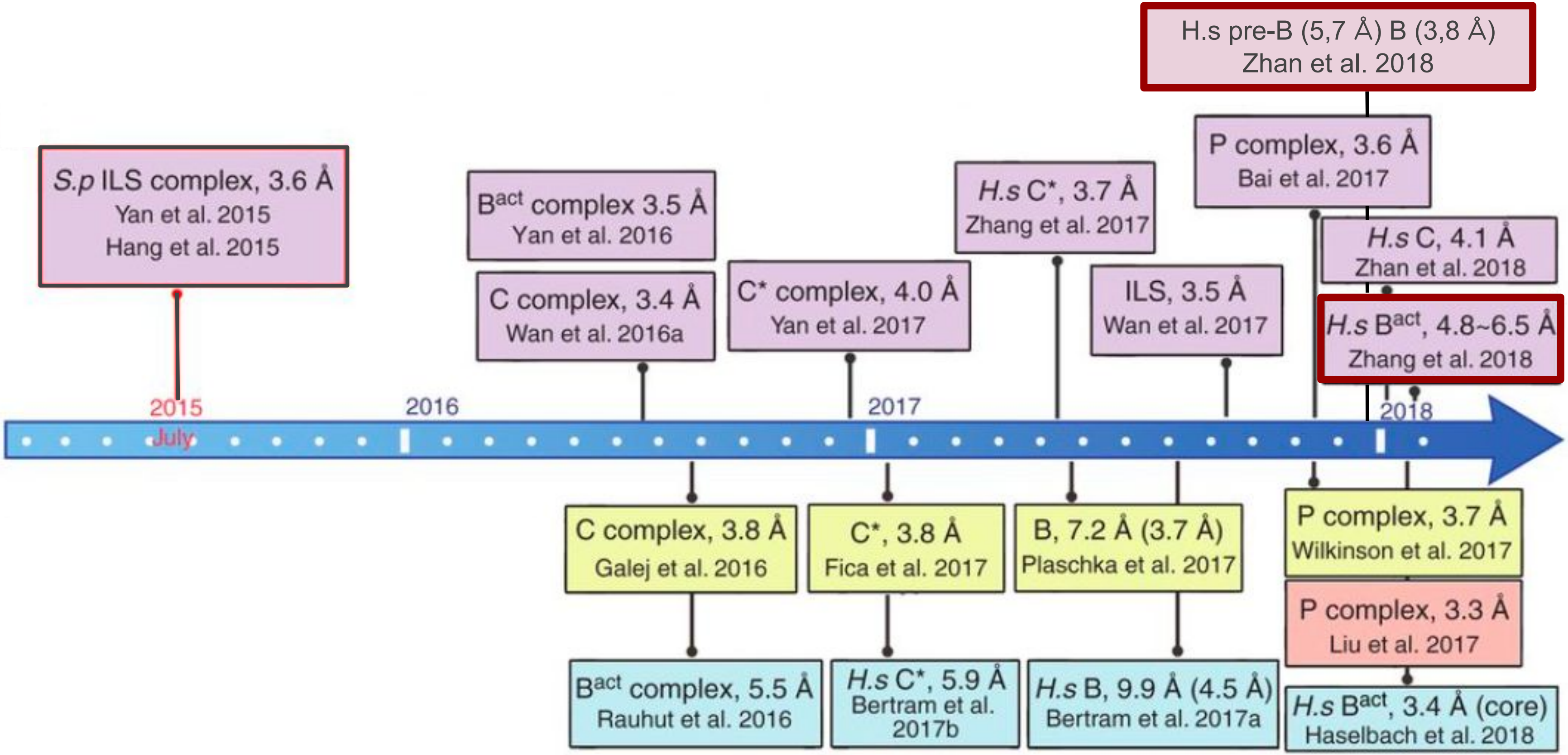


EM density for the yeast spliceosome. The resolution goes to 2.9-3.2 Å in the center of the spliceosome

Extracted from: Yan, C., Hang, J., Wan, R., Huang, M., Wong, C. and Shi, Y. Structure of a yeast spliceosome at 3.6-angstrom resolution. Science. 2015; 349: 1182-1191.



Extracted from: Song C, Murata K. Cryo-electron Microscopy for Structural Analysis of Dynamic Biological Macromolecules. Journal of Computer Chemistry, Japan. 2018; 17(1): 38-45.



S.p ILS complex, 3.6 Å
Yan et al. 2015
Hang et al. 2015

B^{act} complex 3.5 Å
Yan et al. 2016

C complex, 3.4 Å
Wan et al. 2016a

C* complex, 4.0 Å
Yan et al. 2017

H.s C*, 3.7 Å
Zhang et al. 2017

ILS, 3.5 Å
Wan et al. 2017

P complex, 3.6 Å
Bai et al. 2017

H.s pre-B (5,7 Å) B (3,8 Å)
Zhan et al. 2018

H.s C, 4.1 Å
Zhan et al. 2018

H.s B^{act}, 4.8~6.5 Å
Zhang et al. 2018

C complex, 3.8 Å
Galej et al. 2016

B^{act} complex, 5.5 Å
Rauhut et al. 2016

C*, 3.8 Å
Fica et al. 2017

H.s C*, 5.9 Å
Bertram et al. 2017b

B, 7.2 Å (3.7 Å)
Plaschka et al. 2017

H.s B, 9.9 Å (4.5 Å)
Bertram et al. 2017a

P complex, 3.7 Å
Wilkinson et al. 2017

P complex, 3.3 Å
Liu et al. 2017

H.s B^{act}, 3.4 Å (core)
Haselbach et al. 2018

Extracted from: Yan C, Wan R, Shi Y. Molecular Mechanisms of pre-mRNA Splicing through Structural Biology of the Spliceosome. Cold Spring Harb Perspect Biol. 2019:11(1).

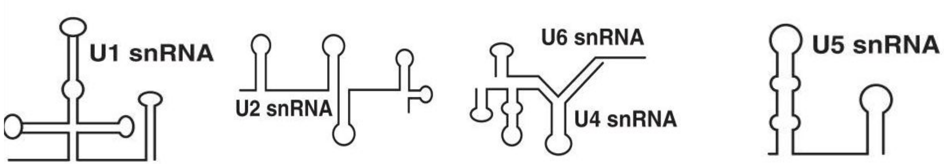
The Human

Major Spliceosome

The Major Spliceosome

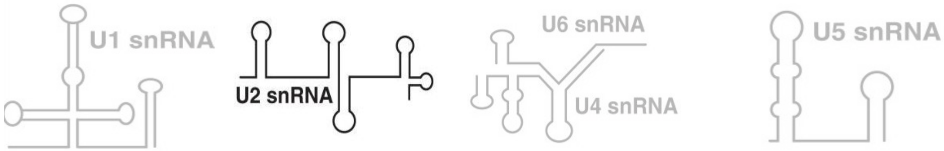
Spliceosome Cycle
Yeast vs Human

Other components:
NTC, NTR, etc.



U1 snRNP	U2 snRNP	U4/U6 snRNP	U5 snRNP
Sm	Sm	Sm (U4)	Sm
70K	U2-A’	LSm (U6)	Prp8
A	U2-B’	Prp31	Prp6
C	**SF3a**	Prp 3	Snu114
	SF3b	Prp4	Brr2
		CypH	40K
		15.5K	52K
			Prp28
			Dib 1

Sm: small nuclear ribonucleoprotein
LSm: Sm-like protein
SF: splicing factor
Prp: pre-m-RNA-processing-splicing factor
NTC: Nine Teen Complex
NTR: NTC-related



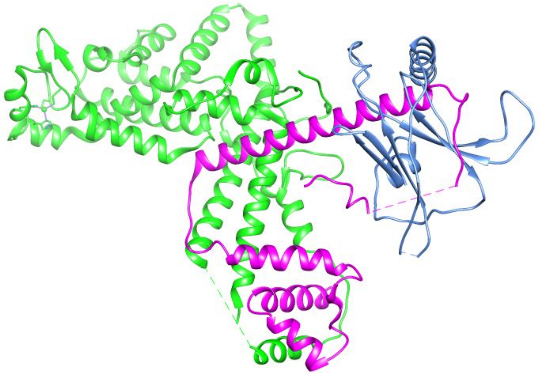
U1 snRNP
- U1 Sm
- 70K
- A
- C

U2 snRNP
- U2 Sm
- U2-A'
- U2-B'
- **SF3a**
- SF3b

U4/U6 snRNP
- U4 Sm
- U6-LSm
- Prp31
- Prp 3
- Prp4
- CypH
- 15.5K

U5 snRNP
- U5 Sm
- Prp8
- Prp6
- Snu114
- Brr2
- 40K
- 52K
- Prp28
- Dib 1

Other components: NTC, NTR, splicing factors, etc.



Sm: small nuclear ribonucleoprotein
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Prp: pre-m-RNA-processing-splicing factor
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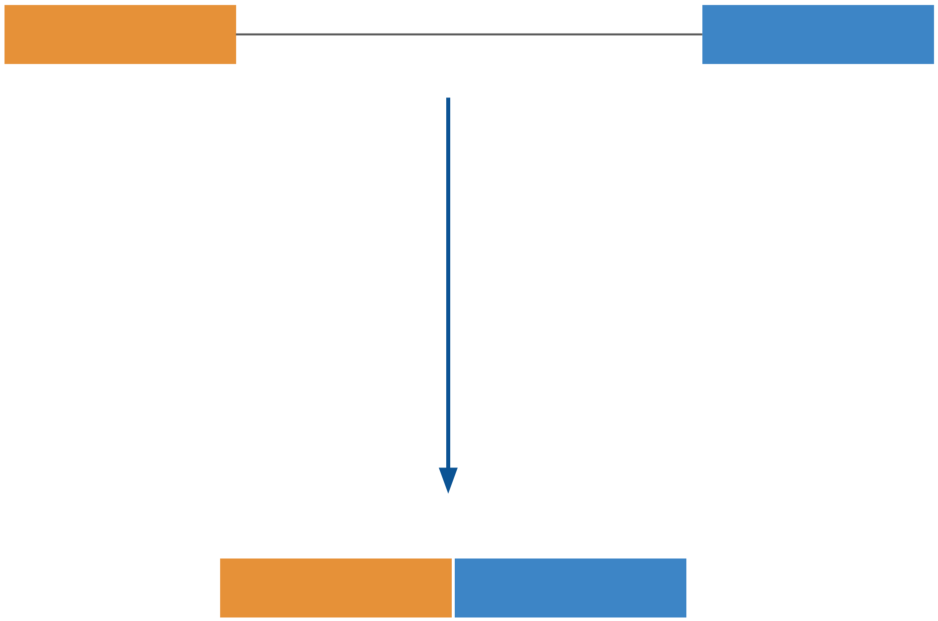
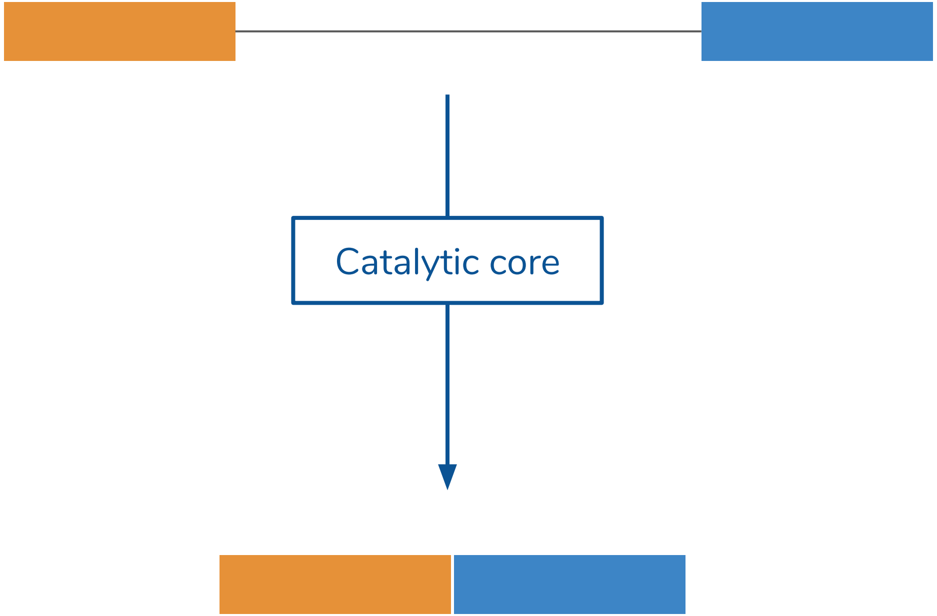
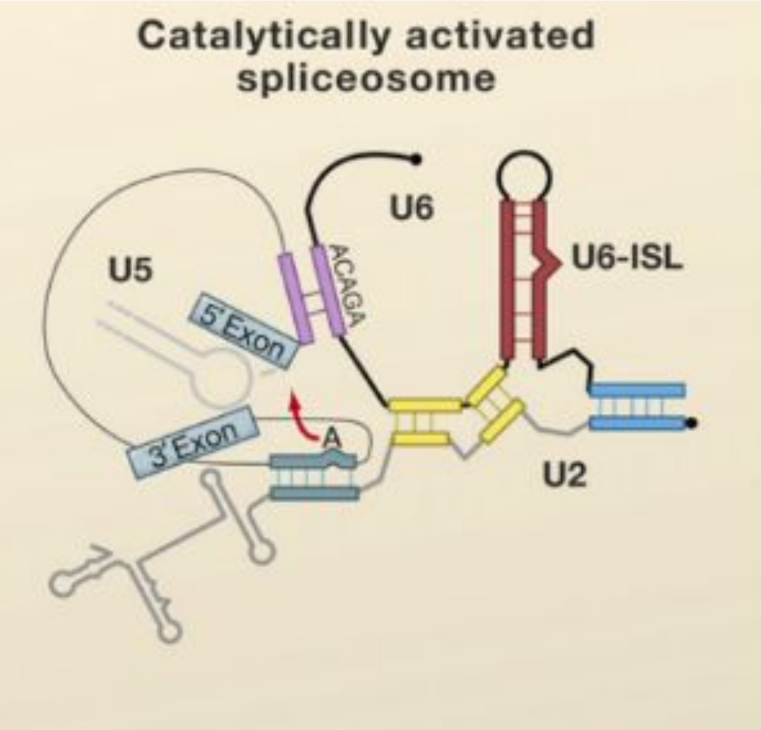


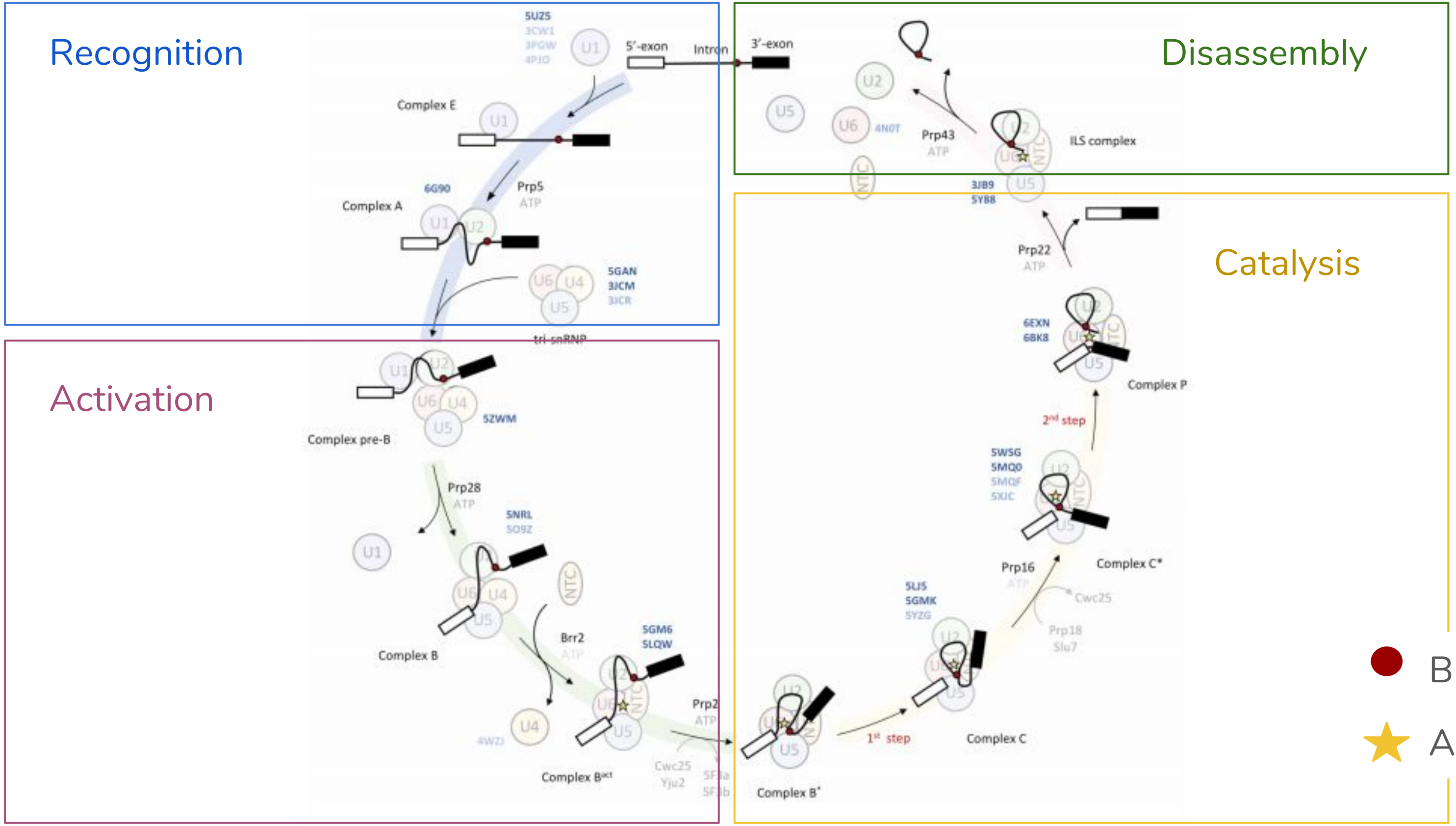


Catalytic core



Extracted from: Wahl M, Will C, Lührmann R. The Spliceosome: Design Principles of a Dynamic RNP Machine. Cell. 2009; 136(4): 701-718.

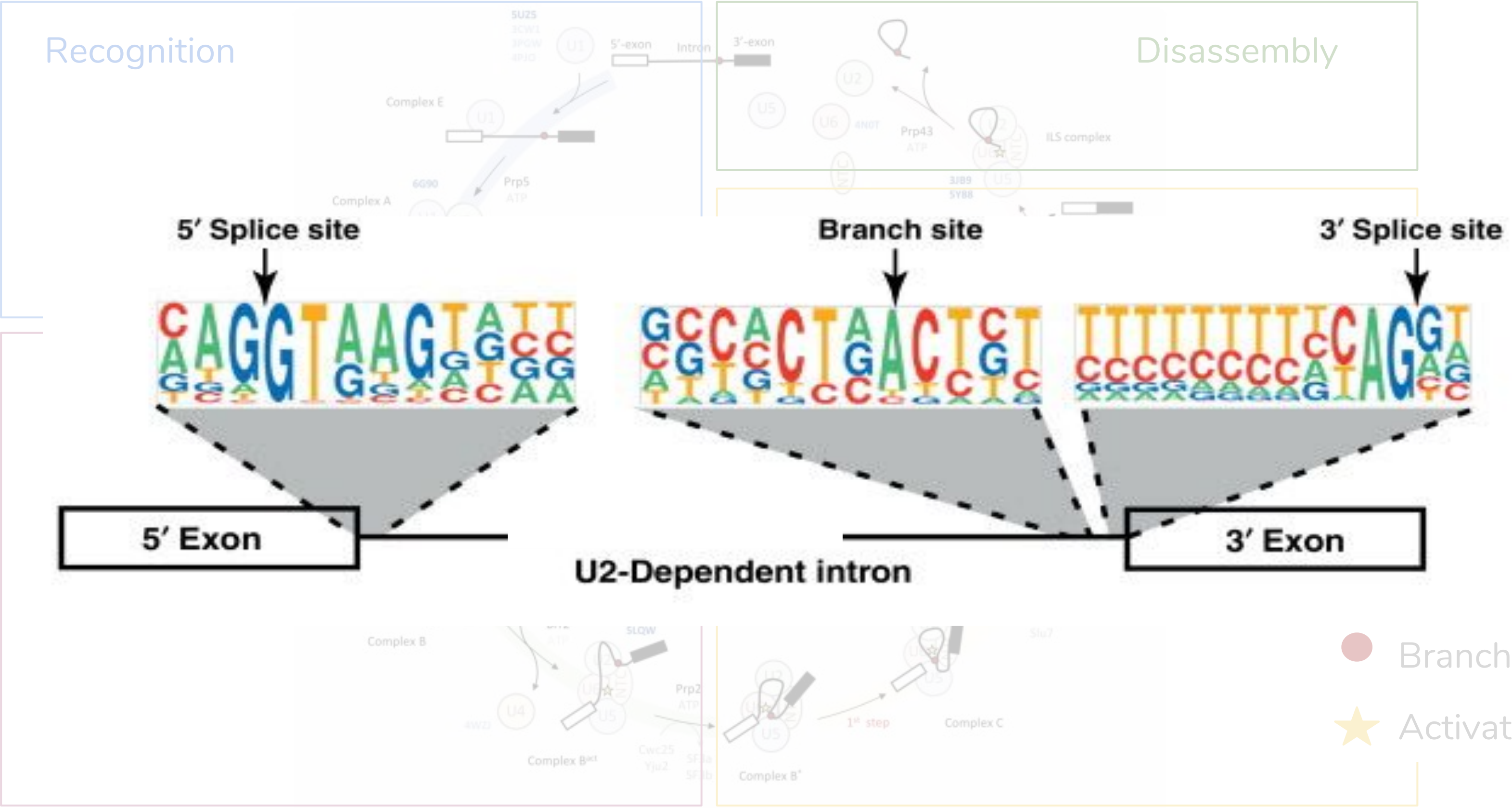
Spliceosome Cycle



● Branch point

★ Activate site

Adapted from: Galej WP. Structural studies of the spliceosome: past, present and future perspectives. Biochem Soc Trans. 2018;46(6):1407-1422.



● Branch point

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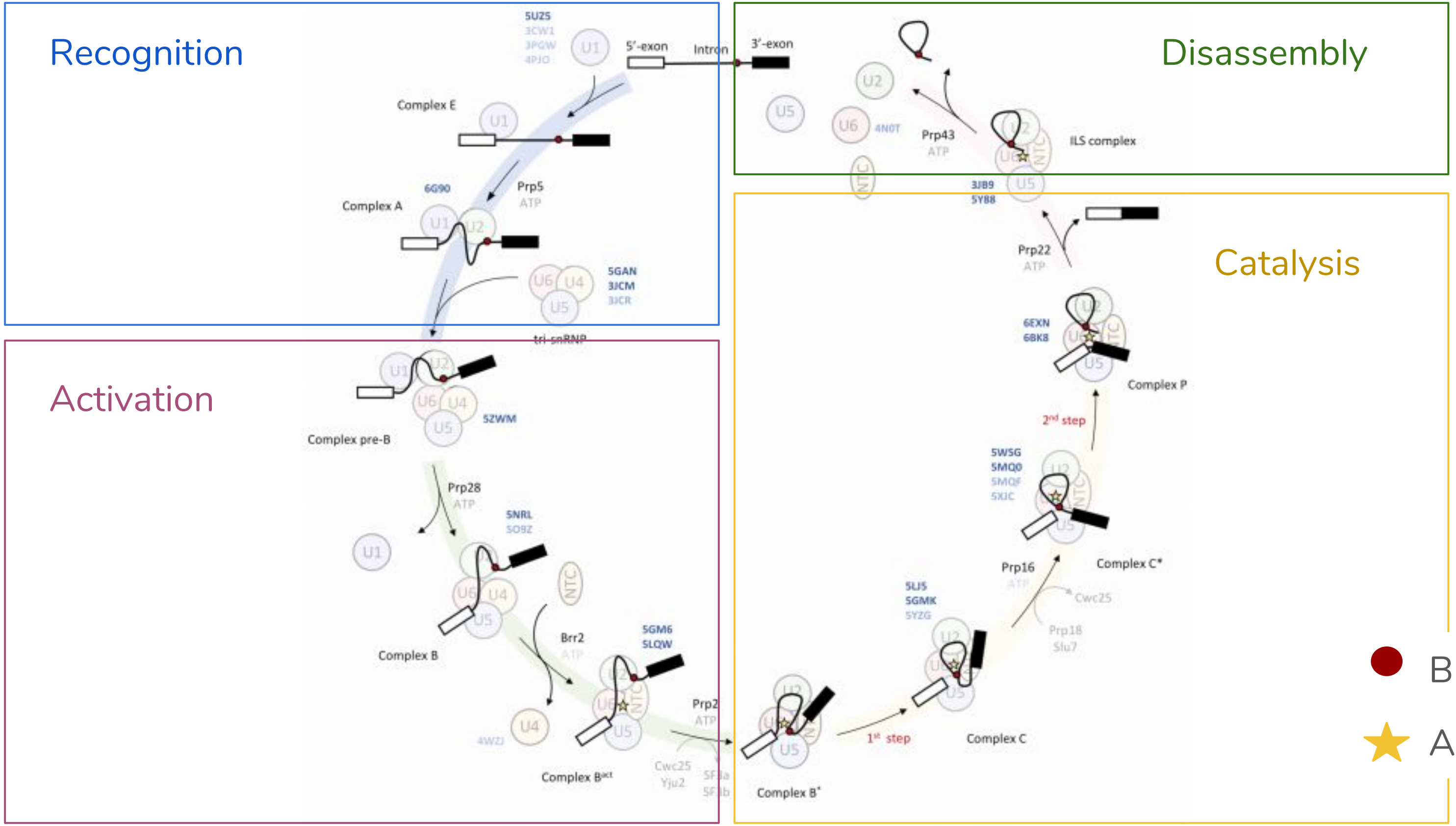

● Branch point

★ Activate site

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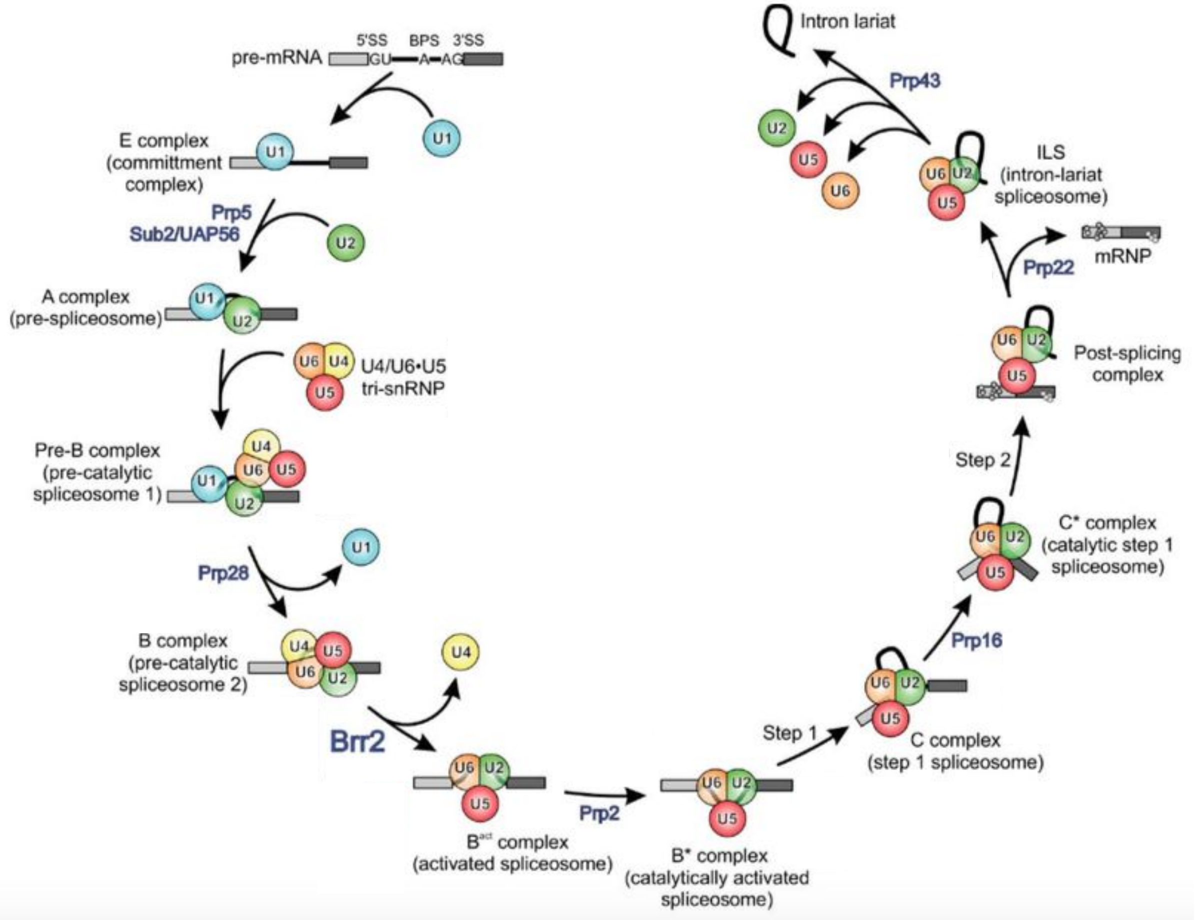
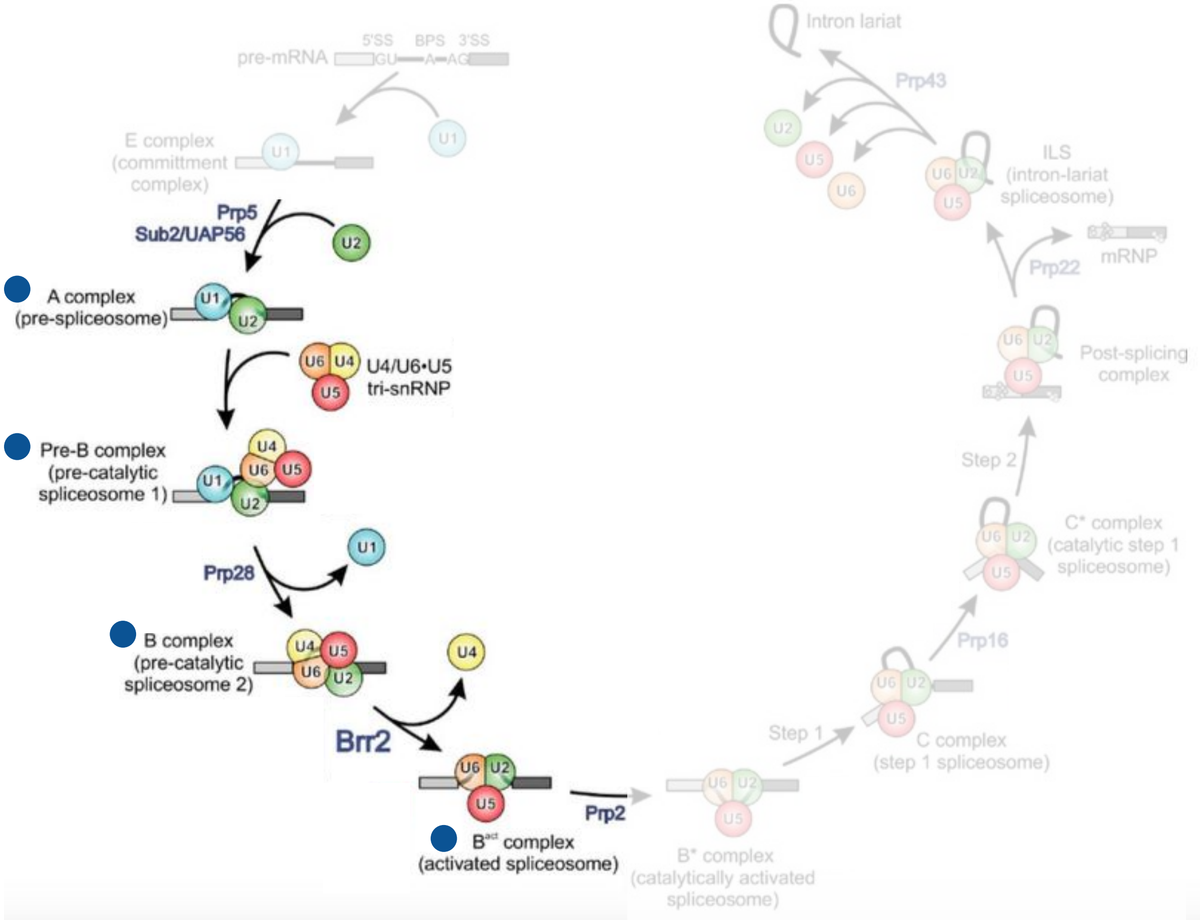
Spliceosome Cycle



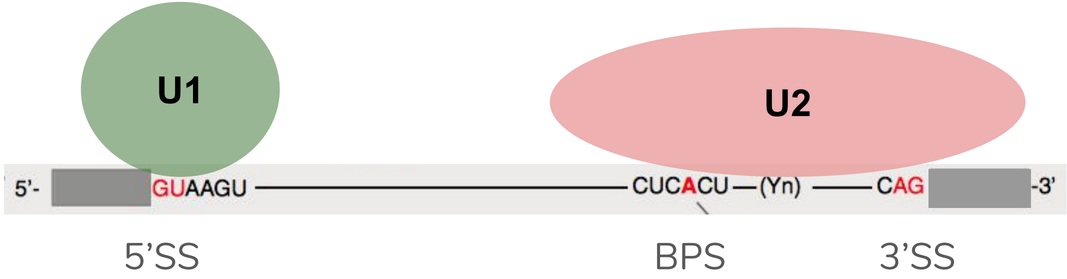
Adapted from: Absmeier E, Santos KF, Whal MC. Functions and regulation of the Brr2 RNA helicase during splicing. Cell Cycle. 201616;15(24):3362-3377.



● SF3a

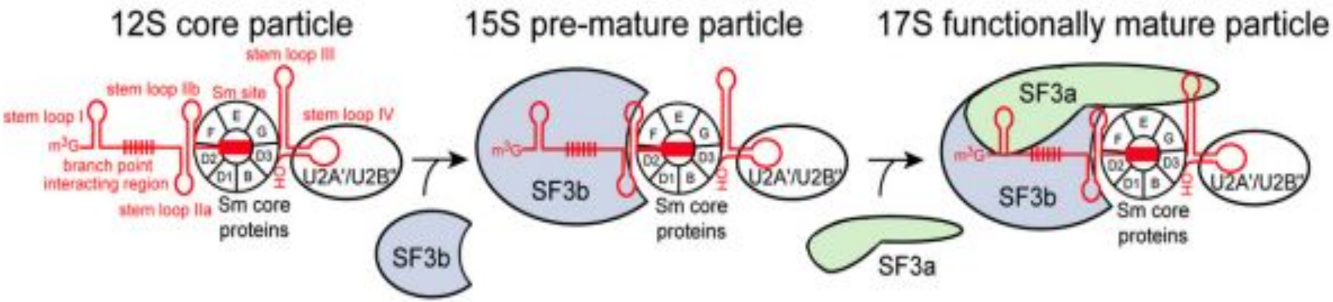
Adapted from: Absmeier E, Santos KF, Whal MC. Functions and regulation of the Brr2 RNA helicase during splicing. Cell Cycle. 201616;15(24):3362-3377.

A complex



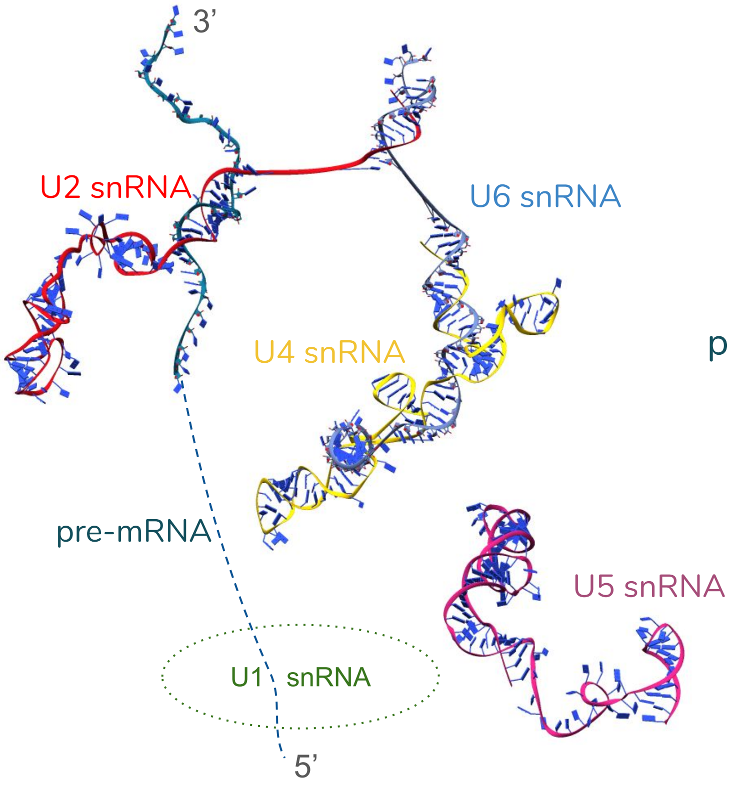
SS: splice site
BPS: branch point sequence

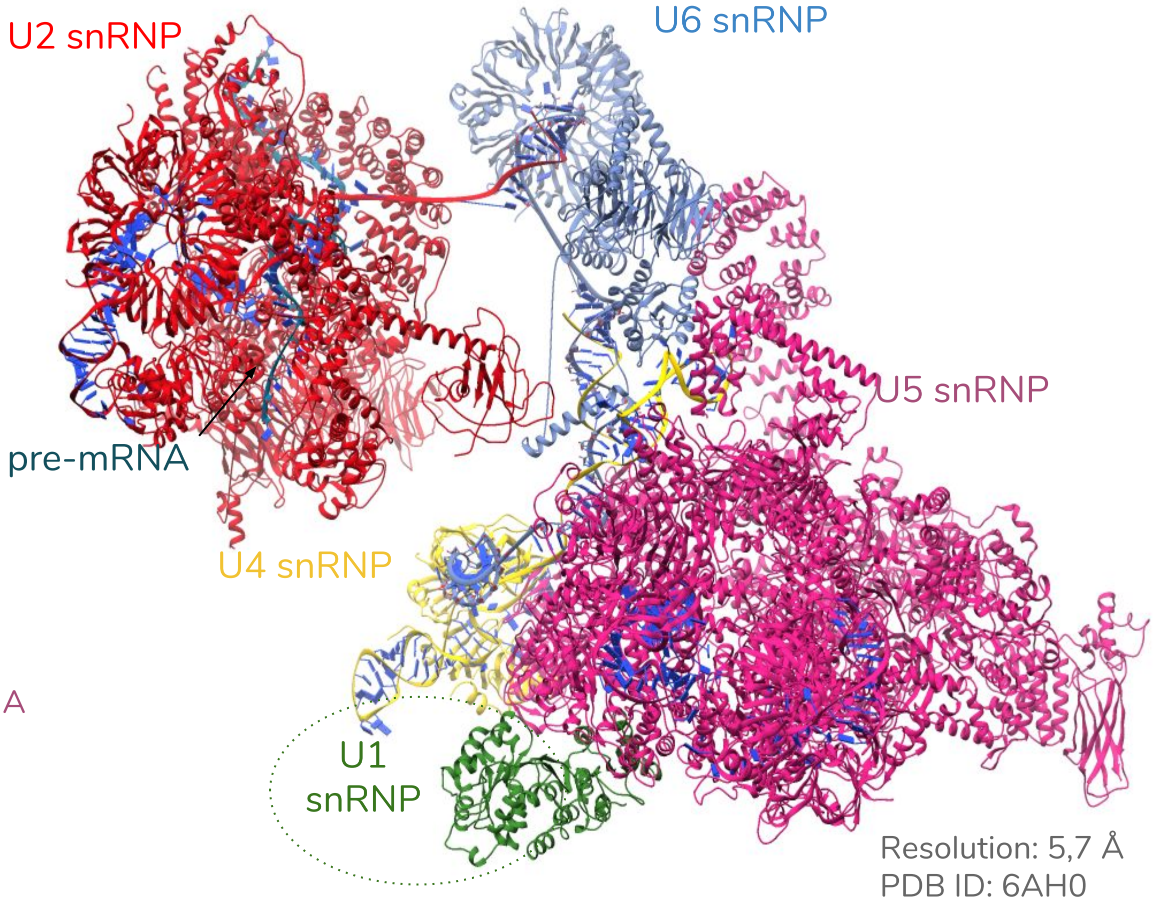
U2 conformation:



Adapted from: Kuwasako K et al. Solution Structures of the SURP Domains and the Subunit-Assembly Mechanism within the Splicing Factor SF3a Complex in 17S U2 snRNP. Structure. 2006;14(11):1677-89.

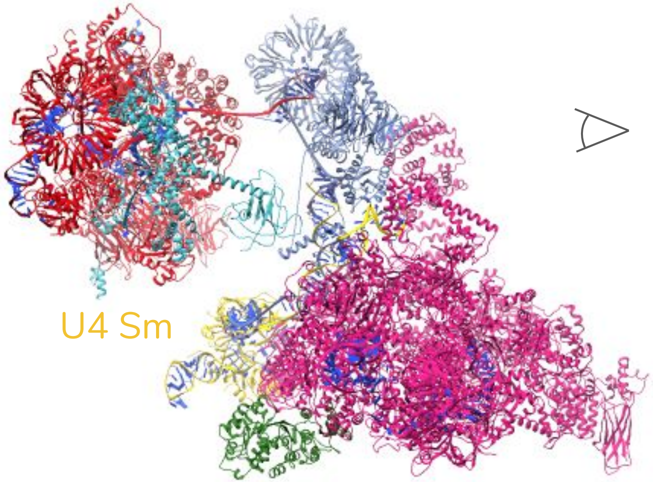
Pre-B complex

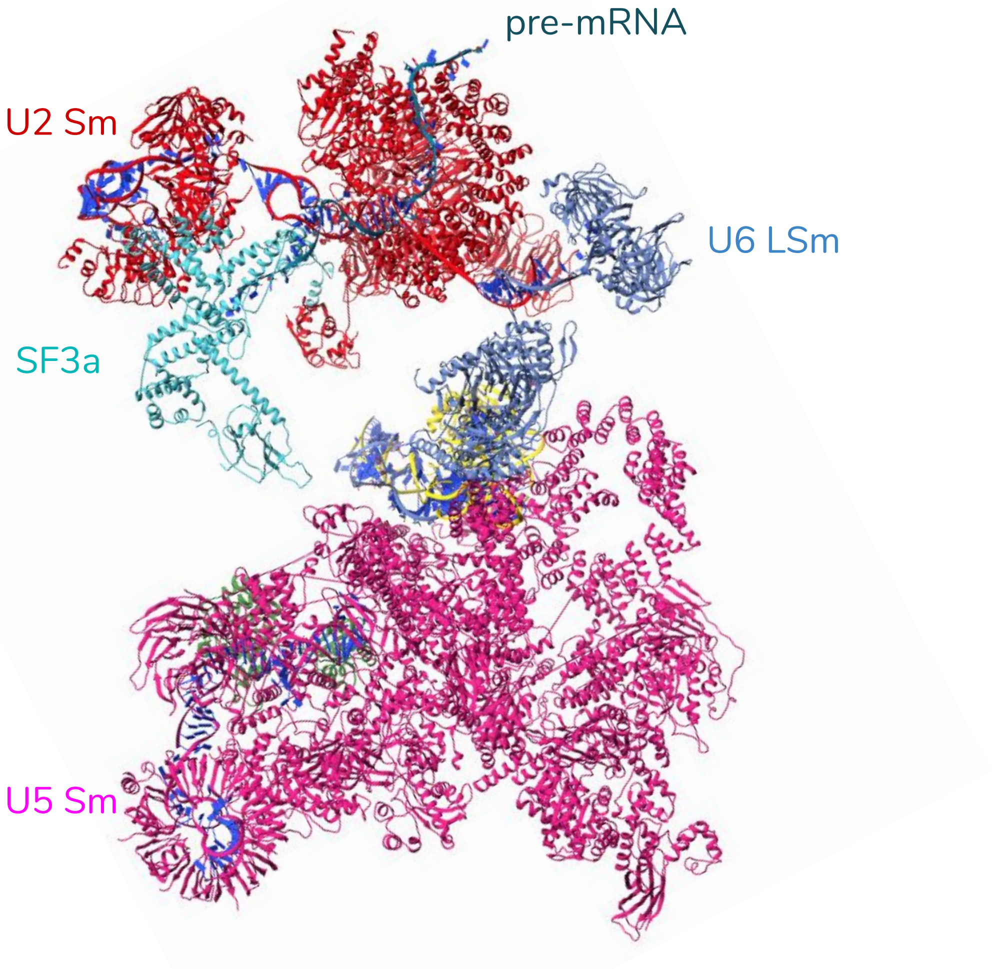




Resolution: 5,7 Å
PDB ID: 6AH0

Pre-B complex



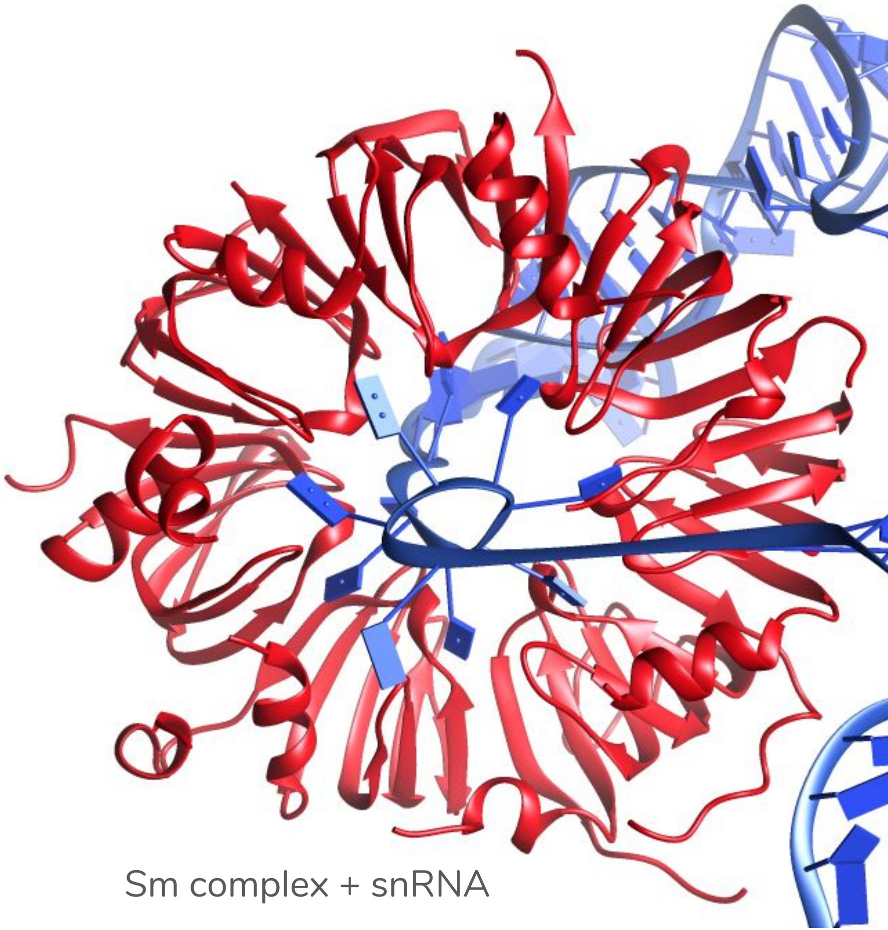


Resolution: 5,7 Å
PDB ID: 6AH0

Sm and LSm complexes

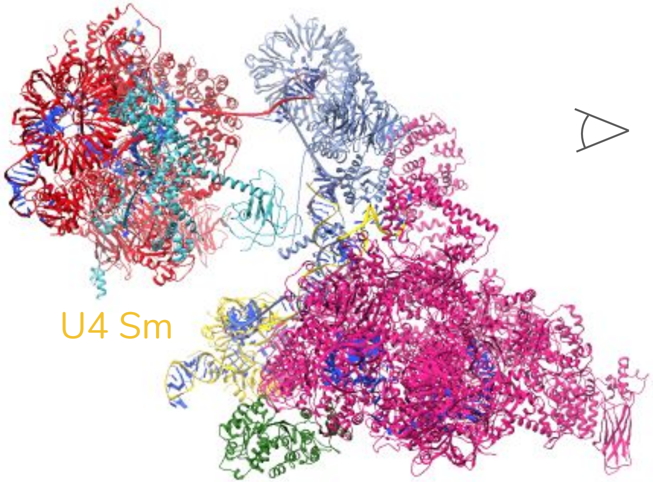
7 subunits
highly conserved

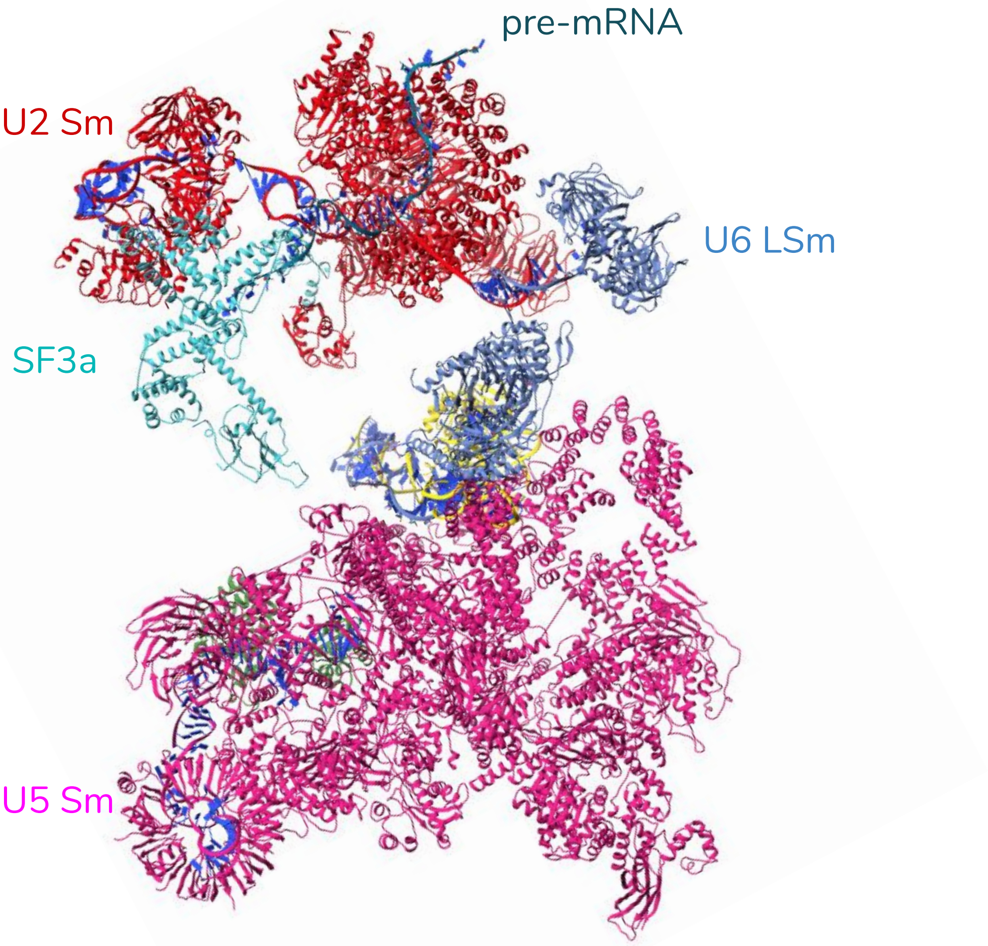
Resolution: 3,8 Å
PDB ID: 6AHD



Sm complex + snRNA

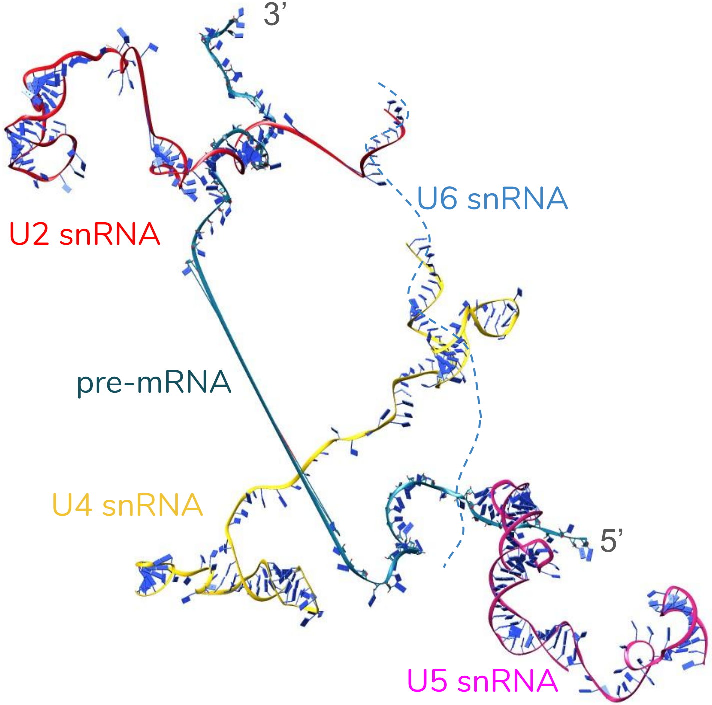
Pre-B complex

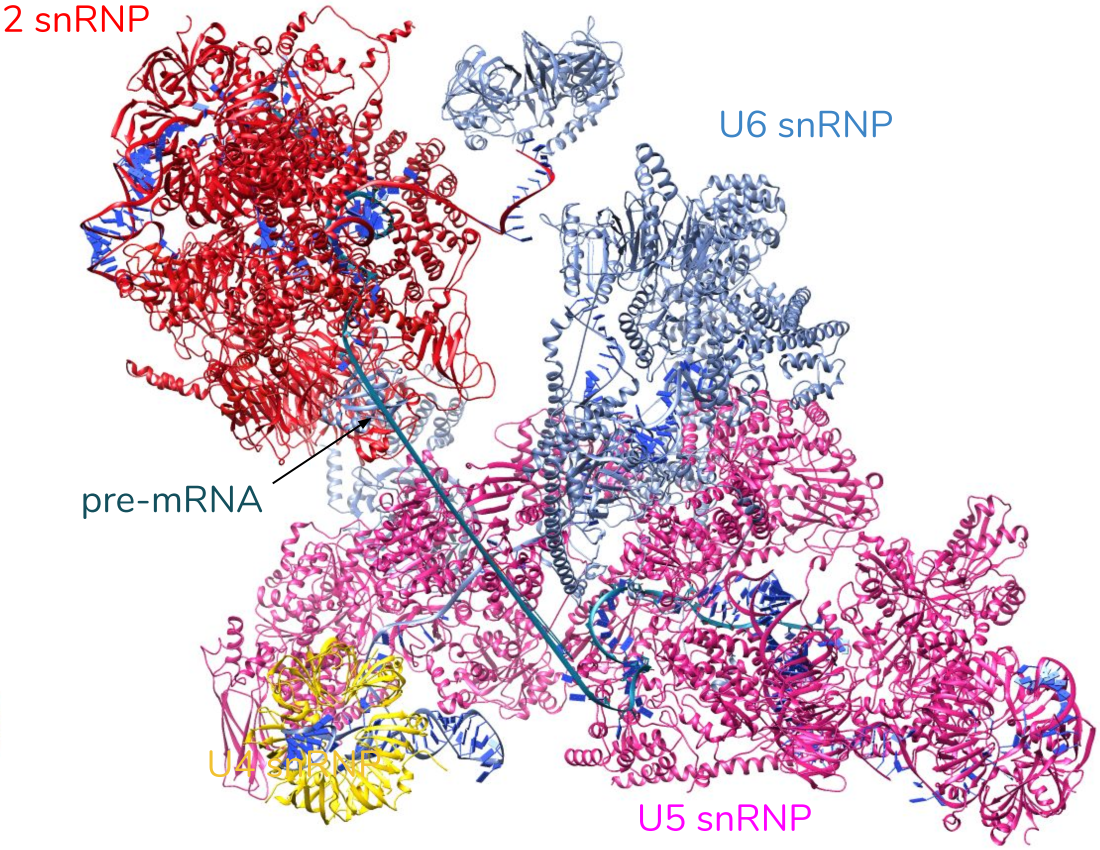




Resolution: 5,7 Å
PDB ID: 6AH0

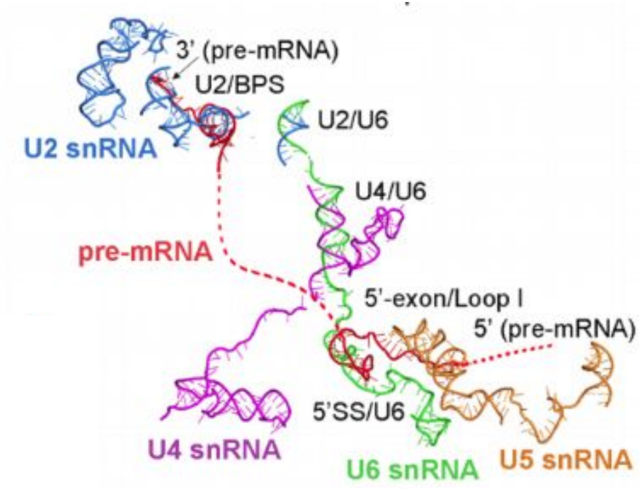
B complex





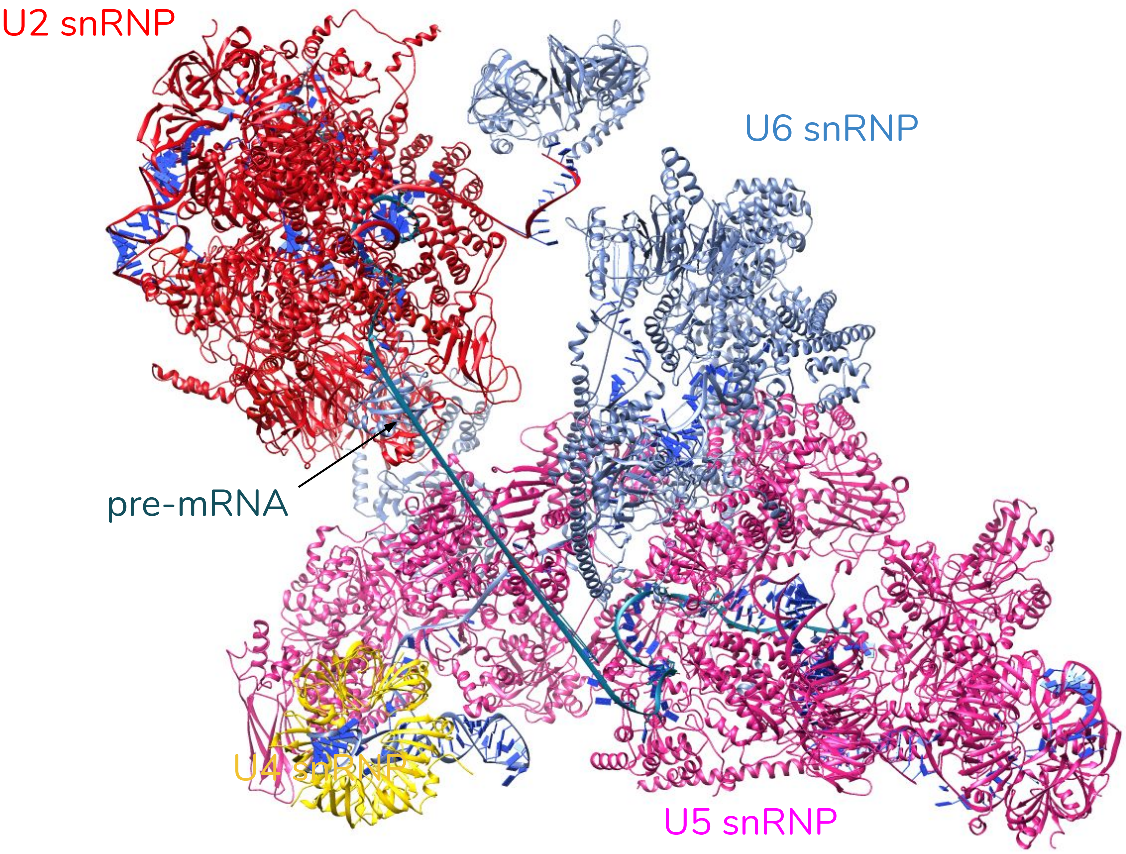
Resolution: 3,8 Å
PDB ID: 6AHD

B complex

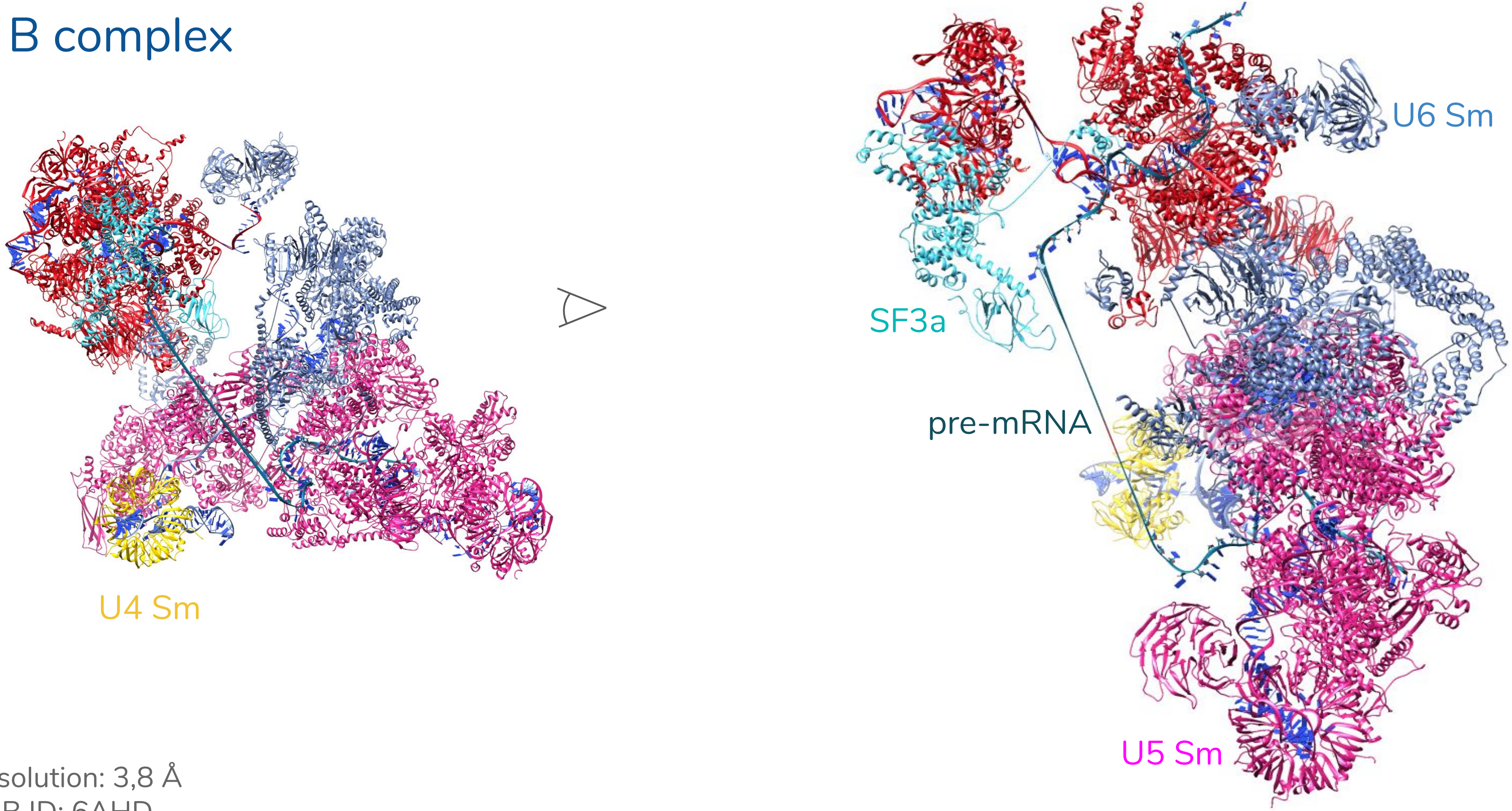


Zhan X, Yan C, Zhang X, Lei J, Shi Y. Structures of the human pre-catalytic spliceosome and its precursor spliceosome. *Cell Research*. 2018; 28(12): 1129-1140.

Resolution: 3,8 Å
PDB ID: 6AHD



B complex



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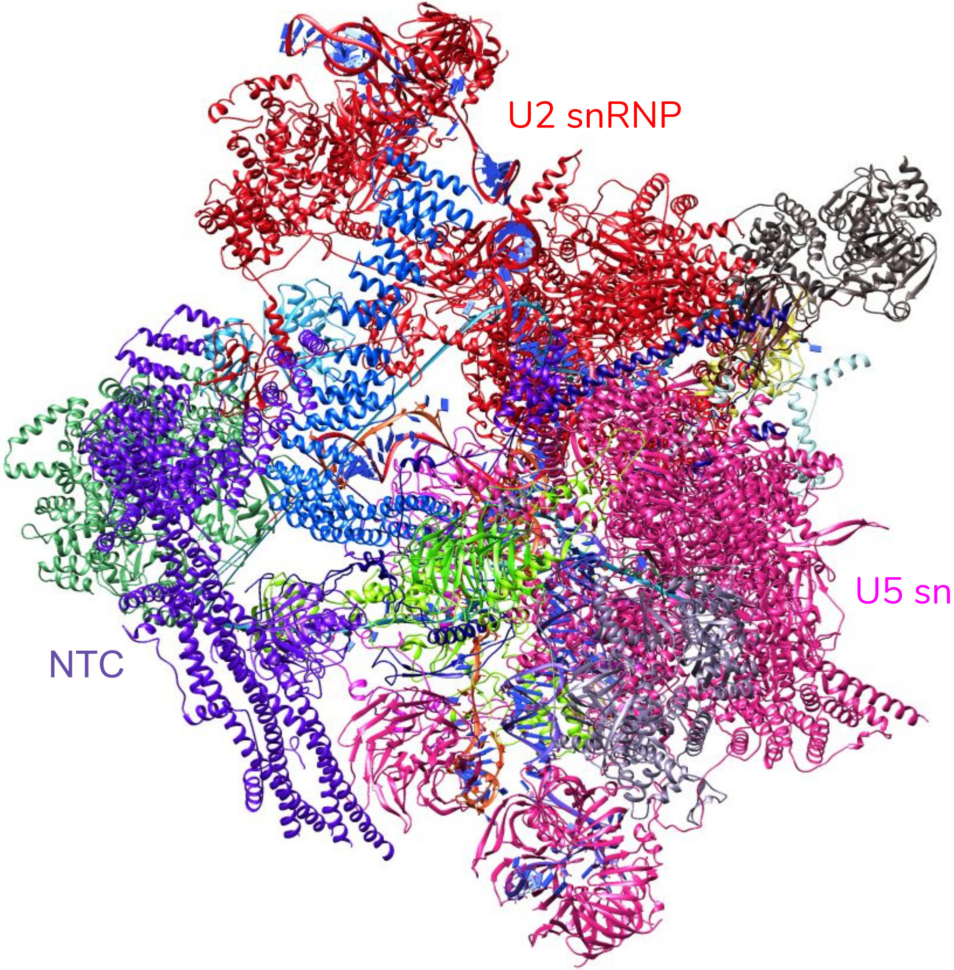
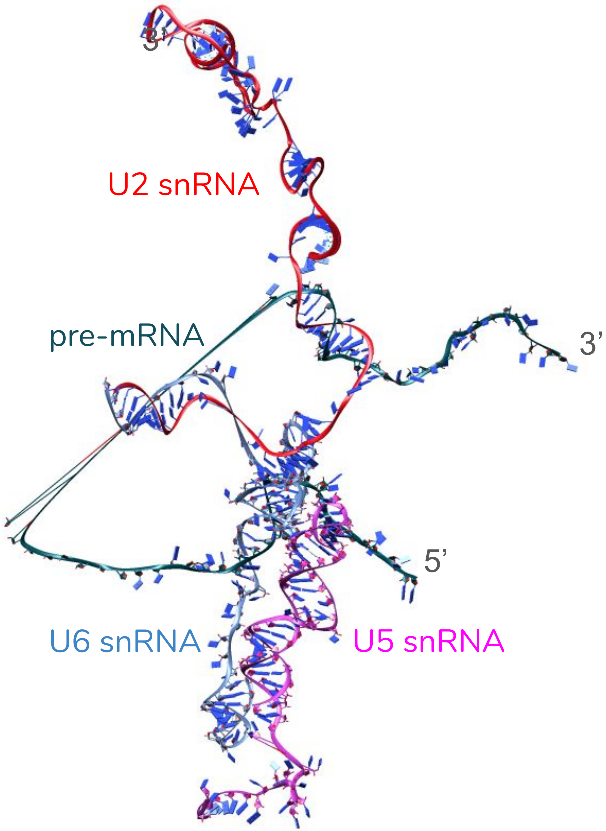
PDB ID: 6AHD

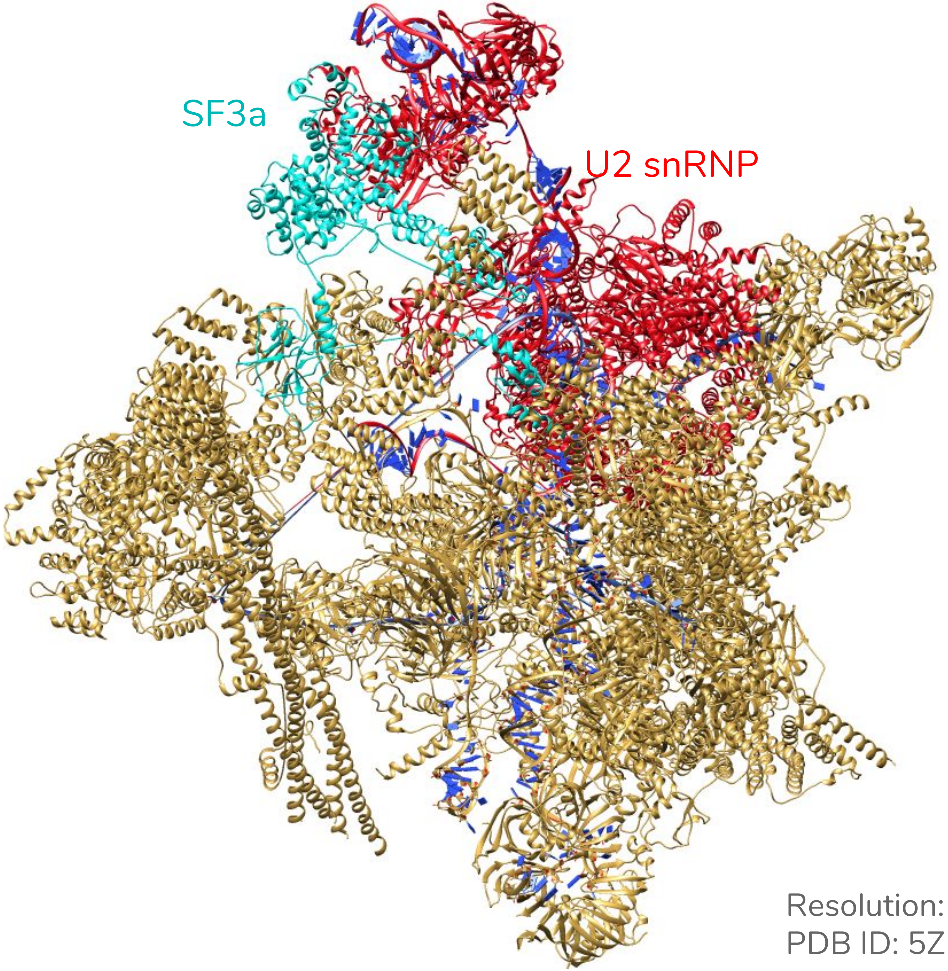
B-act complex



Resolution: 5,1 Å
PDB ID: 5Z56

B-act complex





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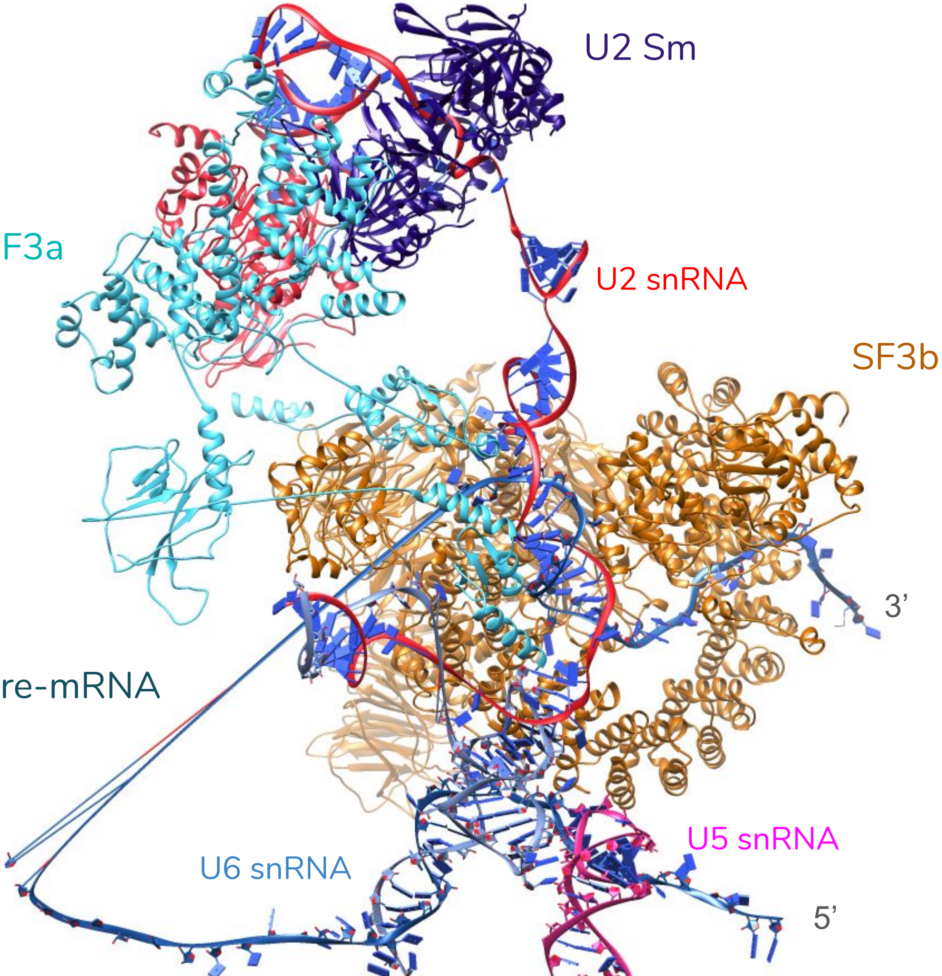
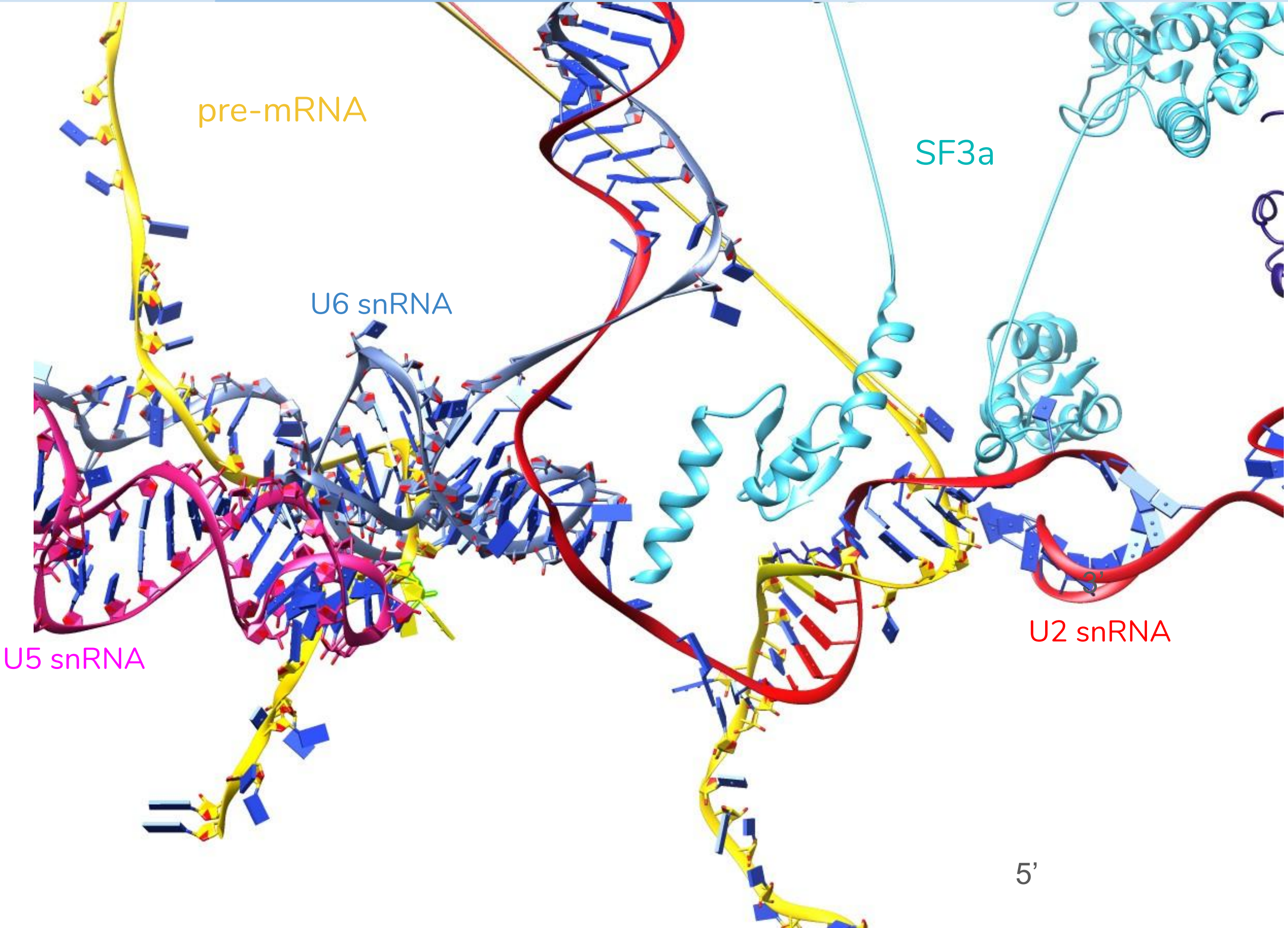
PDB ID: 5Z56

U2 during B-act complex



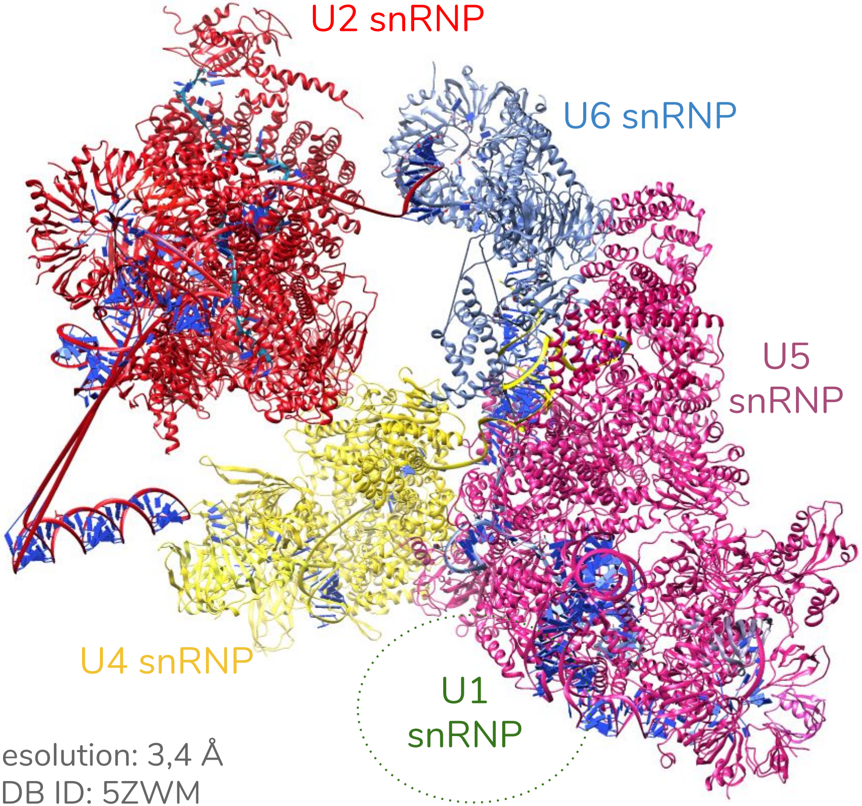
Resolution: 5,1 Å
PDB ID: 5Z56

U2 during B-act complex



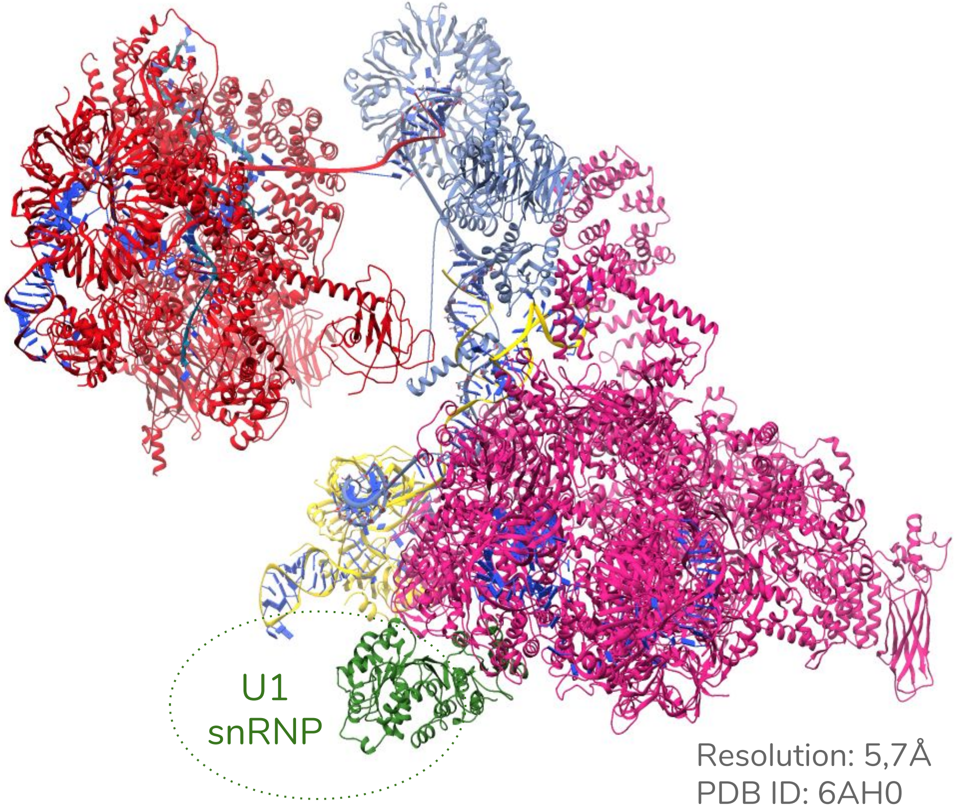
Resolution: 5,1 Å
PDB ID: 5Z56

S. cerevisiae pre-B complex



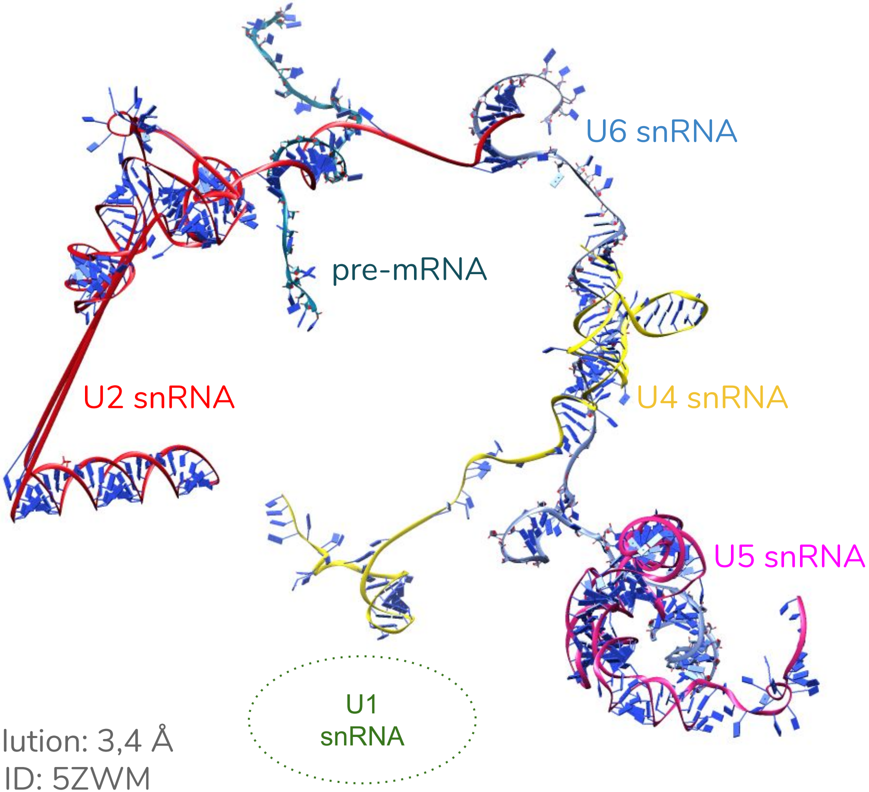
Resolution: 3,4 Å
PDB ID: 5ZWM

H. sapiens pre-B complex



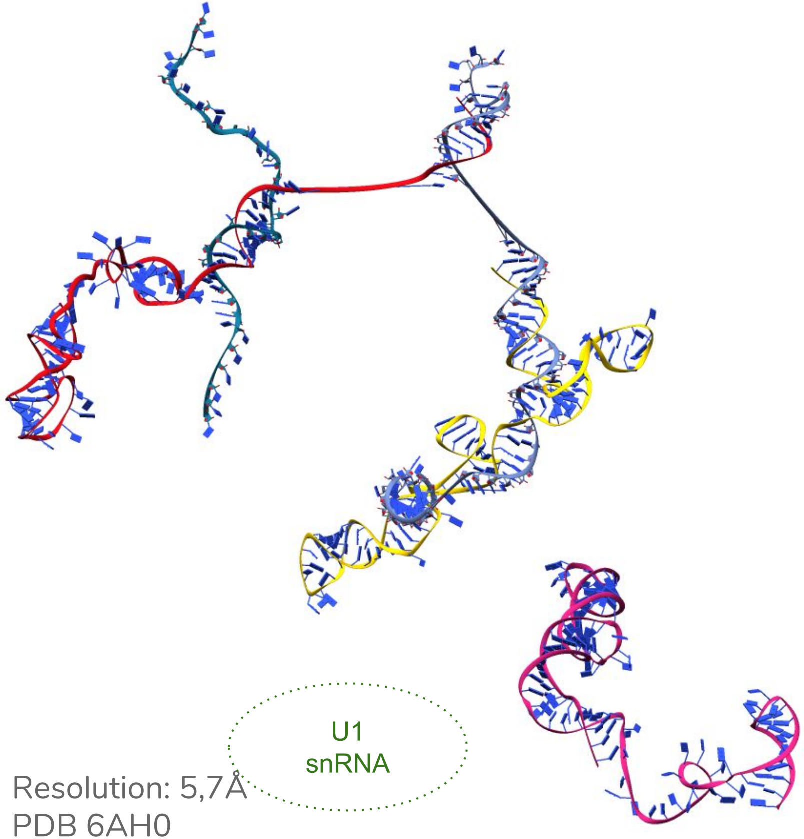
Resolution: 5,7Å
PDB ID: 6AH0

S. cerevisiae pre-B complex RNA



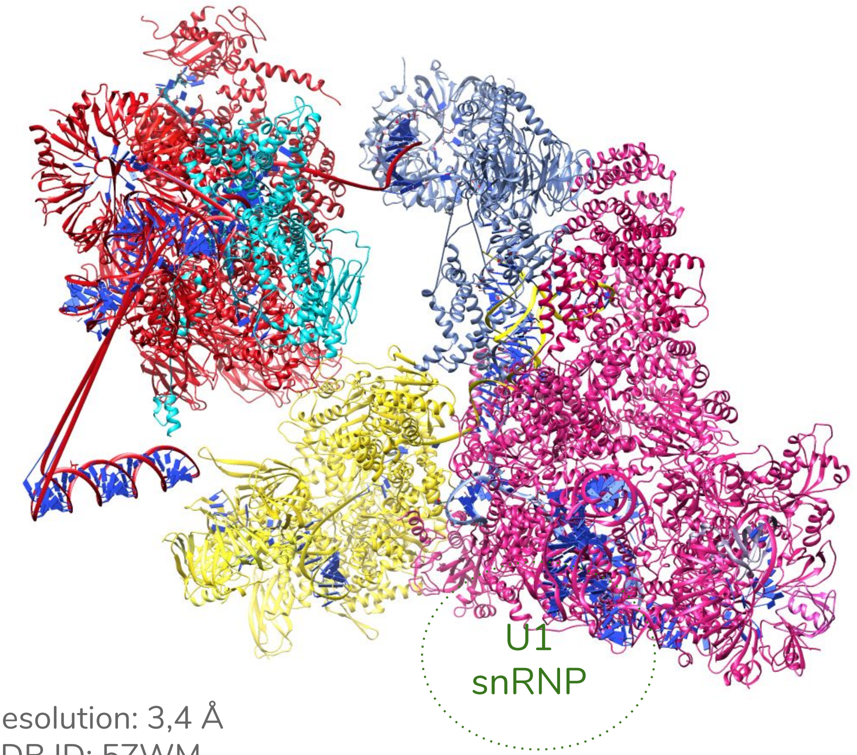
Resolution: 3,4 Å
PDB ID: 5ZWM

H. sapiens pre-B complex RNA



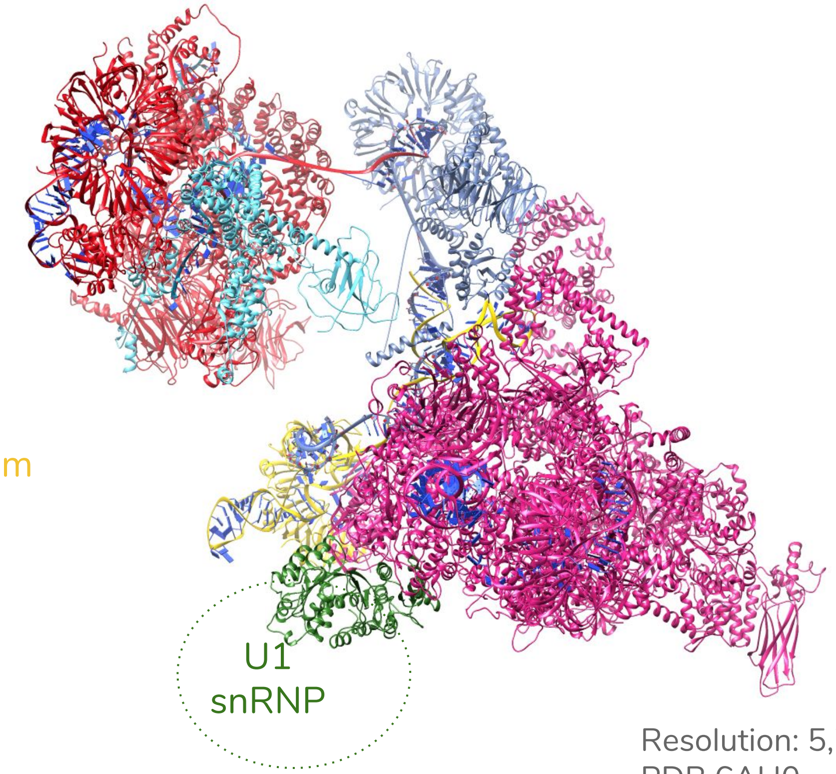
Resolution: 5,7Å
PDB 6AH0

S. cerevisiae pre-B complex



Resolution: 3,4 Å
PDB ID: 5ZWM

H. sapiens pre-B complex



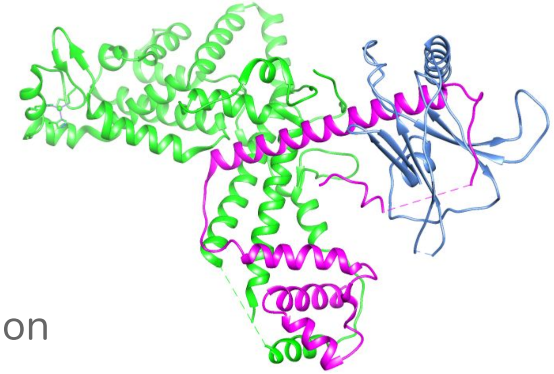
Resolution: 5,7Å
PDB 6AH0

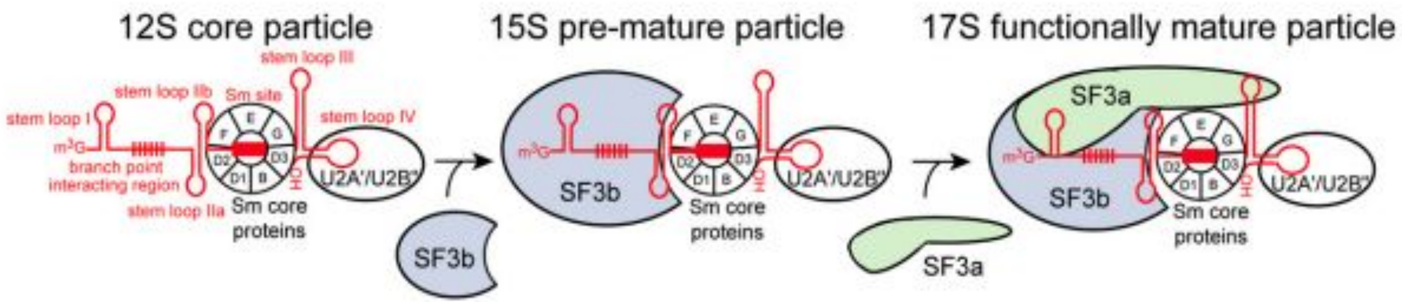
Splicing Factor 3a

→ Crucial component of functionally active 17S U2 complex

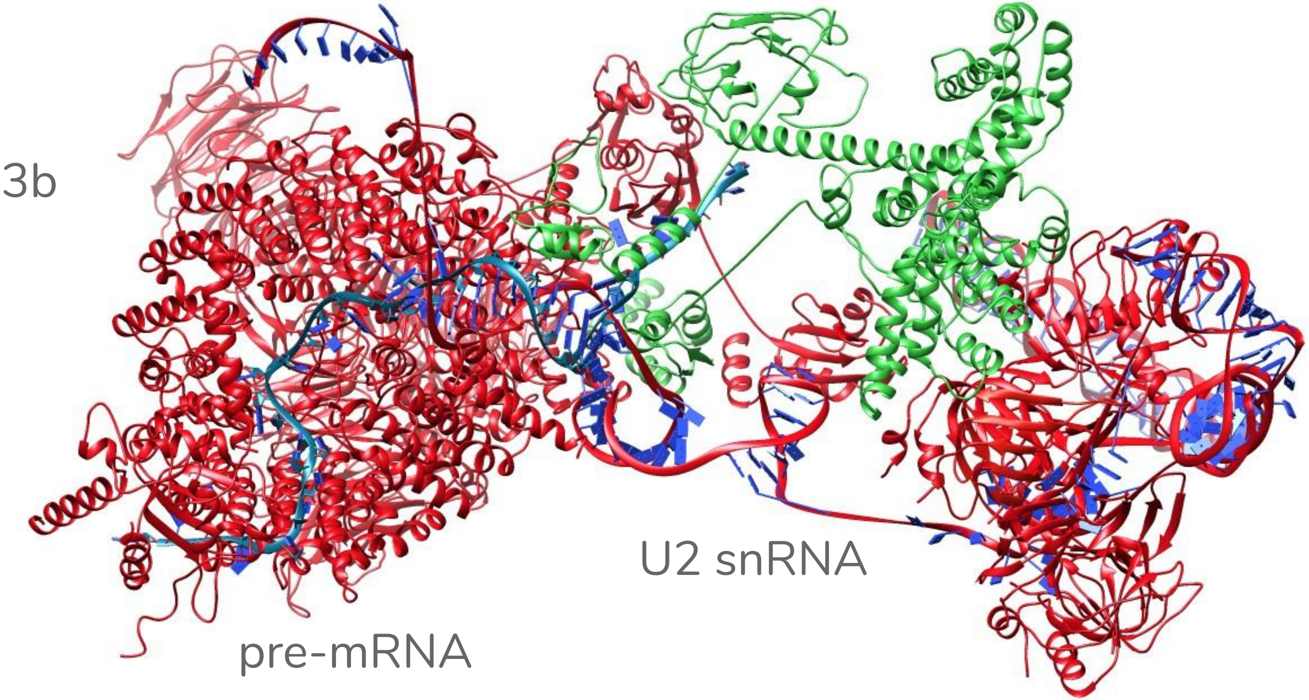
→ Stabilization of U2

→ Its displacement initiates the first step of the splicing reaction





Adapted from: Kuwasako K et al. Solution Structures of the SURP Domains and the Subunit-Assembly Mechanism within the Splicing Factor SF3a Complex in 17S U2 snRNP. Structure. 2006;14(11):1677-89.



SF3a

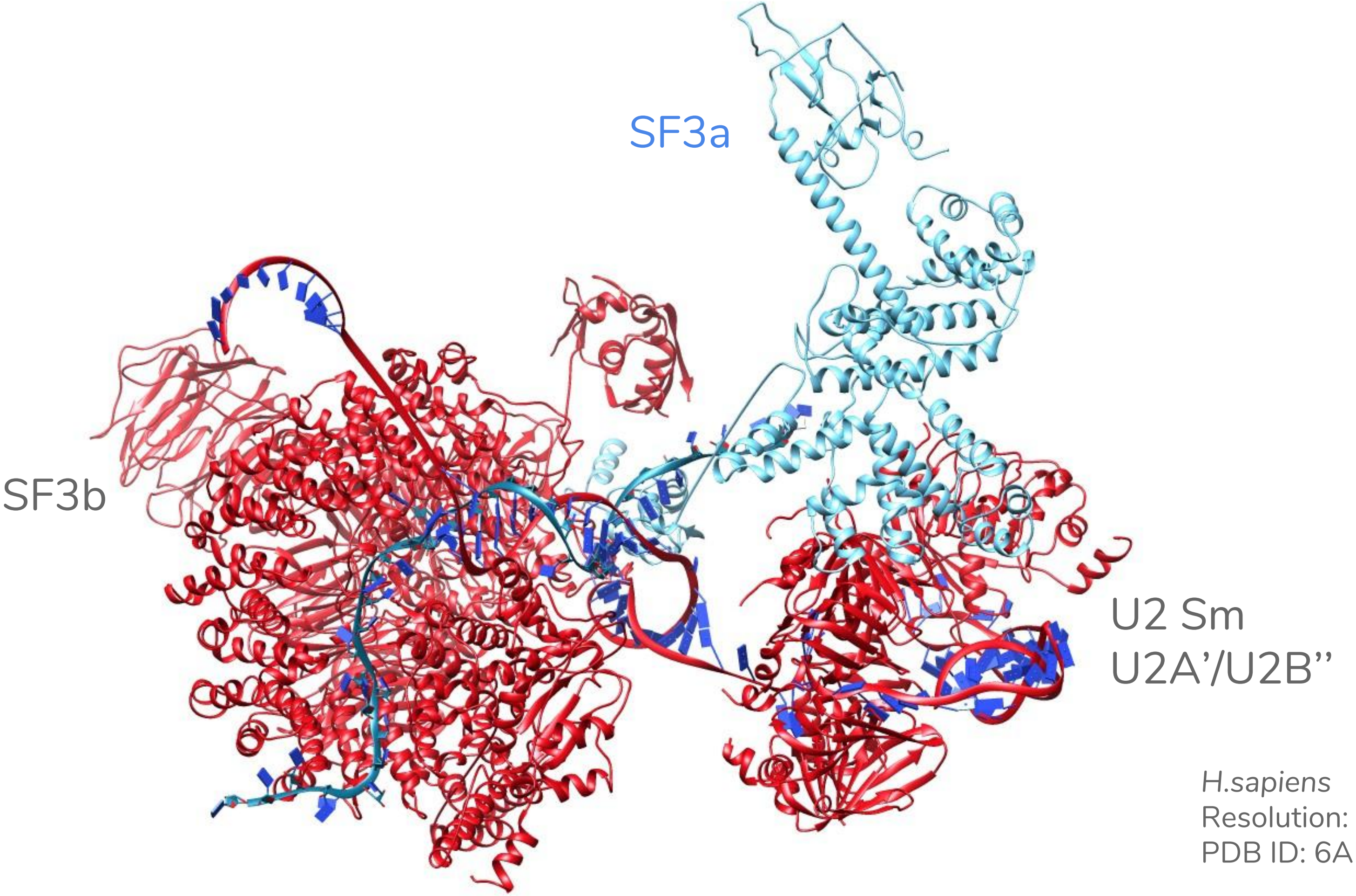
SF3b

U2 Sm
U2A’/U2B”

U2 snRNA

pre-mRNA

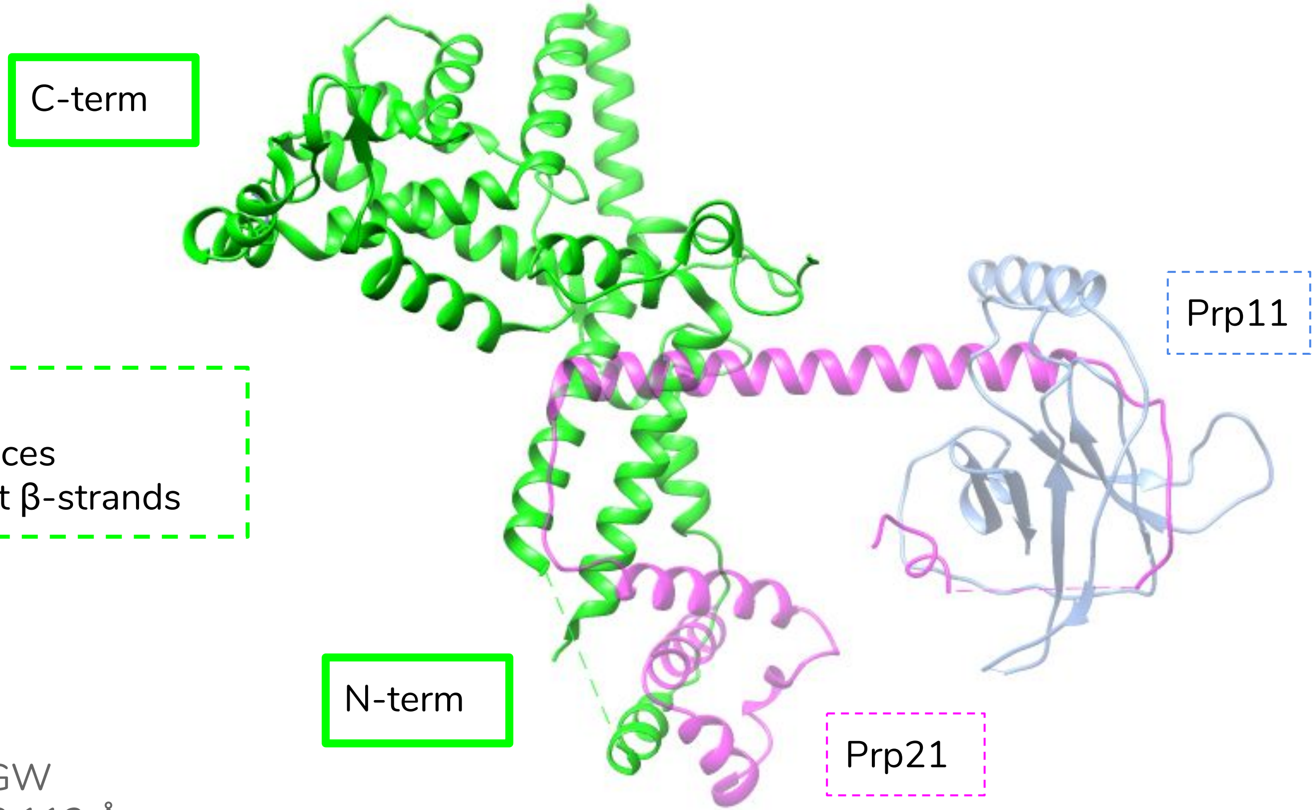
S.cerevisiae
Resolution: 3,4 Å
PDB ID: 5ZWM



H.sapiens
Resolution: 5,7 Å
PDB ID: 6AH0

Prp9 | Prp21 | Prp11

PDB ID: 4DGW
Resolution: 3.112 Å

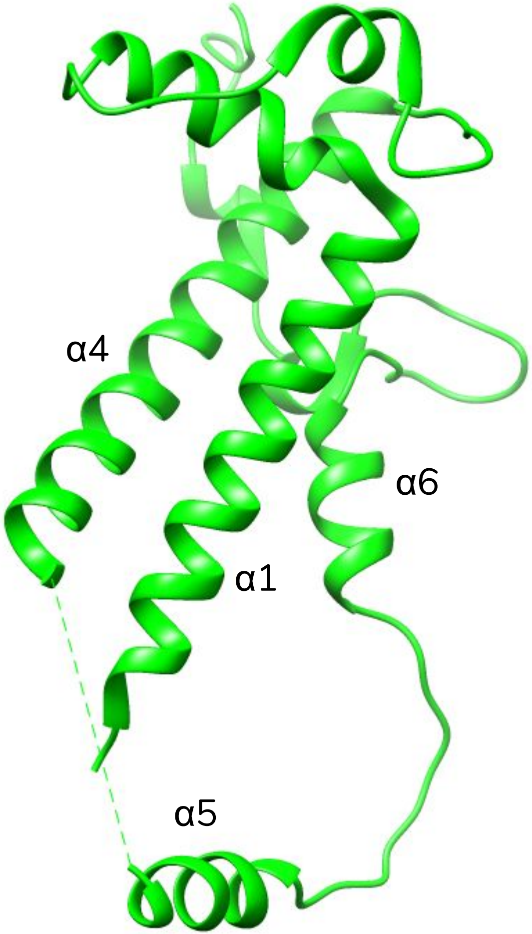


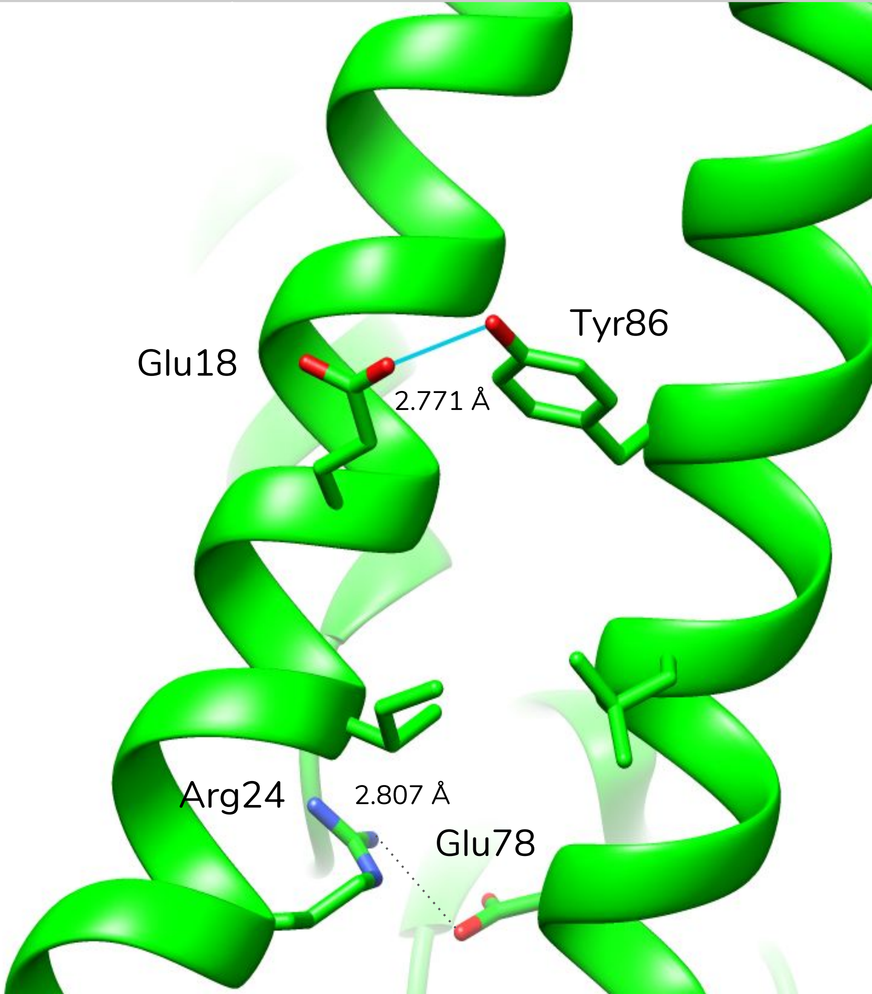
Prp9
13α-helices
+ 2 short β-strands

PDB ID: 4DGW
Resolution: 3.112 Å

Prp9 | Prp21 | Prp11

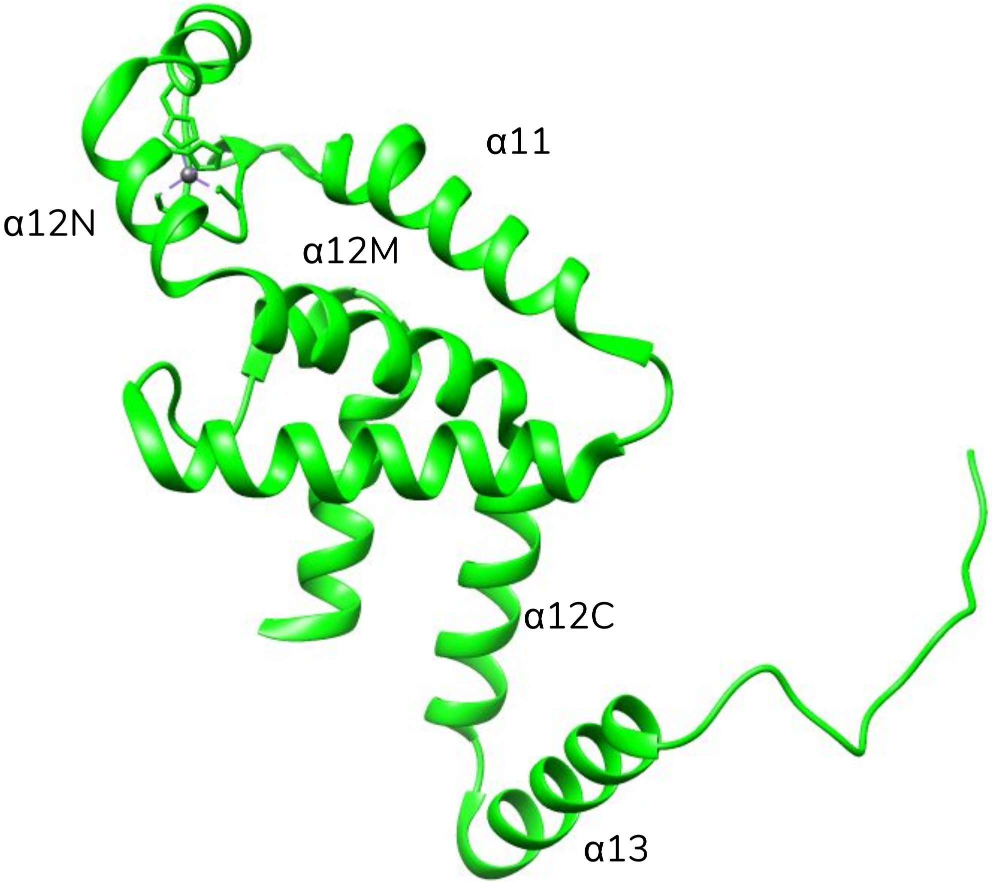
N-term



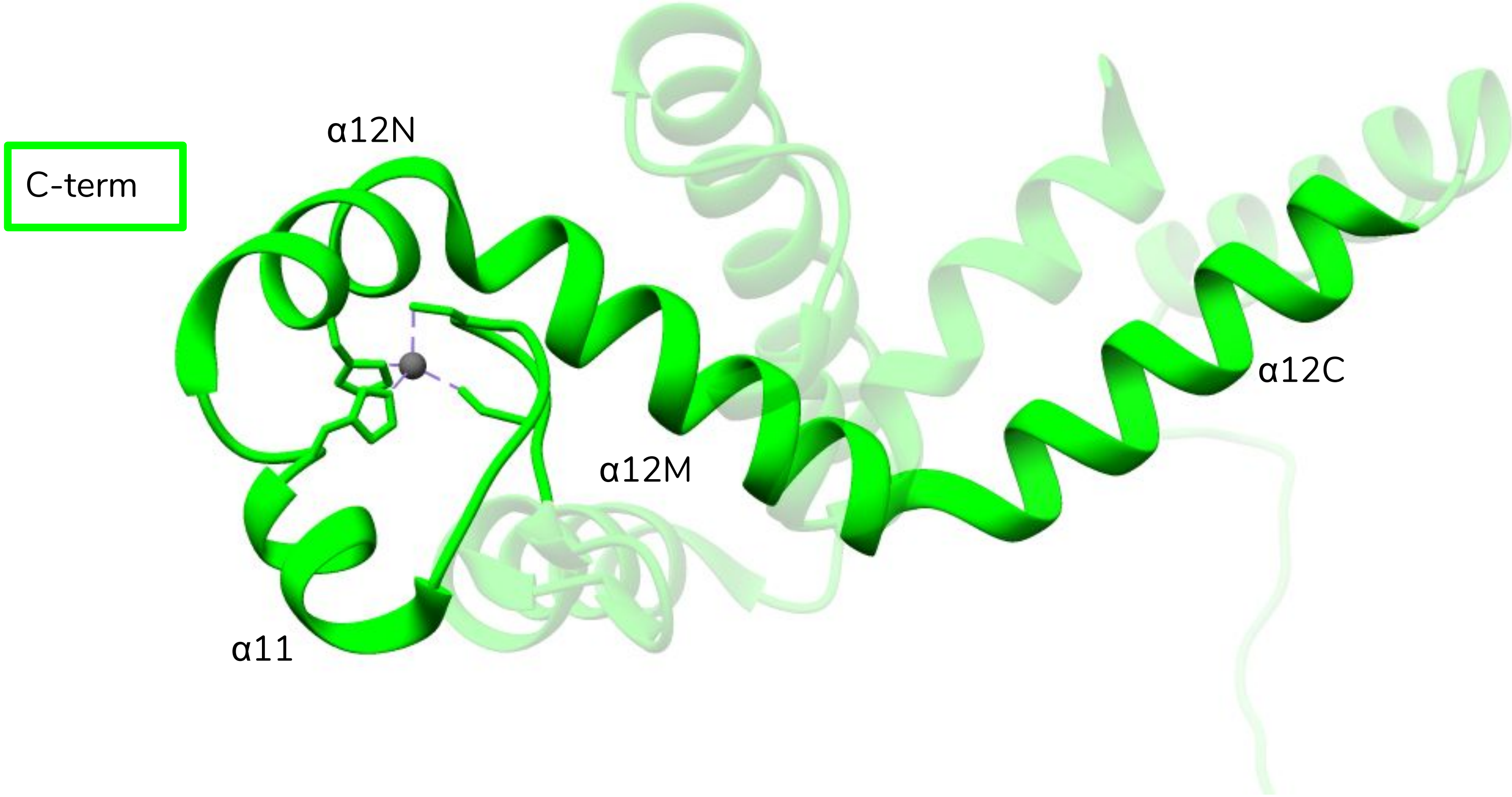


Prp9 | Prp21 | Prp11

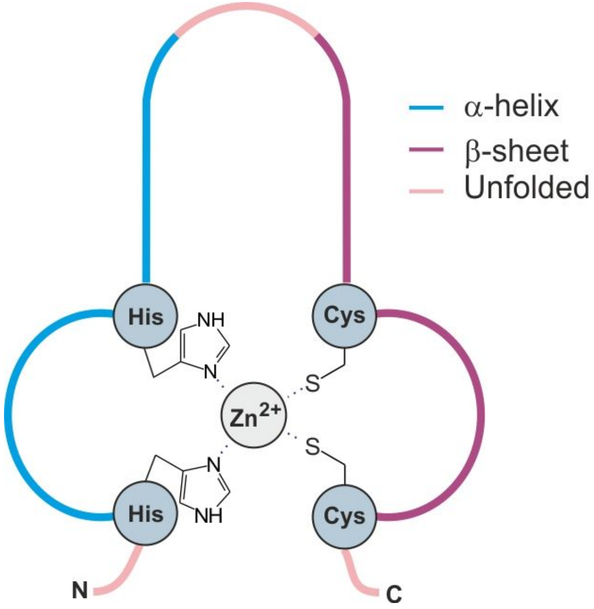
C-term

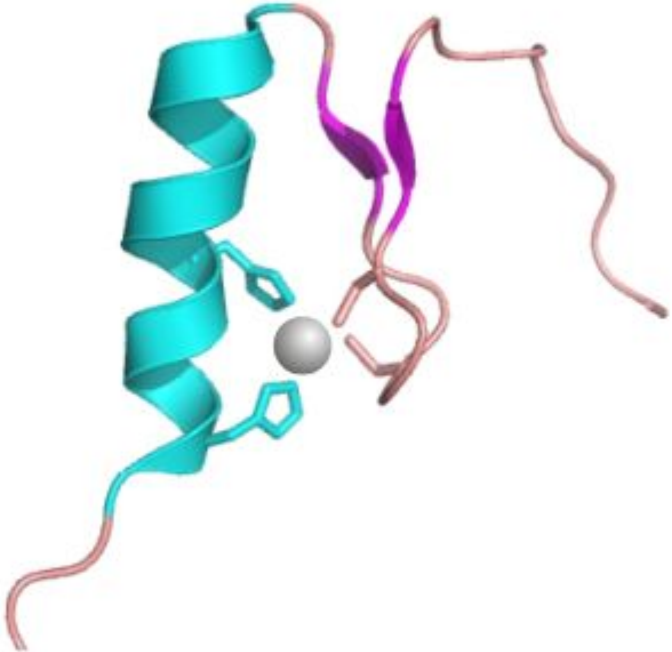


Prp9	Prp21	Prp11



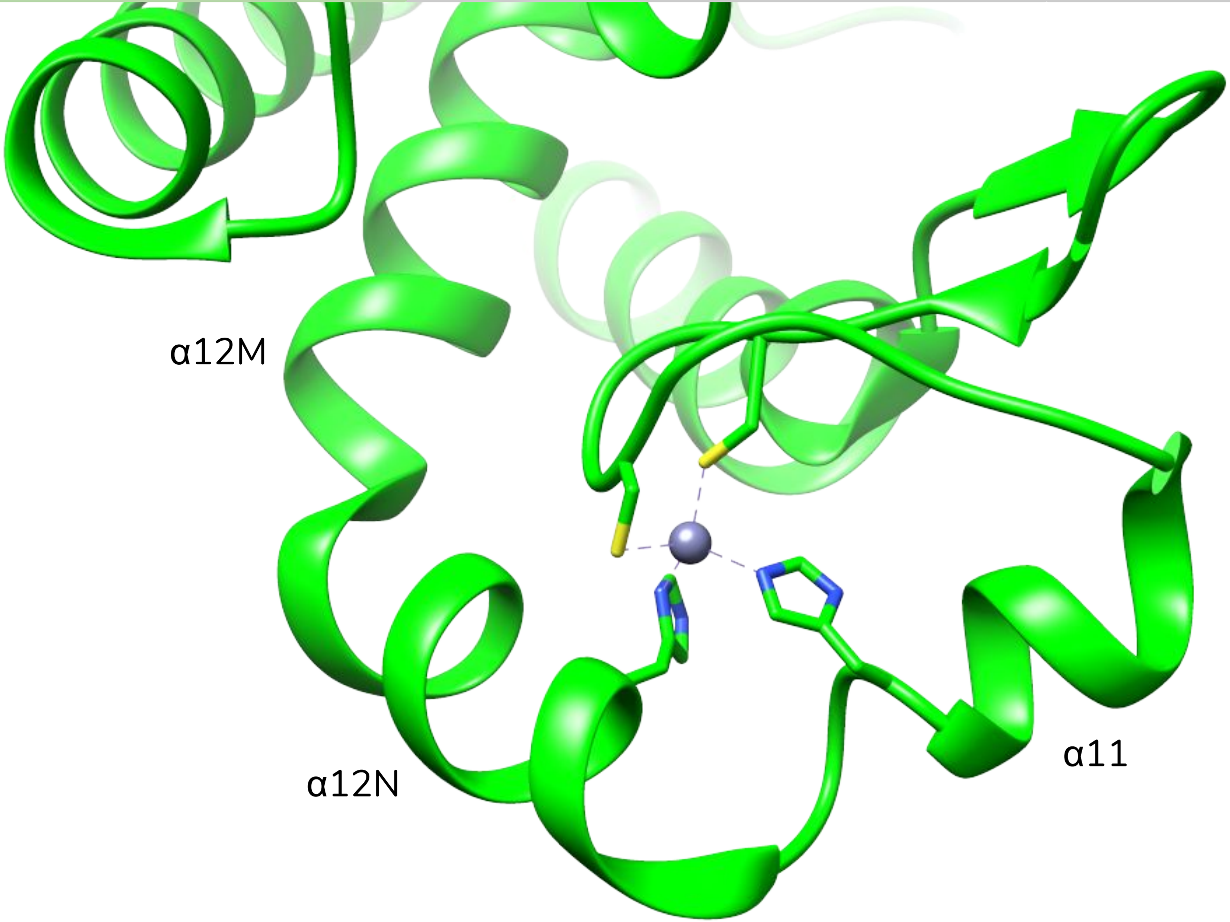
Zn finger



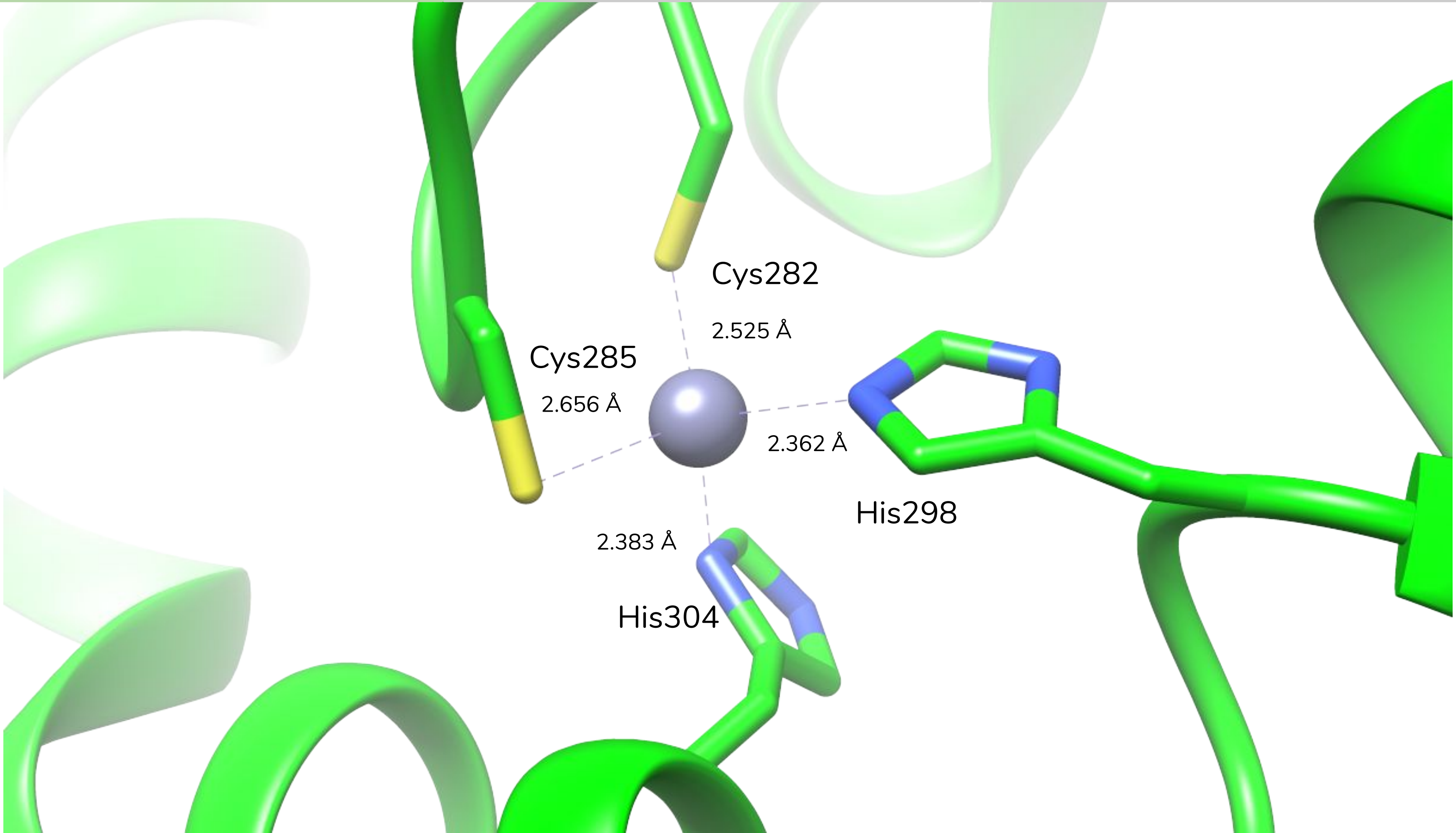


Extracted from: Protein Structures [Internet]. Available from: Peptideweb.com

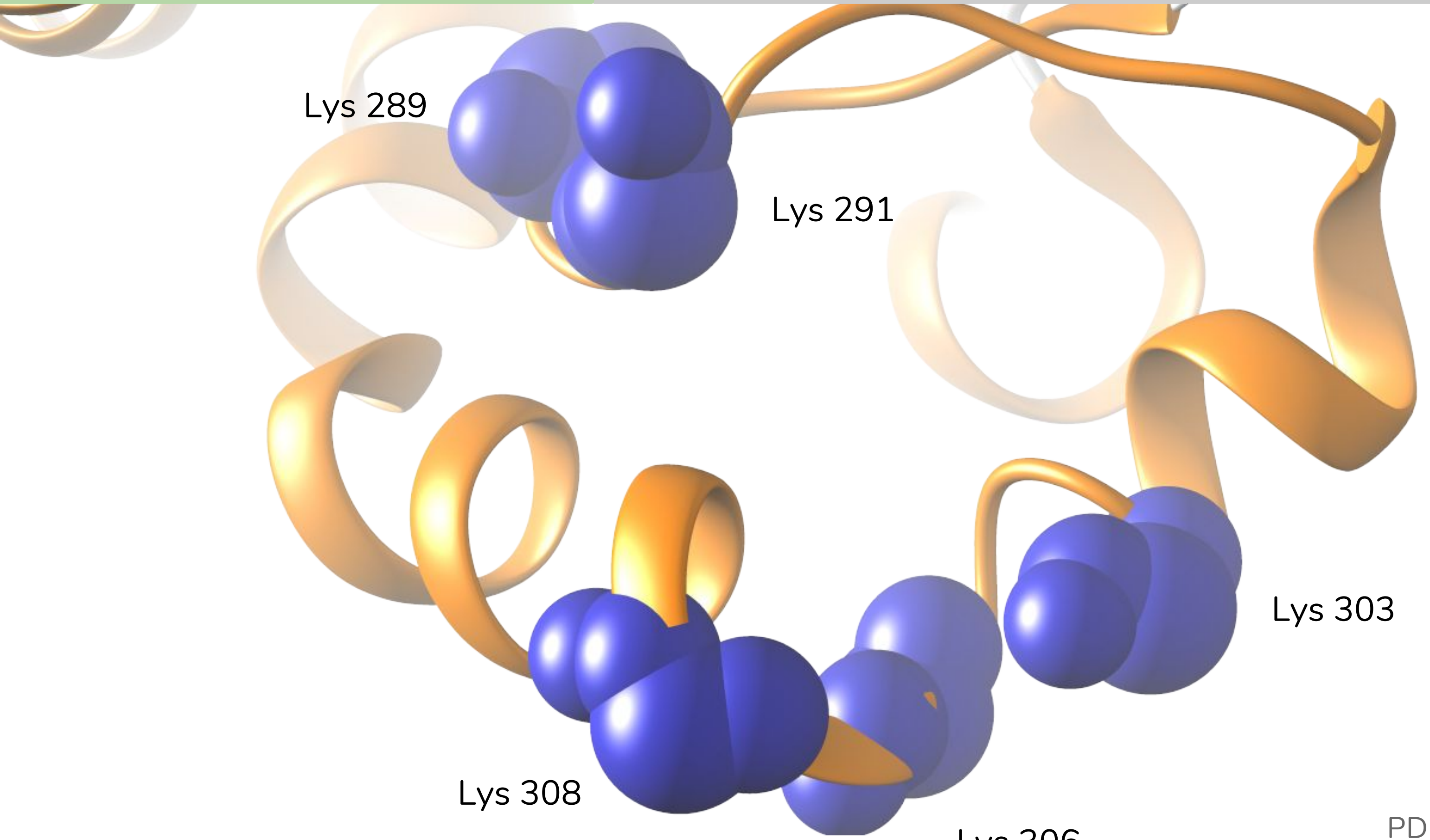
Prp9 | Prp21 | Prp11



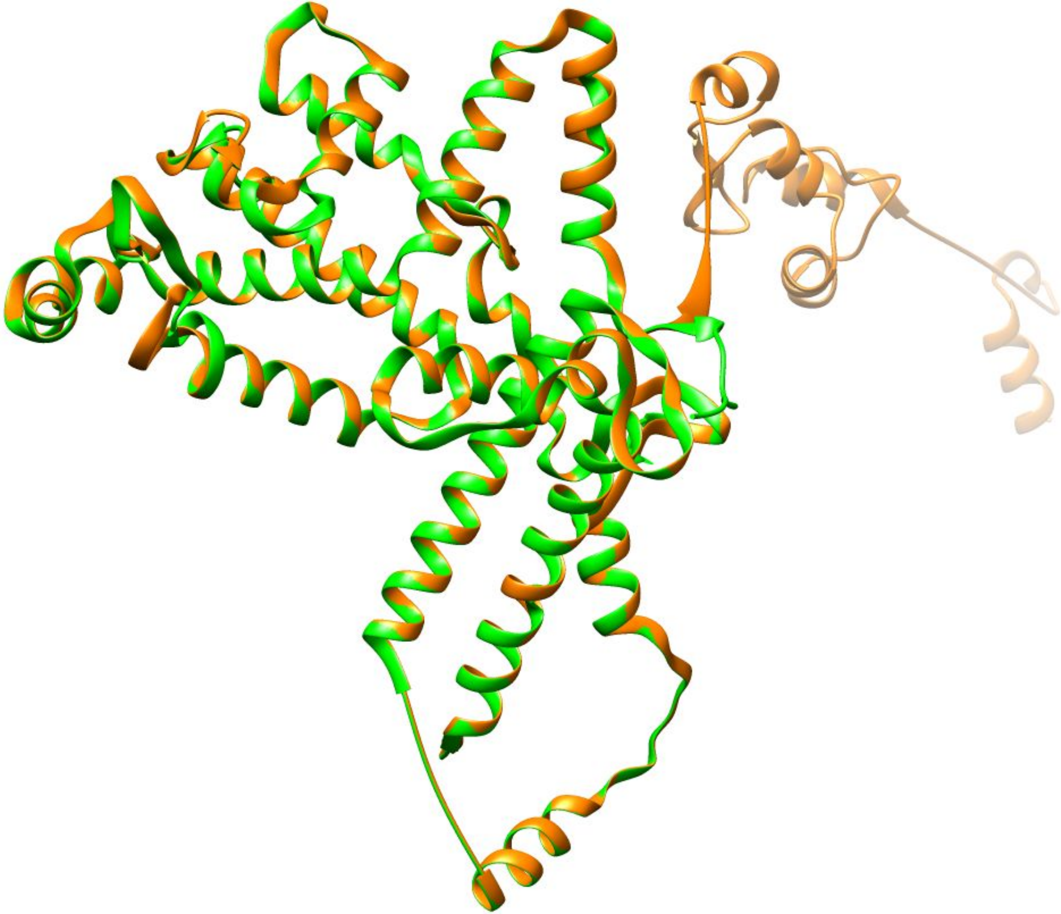
Prp9 Prp21 Prp11



Prp9 | Prp21 | Prp11



PDB ID: 6AH0
Resolution: 5,7Å



ROUGH STAMP
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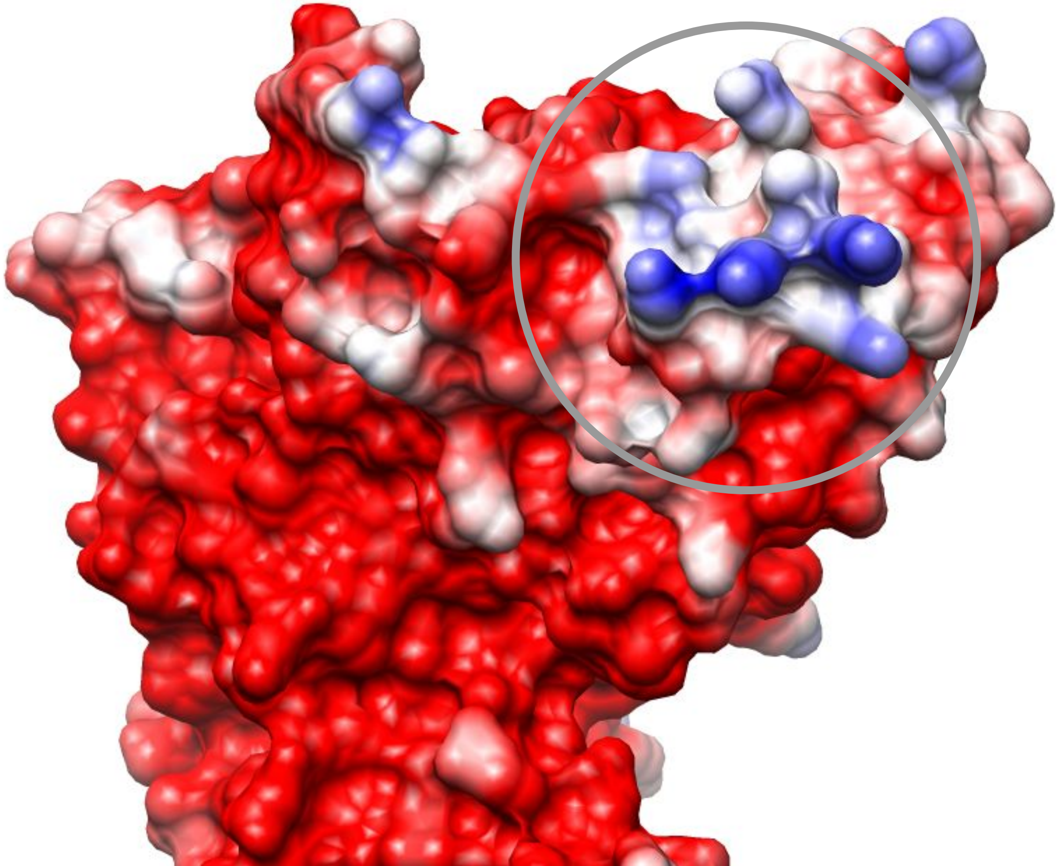
RMS = 0.29

Prp9 | Prp21 | Prp11

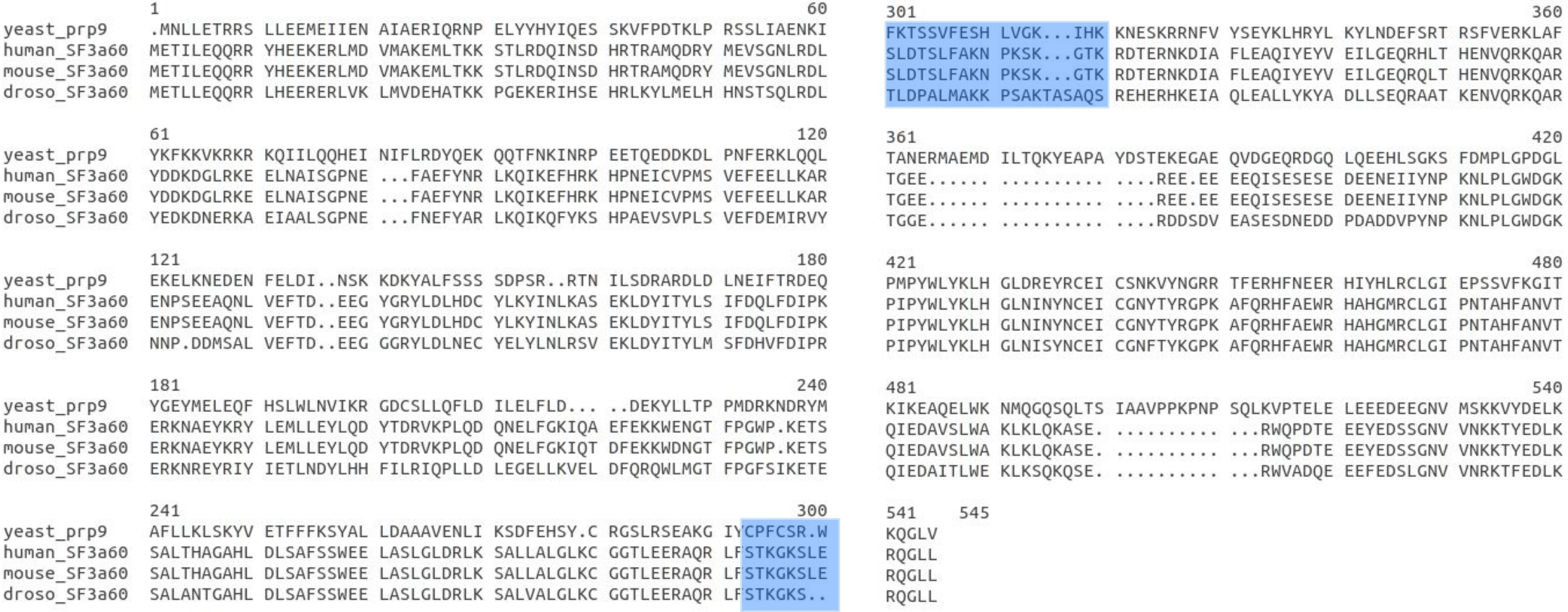


ROUGH STAMP
Sc = 6.95
RMS = 0.29

Prp9 | Prp21 | Prp11

```
                            α1              α2              α3
prp9       E-NLLETRRSLLEE-EIIENAIAERIQRNPELYYHYIQESSKVFPDTKLPRSSLIAENKI
SF3a60     METILEQQRRYHEEKERLMDVMAKEMLTKKSTLRDQINSDHRTRAMQDRYMEVSGNLRDL
                            α4                          α5
prp9       YKFKKVKRKRKQIILQQHEINIFLRDYQEKQQTFNKINFERKLQQLEKELKNEDENFELD
SF3a60     YDDKDGLRKEELNAISGPNEFAEFYNRLKQIKEFHRKHFEELLKARENPSEEAQNLVEFT
                α6                                               α7
prp9       INSKKDKYALFSSSSDPSRRTNILSDRARDLDLNEIFTRDEQYGEY-ELEQFHSLWLNVI
SF3a60     DEEGYGRYLDL-H-Y-INLKASEKLDYITYLSIFDQLFDIPKERKNAEYKRYLEMLLEYL
                      α8                              α9
prp9       KRGDCSLLQFLDILELFLDDEKYLLTPP-DRKNDRY-AFLLKLSKYVETFFFKSYALLDA
SF3a60     QDYTDRVKPLQDQNEL-F-E-KKWENGTFPGWPKETSSALTHAGAHLDLSAFSSWEELAS
                   α10          β1    β2             α11         α12a
prp9       AAVENLIKSDFEHSYCR-GSLRSEAKGIYCP-FCSRWFKTSSVFESHLVGKIHKKNESKR
SF3a60     LGLDRLKSALLALGLKCGGTLEERAQRLFSTKGKSLESLDTSLFAKNPKSKGTKRDTERN
                   α12b            α12c             α13
prp9       RNFVYSEYKLHRYLKYLNDEFSRTRSFVERKLAFTANER-AE-DILTQKYEAPAYDSTEK
SF3a60     KDIAFLEAQIYEYVEILGEQRHLTHENVQRKQARTGEEREEEEEEEQISESESEDEENIPY

prp9       EGAEQVD-----------------------------------------------------
SF3a60     WLYKLHGLNINYNCEICGNYTYRGPKAFQRHFAEWRHAHGMRCLGIPNTAHFANVTQIED

prp9       -----------------------------
SF3a60     AVSLWAKLKEDSSGNVVNKKTYEDLKRQG
```

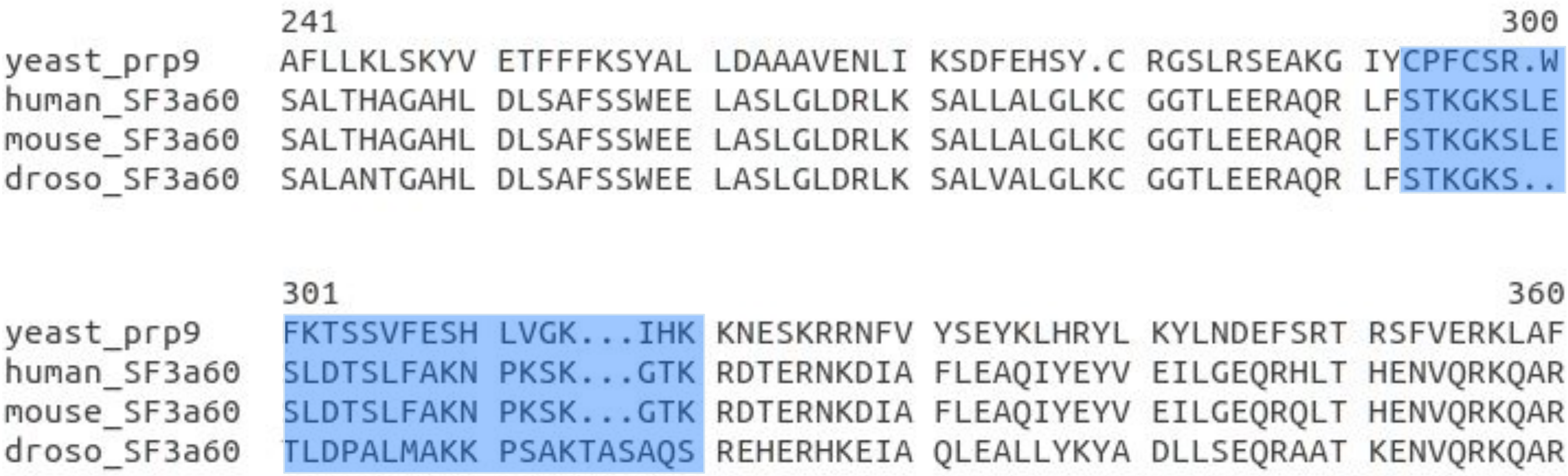
Structural alignment (STAMP)



```
               1                                                          60
yeast_prp9     .MNLLETRRS LLEEMEIIEN AIAERIQRNP ELYYHYIQES SKVFPDTKLP RSSLIAENKI
human_SF3a60   METILEQQRR YHEEKERLMD VMAKEMLTKK STLRDQINSD HRTRAMQDRY MEVSGNLRDL
mouse_SF3a60   METILEQQRR YHEEKERLMD VMAKEMLTKK STLRDQINSD HRTRAMQDRY MEVSGNLRDL
droso_SF3a60   METLLEQQRR LHEERERLVK LMVDEHATKK PGEKERIHSE HRLKYLMELH HNSTSQLRDL

               61                                                        120
yeast_prp9     YKFKKVKRKR KQIILQQHEI NIFLRDYQEK QQTFNKINRP EETQEDDKDL PNFERKLQQL
human_SF3a60   YDDKDGLRKE ELNAISGPNE ...FAEFYNR LKQIKEFHRK HPNEICVPMS VEFEELLKAR
mouse_SF3a60   YDDKDGLRKE ELNAISGPNE ...FAEFYNR LKQIKEFHRK HPNEICVPMS VEFEELLKAR
droso_SF3a60   YEDKDNERKA EIAALSGPNE ...FNEFYAR LKQIKQFYKS HPAEVSVPLS VEFDEMIRVY

               121                                                       180
yeast_prp9     EKELKNEDEN FELDI..NSK KDKYALFSSS SDPSR..RTN ILSDRARDLD LNEIFTRDEQ
human_SF3a60   ENPSEEAQNL VEFTD..EEG YGRYLDLHDC YLKYINLKAS EKLDYITYLS IFDQLFDIPK
mouse_SF3a60   ENPSEEAQNL VEFTD..EEG YGRYLDLHDC YLKYINLKAS EKLDYITYLS IFDQLFDIPK
droso_SF3a60   NNP.DDMSAL VEFTD..EEG GGRYLDLNEC YELYLNLRSV EKLDYITYLM SFDHVFDIPR

               181                                                       240
yeast_prp9     YGEYMELEQF HSLWLNVIKR GDCSLLQFLD ILELFLD... ..DEKYLLTP PMDRKNDRYM
human_SF3a60   ERKNAEYKRY LEMLLEYLQD YTDRVKPLQD QNELFGKIQA EFEKKWENGT FPGWP.KETS
mouse_SF3a60   ERKNAEYKRY LEMLLEYLQD YTDRVKPLQD QNELFGKIQT DFEKKWDNGT FPGWP.KETS
droso_SF3a60   ERKNREYRIY IETLNDYLHH FILRIQPLLD LEGELLKVEL DFQRQWLMGT FPGFSIKETE

               241                                                       300
yeast_prp9     AFLLKLSKYV ETFFFKSYAL LDAAAVENLI KSDFEHSY.C RGSLRSEAKG IYCPFCSR.W
human_SF3a60   SALTHAGAHL DLSAFSSWEE LASLGLDRLK SALLALGLKC GGTLEERAQR LFSTKGKSLE
mouse_SF3a60   SALTHAGAHL DLSAFSSWEE LASLGLDRLK SALLALGLKC GGTLEERAQR LFSTKGKSLE
droso_SF3a60   SALANTGAHL DLSAFSSWEE LASLGLDRLK SALVALGLKC GGTLEERAQR LFSTKGKS..

301                                                        360
FKTSSVFESH LVGK...IHK KNESKRRNFV YSEYKLHRYL KYLNDEFSRT RSFVERKLAF
SLDTSLFAKN PKSK...GTK RDTERNKDIA FLEAQIYEYV EILGEQRHLT HENVQRKQAR
SLDTSLFAKN PKSK...GTK RDTERNKDIA FLEAQIYEYV EILGEQRQLT HENVQRKQAR
TLDPALMAKK PSAKTASAQS REHERHKEIA QLEALLYKYA DLLSEQRAAT KENVQRKQAR

361                                                        420
TANERMAEMD ILTQKYEAPA YDSTEKEGAE QVDGEQRDGQ LQEEHLSGKS FDMPLGPDGL
TGEE...... .......... ....REE.EE EEQISESESE DEENEIIYNP KNLPLGWDGK
TGEE...... .......... ....REE.EE EEQISESESE DEENEIIYNP KNLPLGWDGK
TGGE...... .......... ....RDDSDV EASESDNEDD PDADDVPYNP KNLPLGWDGK

421                                                        480
PMPYWLYKLH GLDREYRCEI CSNKVYNGRR TFERHFNEER HIYHLRCLGI EPSSVFKGIT
PIPYWLYKLH GLNINYNCEI CGNYTYRGPK AFQRHFAEWR HAHGMRCLGI PNTAHFANVT
PIPYWLYKLH GLNINYNCEI CGNYTYRGPK AFQRHFAEWR HAHGMRCLGI PNTAHFANVT
PIPYWLYKLH GLNISYNCEI CGNFTYKGPK AFQRHFAEWR HAHGMRCLGI PNTAHFANVT

481                                                        540
KIKEAQELWK NMQGQSQLTS IAAVPPKPNP SQLKVPTELE LEEEDEEGNV MSKKVYDELK
QIEDAVSLWA KLKLQKASE. .......... ...RWQPDTE EEYEDSSGNV VNKKTYEDLK
QIEDAVSLWA KLKLQKASE. .......... ...RWQPDTE EEYEDSSGNV VNKKTYEDLK
QIEDAITLWE KLKSQKQSE. .......... ...RWVADQE EEFEDSLGNV VNRKTFEDLK

541    545
KQGLV
RQGLL
RQGLL
RQGLL
```

Multiple Sequence Alignment (ClustalW)

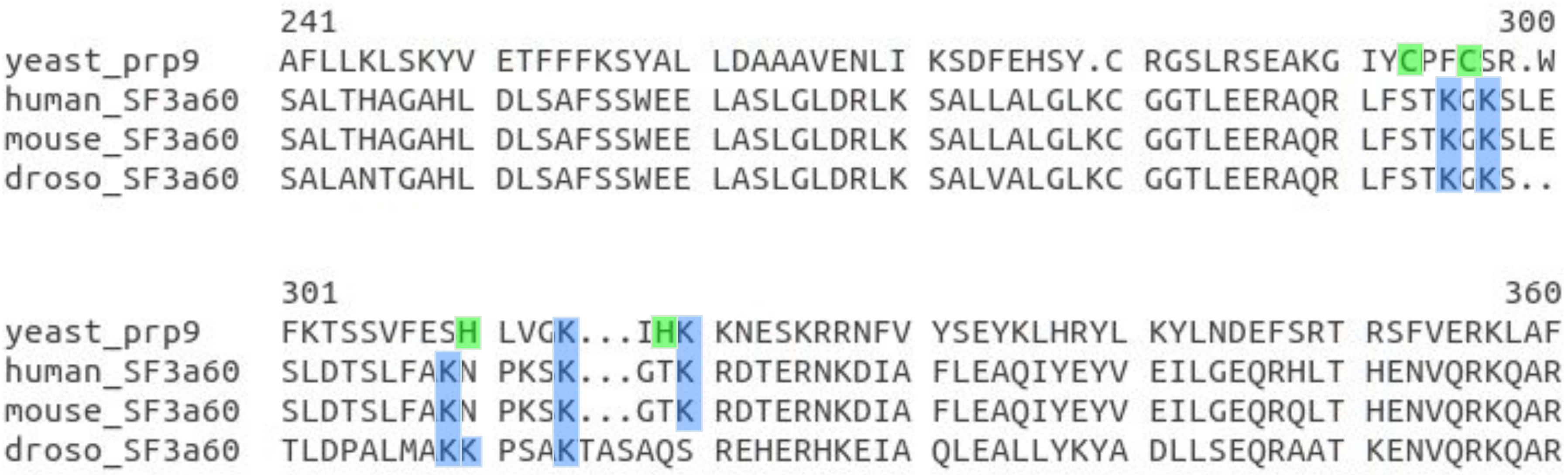
Prp9 Prp21 Prp11



```
                241                                                           300
yeast_prp9      AFLLKLSKYV ETFFFKSYAL LDAAAVENLI KSDFEHSY.C RGSLRSEAKG IYCPFCSR.W
human_SF3a60    SALTHAGAHL DLSAFSSWEE LASLGLDRLK SALLALGLKC GGTLEERAQR LFSTKGKSLE
mouse_SF3a60    SALTHAGAHL DLSAFSSWEE LASLGLDRLK SALLALGLKC GGTLEERAQR LFSTKGKSLE
droso_SF3a60    SALANTGAHL DLSAFSSWEE LASLGLDRLK SALVALGLKC GGTLEERAQR LFSTKGKS..

                301                                                           360
yeast_prp9      FKTSSVFESH LVGK...IHK KNESKRRNFV YSEYKLHRYL KYLNDEFSRT RSFVERKLAF
human_SF3a60    SLDTSLFAKN PKSK...GTK RDTERNKDIA FLEAQIYEYV EILGEQRHLT HENVQRKQAR
mouse_SF3a60    SLDTSLFAKN PKSK...GTK RDTERNKDIA FLEAQIYEYV EILGEQRQLT HENVQRKQAR
droso_SF3a60    TLDPALMAKK PSAKTASAQS REHERHKEIA QLEALLYKYA DLLSEQRAAT KENVQRKQAR
```

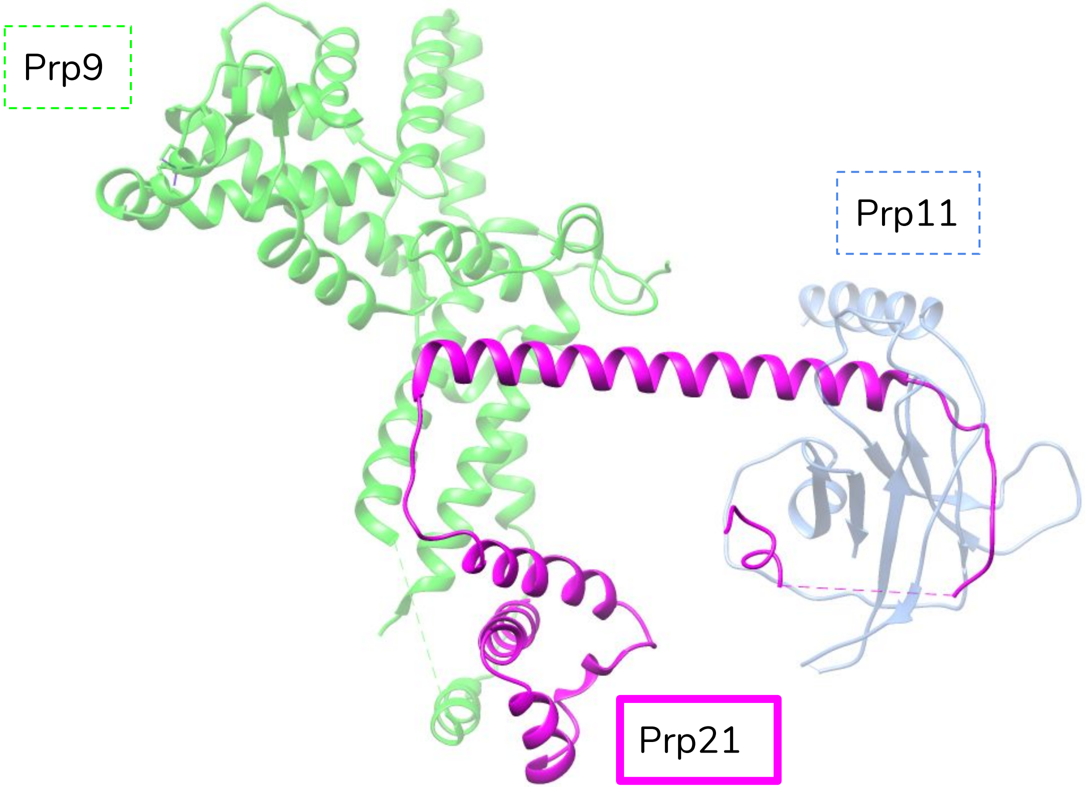
Multiple Sequence Alignment (ClustalW)

Prp9 Prp21 Prp11

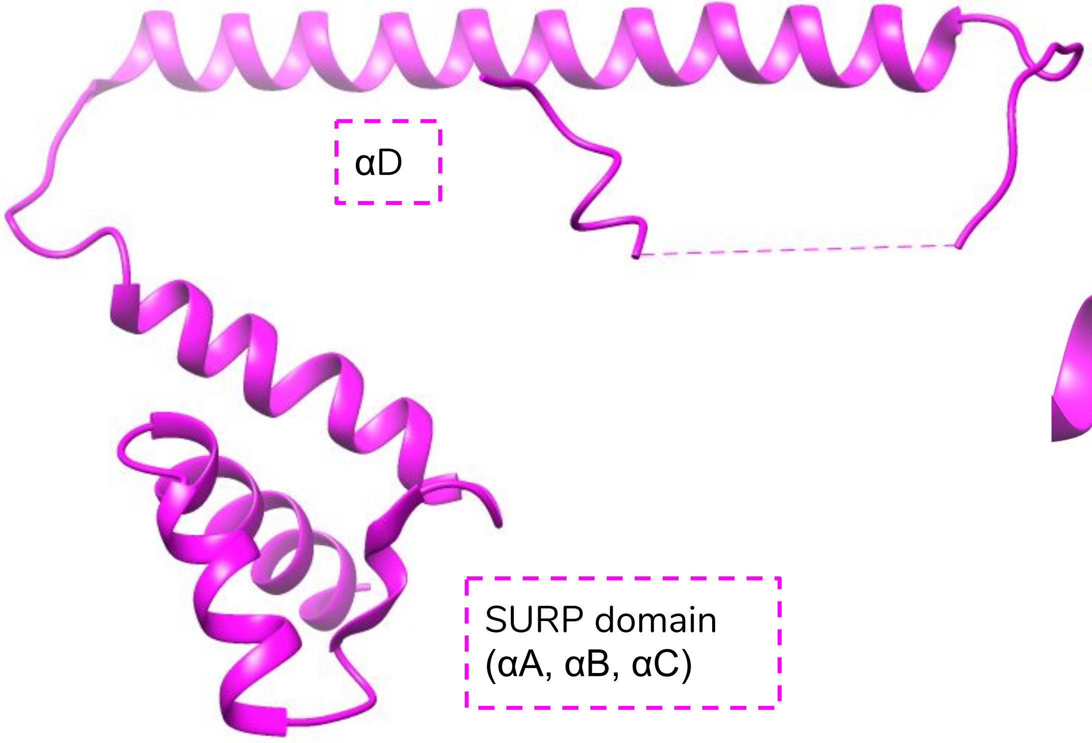


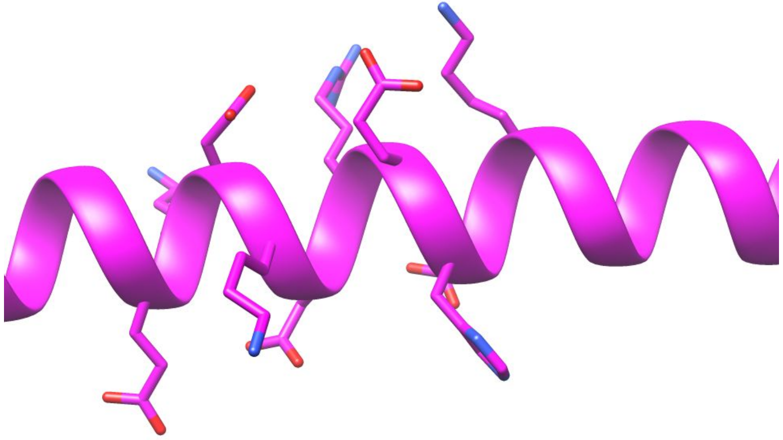
```
                 241                                                         300
yeast_prp9       AFLLKLSKYV ETFFFKSYAL LDAAAVENLI KSDFEHSY.C RGSLRSEAKG IYCPFCSR.W
human_SF3a60     SALTHAGAHL DLSAFSSWEE LASLGLDRLK SALLALGLKC GGTLEERAQR LFSTKGKSLE
mouse_SF3a60     SALTHAGAHL DLSAFSSWEE LASLGLDRLK SALLALGLKC GGTLEERAQR LFSTKGKSLE
droso_SF3a60     SALANTGAHL DLSAFSSWEE LASLGLDRLK SALVALGLKC GGTLEERAQR LFSTKGKS..

                 301                                                         360
yeast_prp9       FKTSSVFESH LVGK...IHK KNESKRRNFV YSEYKLHRYL KYLNDEFSRT RSFVERKLAF
human_SF3a60     SLDTSLFAKN PKSK...GTK RDTERNKDIA FLEAQIYEYV EILGEQRHLT HENVQRKQAR
mouse_SF3a60     SLDTSLFAKN PKSK...GTK RDTERNKDIA FLEAQIYEYV EILGEQRQLT HENVQRKQAR
droso_SF3a60     TLDPALMAKK PSAKTASAQS REHERHKEIA QLEALLYKYA DLLSEQRAAT KENVQRKQAR
```

Multiple Sequence Alignment (ClustalW)



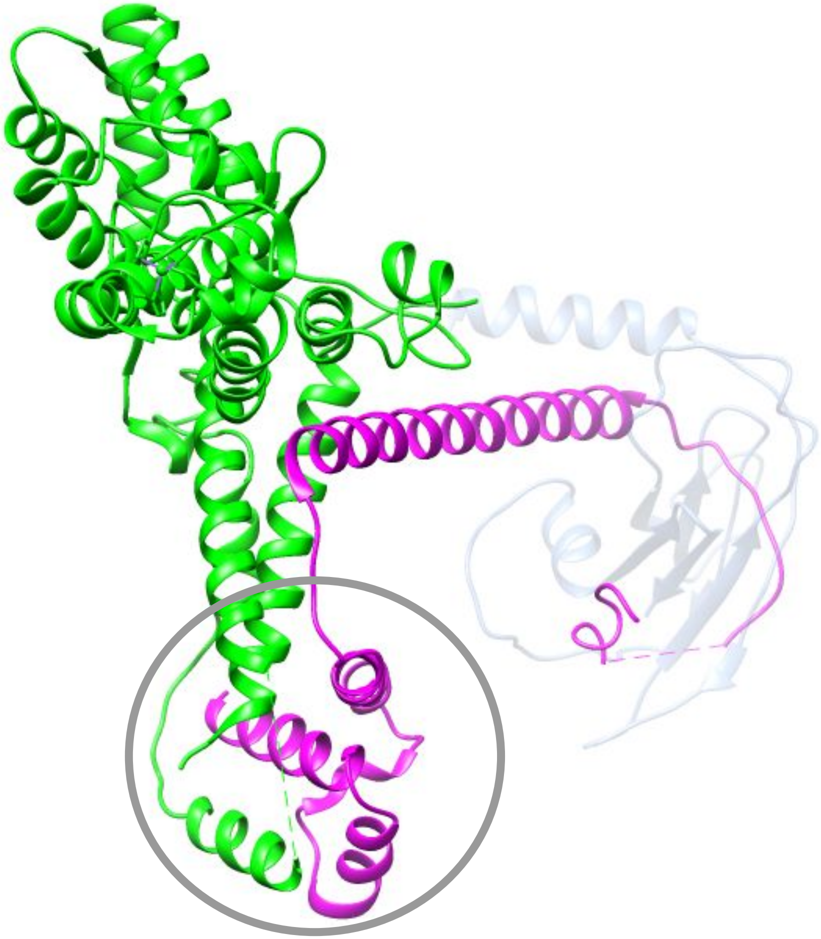
PDB ID: 4DGW
Resolution: 3.112 Å

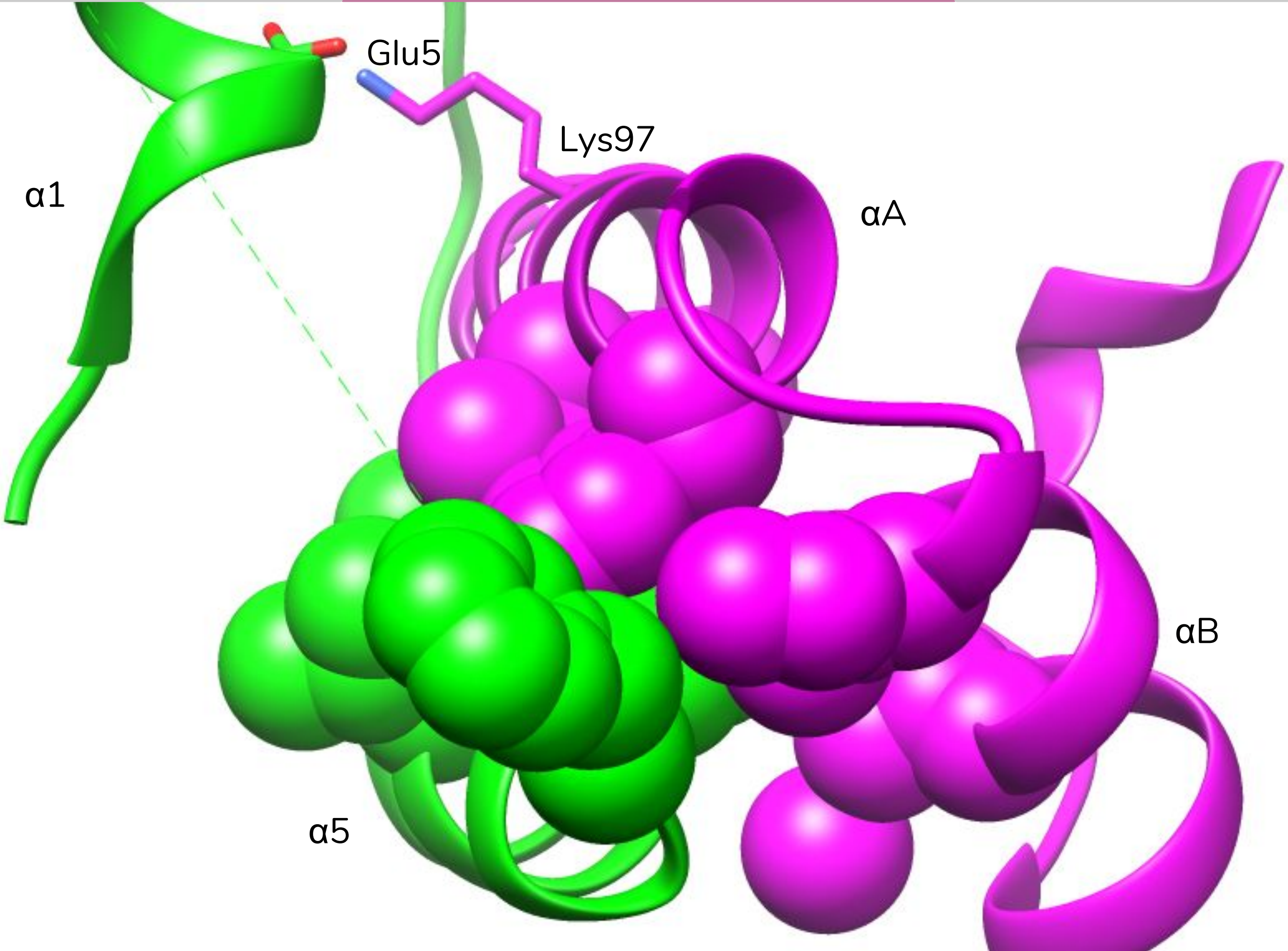


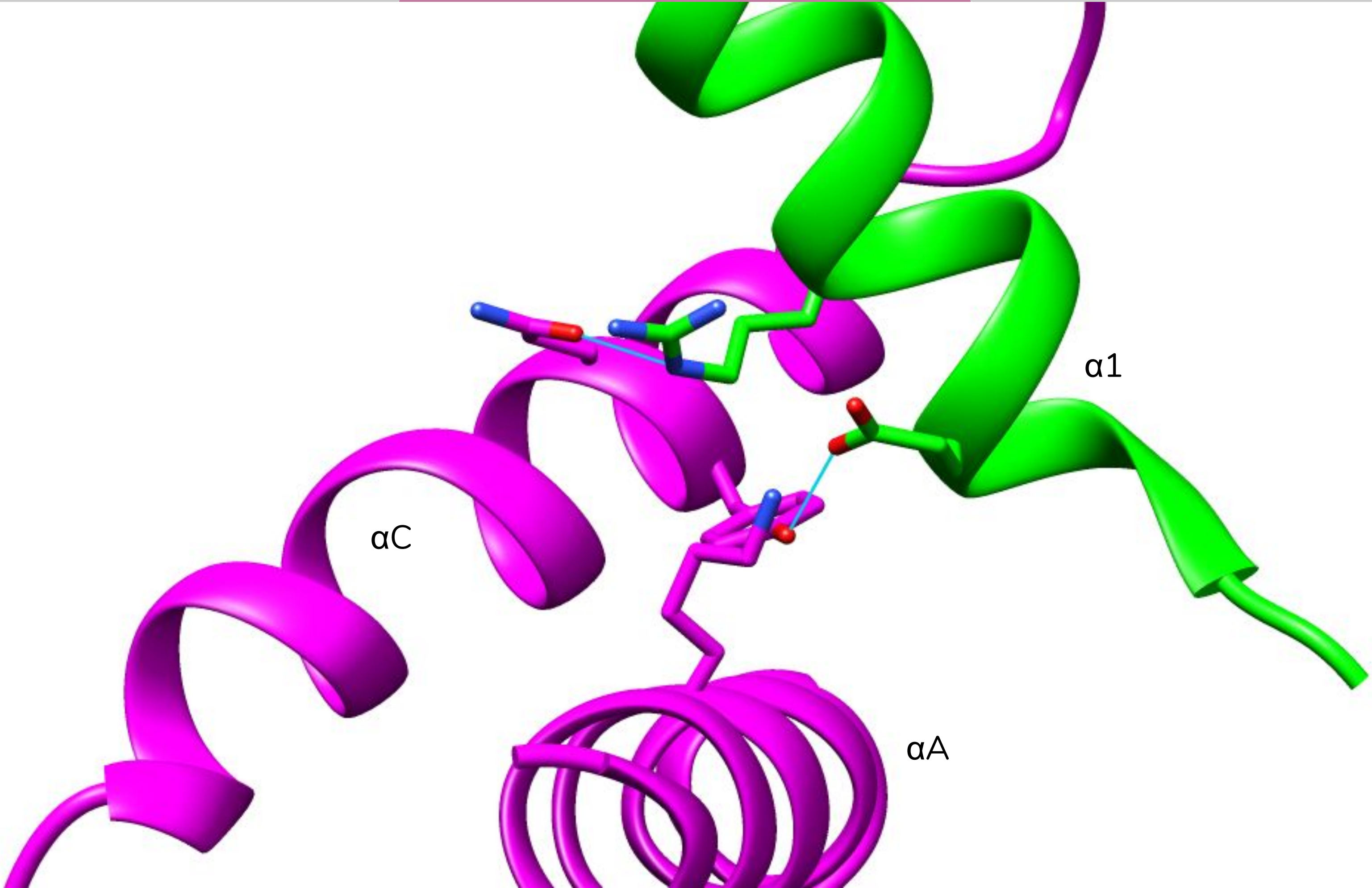


Glu174 - Lys183

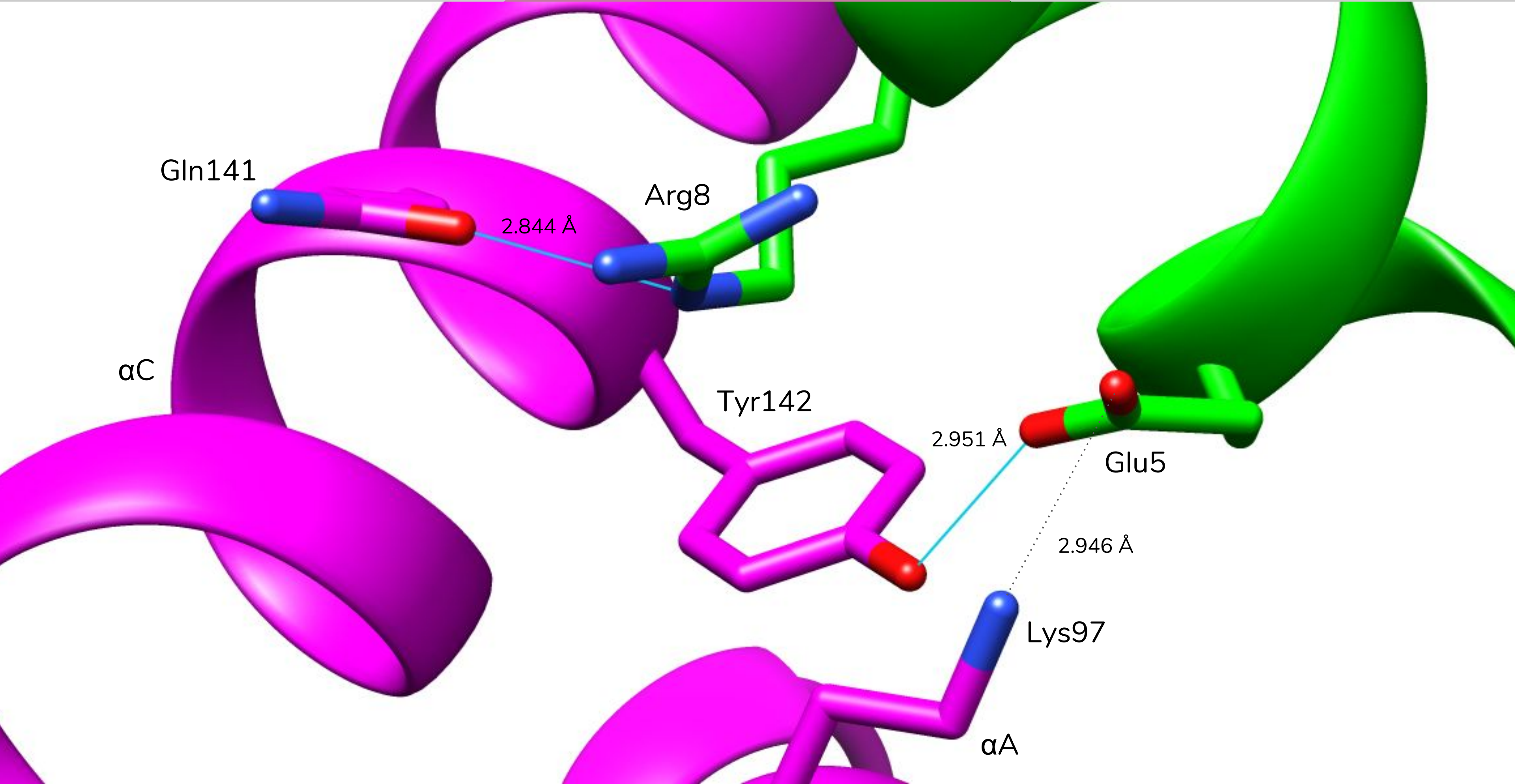
Prp9 | **Prp21** | Prp11



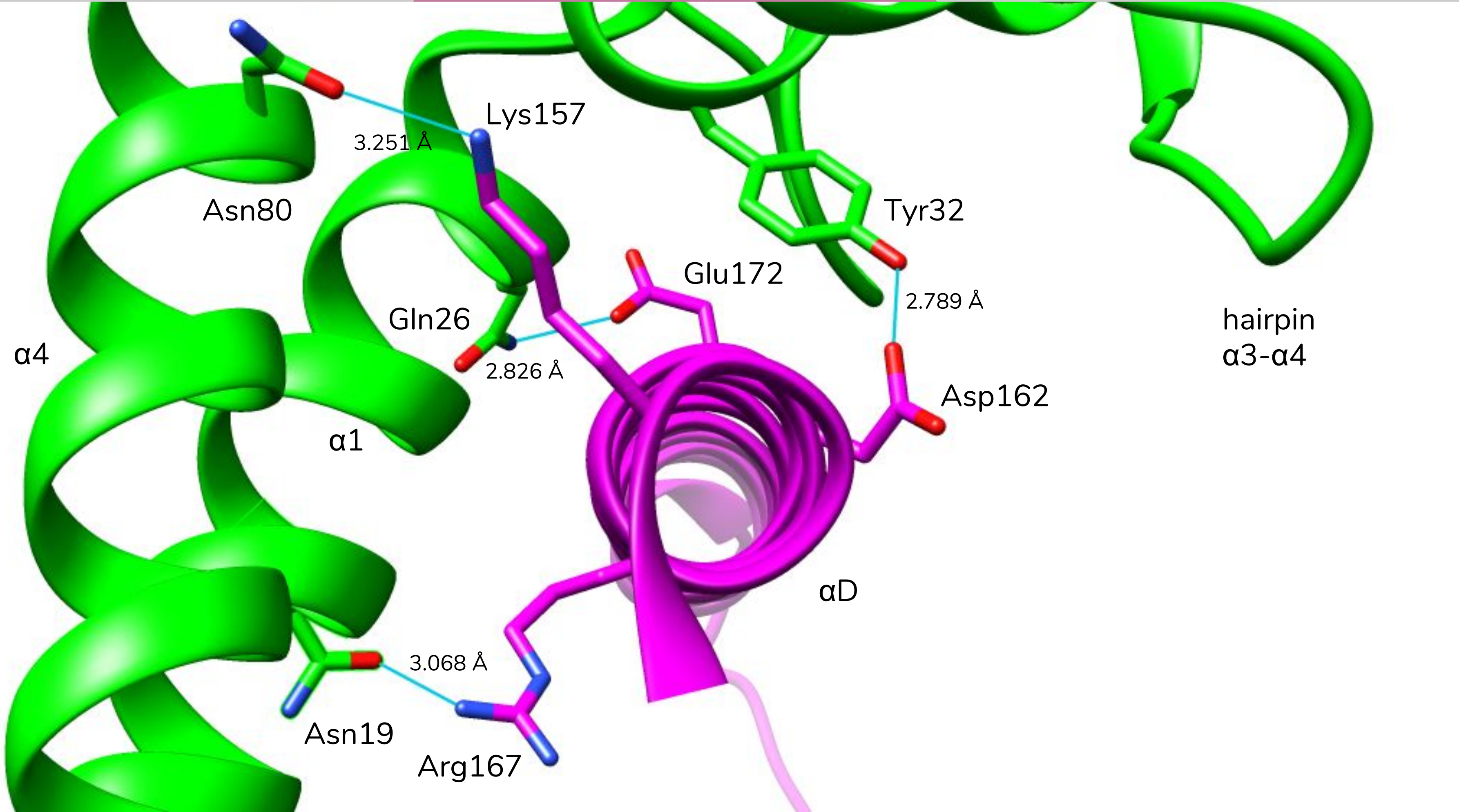

Glu5
Lys97
α1
αA
αB
α5

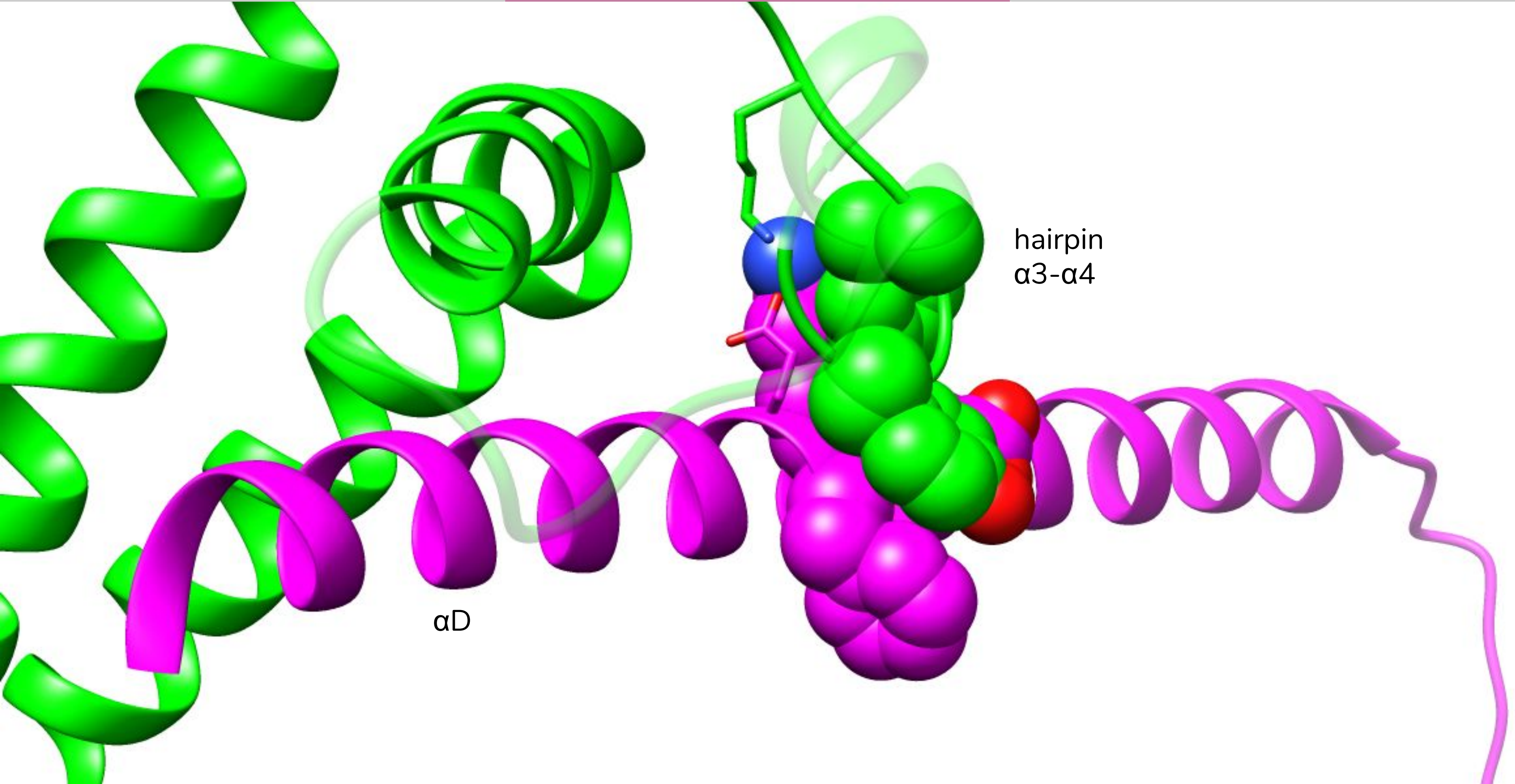

α1
αC
αA

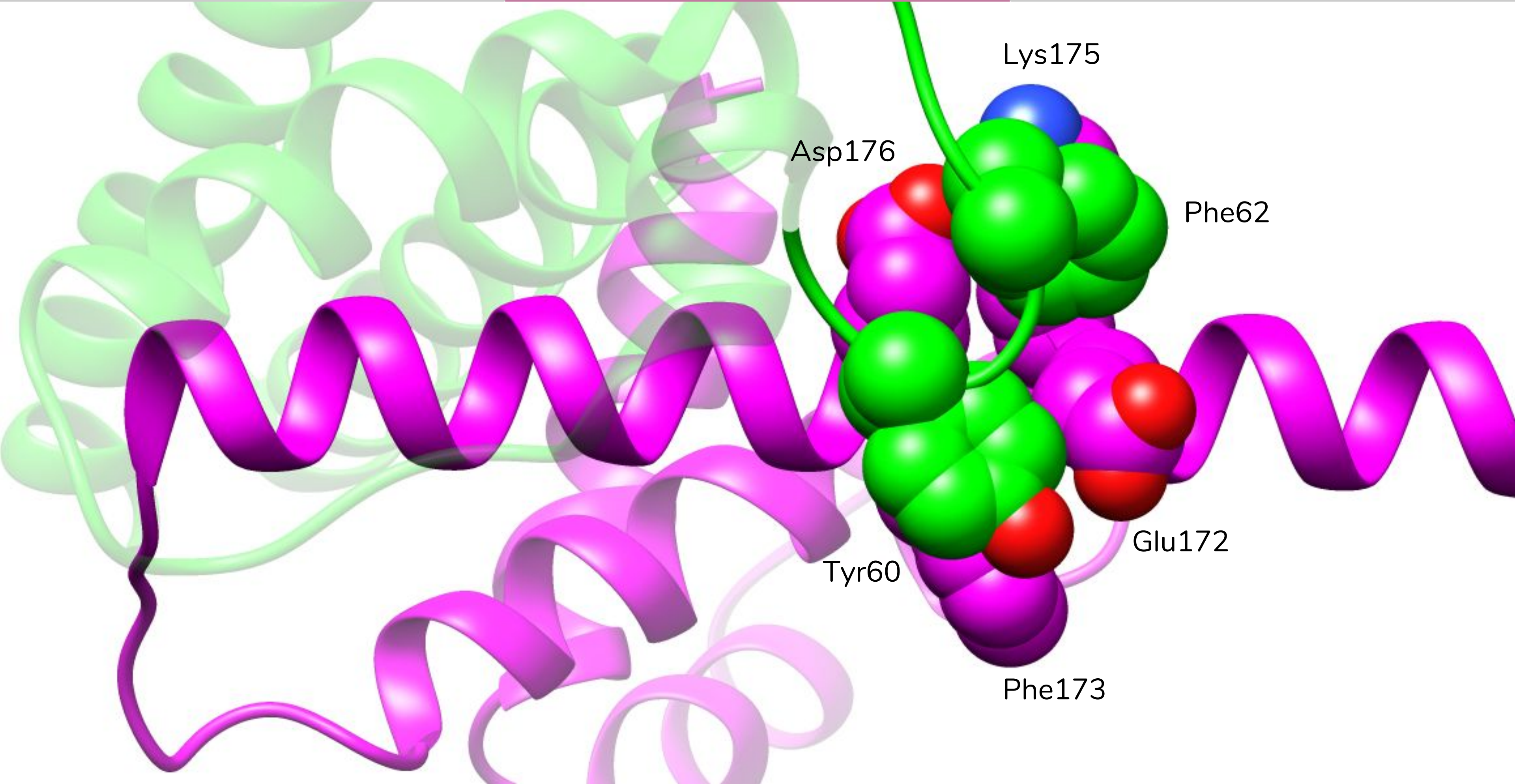
Prp9 | **Prp21** | Prp11

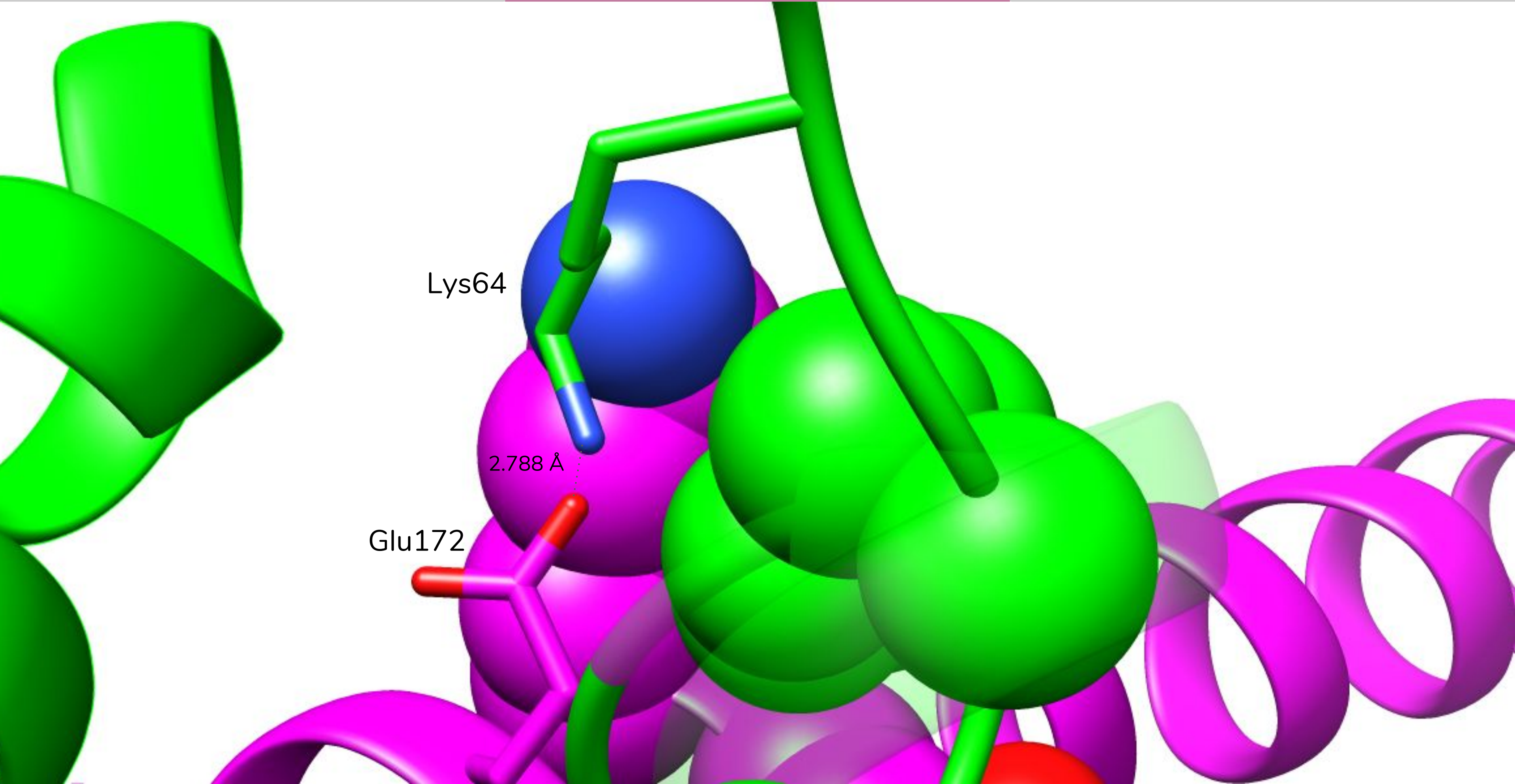


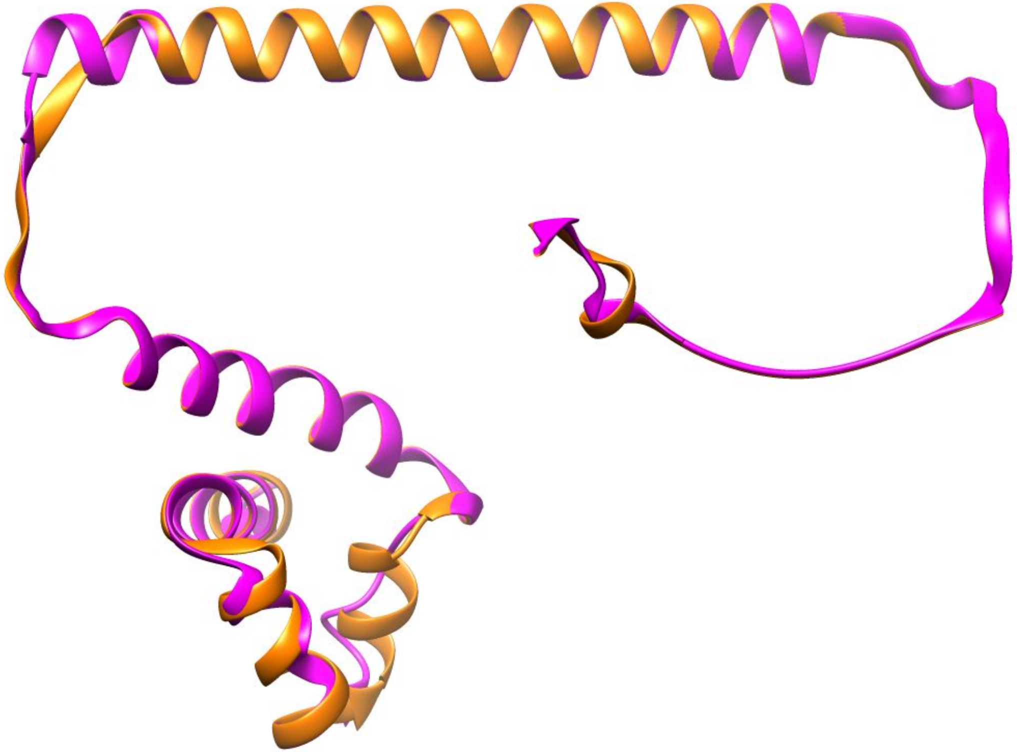
Prp9 | **Prp21** | Prp11


Lys157
3.251 Å
Asn80
Tyr32
Glu172
Gln26
2.789 Å
hairpin
α3-α4
α4
2.826 Å
Asp162
α1
αD
3.068 Å
Asn19
Arg167


hairpin
α3-α4
αD


Lys175
Asp176
Phe62
Glu172
Tyr60
Phe173

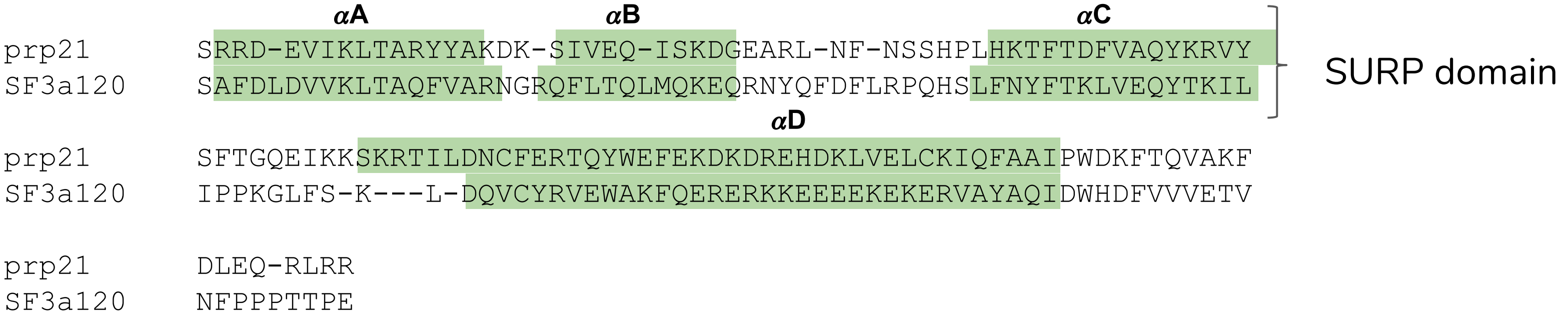

Lys64
2.788 Å
Glu172



● Prp21

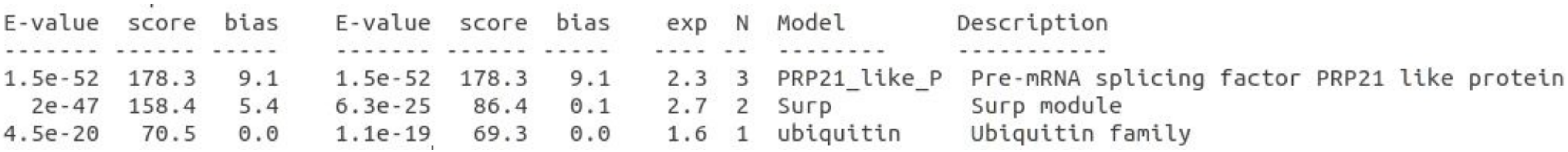
● SF3a120

ROUGH STAMP
Sc = 8.39
RMS = 0.55



```
prp21      SRRD-EVIKLTARYYAKDK-SIVEQ-ISKDGEARL-NF-NSSHPLHKTFTDFVAQYKRVY
SF3a120    SAFDLDVVKLTAQFVARNGRQFLTQLMQKEQRNYQFDFLRPQHSLFNYFTKLVEQYTKIL

prp21      SFTGQEIKKSKRTILDNCFERTQYWEFEKDKDREHDKLVELCKIQFAAIPWDKFTQVAKF
SF3a120    IPPKGLFS-K---L-DQVCYRVEWAKFQERERKKEEEEKEKERVAYAQIDWHDFVVVETV

prp21      DLEQ-RLRR
SF3a120    NFPPPTTPE
```

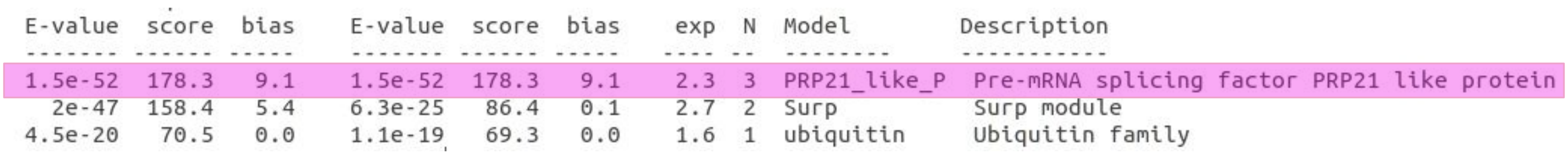
Structural alignment (STAMP)



```
E-value  score  bias    E-value  score  bias    exp  N  Model        Description
------- ------ -----    ------- ------ -----   ---- --  --------     -----------
1.5e-52  178.3   9.1    1.5e-52  178.3   9.1    2.3  3  PRP21_like_P  Pre-mRNA splicing factor PRP21 like protein
  2e-47  158.4   5.4    6.3e-25   86.4   0.1    2.7  2  Surp          Surp module
4.5e-20   70.5   0.0    1.1e-19   69.3   0.0    1.6  1  ubiquitin     Ubiquitin family
```

PFAM HMM search

Prp9 **Prp21** Prp11



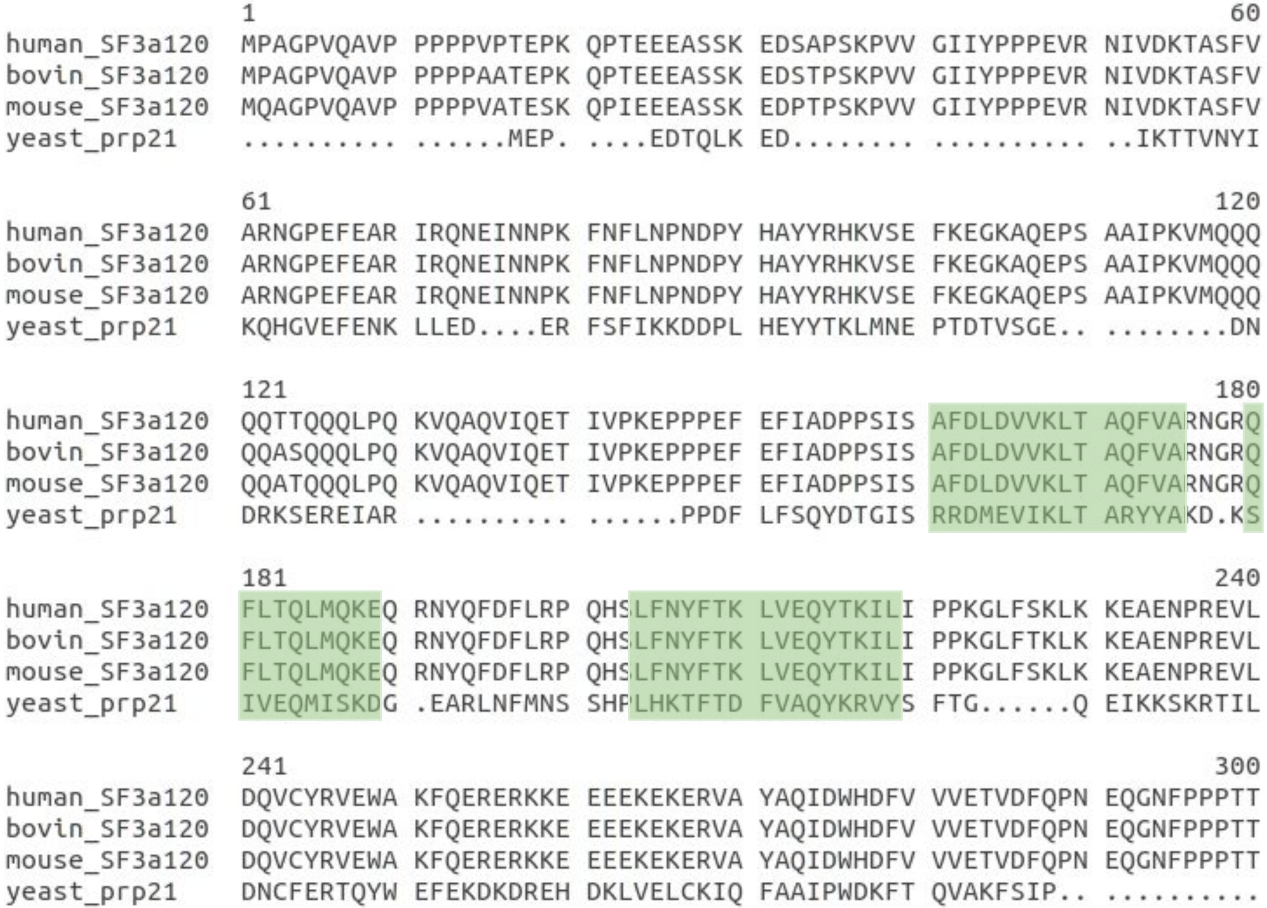
```
 E-value  score  bias    E-value  score  bias    exp  N  Model         Description
 ------- ------ -----    ------- ------ -----   ---- --  --------      -----------
 1.5e-52  178.3   9.1    1.5e-52  178.3   9.1    2.3  3  PRP21_like_P   Pre-mRNA splicing factor PRP21 like protein
   2e-47  158.4   5.4    6.3e-25   86.4   0.1    2.7  2  Surp           Surp module
 4.5e-20   70.5   0.0    1.1e-19   69.3   0.0    1.6  1  ubiquitin      Ubiquitin family
```

PFAM HMM search

```
                 1                                                           60    301                                                       360
human_SF3a120    MPAGPVQAVP PPPPVPTEPK QPTEEEASSK EDSAPSKPVV GIIYPPPEVR NIVDKTASFV    PEELGARILI QERYEKFGES EEVEMEVESD EEDDKQEKAE EPPSQLDQDT QVQDMDEGSD
bovin_SF3a120    MPAGPVQAVP PPPPAATEPK QPTEEEASSK EDSTPSKPVV GIIYPPPEVR NIVDKTASFV    PEELGARILI QERYEKFGES EEVEMEVESD EEDEKQEKAE EPPSQLDQDT QVQDMDEGSD
mouse_SF3a120    MQAGPVQAVP PPPPVATESK QPIEEEASSK EDPTPSKPVV GIIYPPPEVR NIVDKTASFV    PEELGARILI QERYEKFGES EEVEMEVESD EED..QEKAE ETPSQLDQDT QVQDMDEGSD
yeast_prp21      .......... ......MEP. ....EDTQLK ED........ .......... ..IKTTVNYI    .......... .......... .......... .......... .......... ..........

                 61                                                         120    361                                                       420
human_SF3a120    ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ    DEEEGQKVPP PPETPMPPPL PPTPDQVIVR KDYDPKASKP LPPAPAPDEY LVSPITGEKI
bovin_SF3a120    ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ    DEEEGQKVPP PPETPMPPPL PPTPDQVIVR KDYDPKASKP LPPAPAPDEY LVSPITGEKI
mouse_SF3a120    ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ    DEEEGQKVPP PPETPMPPPL PPTPDQVIVR KDYDPKASKP LPPAPAPDEY LVSPITGEKI
yeast_prp21      KQHGVEFENK LLED....ER FSFIKKDDPL HEYYTKLMNE PTDTVSGE.. ........DN    .......... .......... .......... .......... .......... ..........

                 121                                                        180    421                                                       480
human_SF3a120    QQTTQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ    PASKMQEHMR IGLLDPRWLE QRDRSIREKQ SDDEVYAPGL DIESSLKQLA ERRTDIFGVE
bovin_SF3a120    QQASQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ    PASKMQEHMR IGLLDPRWLE QRDRSIREKQ SDDEVYAPGL DIESSLKQLA ERRTDIFGVE
mouse_SF3a120    QQATQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ    PASKMQEHMR IGLLDPRWLE QRDRSIREKQ SDDEVYAPGL DIESSLKQLA ERRTDIFGVE
yeast_prp21      DRKSEREIAR .......... ......PPDF LFSQYDTGIS RRDMEVIKLT ARYYAKD.KS    .......... .......... .......... EDTEIFEGSL DLEQMRLRRV QTGIKLFDSI

                 181                                                        240    481                                                       540
human_SF3a120    FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFSKLK KEAENPREVL    ETAIGKKIGE EEIQKPEEKV TWDGHSGSMA RTQQAAQANI TLQEQIEAIH KAKGLVPEDD
bovin_SF3a120    FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFTKLK KEAENPREVL    ETAIGKKIGE EEIQKPEEKV TWDGHSGSMA RTQQAAQANI TLQEQIEAIH KAKGLVPEDD
mouse_SF3a120    FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFSKLK KEAENPREVL    ETAIGKKIGE EEIQKPEEKV TWDGHSGSMA RTQQAAQANI TLQEQIEAIH KAKGLVPEDD
yeast_prp21      IVEQMISKDG .EARLNFMNS SHPLHKTFTD FVAQYKRVYS FTG......Q EIKKSKRTIL    KPTN....EE EKIVSDQGKQ KGGDSKGKKR KIRAVGETRL KKSKK..... ..........

                 241                                                        300    541                                                       600
human_SF3a120    DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT    TKEKIGPSKP NEIPQQPPPP SSATNIPSSA PPITSVPRPP TMPPPVRTTV VSAVPVMPRP
bovin_SF3a120    DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT    TKEKIGPSKP NEIPQQPPPP SSATNIPSSA PPITSVPRPP AMPPPVRTTV VSAVPVMPRP
mouse_SF3a120    DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT    TKEKIGPSKP NEIPQQPPPP SSATNIPSSA PPITSVPRPP AMPPPVRTTV VSAVPVMPRP
yeast_prp21      DNCFERTQYW EFEKDKDREH DKLVELCKIQ FAAIPWDKFT QVAKFSIP.. ..........    .......... .......... .......... .......... .......... ..........
```

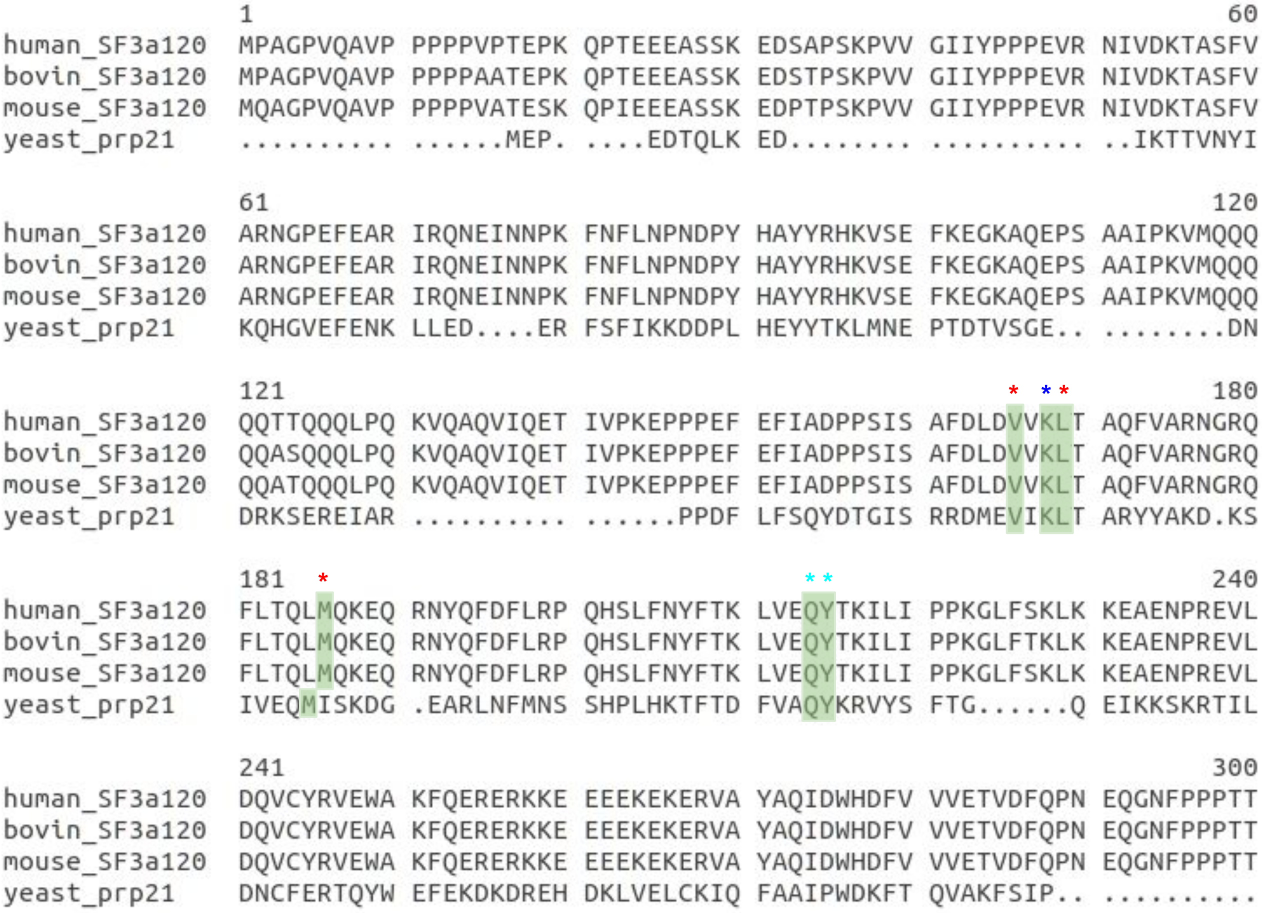
Sequence alignment (ClustalW)

Prp9 | **Prp21** | Prp11



```
                   1                                                         60
human_SF3a120   MPAGPVQAVP PPPPVPTEPK QPTEEEASSK EDSAPSKPVV GIIYPPPEVR NIVDKTASFV
bovin_SF3a120   MPAGPVQAVP PPPPAATEPK QPTEEEASSK EDSTPSKPVV GIIYPPPEVR NIVDKTASFV
mouse_SF3a120   MQAGPVQAVP PPPPVATESK QPIEEEASSK EDPTPSKPVV GIIYPPPEVR NIVDKTASFV
yeast_prp21     .......... ......MEP. ....EDTQLK ED........ .......... ..IKTTVNYI

                61                                                          120
human_SF3a120   ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ
bovin_SF3a120   ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ
mouse_SF3a120   ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ
yeast_prp21     KQHGVEFENK LLED....ER FSFIKKDDPL HEYYTKLMNE PTDTVSGE.. ........DN

                121                                                         180
human_SF3a120   QQTTQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ
bovin_SF3a120   QQASQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ
mouse_SF3a120   QQATQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ
yeast_prp21     DRKSEREIAR .......... ......PPDF LFSQYDTGIS RRDMEVIKLT ARYYAKD.KS

                181                                                         240
human_SF3a120   FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFSKLK KEAENPREVL
bovin_SF3a120   FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFTKLK KEAENPREVL
mouse_SF3a120   FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFSKLK KEAENPREVL
yeast_prp21     IVEQMISKDG .EARLNFMNS SHPLHKTFTD FVAQYKRVYS FTG......Q EIKKSKRTIL

                241                                                         300
human_SF3a120   DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT
bovin_SF3a120   DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT
mouse_SF3a120   DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT
yeast_prp21     DNCFERTQYW EFEKDKDREH DKLVELCKIQ FAAIPWDKFT QVAKFSIP.. ..........
```

Prp9 | **Prp21** | Prp11

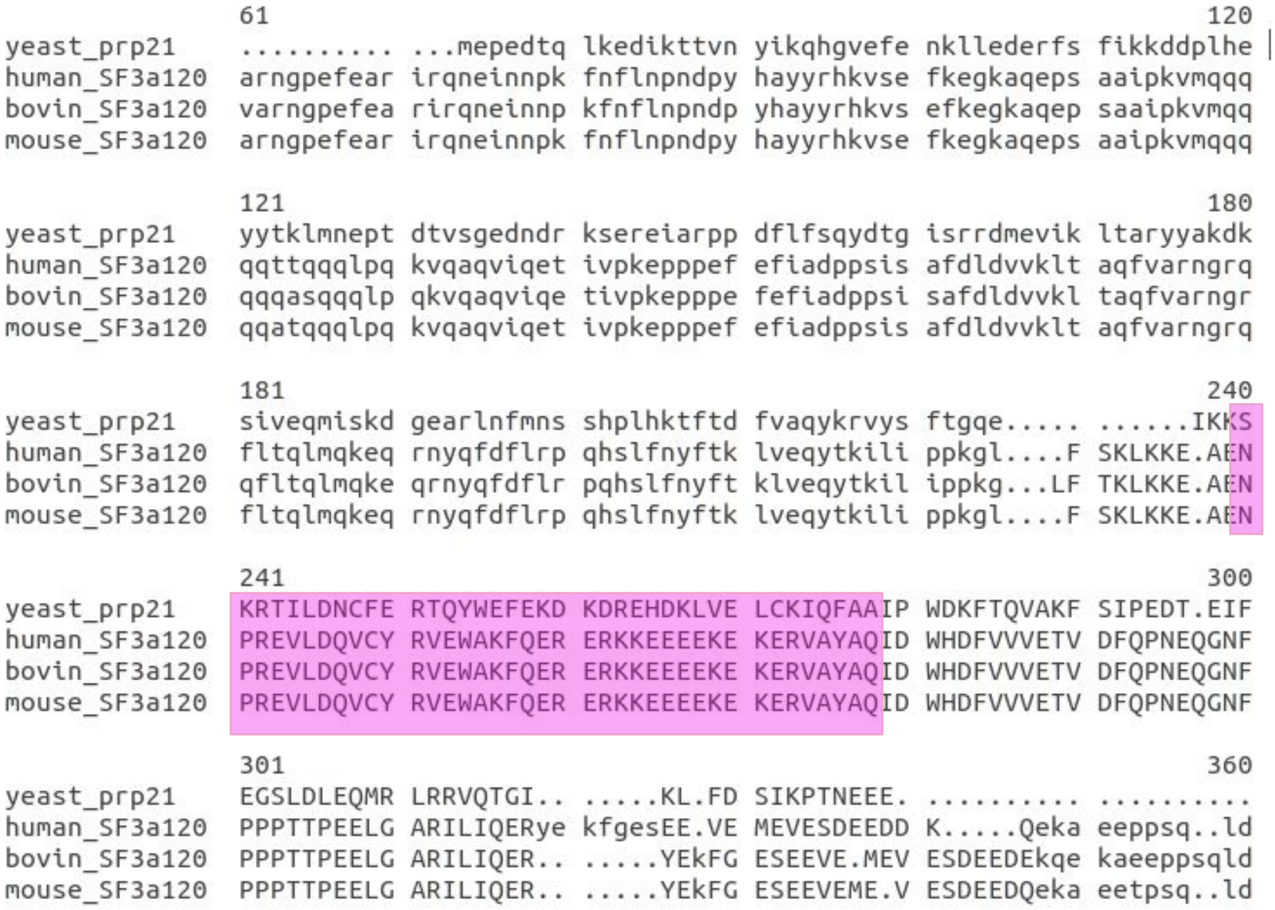


```
               1                                                              60
human_SF3a120  MPAGPVQAVP PPPPVPTEPK QPTEEEASSK EDSAPSKPVV GIIYPPPEVR NIVDKTASFV
bovin_SF3a120  MPAGPVQAVP PPPPAATEPK QPTEEEASSK EDSTPSKPVV GIIYPPPEVR NIVDKTASFV
mouse_SF3a120  MQAGPVQAVP PPPPVATESK QPIEEEASSK EDPTPSKPVV GIIYPPPEVR NIVDKTASFV
yeast_prp21    .......... ......MEP. ....EDTQLK ED........ .......... ..IKTTVNYI

               61                                                            120
human_SF3a120  ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ
bovin_SF3a120  ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ
mouse_SF3a120  ARNGPEFEAR IRQNEINNPK FNFLNPNDPY HAYYRHKVSE FKEGKAQEPS AAIPKVMQQQ
yeast_prp21    KQHGVEFENK LLED....ER FSFIKKDDPL HEYYTKLMNE PTDTVSGE.. ........DN

               121                                              * **         180
human_SF3a120  QQTTQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ
bovin_SF3a120  QQASQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ
mouse_SF3a120  QQATQQQLPQ KVQAQVIQET IVPKEPPPEF EFIADPPSIS AFDLDVVKLT AQFVARNGRQ
yeast_prp21    DRKSEREIAR .......... ......PPDF LFSQYDTGIS RRDMEVIKLT ARYYAKD.KS

               181  *                              **                        240
human_SF3a120  FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFSKLK KEAENPREVL
bovin_SF3a120  FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFTKLK KEAENPREVL
mouse_SF3a120  FLTQLMQKEQ RNYQFDFLRP QHSLFNYFTK LVEQYTKILI PPKGLFSKLK KEAENPREVL
yeast_prp21    IVEQMISKDG .EARLNFMNS SHPLHKTFTD FVAQYKRVYS FTG......Q EIKKSKRTIL

               241                                                           300
human_SF3a120  DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT
bovin_SF3a120  DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT
mouse_SF3a120  DQVCYRVEWA KFQERERKKE EEEKEKERVA YAQIDWHDFV VVETVDFQPN EQGNFPPPTT
yeast_prp21    DNCFERTQYW EFEKDKDREH DKLVELCKIQ FAAIPWDKFT QVAKFSIP.. ..........
```

Conserved Prp21 residues involved in interactions between Prp21 - Prp9

* hydrophobic
* ionic
* Hbond

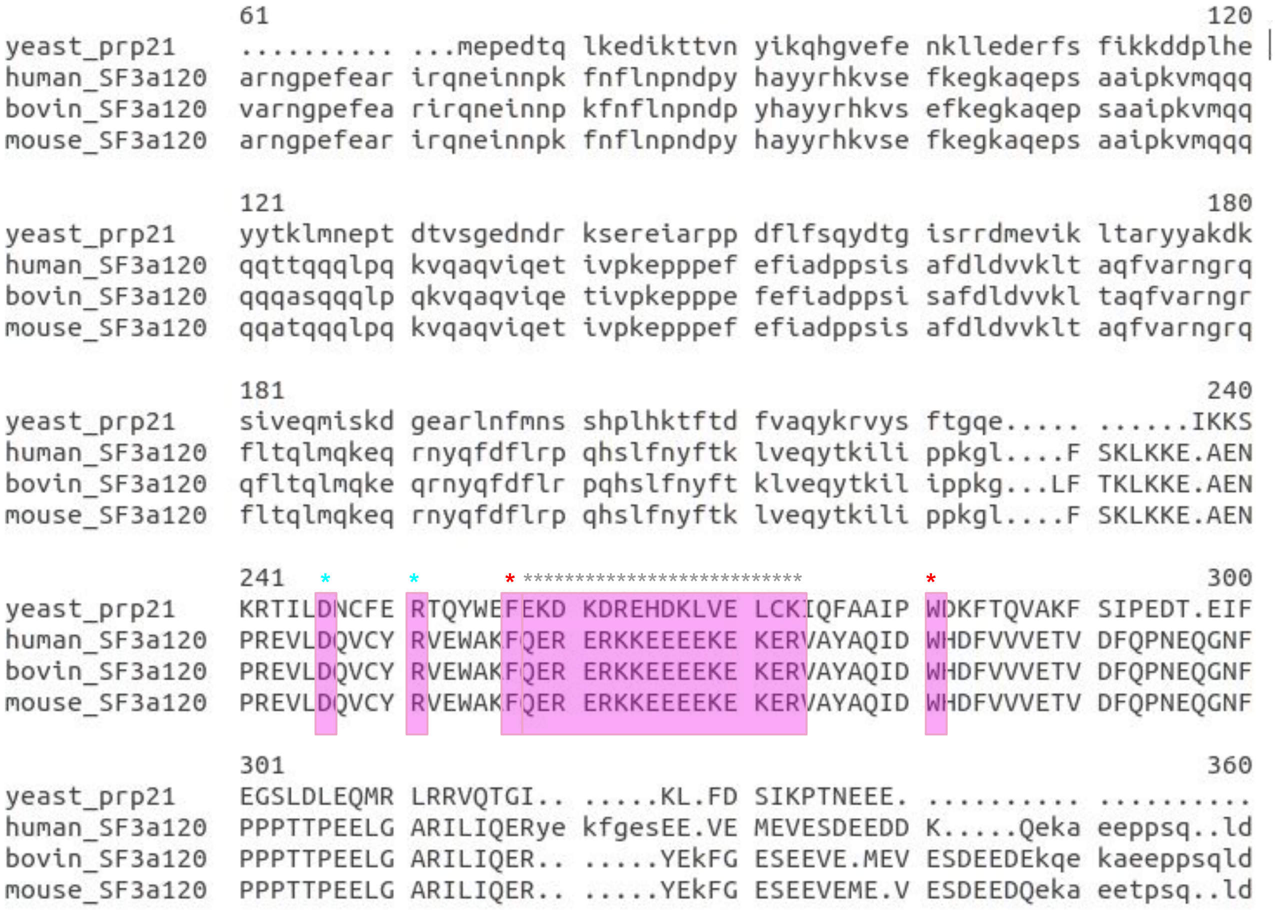
Prp9 | **Prp21** | Prp11



```
                61                                                         120
yeast_prp21     .......... ...mepedtq lkedikttvn yikqhgvefe nkllederfs fikkddplhe
human_SF3a120   arngpefear irqneinnpk fnflnpndpy hayyrhkvse fkegkaqeps aaipkvmqqq
bovin_SF3a120   varngpefea rirqneinnp kfnflnpndp yhayyrhkvs efkegkaqep saaipkvmqq
mouse_SF3a120   arngpefear irqneinnpk fnflnpndpy hayyrhkvse fkegkaqeps aaipkvmqqq

                121                                                        180
yeast_prp21     yytklmnept dtvsgedndr ksereiarpp dflfsqydtg isrrdmevik ltaryyakdk
human_SF3a120   qqttqqqlpq kvqaqviqet ivpkepppef efiadppsis afdldvvklt aqfvarngrq
bovin_SF3a120   qqqasqqqlp qkvqaqviqe tivpkepppe fefiadppsi safdldvvkl taqfvarngr
mouse_SF3a120   qqatqqqlpq kvqaqviqet ivpkepppef efiadppsis afdldvvklt aqfvarngrq

                181                                                        240
yeast_prp21     siveqmiskd gearlnfmns shplhktftd fvaqykrvys ftgqe..... ......IKKS
human_SF3a120   fltqlmqkeq rnyqfdflrp qhslfnyftk lveqytkili ppkgl....F SKLKKE.AEN
bovin_SF3a120   qfltqlmqke qrnyqfdflr pqhslfnyft klveqytkil ippkg...LF TKLKKE.AEN
mouse_SF3a120   fltqlmqkeq rnyqfdflrp qhslfnyftk lveqytkili ppkgl....F SKLKKE.AEN

                241                                                        300
yeast_prp21     KRTILDNCFE RTQYWEFEKD KDREHDKLVE LCKIQFAAIP WDKFTQVAKF SIPEDT.EIF
human_SF3a120   PREVLDQVCY RVEWAKFQER ERKKEEEEKE KERVAYAQID WHDFVVVETV DFQPNEQGNF
bovin_SF3a120   PREVLDQVCY RVEWAKFQER ERKKEEEEKE KERVAYAQID WHDFVVVETV DFQPNEQGNF
mouse_SF3a120   PREVLDQVCY RVEWAKFQER ERKKEEEEKE KERVAYAQID WHDFVVVETV DFQPNEQGNF

                301                                                        360
yeast_prp21     EGSLDLEQMR LRRVQTGI.. .....KL.FD SIKPTNEEE. .......... ..........
human_SF3a120   PPPTTPEELG ARILIQERye kfgesEE.VE MEVESDEEDD K.....Qeka eeppsq..ld
bovin_SF3a120   PPPTTPEELG ARILIQER.. .....YEkFG ESEEVE.MEV ESDEEDEkqe kaeeppsqld
mouse_SF3a120   PPPTTPEELG ARILIQER.. .....YEkFG ESEEVEME.V ESDEEDQeka eetpsq..ld
```

Sequence alignment (HMM fetched from PFAM)

Prp9 | **Prp21** | Prp11

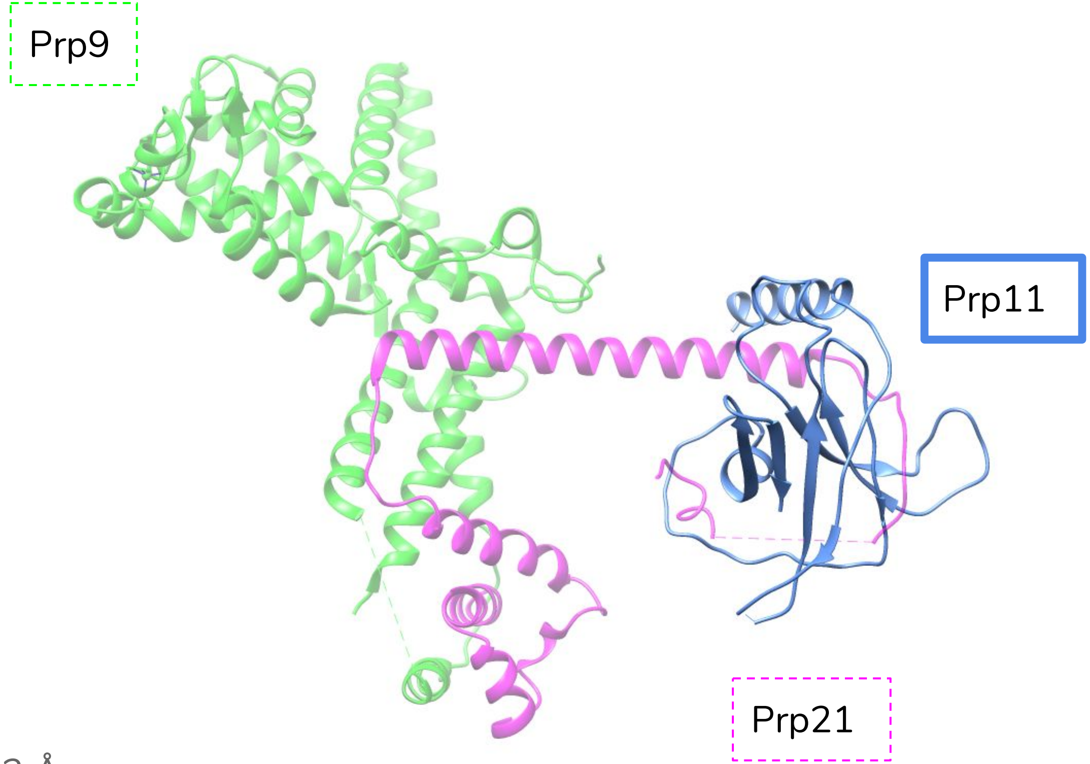


```
                 61                                                          120
yeast_prp21      .......... ...mepedtq lkedikttvn yikqhgvefe nkllederfs fikkddplhe |
human_SF3a120    arngpefear irqneinnpk fnflnpndpy hayyrhkvse fkegkaqeps aaipkvmqqq
bovin_SF3a120    varngpefea rirqneinnp kfnflnpndp yhayyrhkvs efkegkaqep saaipkvmqq
mouse_SF3a120    arngpefear irqneinnpk fnflnpndpy hayyrhkvse fkegkaqeps aaipkvmqqq

                 121                                                         180
yeast_prp21      yytklmnept dtvsgedndr ksereiarpp dflfsqydtg isrrdmevik ltaryyakdk
human_SF3a120    qqttqqqlpq kvqaqviqet ivpkepppef efiadppsis afdldvvklt aqfvarngrq
bovin_SF3a120    qqqasqqqlp qkvqaqviqe tivpkepppe fefiadppsi safdldvvkl taqfvarngr
mouse_SF3a120    qqatqqqlpq kvqaqviqet ivpkepppef efiadppsis afdldvvklt aqfvarngrq

                 181                                                         240
yeast_prp21      siveqmiskd gearlnfmns shplhktftd fvaqykrvys ftgqe..... ......IKKS
human_SF3a120    fltqlmqkeq rnyqfdflrp qhslfnyftk lveqytkili ppkgl....F SKLKKE.AEN
bovin_SF3a120    qfltqlmqke qrnyqfdflr pqhslfnyft klveqytkil ippkg...LF TKLKKE.AEN
mouse_SF3a120    fltqlmqkeq rnyqfdflrp qhslfnyftk lveqytkili ppkgl....F SKLKKE.AEN

                 241  *     *     * ***************************      *           300
yeast_prp21      KRTILDNCFE RTQYWEFEKD KDREHDKLVE LCKIQFAAIP WDKFTQVAKF SIPEDT.EIF
human_SF3a120    PREVLDQVCY RVEWAKFQER ERKKEEEEKE KERVAYAQID WHDFVVVETV DFQPNEQGNF
bovin_SF3a120    PREVLDQVCY RVEWAKFQER ERKKEEEEKE KERVAYAQID WHDFVVVETV DFQPNEQGNF
mouse_SF3a120    PREVLDQVCY RVEWAKFQER ERKKEEEEKE KERVAYAQID WHDFVVVETV DFQPNEQGNF

                 301                                                         360
yeast_prp21      EGSLDLEQMR LRRVQTGI.. .....KL.FD SIKPTNEEE. .......... ..........
human_SF3a120    PPPTTPEELG ARILIQERye kfgesEE.VE MEVESDEEDD K.....Qeka eeppsq..ld
bovin_SF3a120    PPPTTPEELG ARILIQER.. .....YEkFG ESEEVE.MEV ESDEEDEkqe kaeeppsqld
mouse_SF3a120    PPPTTPEELG ARILIQER.. .....YEkFG ESEEVEME.V ESDEEDQeka eetpsq..ld
```

Conserved Prp21 residues involved in interactions between Prp21 - Prp9 / 11

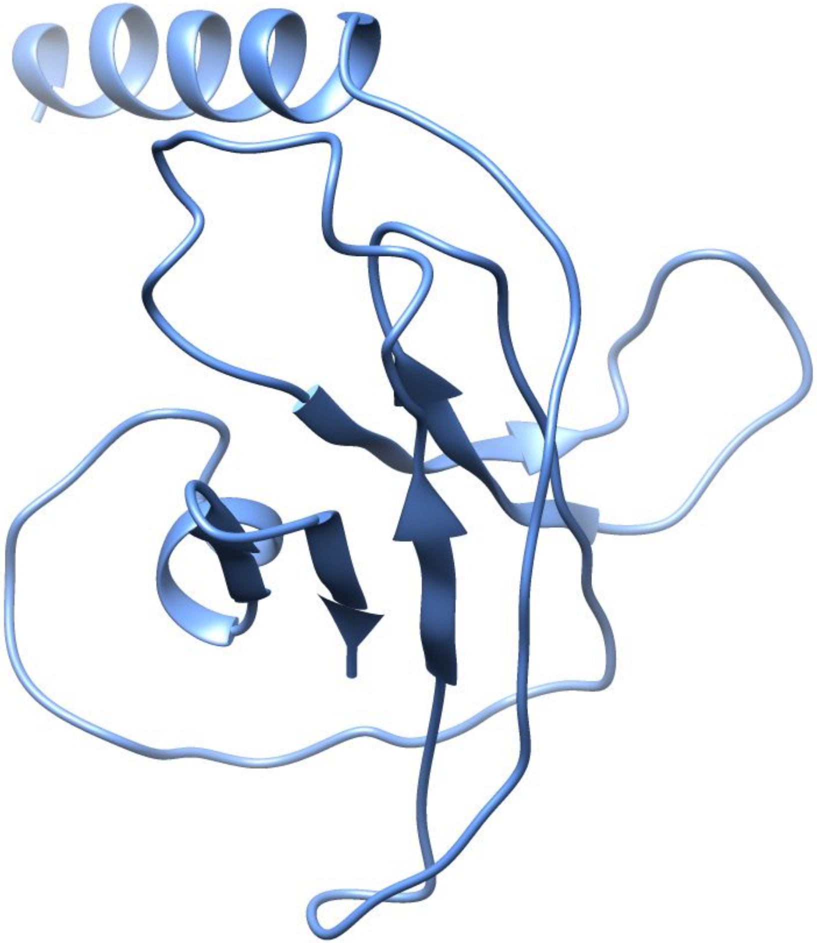
* hydrophobic
* ionic
* Hbond
*solvent exposed

Prp9 | Prp21 | **Prp11**

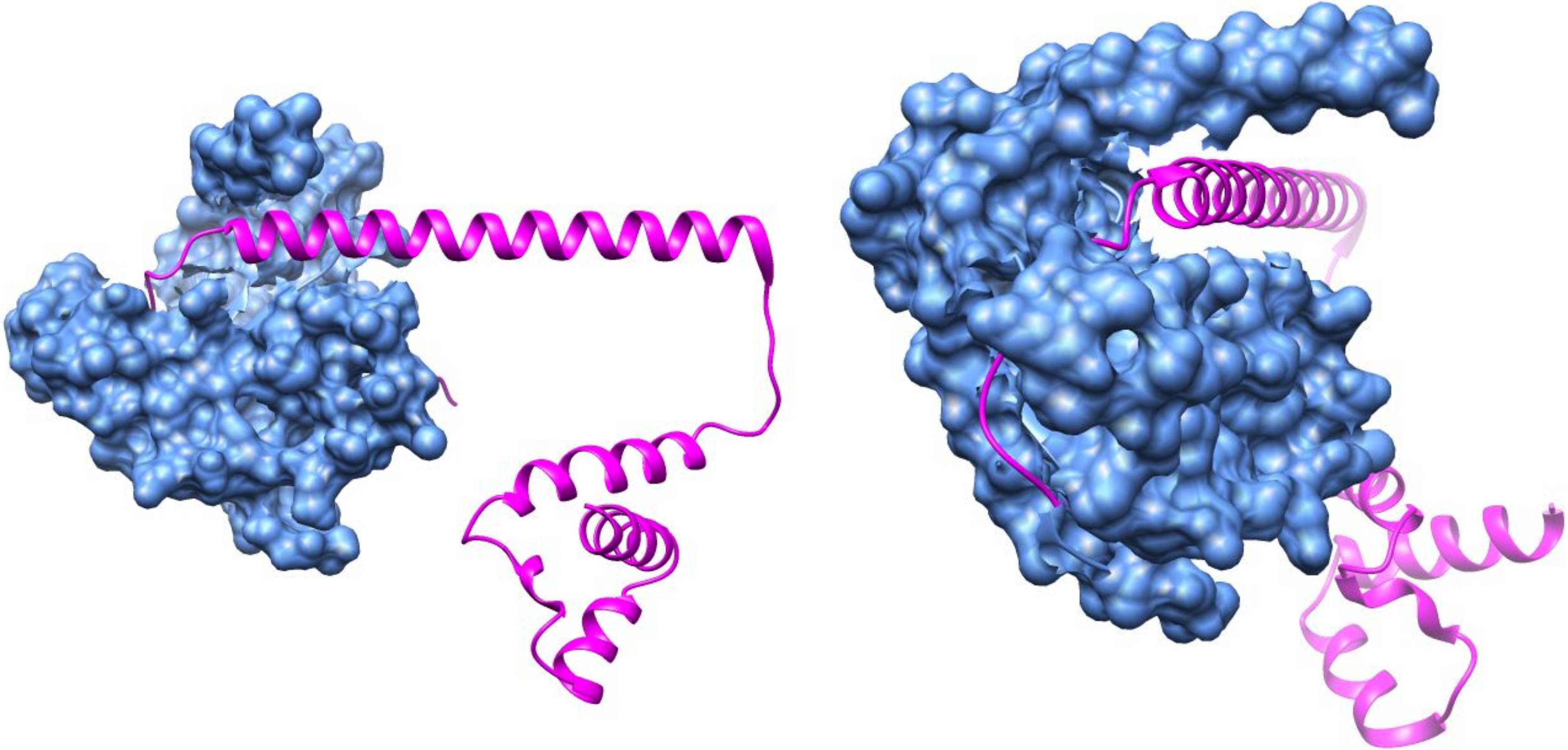


PDB ID: 4DGW
Resolution: 3.112 Å

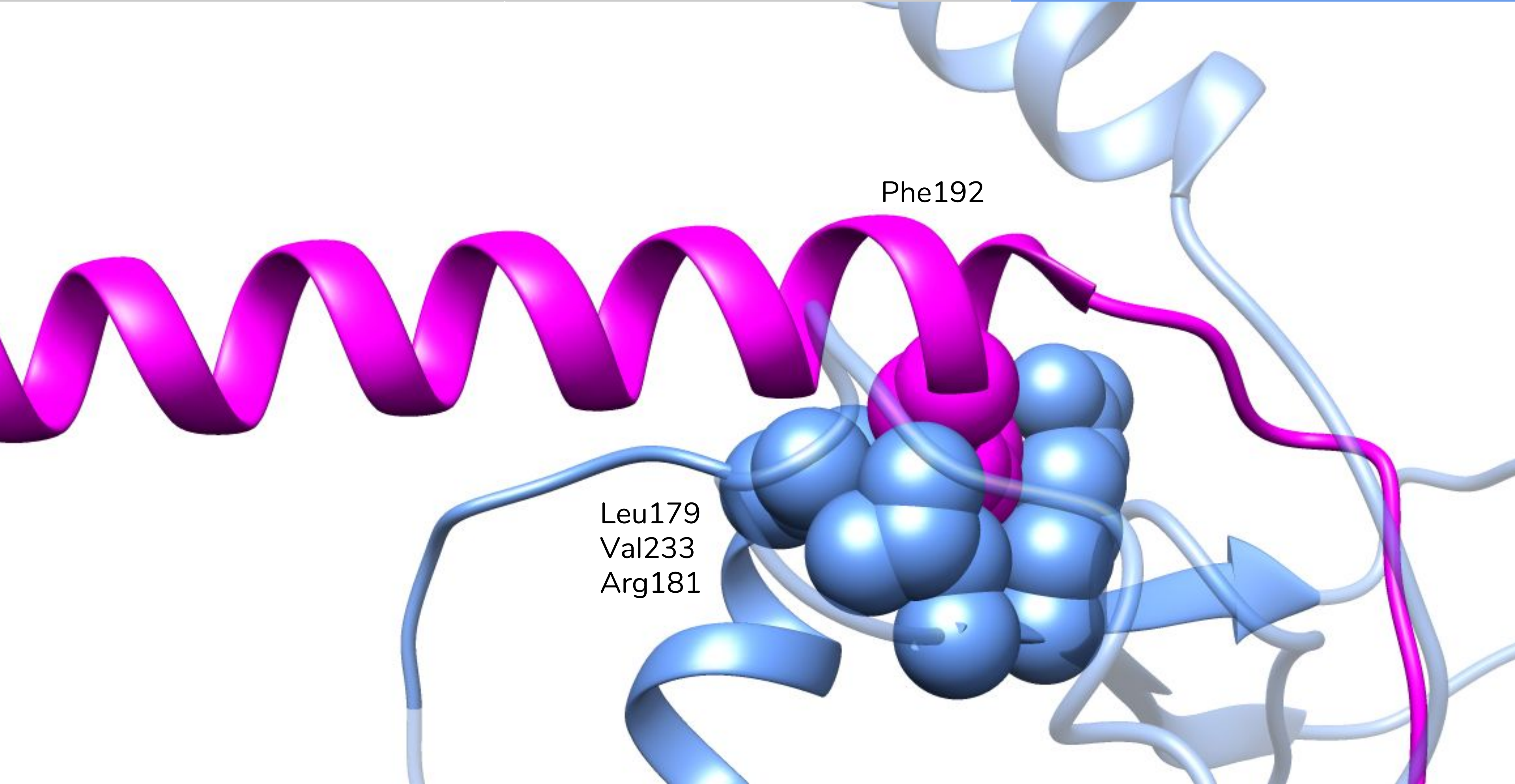
Prp9 | Prp21 | **Prp11**



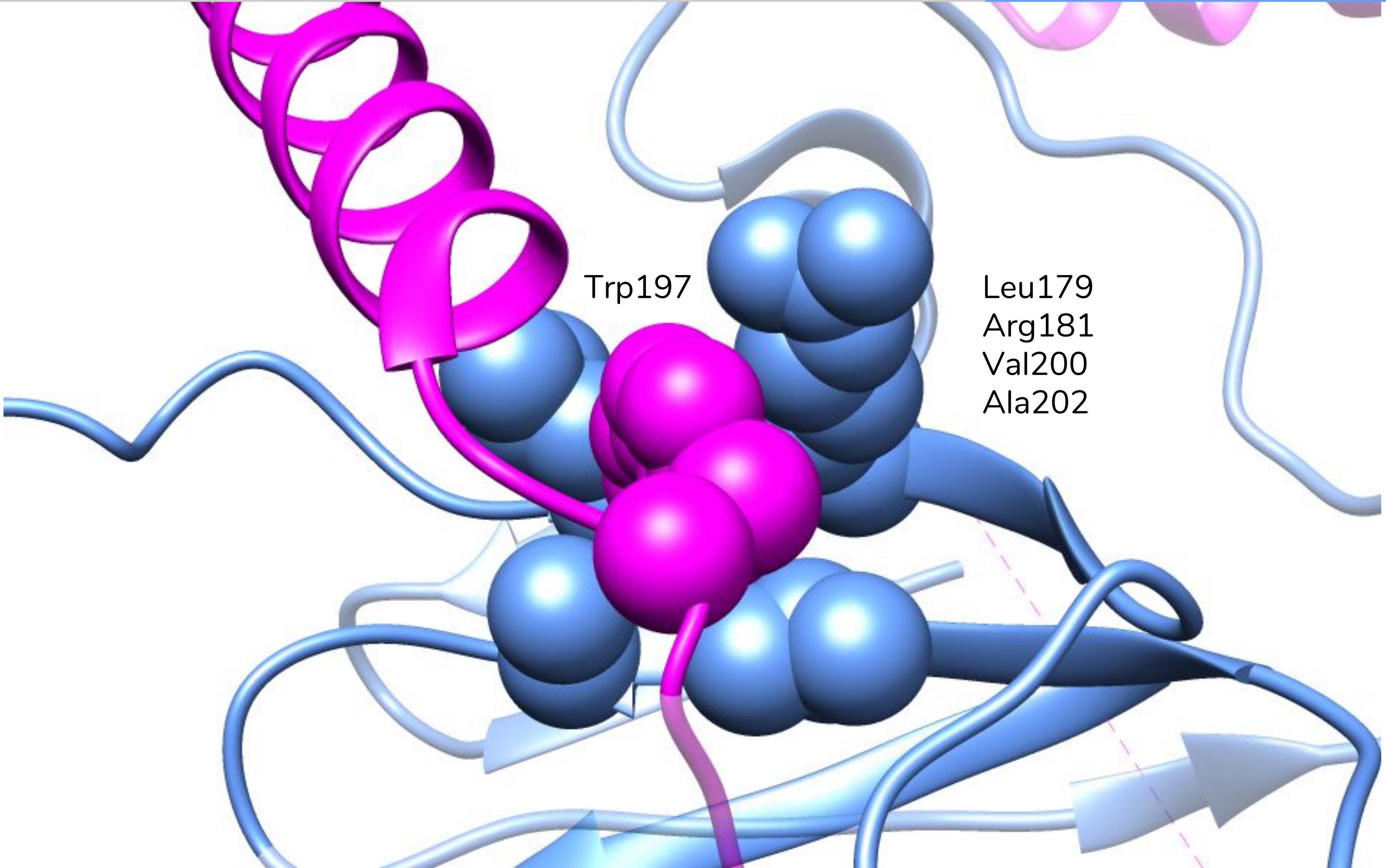
Prp9 | Prp21 | **Prp11**



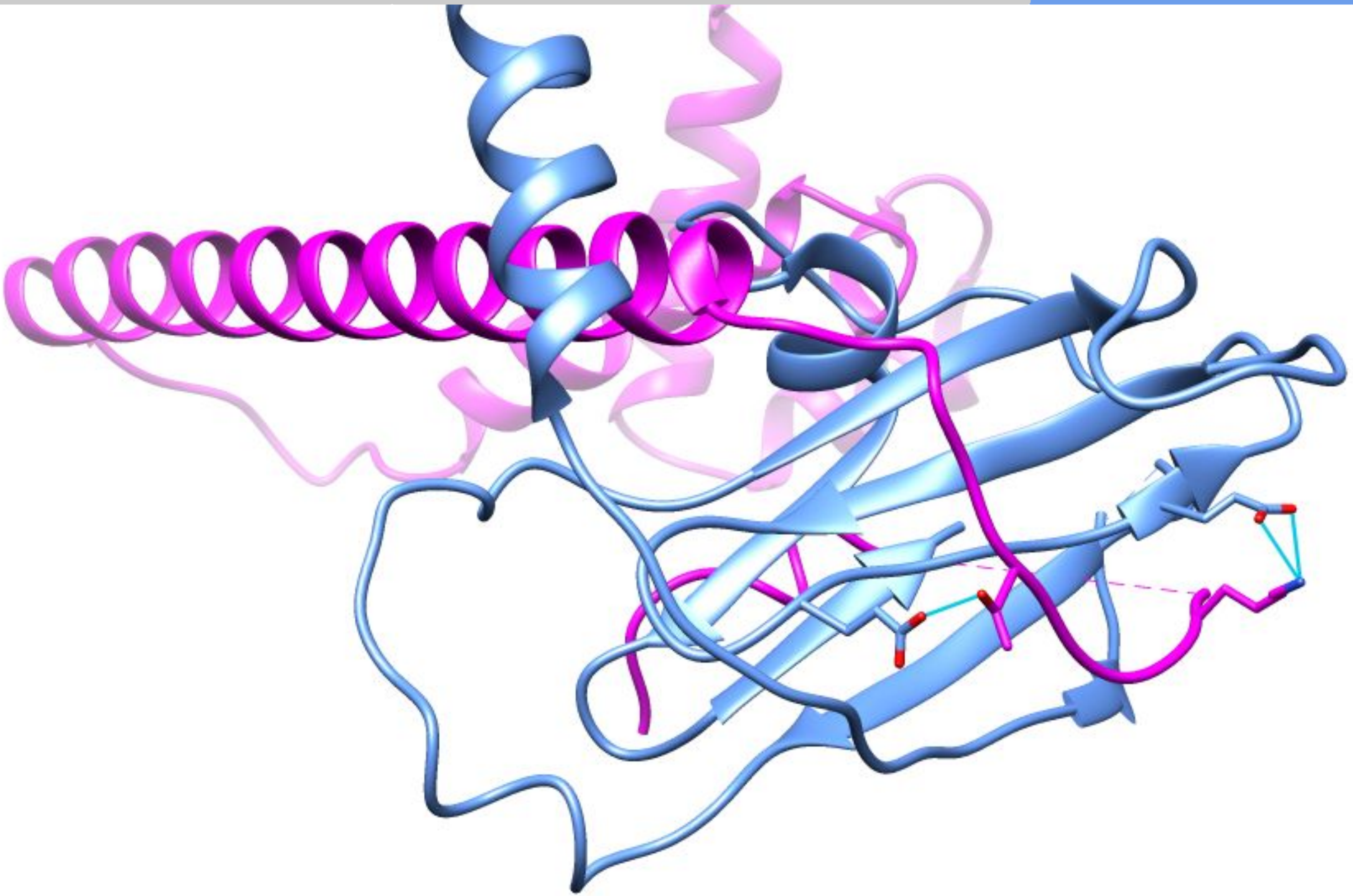
Prp9 | Prp21 | **Prp11**



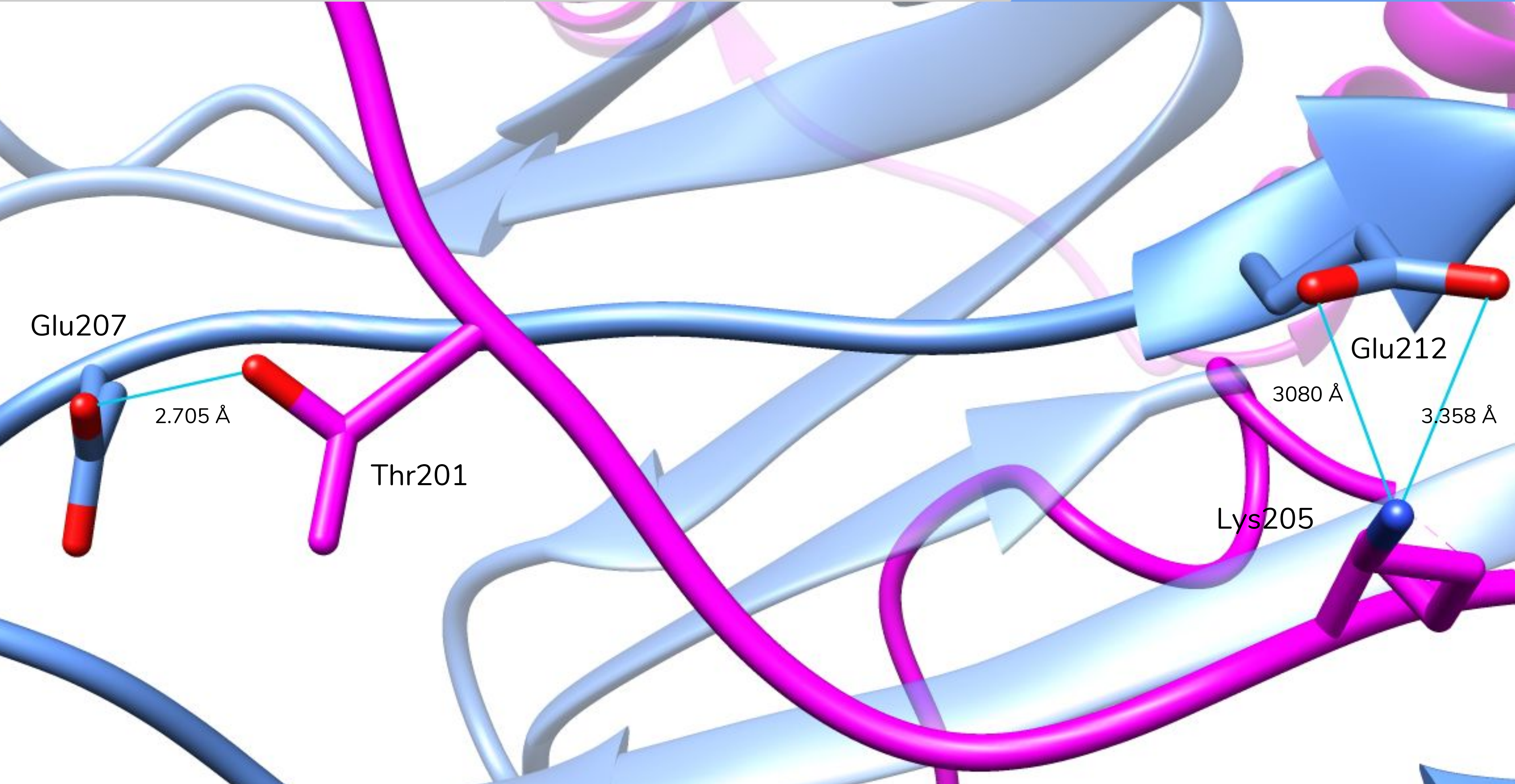
Prp9 | Prp21 | **Prp11**

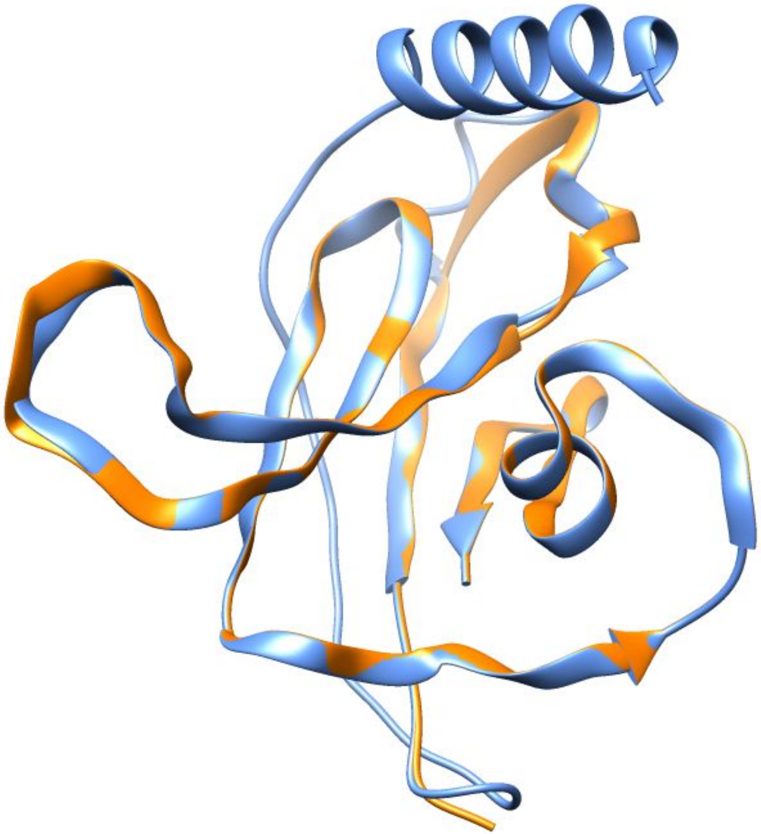


Prp9 Prp21 **Prp11**



Prp9 Prp21 **Prp11**

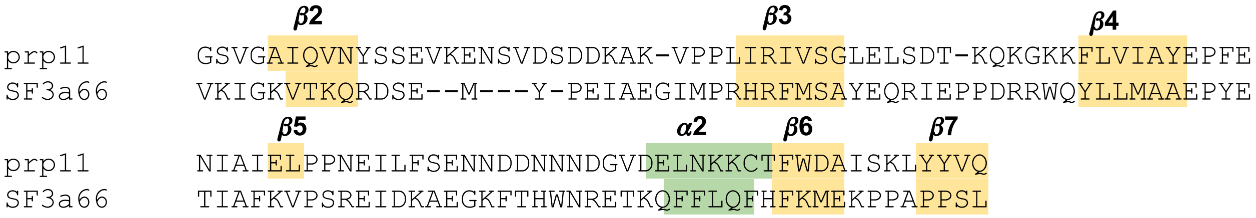




● Prp11

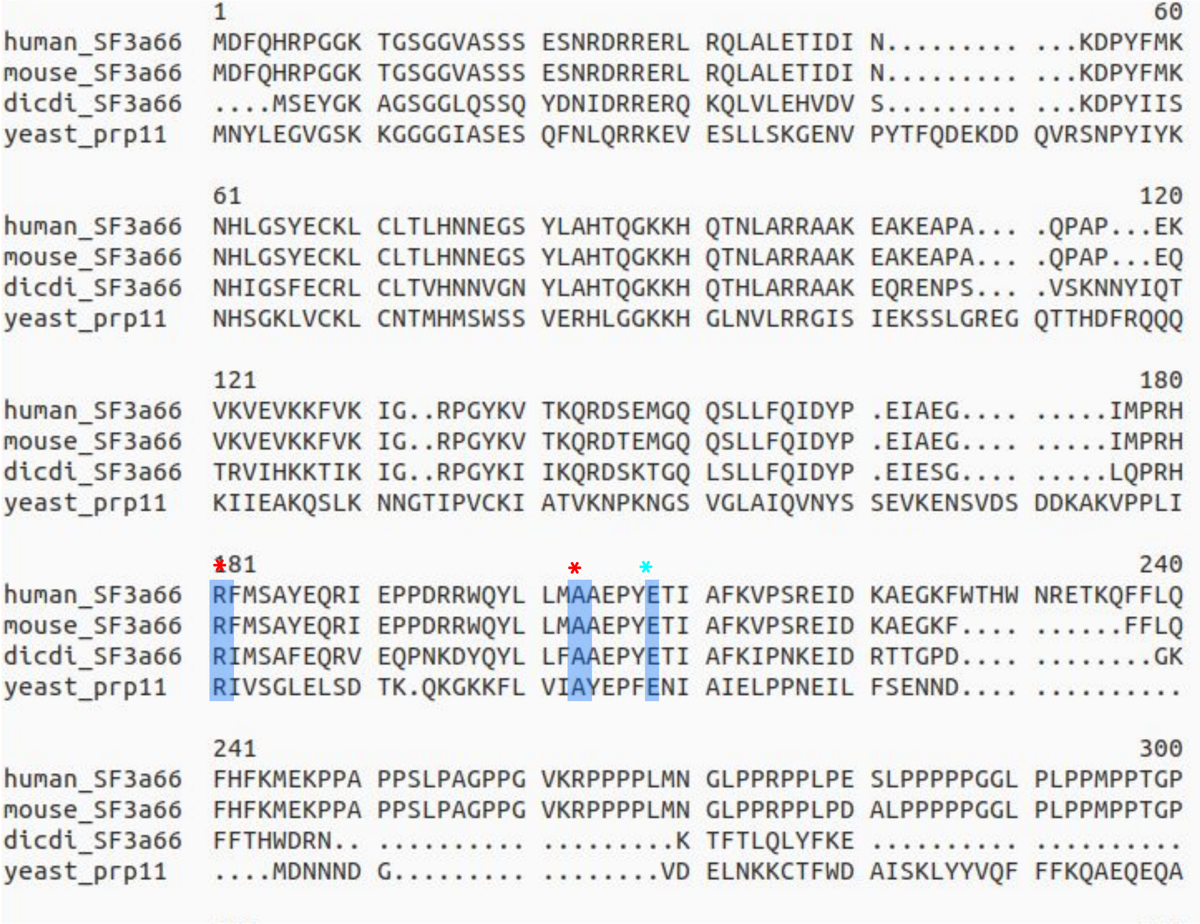
● SF3a66

ALIGNFIT STAMP
Sc = 6.47
RMS = 0.38



```
                β2                        β3                β4
prp11     GSVGAIQVNYSSEVKENSVDSDDKAK-VPPLIRIVSGLELSDT-KQKGKKFLVIAYEPFE
SF3a66    VKIGKVTKQRDSE--M---Y-PEIAEGIMPRHRFMSAYEQRIEPPDRRWQYLLMAAEPYE
               β5                    α2    β6      β7
prp11     NIAIELPPNEILFSENNDDNNNDGVDELNKKCTFWDAISKLYYVQ
SF3a66    TIAFKVPSREIDKAEGKFTHWNRETKQFFLQFHFKMEKPPAPPSL
```

Structural alignment (STAMP)



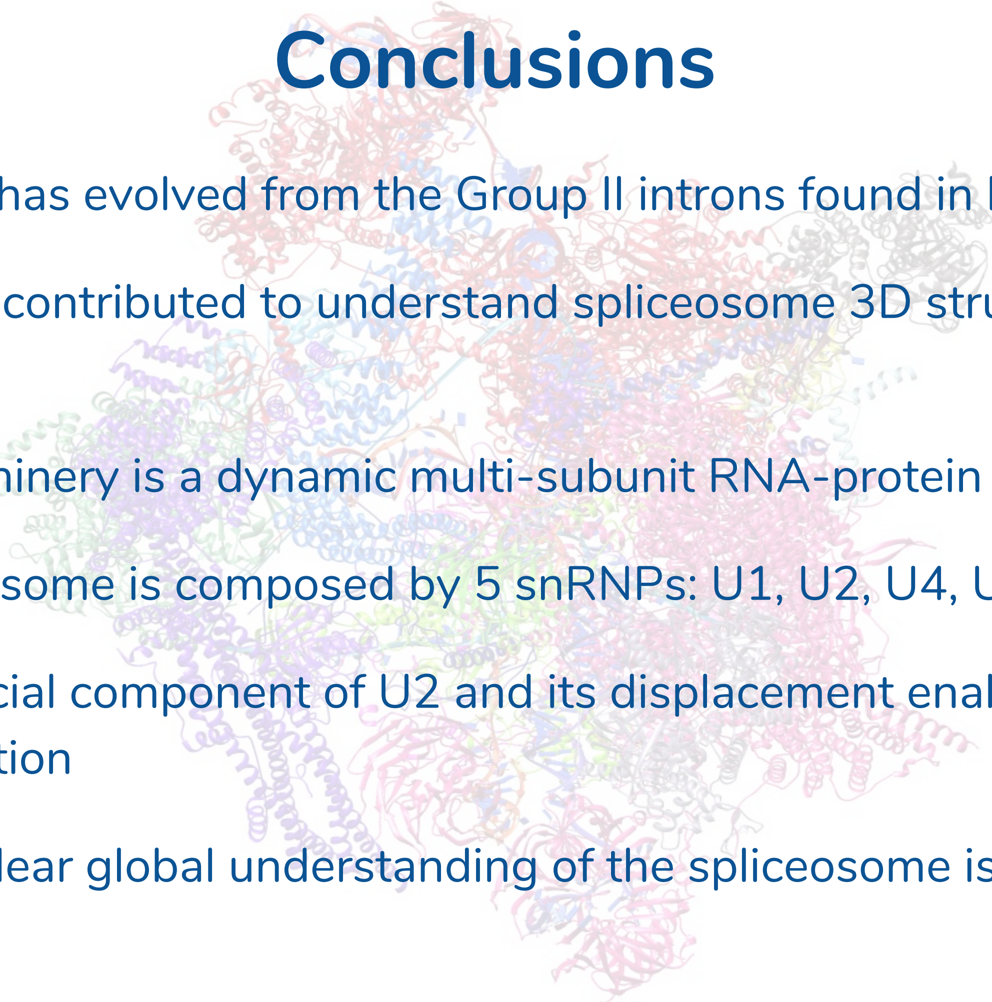
```
              1                                                              60
human_SF3a66  MDFQHRPGGK TGSGGVASSS ESNRDRRERL RQLALETIDI N......... ...KDPYFMK
mouse_SF3a66  MDFQHRPGGK TGSGGVASSS ESNRDRRERL RQLALETIDI N......... ...KDPYFMK
dicdi_SF3a66  ....MSEYGK AGSGGLQSSQ YDNIDRRERQ KQLVLEHVDV S......... ...KDPYIIS
yeast_prp11   MNYLEGVGSK KGGGGIASES QFNLQRRKEV ESLLSKGENV PYTFQDEKDD QVRSNPYIYK

              61                                                            120
human_SF3a66  NHLGSYECKL CLTLHNNEGS YLAHTQGKKH QTNLARRAAK EAKEAPA... .QPAP...EK
mouse_SF3a66  NHLGSYECKL CLTLHNNEGS YLAHTQGKKH QTNLARRAAK EAKEAPA... .QPAP...EQ
dicdi_SF3a66  NHIGSFECRL CLTVHNNVGN YLAHTQGKKH QTHLARRAAK EQRENPS... .VSKNNYIQT
yeast_prp11   NHSGKLVCKL CNTMHMSWSS VERHLGGKKH GLNVLRRGIS IEKSSLGREG QTTHDFRQQQ

              121                                                           180
human_SF3a66  VKVEVKKFVK IG..RPGYKV TKQRDSEMGQ QSLLFQIDYP .EIAEG.... .....IMPRH
mouse_SF3a66  VKVEVKKFVK IG..RPGYKV TKQRDTEMGQ QSLLFQIDYP .EIAEG.... .....IMPRH
dicdi_SF3a66  TRVIHKKTIK IG..RPGYKI IKQRDSKTGQ LSLLFQIDYP .EIESG.... .....LQPRH
yeast_prp11   KIIEAKQSLK NNGTIPVCKI ATVKNPKNGS VGLAIQVNYS SEVKENSVDS DDKAKVPPLI

              *                       *    *
              181                                                           240
human_SF3a66  RFMSAYEQRI EPPDRRWQYL LMAAEPYETI AFKVPSREID KAEGKFWTHW NRETKQFFLQ
mouse_SF3a66  RFMSAYEQRI EPPDRRWQYL LMAAEPYETI AFKVPSREID KAEGKF.... ......FFLQ
dicdi_SF3a66  RIMSAFEQRV EQPNKDYQYL LFAAEPYETI AFKIPNKEID RTTGPD.... ........GK
yeast_prp11   RIVSGLELSD TK.QKGKKFL VIAYEPFENI AIELPPNEIL FSENND.... ..........

              241                                                           300
human_SF3a66  FHFKMEKPPA PPSLPAGPPG VKRPPPPLMN GLPPRPPLPE SLPPPPPGGL PLPPMPPTGP
mouse_SF3a66  FHFKMEKPPA PPSLPAGPPG VKRPPPPLMN GLPPRPPLPD ALPPPPPGGL PLPPMPPTGP
dicdi_SF3a66  FFTHWDRN.. .......... .........K TFTLQLYFKE .......... ..........
yeast_prp11   ....MDNNND G......... ........VD ELNKKCTFWD AISKLYYVQF FFKQAEQEQA
```

Conserved Prp11 residues involved in interactions between Prp21 - Prp11

* hydrophobic
* Hbond

Sequence alignment (ClustalW)

Conclusions



Spliceosome has evolved from the Group II introns found in bacteria

Cryo-EM has contributed to understand spliceosome 3D structure and its dynamics

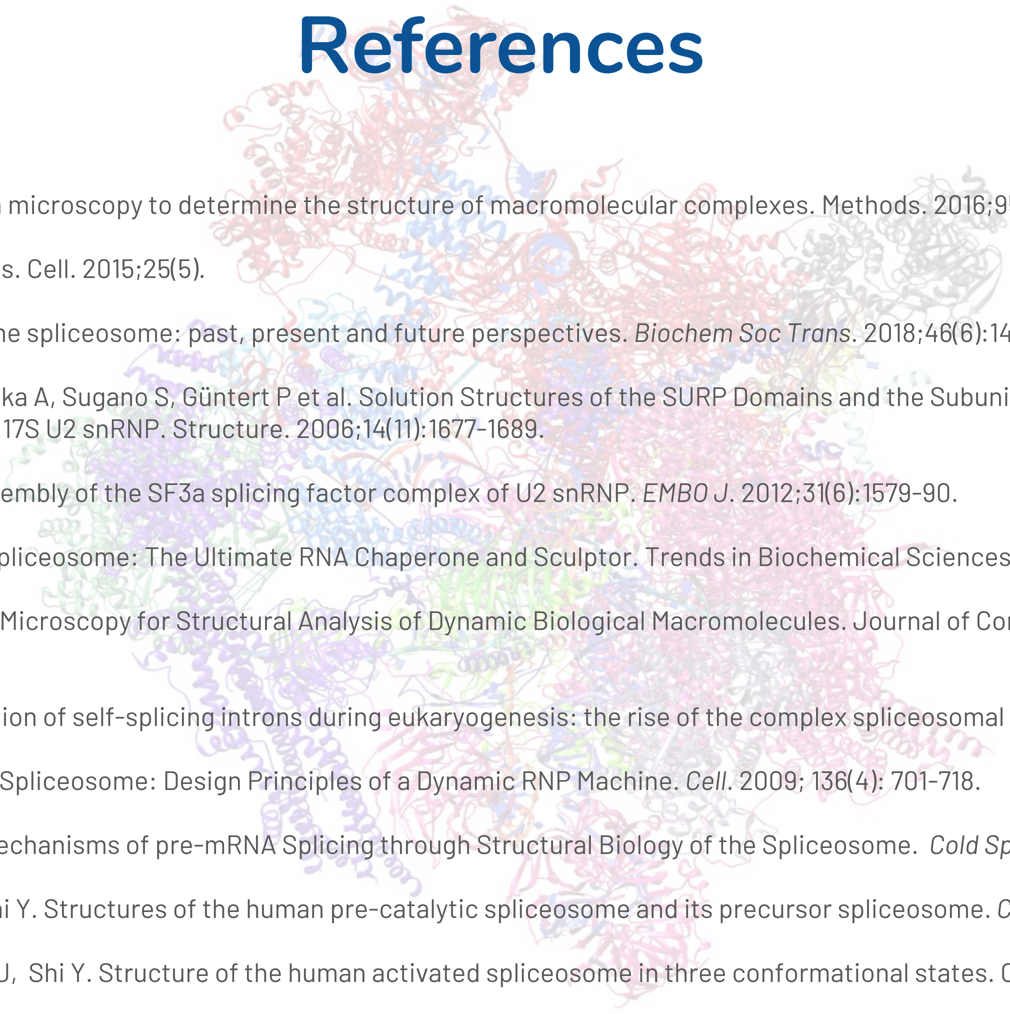
This cell machinery is a dynamic multi-subunit RNA-protein complex

Major Spliceosome is composed by 5 snRNPs: U1, U2, U4, U5 and U6

SF3a is a crucial component of U2 and its displacement enables the first catalytic reaction

A deep and clear global understanding of the spliceosome is still lacking

References



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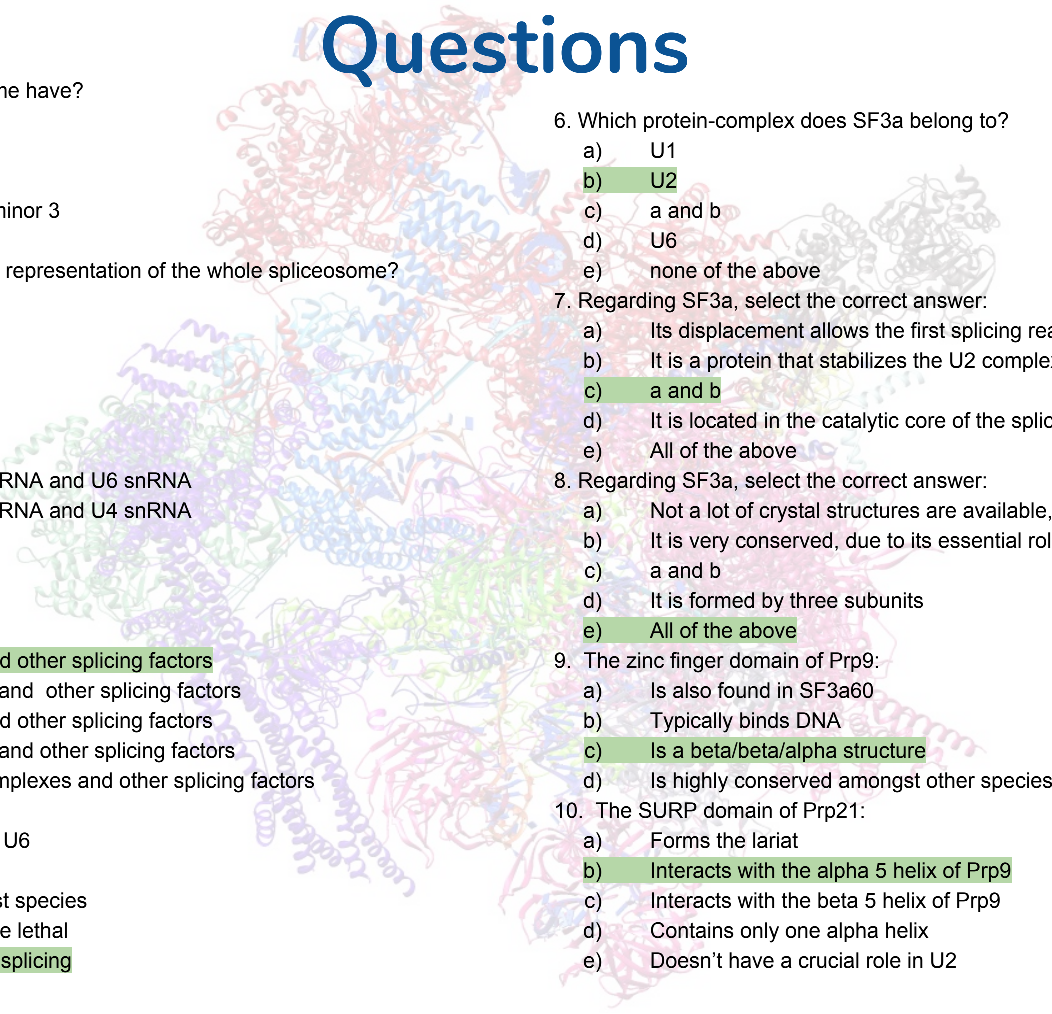
Questions



1. How many snRNP does the spliceosome have?
a) < 5
b) > 5
c) 5
d) Major spliceosome has 5 and minor 3
e) None of the above

2. Which is the best technique to obtain a representation of the whole spliceosome?
a) X-ray diffraction
b) NMR
c) a and b
d) Cryo - Electron Microscopy
e) All of the above

3. Regarding Major Spliceosome,
a) U2 snRNA interacts with pre-mRNA and U6 snRNA
b) U6 snRNA interacts with pre-mRNA and U4 snRNA
c) U1 interacts with pre-mRNA
d) All of the above
e) None of the above

4. snRNP has:
a) snRNA, 1 Sm/LSm complex and other splicing factors
b) snRNA, 2 Sm/LSm complexes and other splicing factors
c) snDNA, 1 Sm/LSm complex and other splicing factors
d) snDNA, 2 Sm/LSm complexes and other splicing factors
e) snRNA, snDNA, 2 Sm/LSm complexes and other splicing factors

5. Regarding the Sm complex,
a) It is present only in U2, U5 and U6
a) It has eight subunits
b) It is not well conserved amongst species
c) Mutations in this proteins can be lethal
d) Doesn't play any crucial role in splicing

6. Which protein-complex does SF3a belong to?
a) U1
b) U2
c) a and b
d) U6
e) none of the above

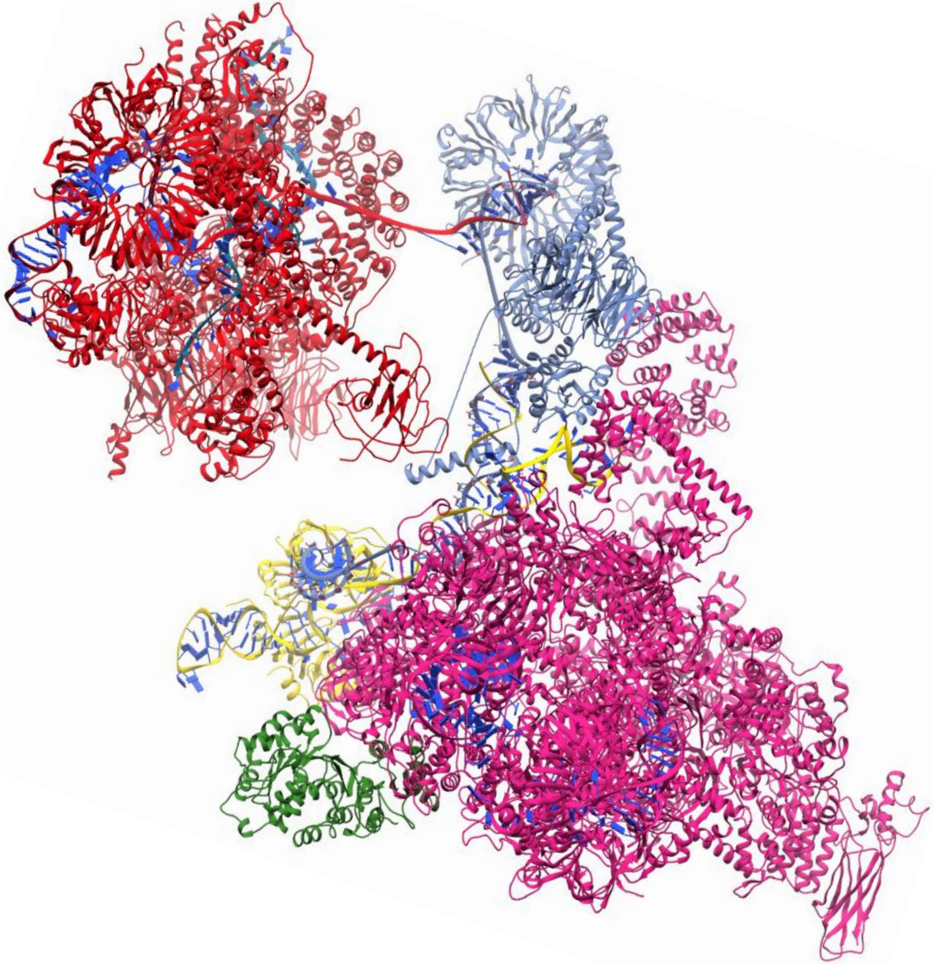
7. Regarding SF3a, select the correct answer:
a) Its displacement allows the first splicing reaction to happen
b) It is a protein that stabilizes the U2 complex
c) a and b
d) It is located in the catalytic core of the spliceosome
e) All of the above

8. Regarding SF3a, select the correct answer:
a) Not a lot of crystal structures are available, due to the complexity of the spliceosome
b) It is very conserved, due to its essential role in splicing
c) a and b
d) It is formed by three subunits
e) All of the above

9. The zinc finger domain of Prp9:
a) Is also found in SF3a60
b) Typically binds DNA
c) Is a beta/beta/alpha structure
d) Is highly conserved amongst other species

10. The SURP domain of Prp21:
a) Forms the lariat
b) Interacts with the alpha 5 helix of Prp9
c) Interacts with the beta 5 helix of Prp9
d) Contains only one alpha helix
e) Doesn't have a crucial role in U2

Thank you for your attention!



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