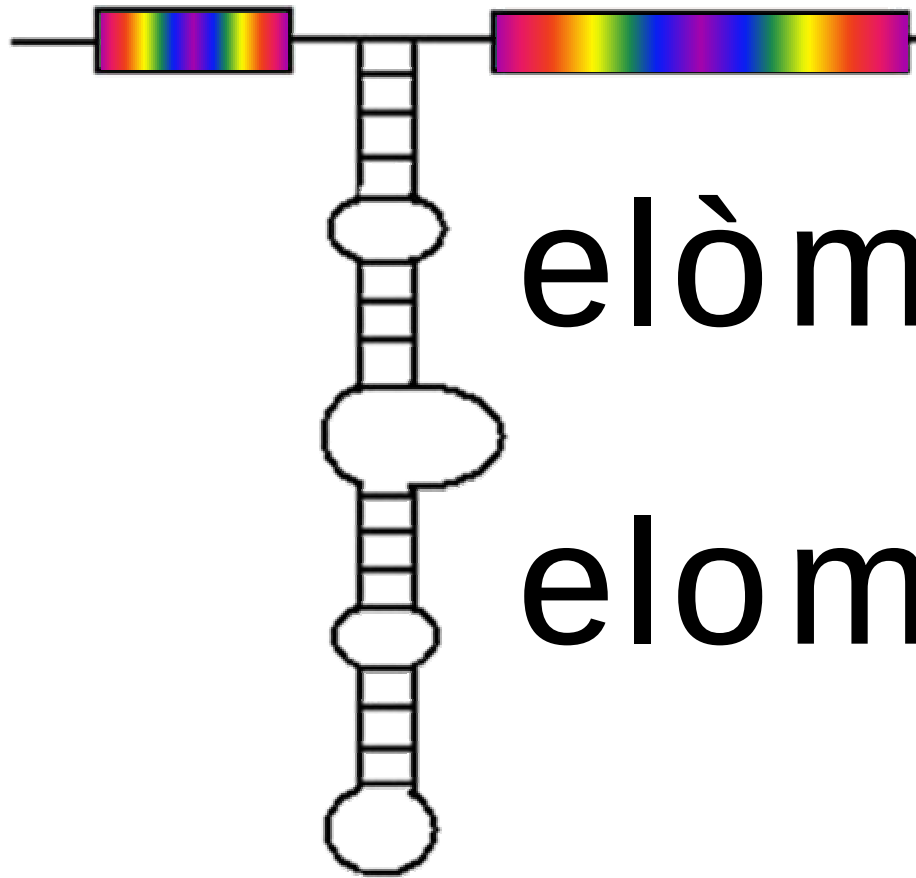




elòmers i elomerasa

Jesús Bertran
Raquel Clivillé
Marta Massanella
Ingrid Pallàs
Miriam Sánchez

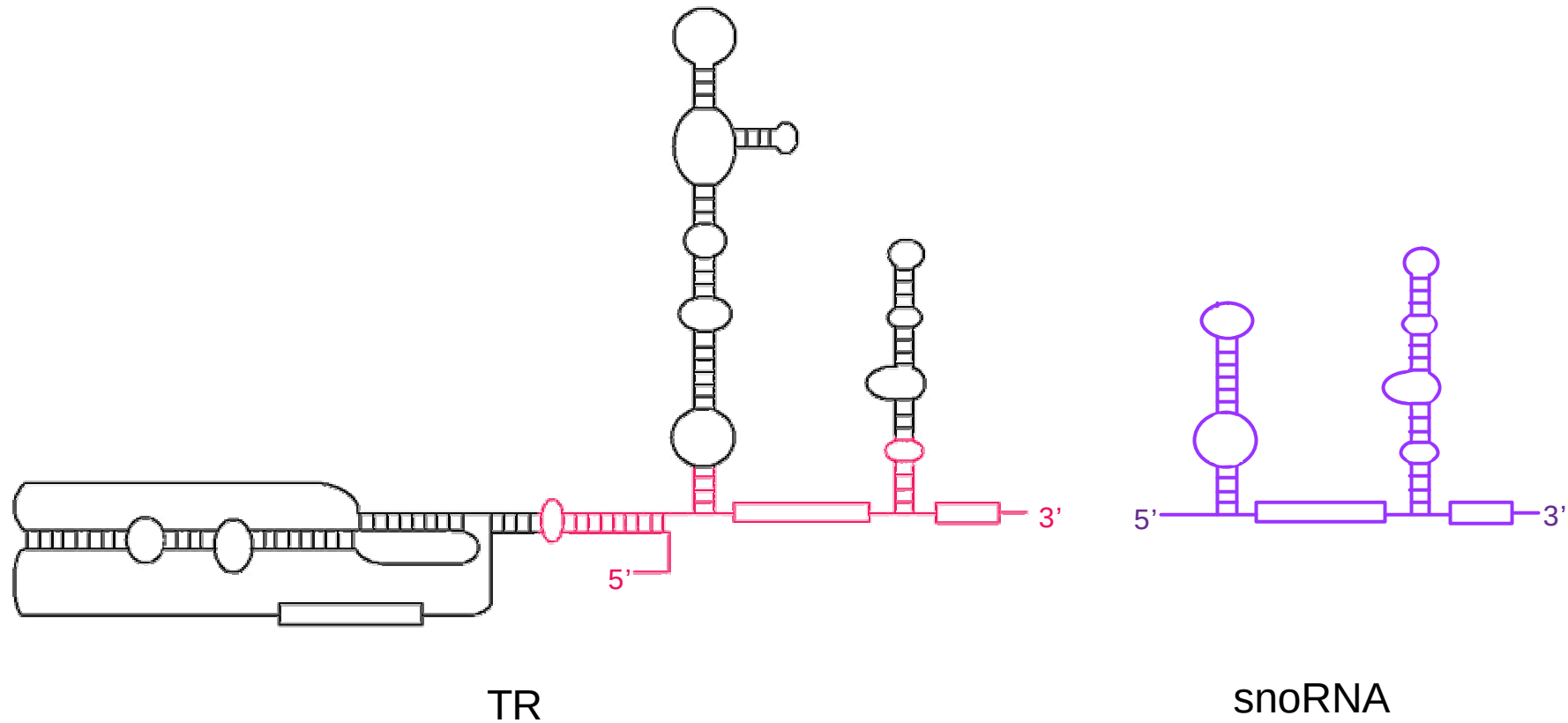


Alineament SnoRNA - TR

ACA box

Homo_sapie	GGACTCGGCTCA'ACATGC
Bos_taurus	GGACTCGGCTCAGACATCC
Sus_scrofa	GGACTCGGCTCAGACACTT
Equus_caba	GGACTCGGCTCAAACACGT
Felis_catu	GGACTGGGCTCAGACACAT
Mustela_pu	GGACTAGGCTCACACACAC
Procyon_lo	GGACTAGGCTCACACACAT
Oryctolagu	GGACTCGGCTCAAACACGC
Trichechus	GGACTCAGCTCCGACAGGT
Dasypus_no	GGACTCGGCTCAGACACGT
Elephas_ma	GGGCTCAGCTCCGACAGGT
Xenopus_la	CAGCCAGTCCCCGACATGT
Microtus_o	GAGCTCGGCTCCTACAACC
Chelydra_s	GGGCTGCGCTCAGACACGC
Mus_muscul	GAACTCGGTTCTCACAAACC
Cavia_porc	GGGACGGGCTCCTACAAGC
Gallus_gal	CGGCGTCGCTCCCACACGC
gi 6041649	AACAACCTTCTGGAACAACG
gi 6010124	GATTAGCACTCATACAGTC
gi 5031301	CTTGGTACGCATCACATCG
gi 4609203	CATAACTGTCACCACAATT
gi 3860192	TTGGTGATAAGGAACAGCT
gi 3860195	GATTCTGACTTGCAACAAGT
gi 5702104	TTTGAAGGCTGTAAACATTT
AJ310189.1	AACCATGCAGTGTACAACCT
L16792.1/3	AACCATGCAGGAAACATAT
AJ306560.1	AACCATGCAGGTTACAACCT

Conservació estructura secundària



Què són els snoRNA?

Small nucleolar ribonucleic acid

snoRNP: snoRNA associat a un core de quatre proteïnes

Funció:

- ✓ modificació post-transcripcional rRNA i snRNA
- ✓ processament i estabilització de les RNP

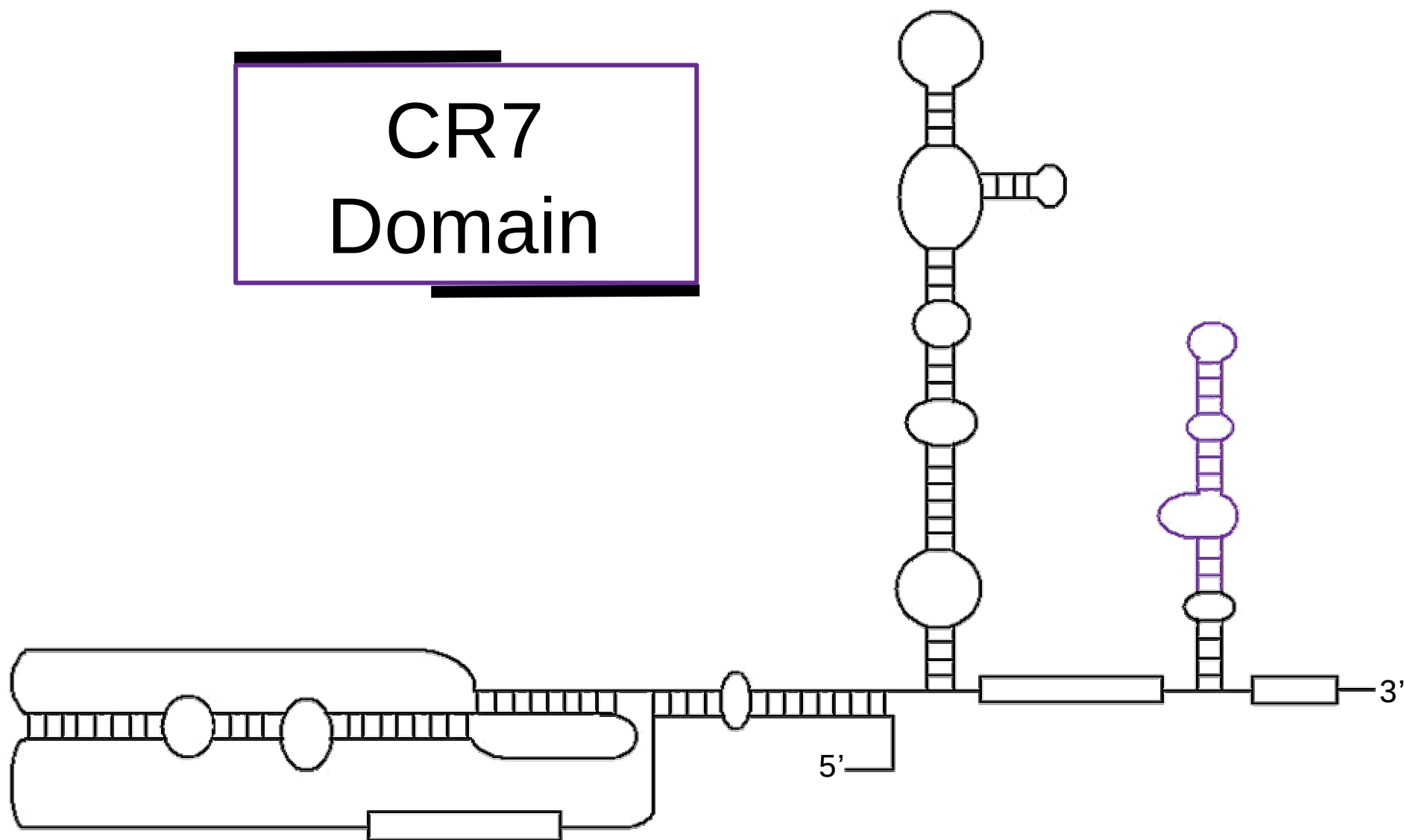
Característiques que comparteixen les snoRNP:

- ✓ localització nucleolar estable
- ✓ processament 3' i 5' comú
- ✓ associades sempre a les mateixes proteïnes

Funcions del domini H/ACA

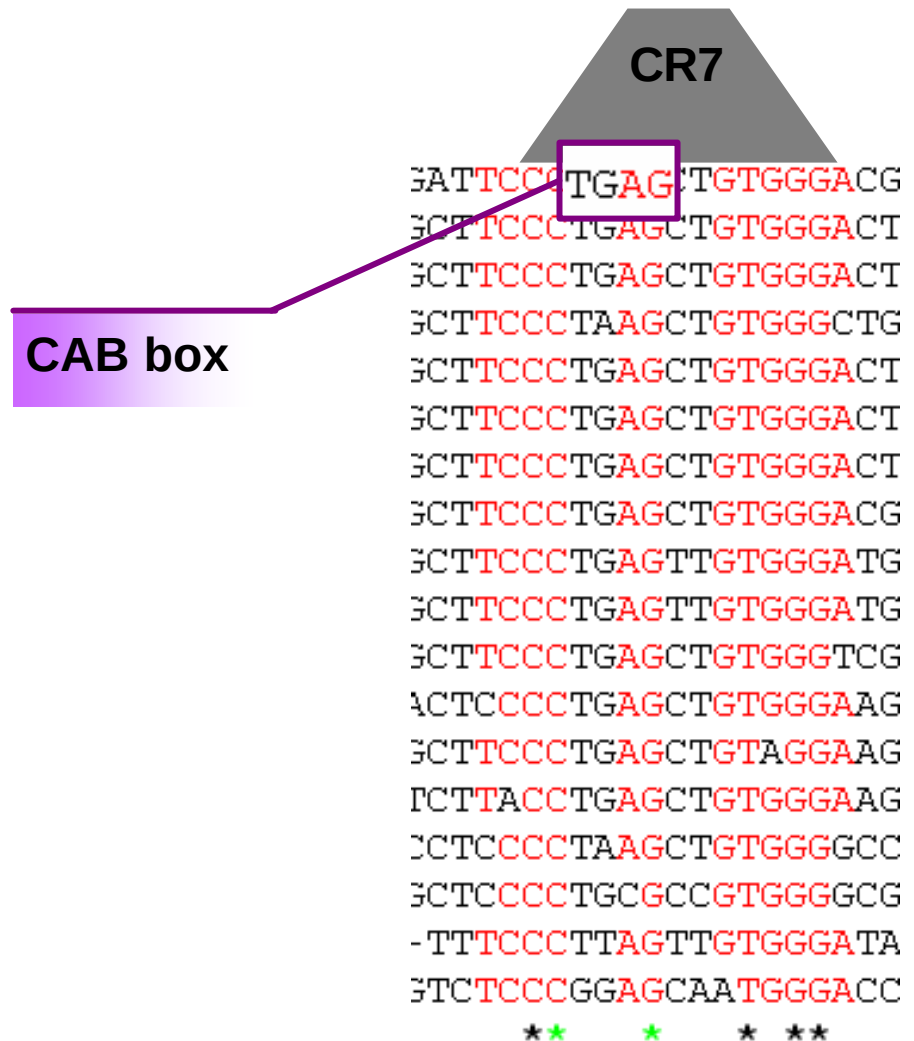
- ✓ Localització cel·lular
- ✓ Associació a les mateixes proteïnes
- ✓ Processament 3' (no el 5')

CR7 Domain

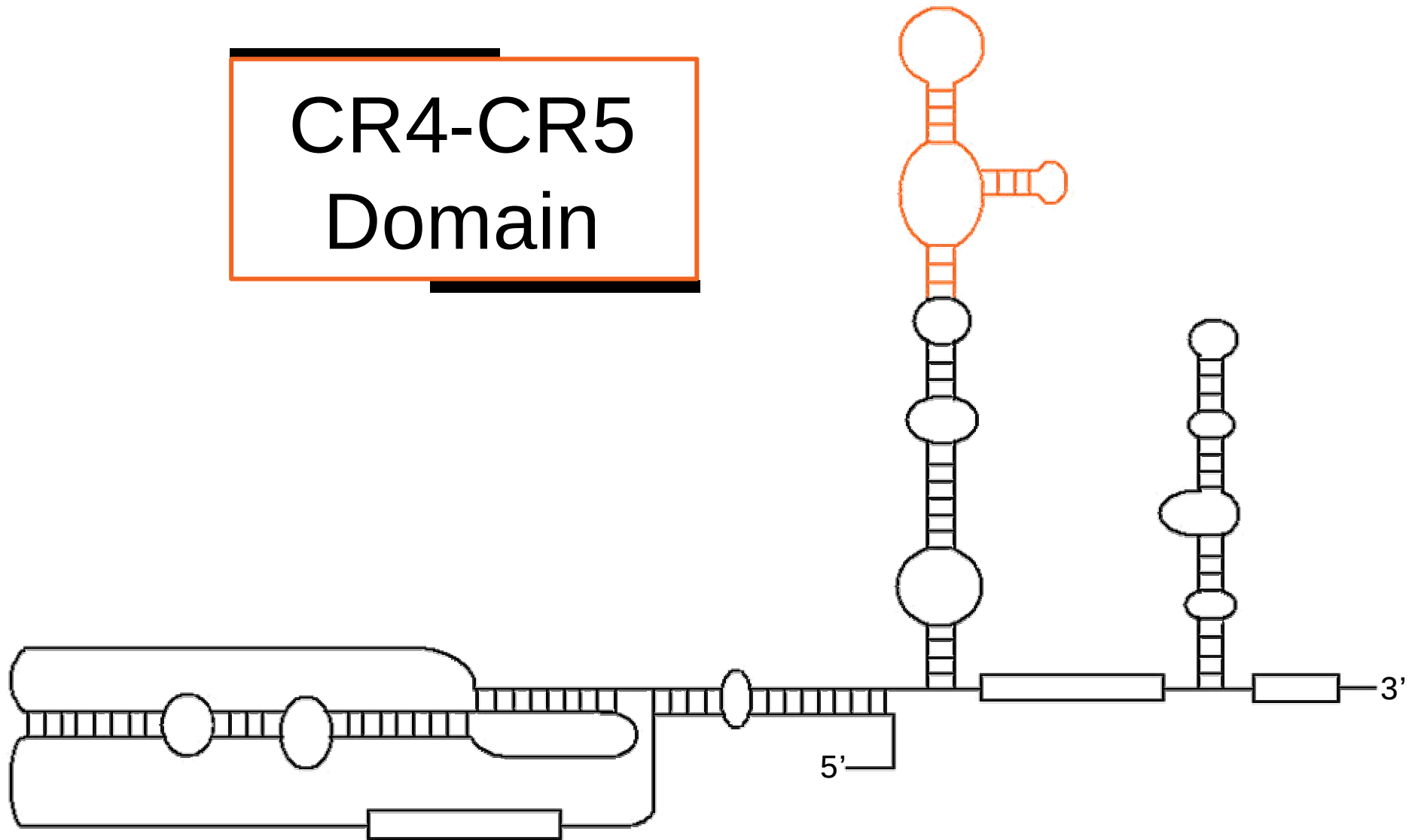


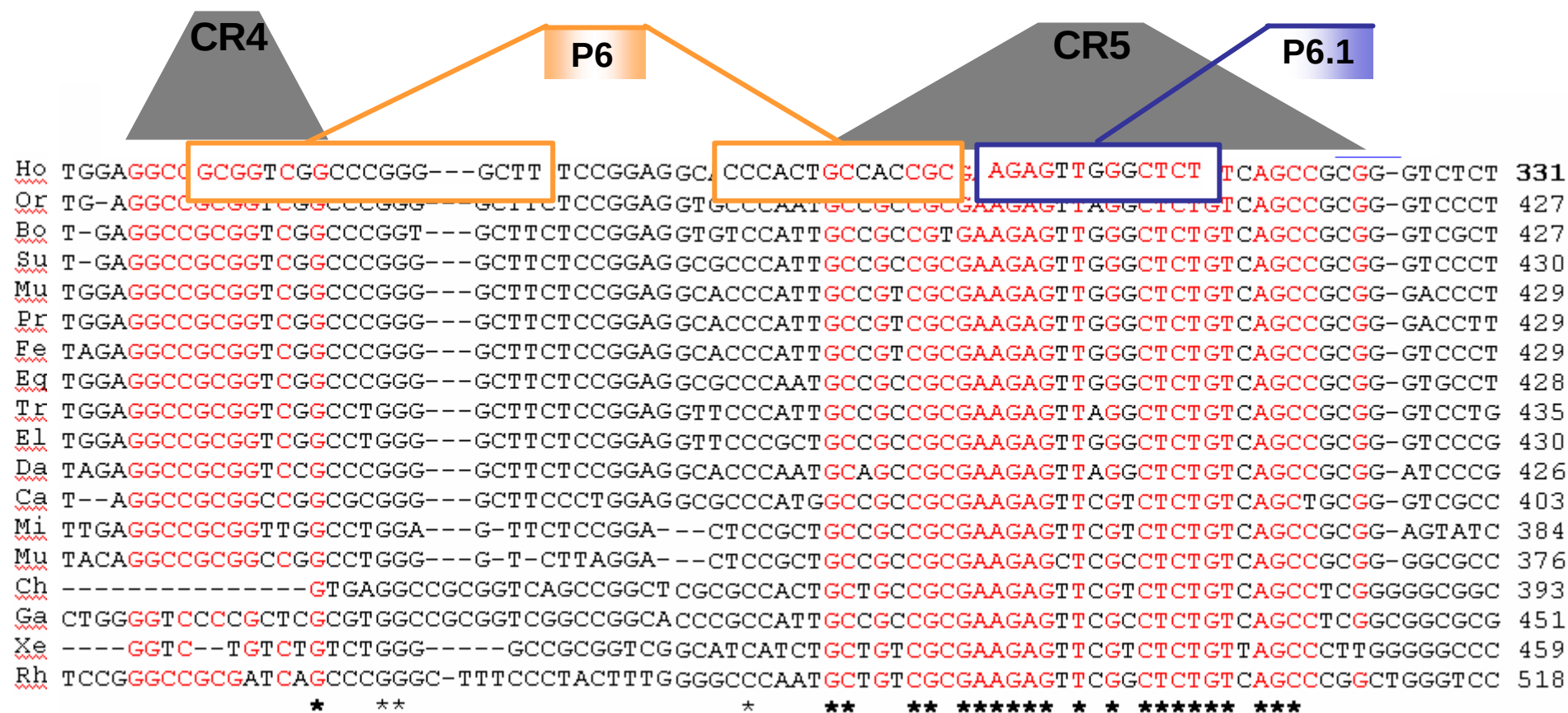
Funcions del domini CR7

- ✓ Poc conegut
- ✓ Té seqüència targetting cap a cossos de Cajal (nuclèol)

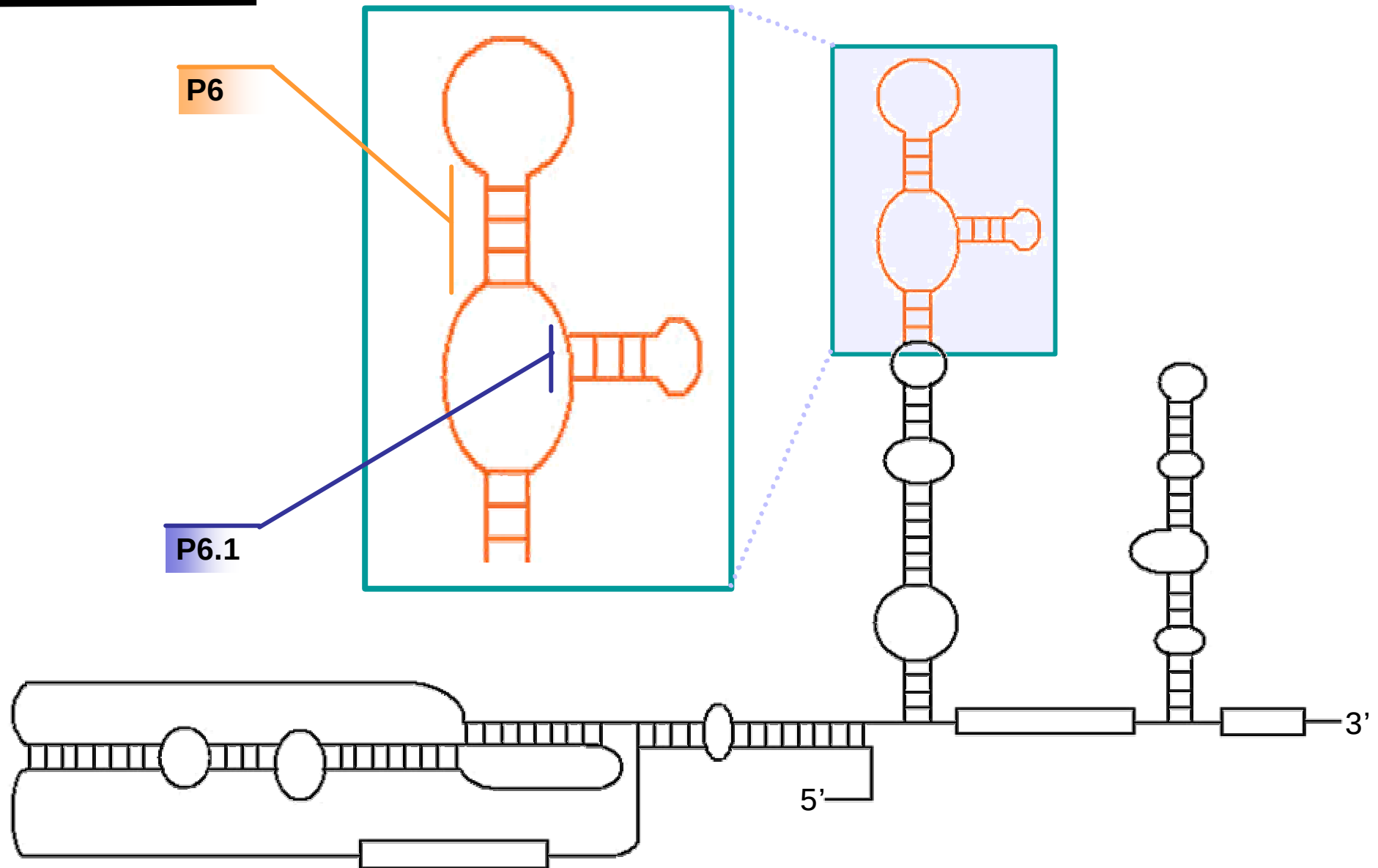


CR4-CR5 Domain





Domini CR4-CR5. Domini d'activació

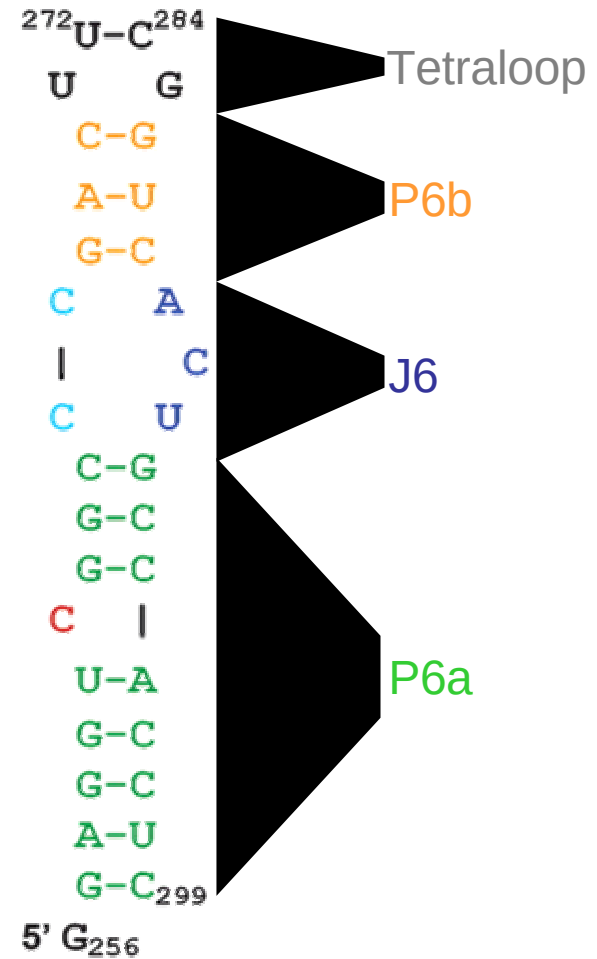


Domini CR4-CR5. Estructura P6

P6

GAGGTCGGCCCG - - - GCTT

CGGTCACTGCCACCGC



Domini CR4-CR5. Stem P6a

P6a

GAGGT**C**GGC GCC-ACCTC

²⁷²U-C²⁸⁴

U G

C-G

A-U

G-C

C A

I C

C U

C-G

G-C

G-C

C |

U-A

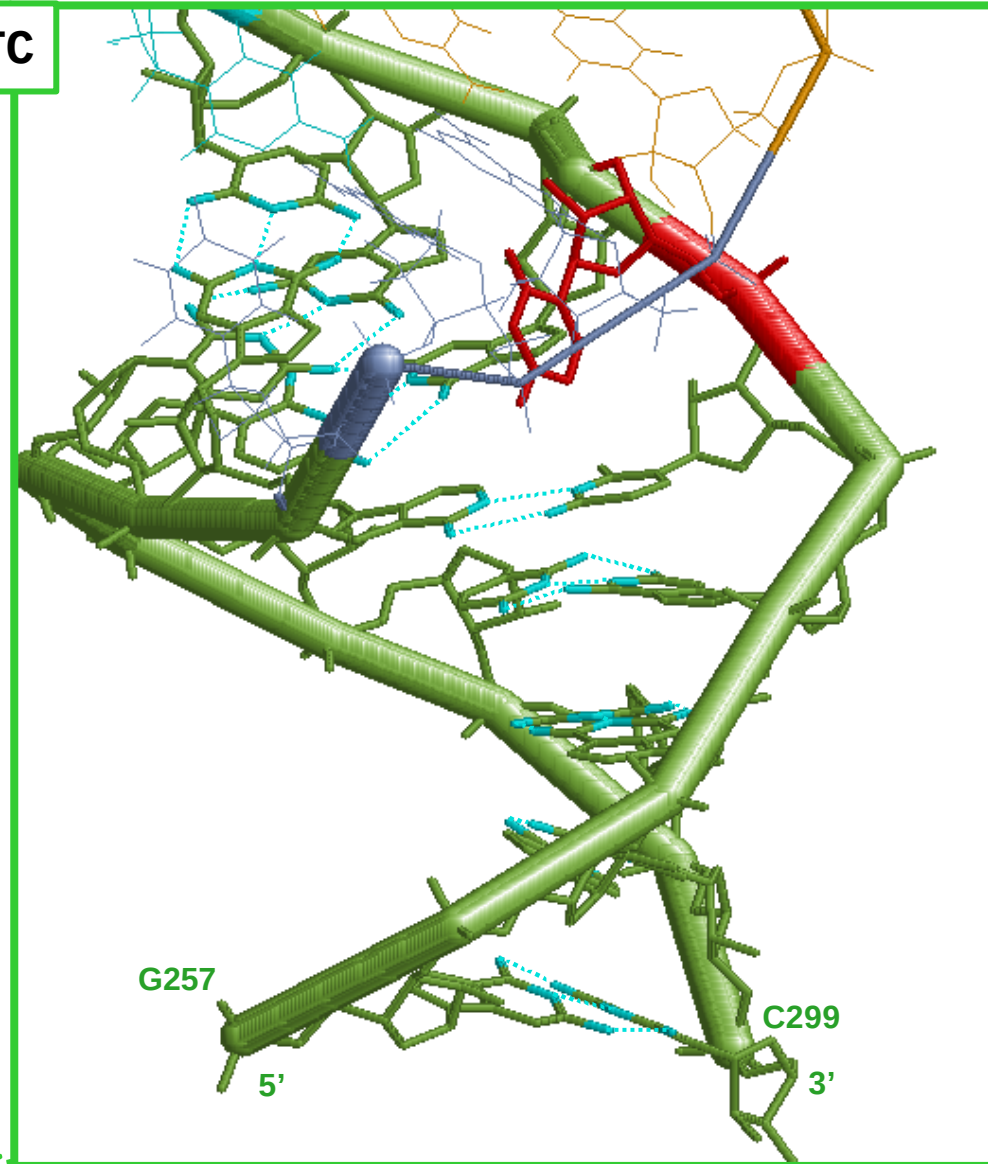
G-C

G-C

A-U

G-C²⁹⁹

5' G₂₅₆



Domini CR4-CR5. Stem P6a

P6a

GAGGT**C**GGC GCC-ACCTC

²⁷²U-C²⁸⁴

U G

C-G

A-U

G-C

C A

| C

C U

C-G

G-C

G-C

C |

U-A

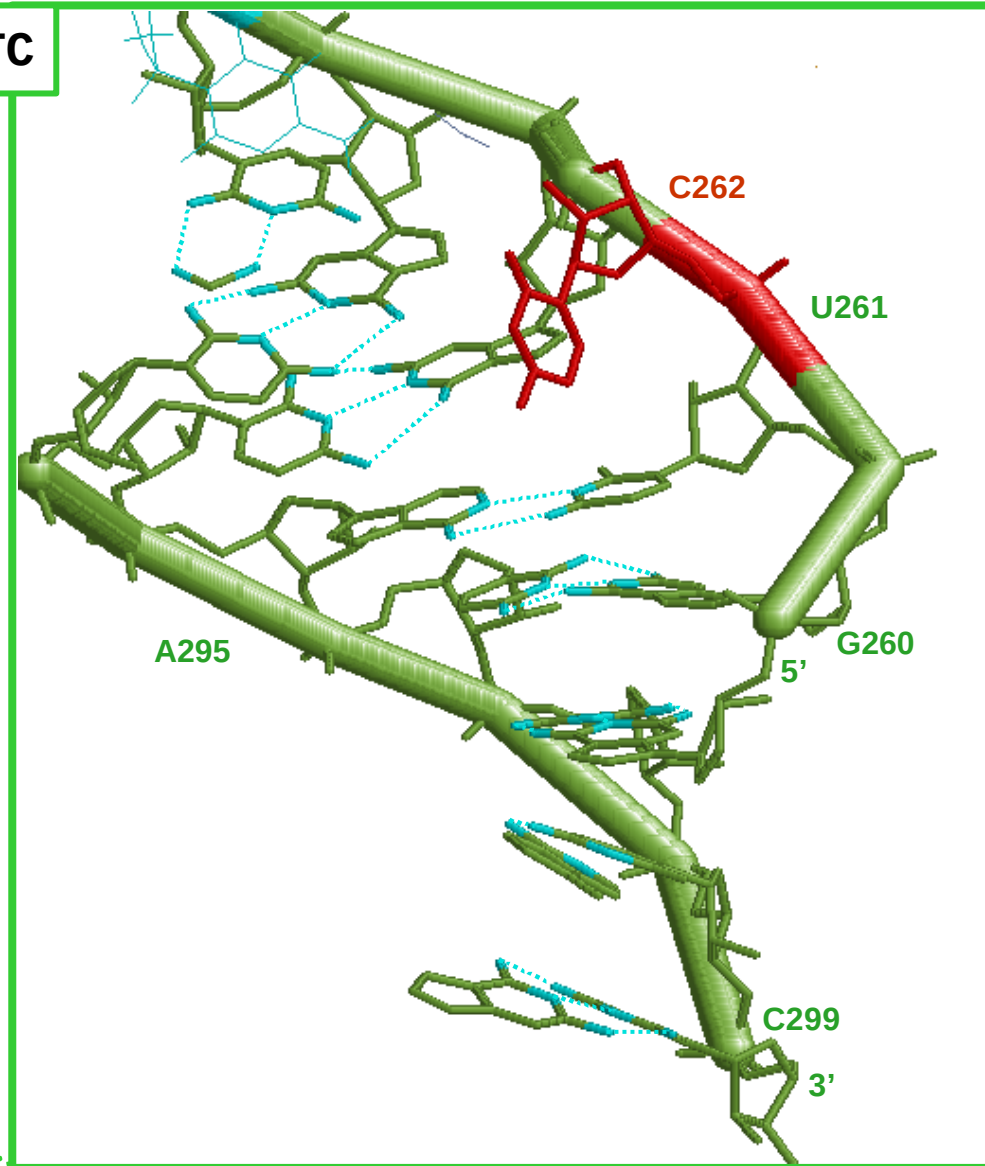
G-C

G-C

A-U

G-C²⁹⁹

5' G₂₅₆



Domini CR4-CR5. Stem P6a

A/G 295

```
GCACCCACTGCCGCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GTCTCT 331
GTGCCCAATGCCGCGCGAAGAGTTAGGCTCTGT CAGCCGCGG-GTCCCT 427
GTGTCCATTGCCGCGGTGAAGAGTTGGGCTCTGT CAGCCGCGG-GTCGCT 427
GCGCCCATTCGCCGCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GTCCCT 430
GCACCCATTGCCGTCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GACCCT 429
GCACCCATTGCCGTCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GACCTT 429
GCACCCATTGCCGTCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GTCCCT 429
GCGCCCAATGCCGCGCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GTGCCT 428
GTTCCCATTCGCCGCGCGAAGAGTTAGGCTCTGT CAGCCGCGG-GTCCTG 435
GTTCCCGCTGCCGCGCGCGAAGAGTTGGGCTCTGT CAGCCGCGG-GTCCCG 430
GCACCCAATGCAGCCGCGCGAAGAGTTAGGCTCTGT CAGCCGCGG-ATCCCG 426
GCGCCCATGGCCGCGCGCGAAGAGTTCGTCTCTGT CAGCTGCGG-GTCGCC 403
--CTCCGCTGCCGCGCGCGAAGAGTTCGTCTCTGT CAGCCGCGG-AGTATC 384
--CTCCGCTGCCGCGCGCGAAGAGCTCGCCTCTGT CAGCCGCGG-GGCGCC 376
CGCGCCACTGCTGCCGCGCGAAGAGTTCGTCTCTGT CAGCCTCGGGGGCGGC 393
CCCGCCATTGCCGCGCGCGAAGAGTTCGCCTCTGT CAGCCTCGGCGGCGCG 451
GCATCATCTGCTGTCGCGAAGAGTTCGTCTCTGT TAGCCCTTGGGGGCC 459
GGGCCCAATGCTGTCGCGAAGAGTTCGGCTCTGT CAGCCCGGCTGGGTCC 518
*      **      **      *****      *      *      *****      ***
```

Domini CR4-CR5. Stem P6a

P6a

GAGGT**C**GGC GCC-ACCTC

²⁷²U-C²⁸⁴

U G

C-G

A-U

G-C

C A

I C

C U

C-G

G-C

G-C

C |

U-A

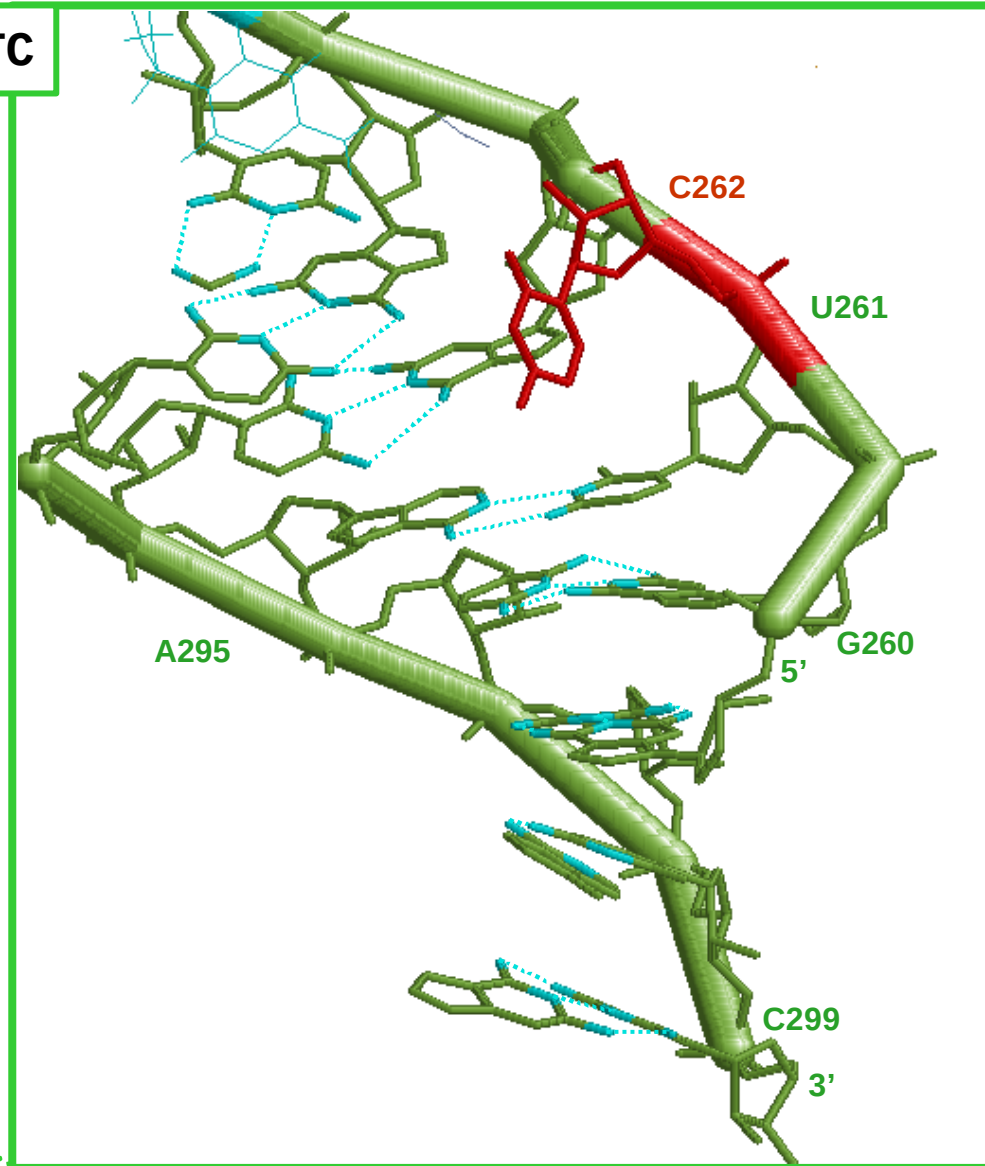
G-C

G-C

A-U

G-C₂₉₉

5' G₂₅₆



Domini CR4-CR5. Stem P6a

P6a

GAGGT**C**GGC GCC-ACCTC

²⁷²U-C²⁸⁴

U G

C-G

A-U

G-C

C A

| C

C U

C-G

G-C

G-C

C |

U-A

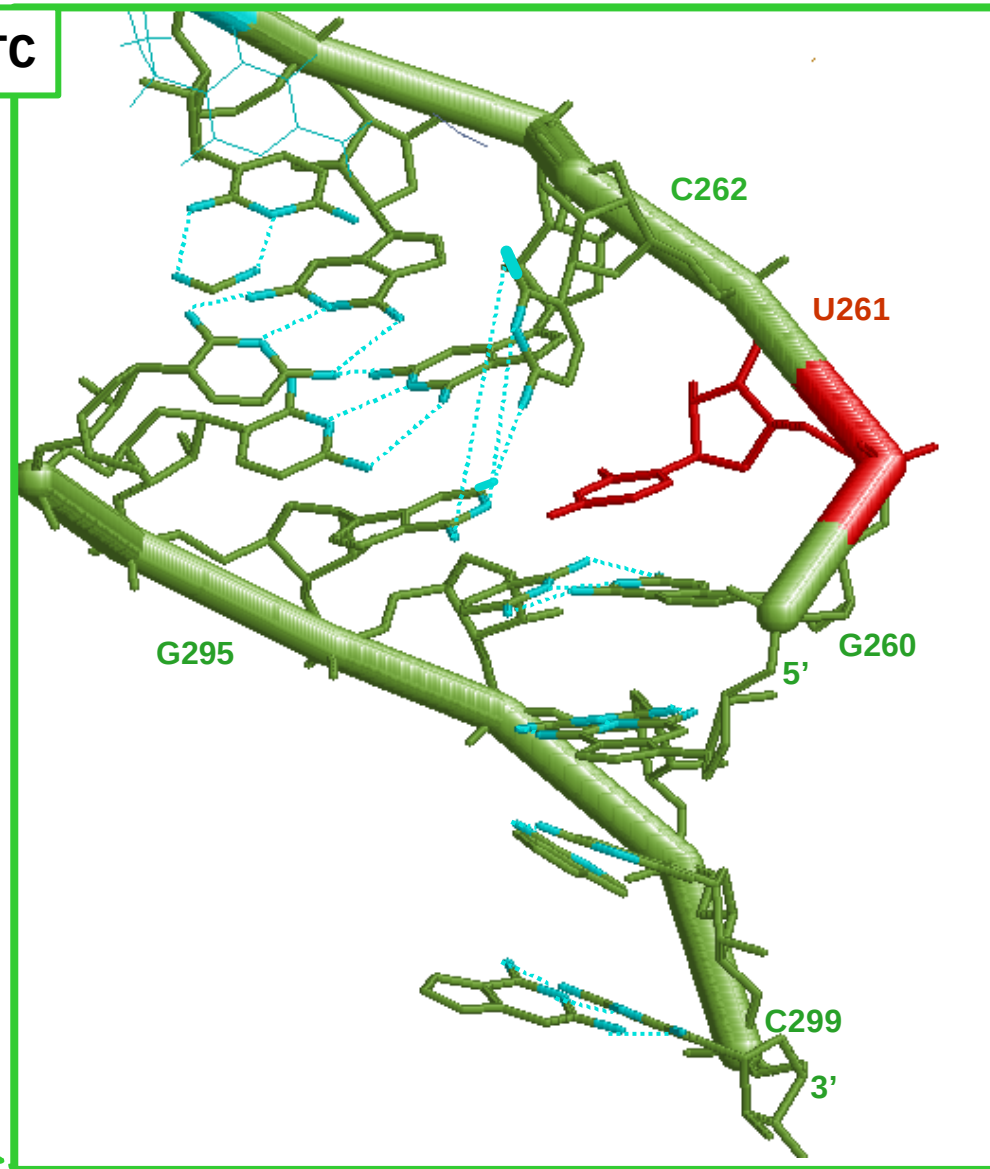
G-C

G-C

A-U

G-C²⁹⁹

5' G₂₅₆



Domini CR4-CR5. Loop Intern J6

J6

CCCG CACTG

²⁷²U-C²⁸⁴

U G

C-G

A-U

G-C

C A

| C

C U

C-G

G-C

G-C

C |

U-A

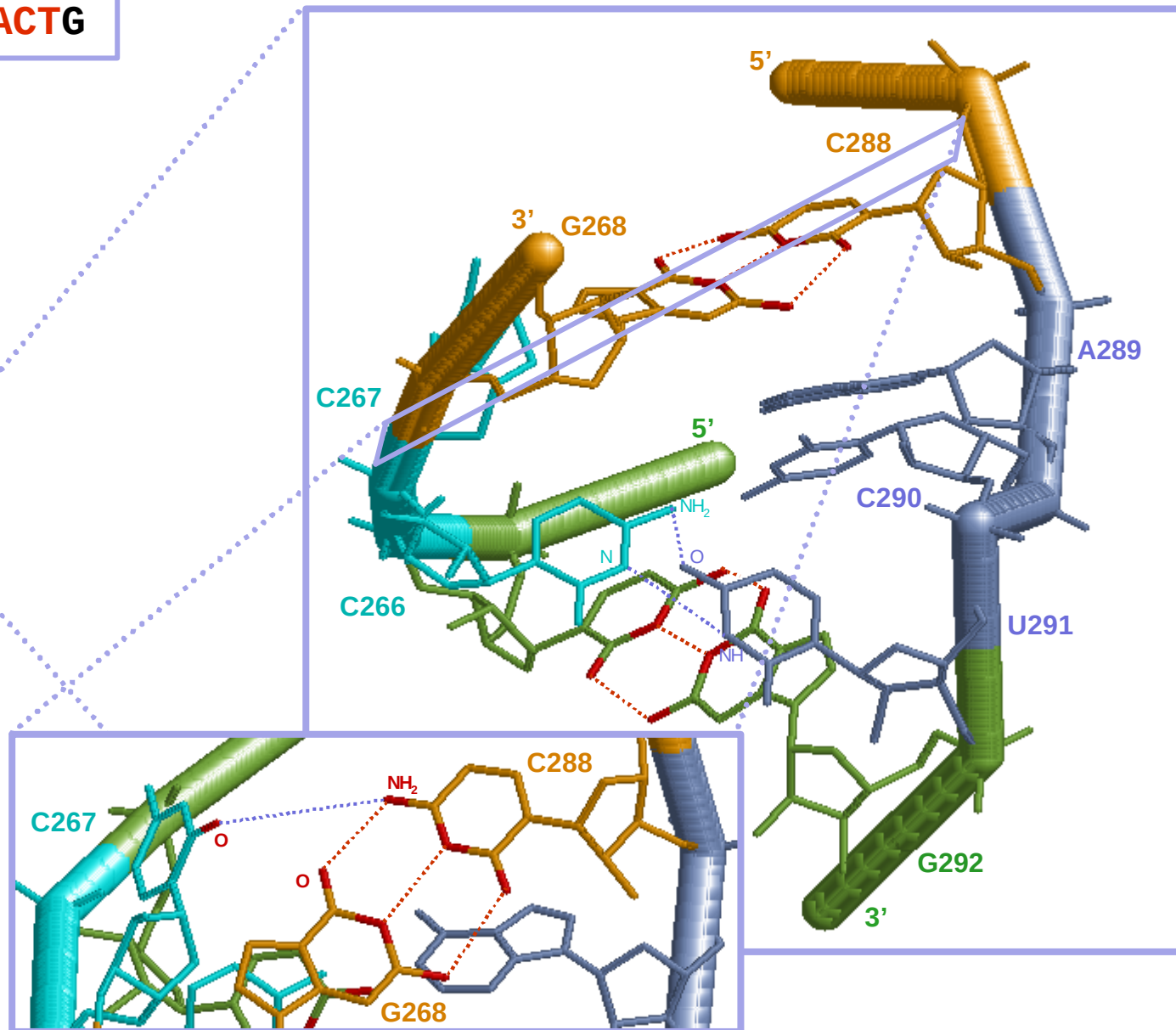
G-C

G-C

A-U

G-C²⁹⁹

5' G₂₅₆



Domini CR4-CR5. Loop Intern J6

J6

CCCG CACTG

²⁷²U-C²⁸⁴

U G

C-G

A-U

G-C

C A

| C

C U

C-G

G-C

G-C

C |

U-A

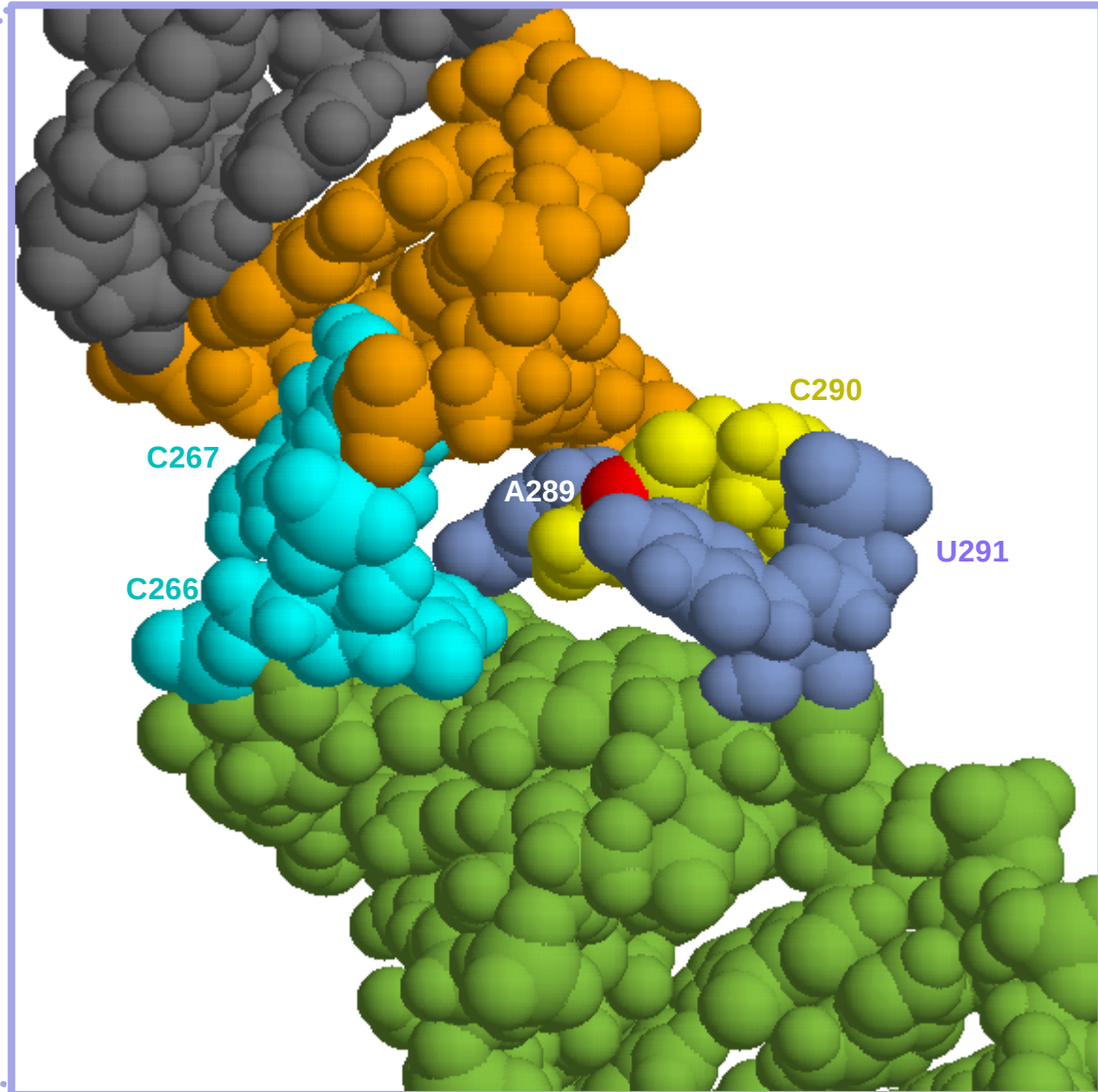
G-C

G-C

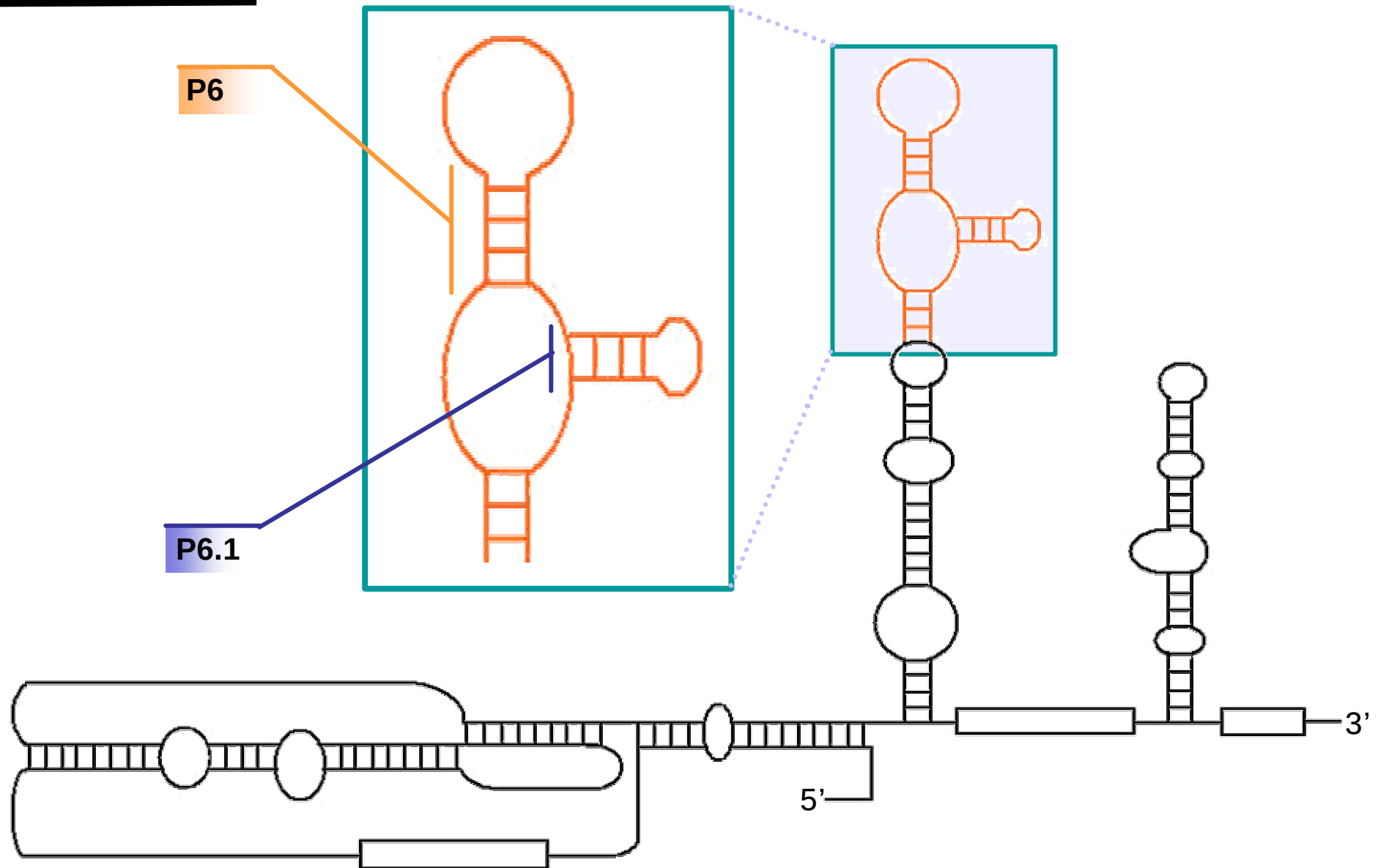
A-U

G-C²⁹⁹

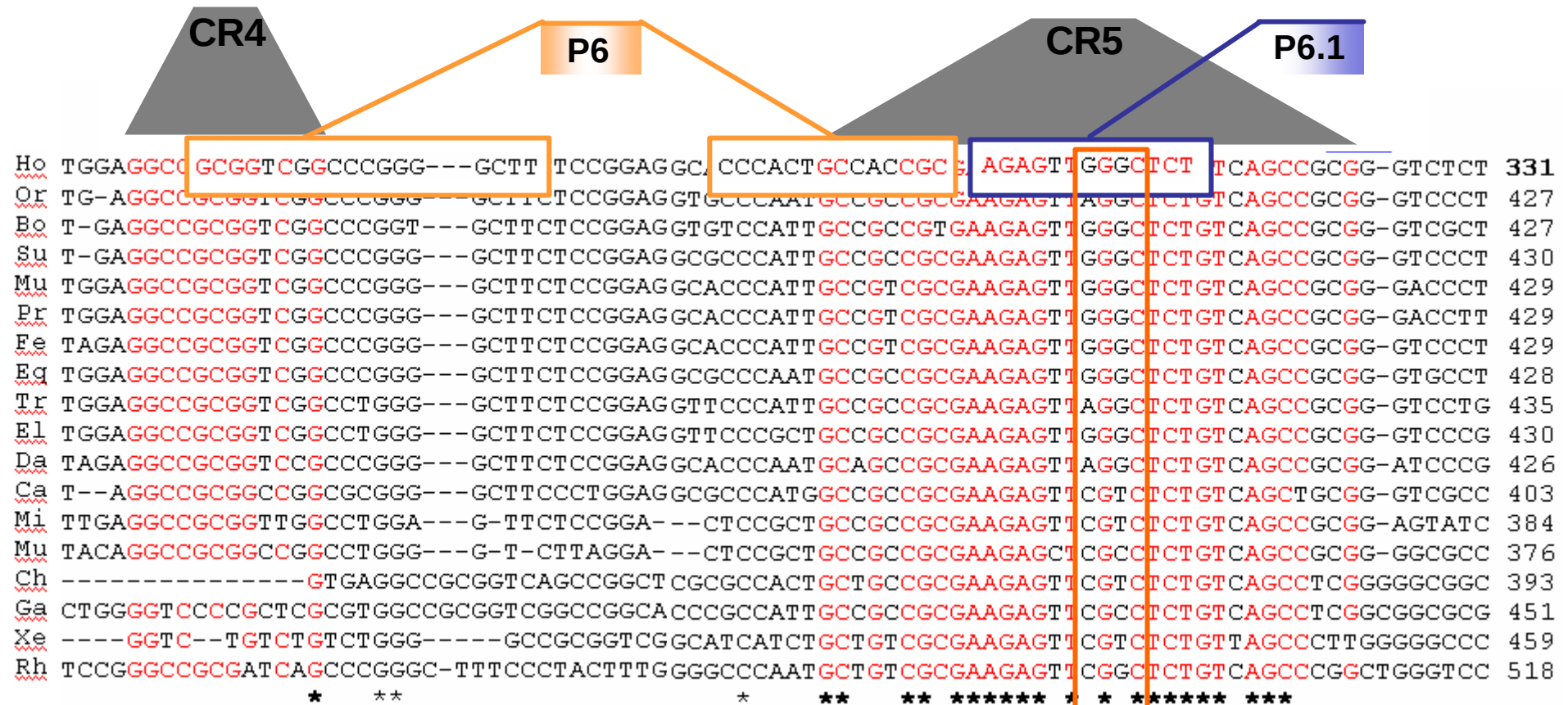
5' G₂₅₆



Domini CR4-CR5. Domini d'activació



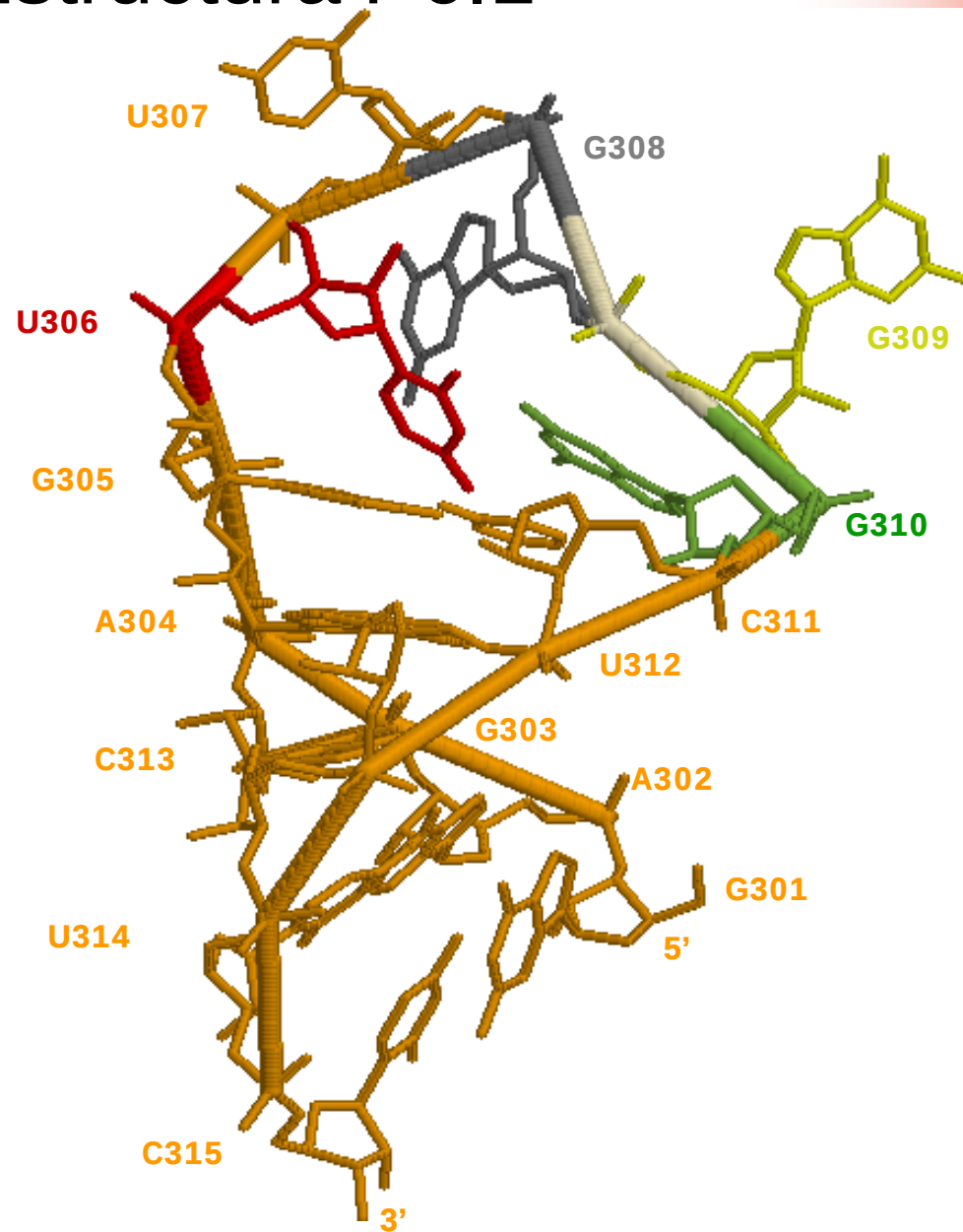
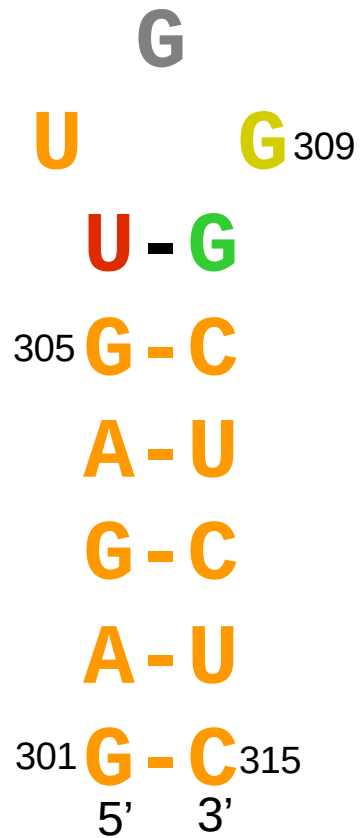
Domini CR4-CR5. Alineamento inicial



Domini CR4-CR5. Estructura P6.1

P6.1

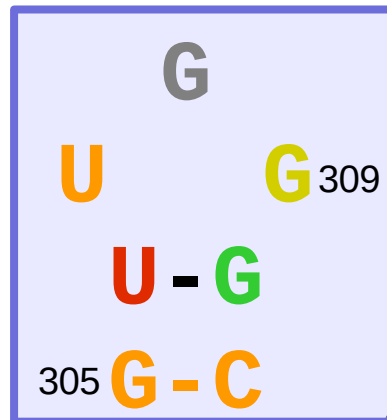
AGAGTTGGGCTCT



Domini CR4-CR5. Estructura P6.1

P6.1

AGAGTTGGCTCT



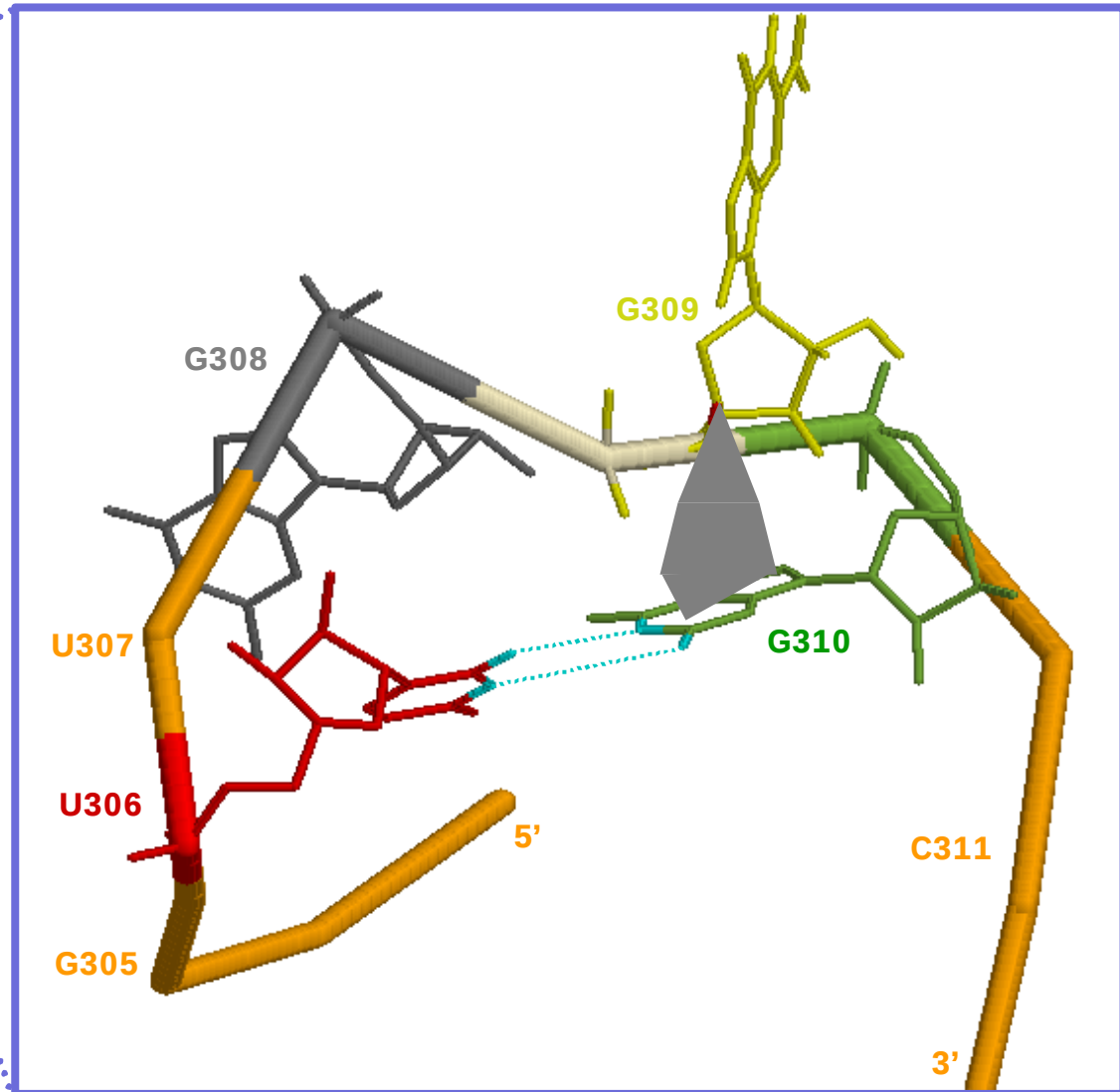
A - U

G - C

A - U

301 G - C₃₁₅

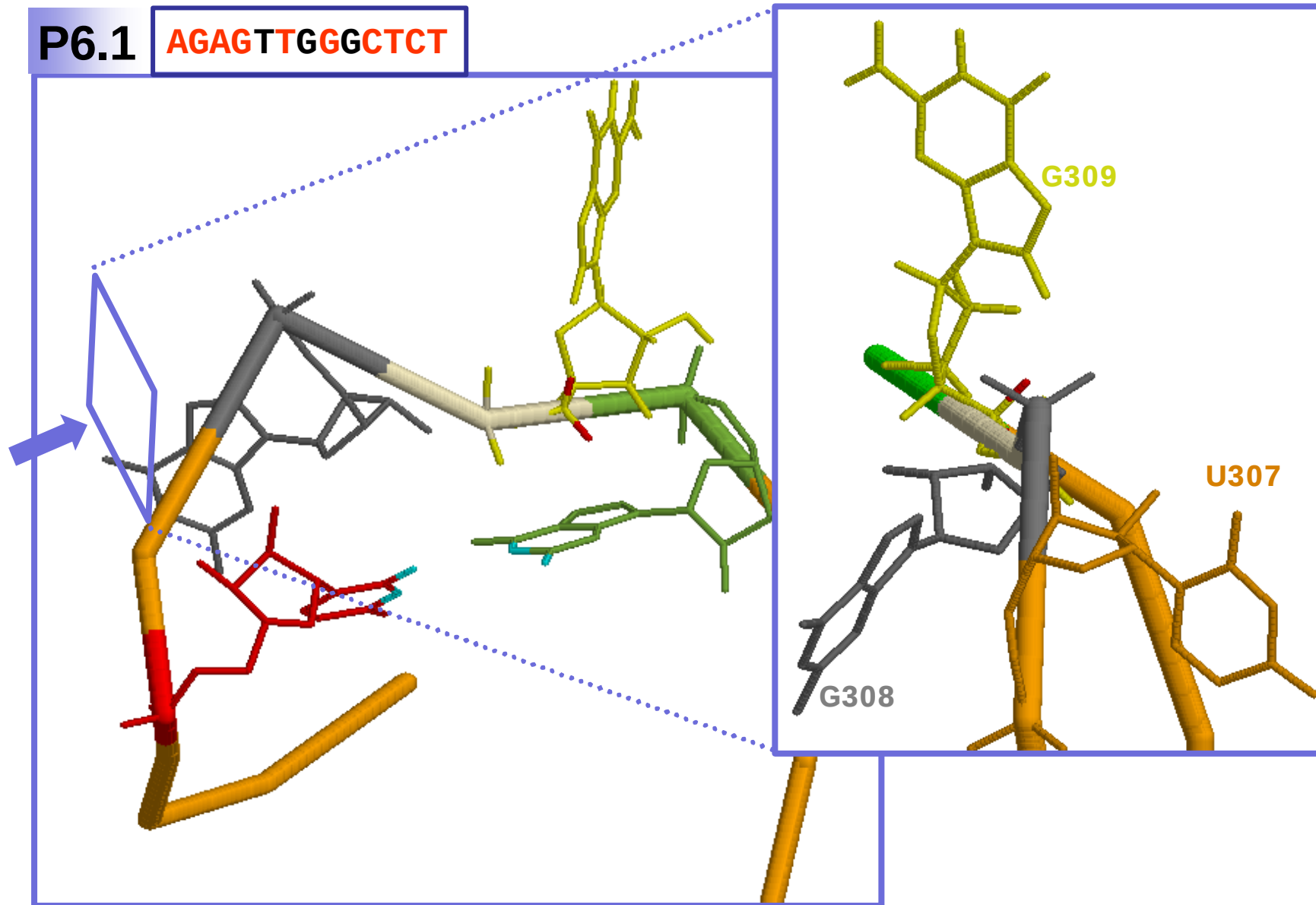
5' 3'



Domini CR4-CR5. Estructura P6.1

P6.1

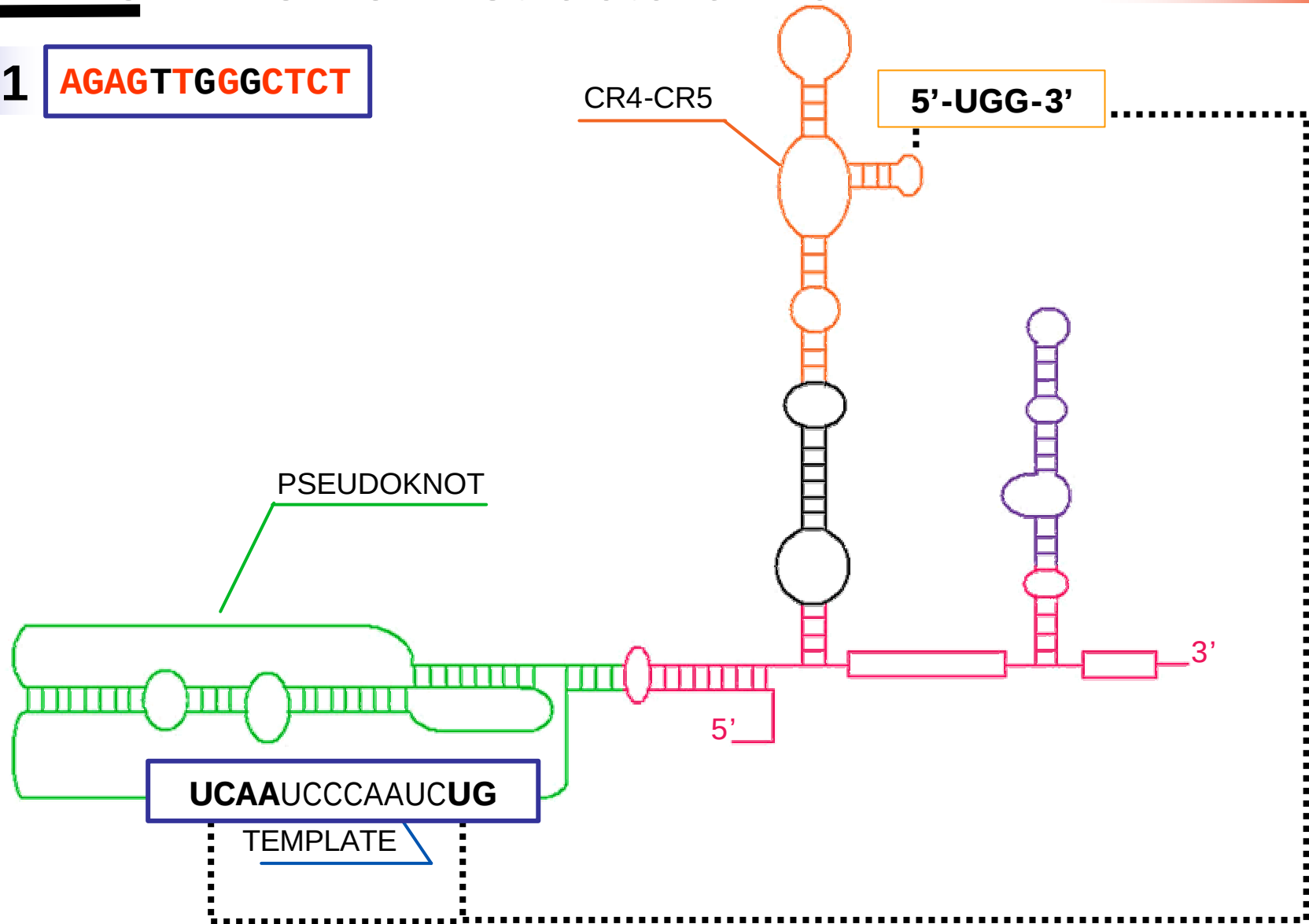
AGAGTTGGCTCT



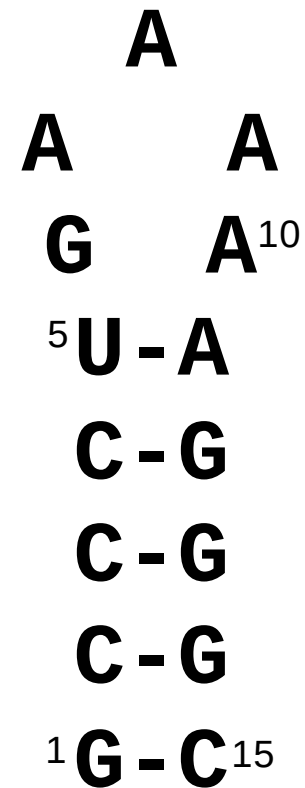
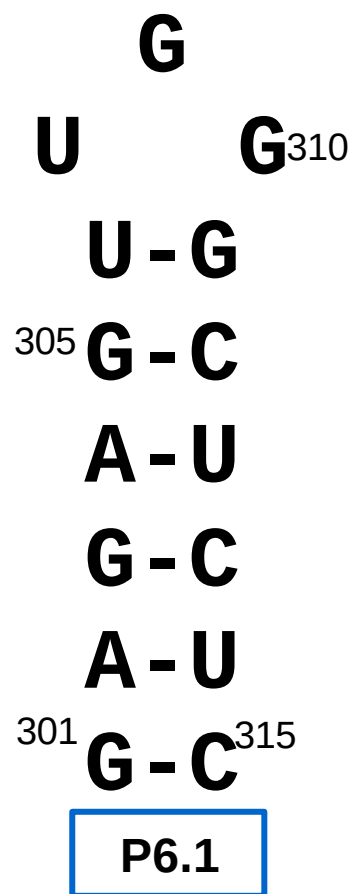
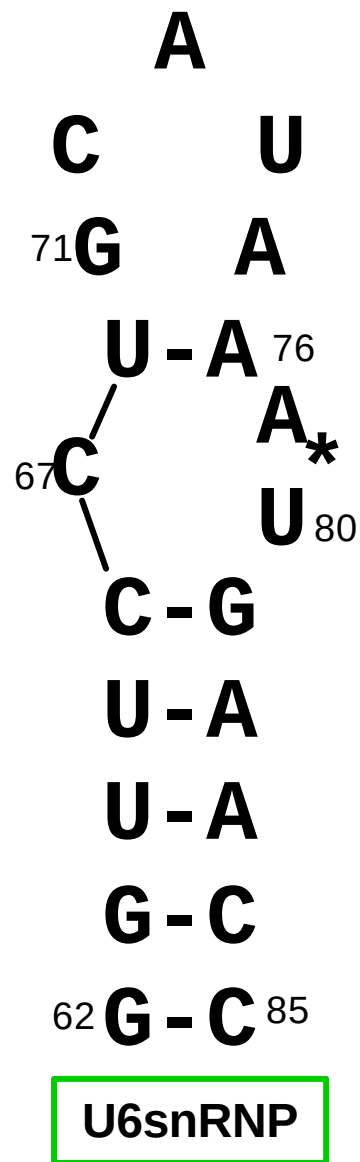
Domini CR4-CR5. Estructura P6.1

P6.1

AGAGTTGGCTCT



XAM: buscant homologies estructurals



CLUSTAL W(1.60) multiple sequence alignment

1LC6_A_U6

GGTTCCCCTGCATAAGGATGAACC

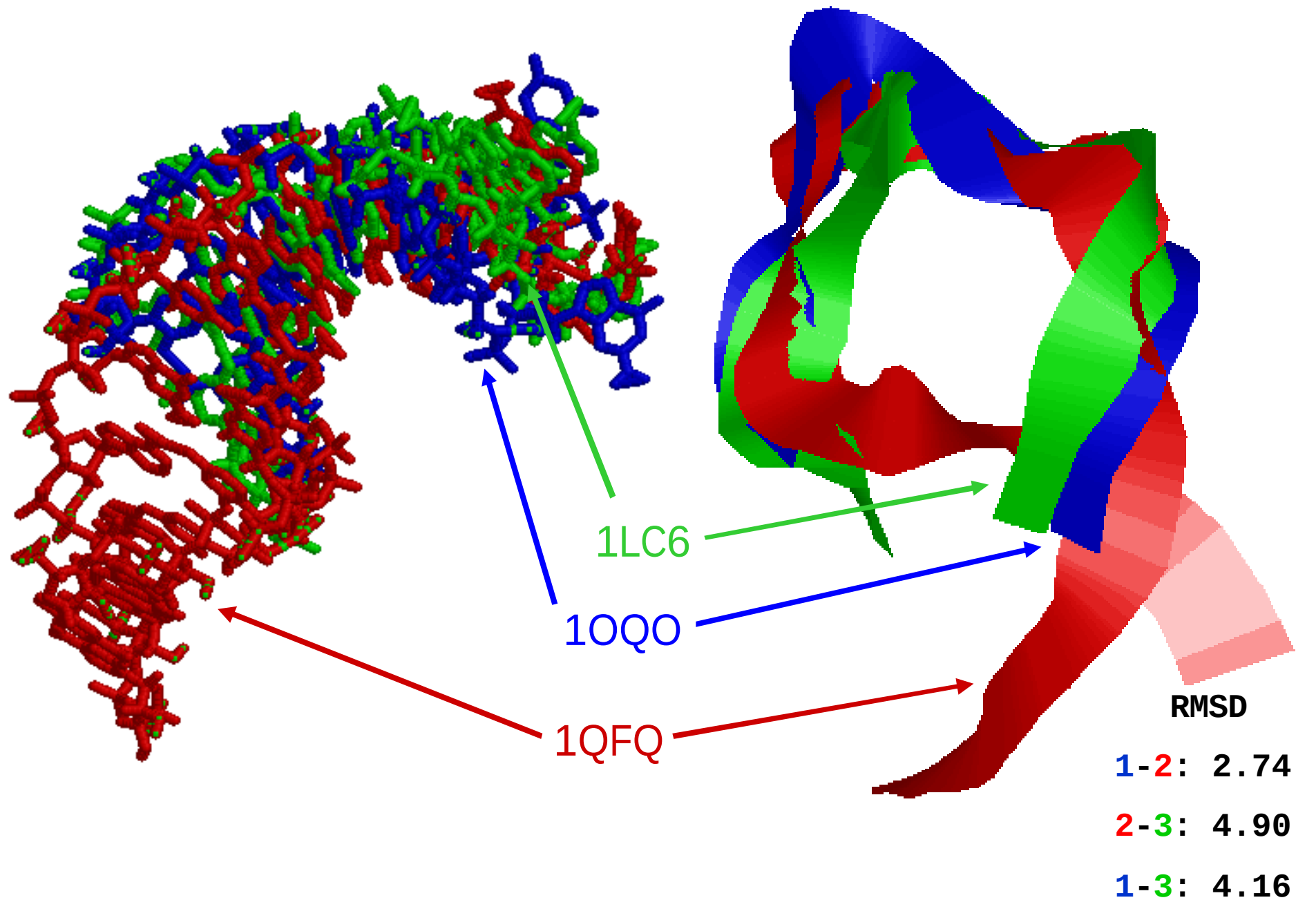
10Q0_A_P6.

-----GAGAGTTGGGCTCTC-

1QFQ_A_15-

----GCCCTGAAAAAGGGC-----

XAM: buscant homologies estructurals



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Preguntas PEM

1. Respecte la subunitat catalítica de la telomerasa (TERT), és cert que:

1. Té un 20% d'identitat amb la retrotranscriptasa del HIV-1.
2. Es creu que conserva l'estructura de fingers-palm-thumb.
3. Els residus importants per l'addició de nucleòtids estan conservats (p.e. Triada catalítica i residus del finger domain).
4. La cristal·lització de la TERT (Març 2005) confirma la homologia amb el virus HIV humà.

a) 1, 2 i 3

b) 1 i 3.

c) 2 i 4.

d) 4

e) 1, 2, 3 i 4.

2. Pel què fa al plegament de l'RNA, assenyala la resposta correcta:

- a) La unió a cations divalents estabilitza el plegament
- b) Es creen ponts d'hidrogen entre unions canòniques i no-canòniques

c) Les dues anteriors

d) No es pot plegar en forma de doble hèlix

e) Totes les anteriors

3. Respecte al template de la telomerasa, és cert que:

- a) Està molt conservat en vertebrats.
- b) Està situat suficientment exposat per interaccionar i allargar el DNA telomèric i alhora a prop del domini funcional pseudoknot per tal d'interaccionar amb el centre actiu de la subunitat catalítica (TERT).
- c) Les dues anteriors.**
- d) La seqüència no és complementària al DNA telomèric.
- e) Totes les anteriors.

4. Respecte al domini pseudoknot de la telomerasa, és cert que:

- a) Es tracta d'una estructura terciària de l'RNA.
- b) Està format per 2 stems i per 2 loops.
- c) Les dues anteriors
- d) Es troba a l'extrem 5' del RNA
- e) Totes les anteriors són certes.**

5. L'estructura característica de triples bases del domini pseudoknot de la telomerasa ve donada per l'interacció de:

- a) Pseudoknot i template
- b) Pseudoknot i subunitat catalítica de la telomerasa (TERT)
- c) Primer residu del loop 1 i últim residu del loop2.**
- d) Pseudoknot i altres dominis de RNA.
- e) El domini pseudoknot de la telomerasa no té característiques diferencials respecte la resta de pseudoknots.

6. Assenyala la resposta correcta. El domini H/ACA de la Telomerasa RNA:

- a) Es troba a la telomerasa de llevats, ciliats i vertebrats
- b) La caixa ACA uneix sempre les mateixes proteïnes formant un core**
- c) La telomerasa s'emmagatzema al citoplasma
- d) La caixa ACA es localitza a prop de l'extrem 5'
- e) El domini H/ACA només el té la telomerasa RNA

7. Respecte als dominis dels RNAs amb funció catalítica, indica les afirmacions certes:

- a) És comú trobar una elevada conservació de seqüència en diferents ribonucleoproteïnes.
- b) La seqüència d'aquests RNA es conserva més que la seqüència d'aminoàcids de la proteïna amb què formen complex.
- c) Les dues anteriors són certes.
- d) És possible trobar una bona conservació estructural d'alguns dominis, malgrat la conservació de seqüència sigui nula.**
- e) Totes les anteriors són certes.

8. El domini de l'RNA de la telomerasa CR4CR5, que engloba els subdominis P6 i P6.1, està involucrat més aviat en:

- a) Funció estructural.
- b) Funció catalítica.
- c) Les dues anteriors.
- d) Funció d'activació de la part proteica TERT de la telomerasa.**
- e) Totes les anteriors.

9. **P6.1 és un petit *stem-loop* del domini CR4CR5 de la TR (RNA que forma part del complex telomerasa). S'ha vist que és possible trobar homòlegs estructurals a P6.1 en d'altres RNAs catalítics amb RMSD significatius, però que tanmateix no es produeix conservació entre les seqüències. Com explicaries aquest fenomen?**

- a) En tractar-se d'un domini compost per tant pocs nucleòtids és fàcil que la similaritat estructural sigui casual.
- b) En RNA no és possible trobar homologia estructural sense conservació de seqüència.
- c) Pot tractar-se d'un cas d'homologia remota, on s'ha preservat acuradament l'estructura però s'ha perdut l'homologia de seqüència.**
- d) És impossible determinar l'estructura de l'RNA, ja què és massa inestable.
- e) Pot tractar-se d'un cas d'analogia (convergència evolutiva), donat que tots aquests dominis tenen funcions gairebé idèntiques.

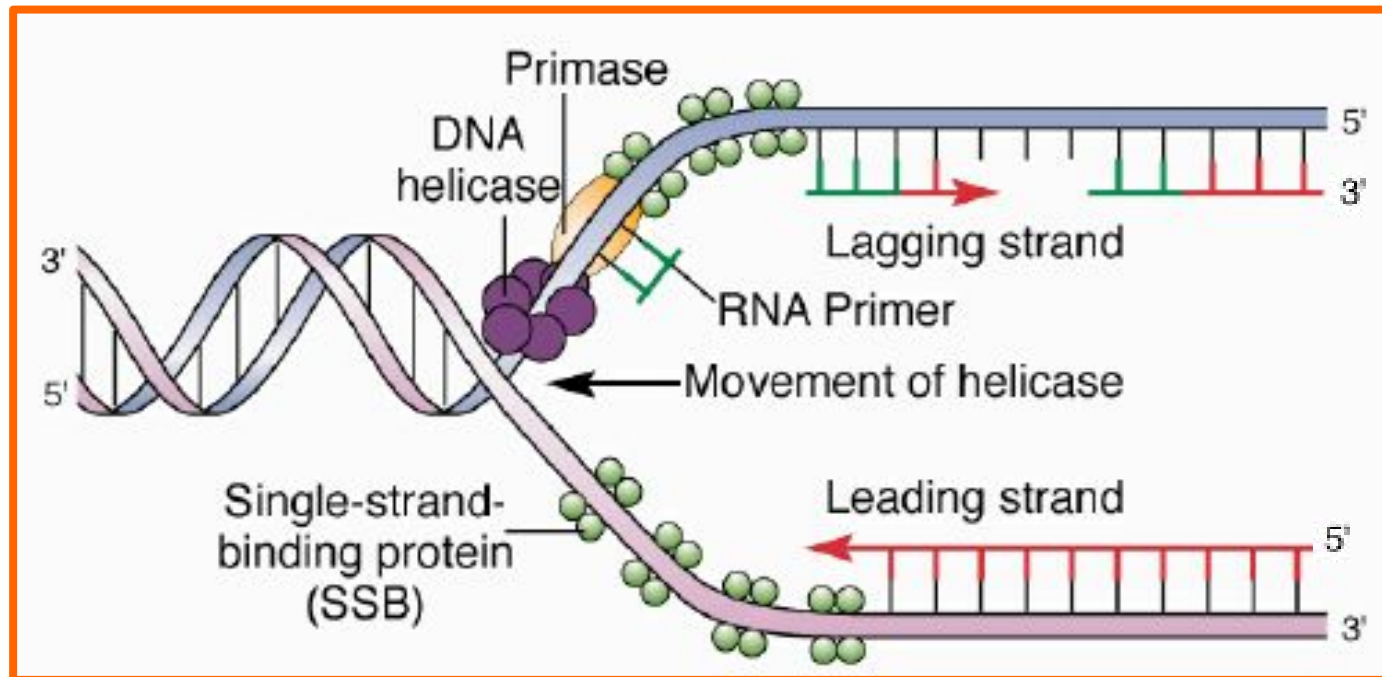
10. **Pel que fa als stem-loops P6 i P6.1, indica les certes:**

- a) Podem trobar bases (nucleòtids) desaparellades tant als extrems com enmig del stem-loop.
- b) Les bases desaparellades són un bon punt d'interacció amb altres regions de la telomerasa.
- c) Les dues anteriors són certes.**
- d) Tots els stem-loops segueixen un patró canònic.
- e) Totes les anteriors.

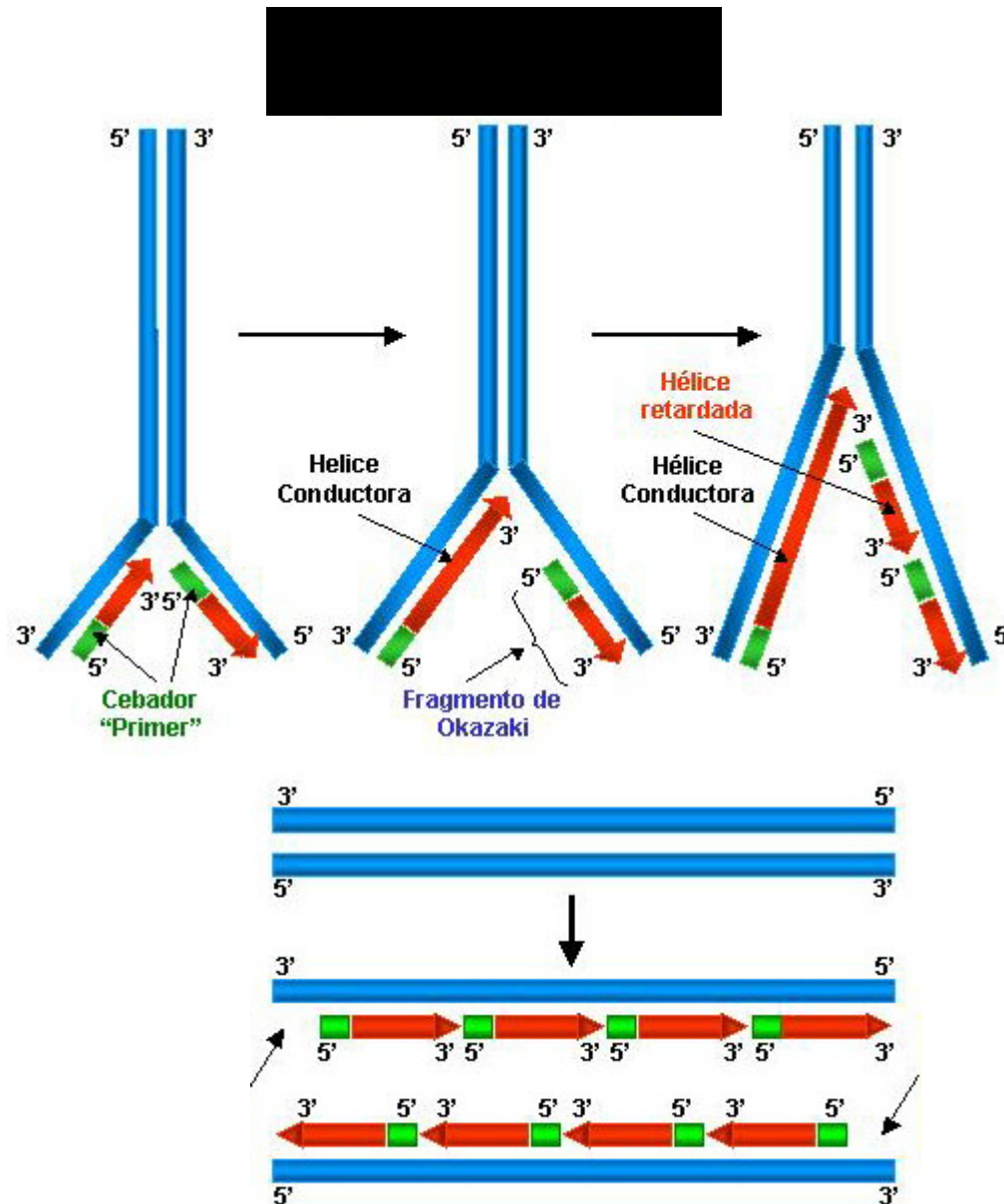
INTRODUCCIÓ

Replicació del DNA

- Replicació de DNA: DNA polimerases DNA dependents
- Sentit 5'- 3' (addició nt al grup 3'- OH)
- Fragments d'Okazaki (RNA-DNA)



“End Replication Problem”



- L'extrem 3' de cada cadena de DNA, que es replica, queda més curt degut a la col·locació de l'encebador

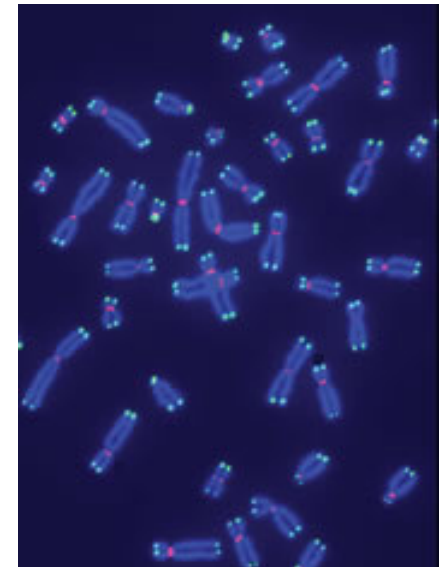
Solucions a l'escurçament de cromosomes

- ✓ Plegar el DNA de manera semblant a la circular
- ✓ Posar una proteïna que doni un 3-OH a la polimerasa
- ✓ Introduir seqüències no codificants: TELÒMERS

Telòmers

- Repeticions simples en tàndem riques en G.
- Afegides a l'extrem 3'-OH
- Seqüència en humans: (TTAGGG) n
- Afegits per la telomerasa

Tinció dels *telòmers* i
centròmers amb Fish



Telomerasa

✓ Classificació SCOP:

Classe: multi-domain protein (alpha and beta)

Fold: DNA/RNA polymerases

Superfamily: DNA/RNA polymerases

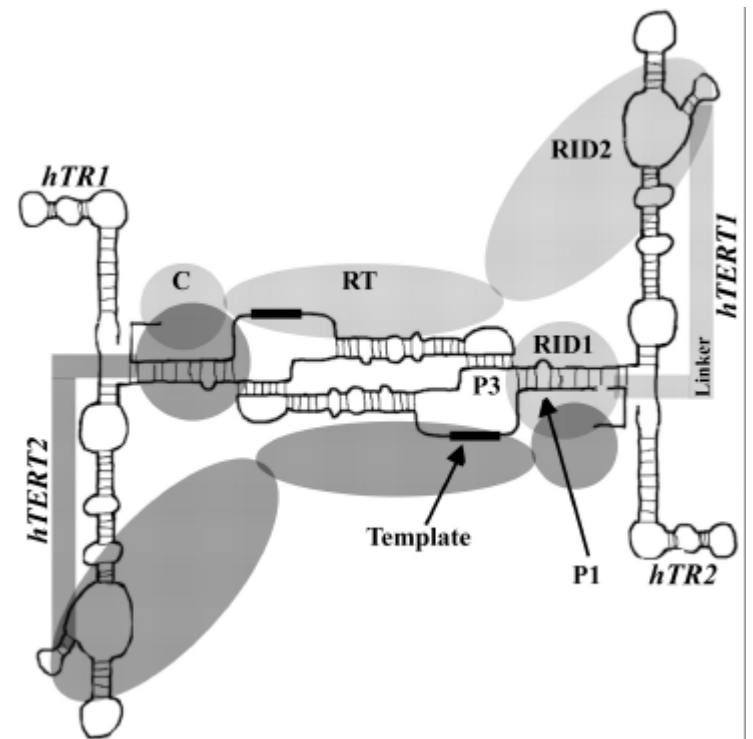
Family: Reverse Transcriptase (DNA pol RNA dep)

✓ Components:

Subunitat proteica (TERT)

Subunitat nucleotídica (TR)

Proteïnes associades

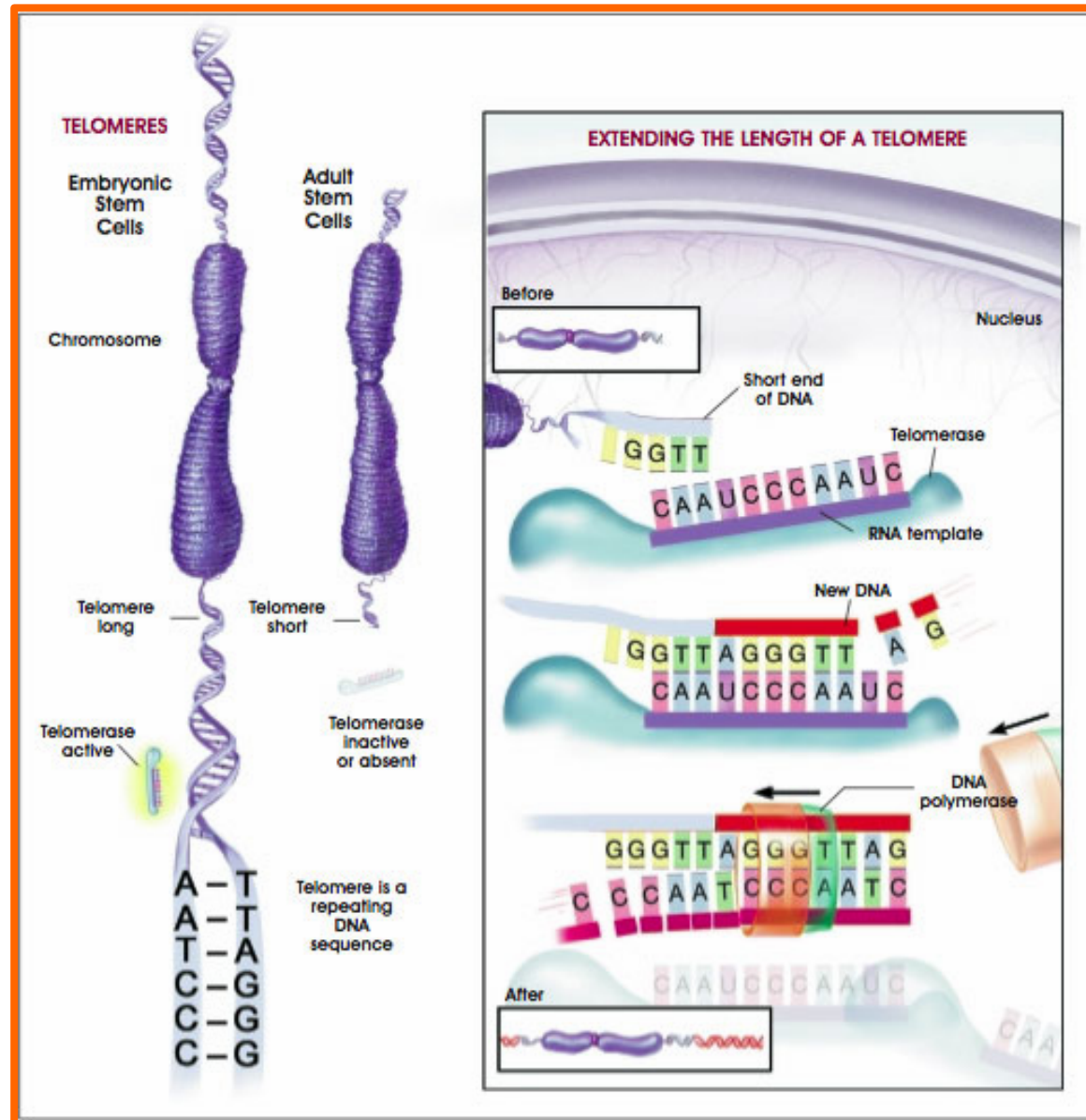


Característiques de la Telomerasa

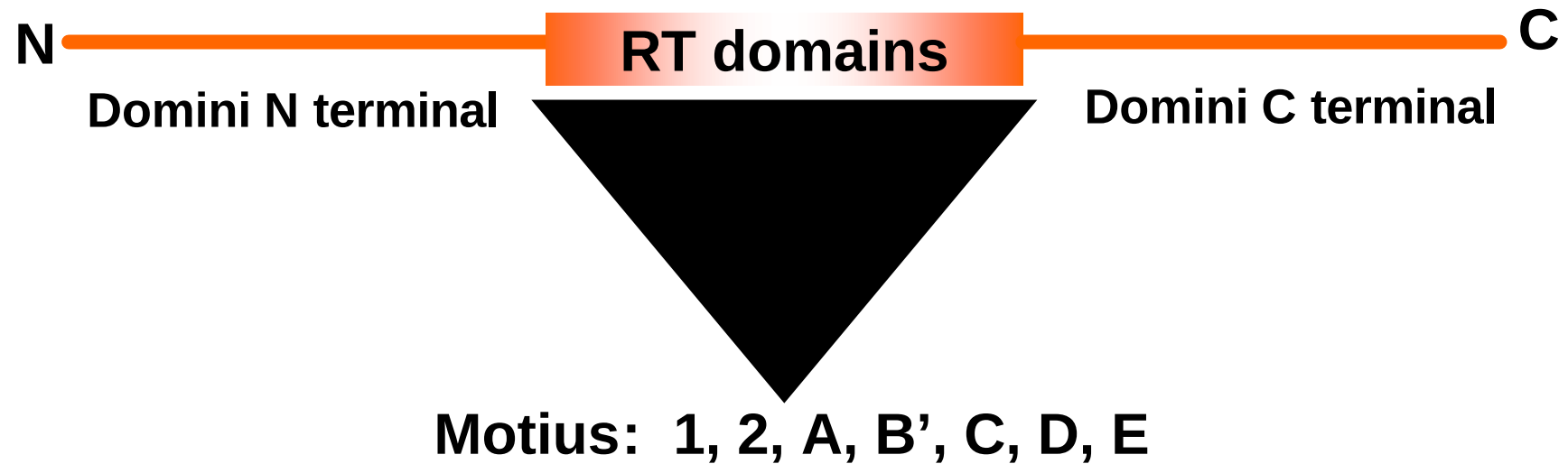


- ✓ Localitzada al nucli, on es replica el DNA
- ✓ No totes les cèl·lules tenen evidència d'activitat telomerasa
- ✓ El component catalític (TERT) s'expressa només quan hi ha evidència d'activitat telomerasa, mentre que el component de RNA ho fa de manera generalitzada (TR).
- ✓ Molta activitat a cèl·lules fetals, que mantenen un alt nivell proliferatiu, però molt poc en cèl·lules de teixits adults.
- ✓ S'observa gran activitat en cèl·lules tumorals (*relació amb càncer; possibles dianes terapèutiques*)

Funcionament de la telomerasa



Subunitat Catalítica: TERT



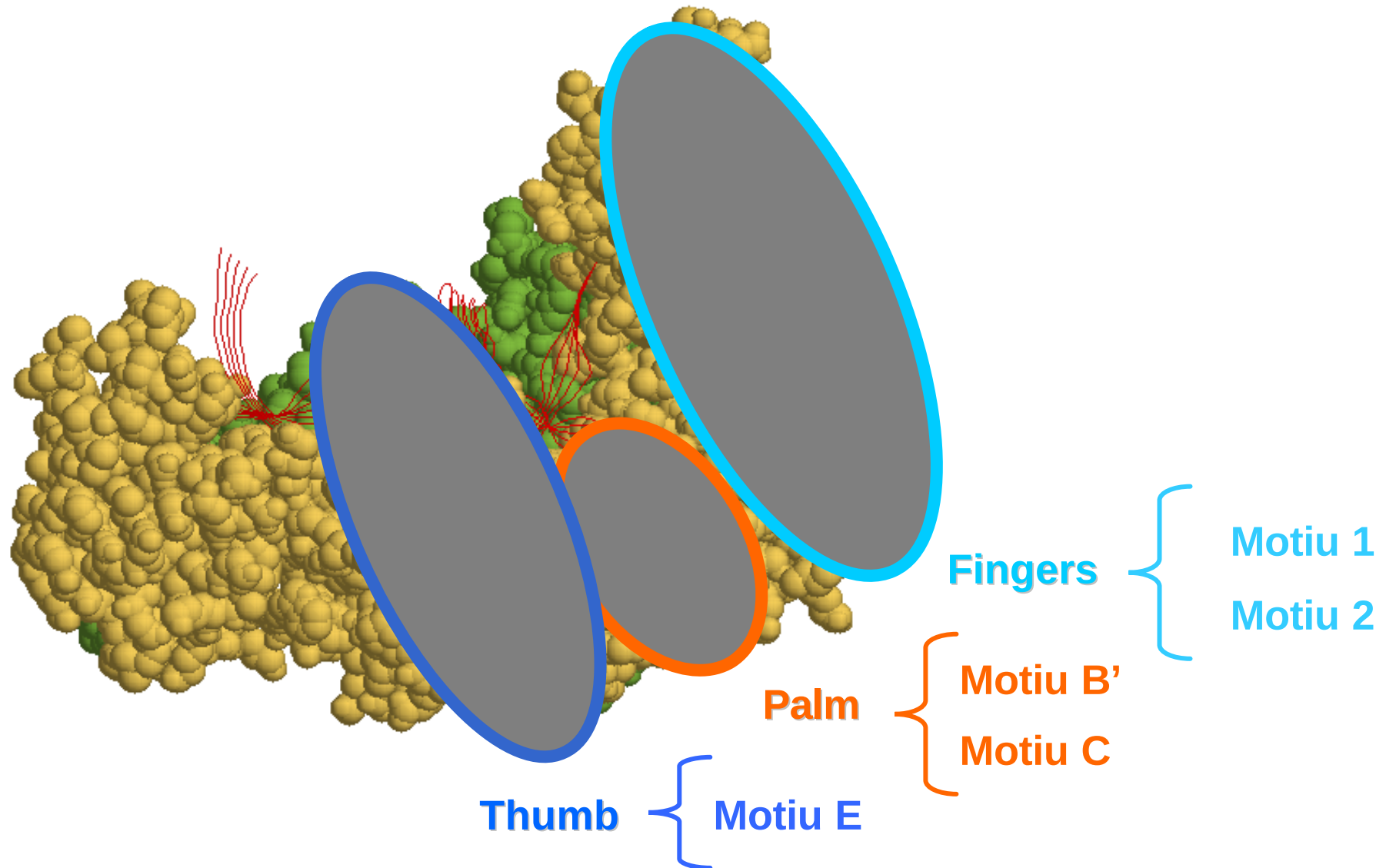
Centre Actiu en RTs de virus:

- Unió al template
- Unió als nts
- Unió al primer

Homòleg en TERT

mateixa funció

Homologia estructural amb RT – HIV1



DOMINI RT

HUMA LRRSPGVGCVPAAEHRLREEILAKFLH **WLMS - VYVVELLRSFFYVTEITTFQKNRLFFYRK**
GOS LHGNPGACCVPAAEHRRREEILARFLV **LVDGHIYVVKLLRSFFYVTETTFQKNRLFFYRK**
RATOLI LRSSPGKDRVPAAEHRLRERILATFLF **WLMD - TYVVQLLSFFYITESTTFQKNRLFFYRK**
RATA LRSSPEKDTVPAAEHRLRERILAMFLF **WLMD - TYVVQLLSFFYITETTFQKNRLFFYRK**
* *

Motiu 2

HUMA SVWSKLQSIGIRQHLLRVQLRELSAEVVRQHREARPALLTSRLRFIFKPDGLFFIVNMDY
 GOS SVWSQLQSIGIRQLFNSVHLRELSAEVVRRHREARPALLTSRLRFLFKPSGLFFIVNMDY
 RATOLI SVWSKLQSIGVRQHLEERVQLRELSQEEVVRHHQDTWLAMPICRLRFIFKPNGLFFIVNMSY
 RATA SVWSKLQSIGIRQQLERVQLRELSQEEVKHHQDTWLAMPICRLRFIFKLNGLFFIVNMSY
 * * * * *

Motiu A

HUMA VVGARTFRREKRAERLTSRVKALFSLVNIYERARRPGLLGASVLGLDDIHRAWRTFVLRVR
GOS IMGARTFHRDKKVQHLSQLKTLFSLVNIYERARRPSLLGASMLGMDDIHRAWRTFVLRIR
RATOLI SMGTRALGRRKQAQHFTQRLKTLFSLVNIYERTKHPHLMGSSVLGMNDIYRTWRAFLVLRVR
RATA GMDTRAFGKKKTQCFTQSLKTLFSLVNIYERTKHPNLMGASVLGTSDSYRIWRTFVLRVR
* *

Motiu B'

HUMA A Q D P P E L Y F V K V D I T G A Y D I P Q D R L T E V I A S I I K P Q - N T Y C V R R Y A V V Q K A A H G H V R K
GOS A Q N P A P Q L Y F V K V D I T G A Y D A L P Q D R L V E V I A N V I R P Q E S T Y C V R H Y A V V Q R T A R G H V R K
RATOLI ALDQTPRM Y FVKA D I T G A Y D A I P Q G K L V E V A N M I R H S E S T Y C I R Q Y A V V R R D S Q G Q V H K
RATA ALDQTPRM Y FVKA D I T G A Y D A I P Q D K L V E I V A N I I R R S E S M Y C I R Q Y A V V Q K D S Q G Q V H K

* * * * *

HUMA AFKSHVSTLTDLQPYMRQFVAHLQET - - SPLRDAVVIEQSSSLNEASSGLFDVFLRFMCH
GOS AFKRHVSTFADLQPYMRQFVERLQET - - SLLRDAVVIEQSSSLNEAGSSLFHLFLRLVHN
RATOLI SFRRQVTTLSDLQPYMGQFLKHLQSDASALRNSVVIEQSISMNESSSLFDFFLHFLRLH
RATA SFRRQVSTLSDLQPYMGQFTKHLQSDASALRNSVVIEQSISMNETGSSLLHFFLRFVRH
* *

Motiu C

HUMA HAVRIRGKSYVQCQGIPQGSILSTLLCSLCYGD MENKLFAGIRRDGLLLRLVDFLLVTP
GOS HVVRIGGKSYIQCGVPQGSILSTLLCSLCYGD MERRLFPGIEQDGVLLRLVDFLLVTP
RATOLI SVVKIGDRCYTQCQGIPQGSILSTLLCSLCFGD MENKLF AEVQRDGLLLRFVDFLLVTP
RATA SVVKIGDRFYVQCQGIPQGSILSTLLCSLCFGD MENKLF AEVQQDGLLLRFVDFLLVTP

* * * * *

Motiu D

HUMA **H**LT-**H**AK**T**FL**R**TL**V**RG**V**PE**Y**G**V**C**V**N**L**R**K**T**V**VNFPVEDEALGGTAFVQMPA**H**GL**F**P**W**CGLLL
GOS **H**LT-**Q**AQ**A**FL**R**TL**V**KG**V**PE**Y**G**C**RAN**L**Q**K**T**A**VNFPVEDGALGSAAPLQLPA**H**GL**F**P**W**CGLLL
RATOL1 **H**LD-**Q**AK**T**FL**S**TL**V**HG**V**PE**Y**G**C**MIN**L**Q**K**T**V**VNFPVEPTLGGAAPYQLPA**H**CL**F**P**W**CGLLL
RATA **H**LA-**H**AK**A**FL**S**TL**V**HG**V**PE**Y**G**C**MIN**L**Q**K**T**V**VNFPVETGALGGAAPHQLPA**H**CL**F**P**W**CGLLL
* * * * *

>Reverse transcriptase HIV-1
subunitat p66

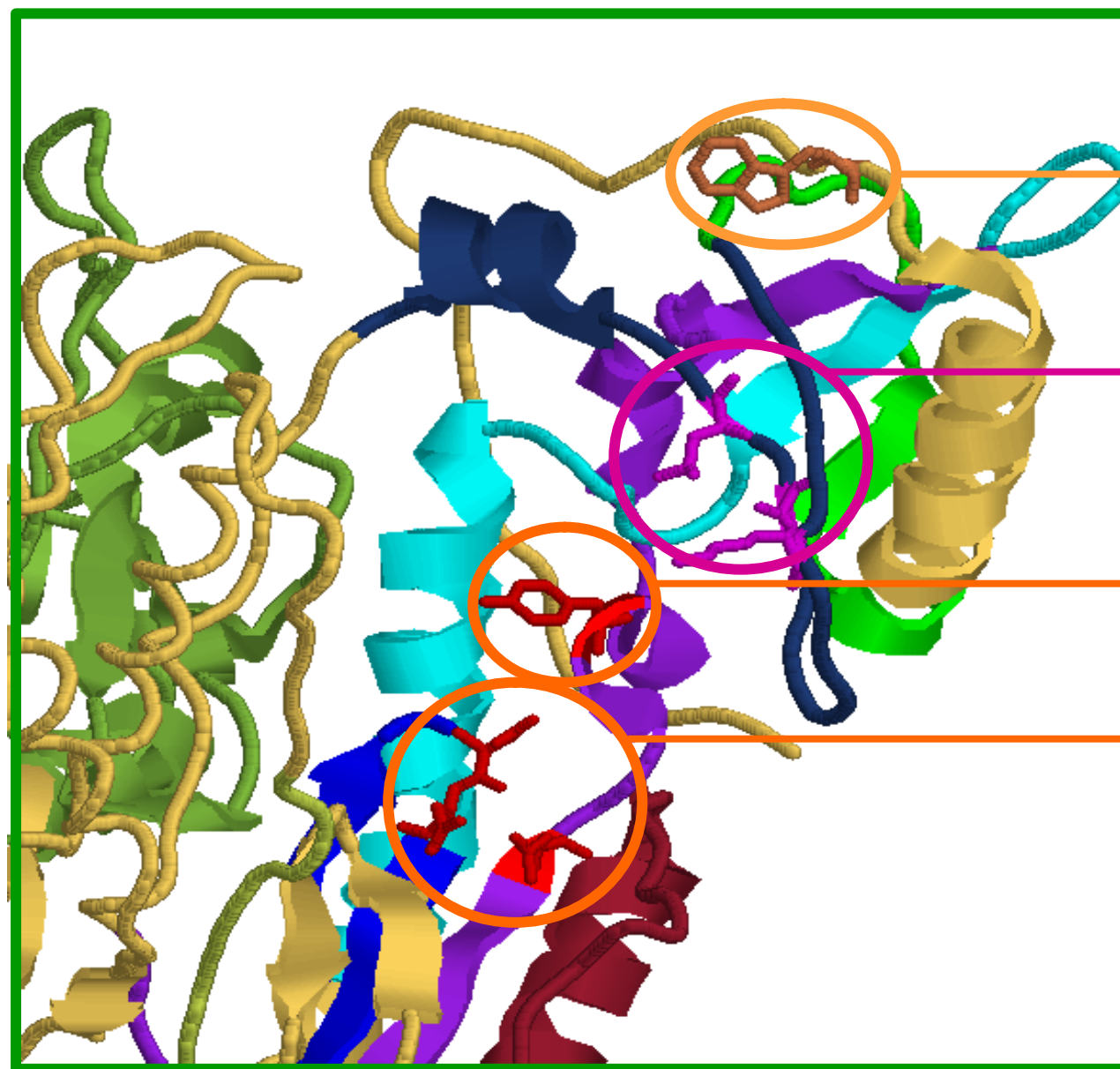
PISPIETVPVKLKPGMDGPKVKQWPLTEEEKIKALVEICTEMEGE
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QLGIPHPAGLKKKKSVTVLIDYGDAYSFVPLDEDFRKYAFTIPSI
NNETPGIRYQYNVLPQGQWKGSPAIFQSSMTKILEPFRKQNPDIVI
YQYNDIYVGSdleIGQHRTKIEELRQHLLRWGLTTPDKKHQKEP
PFLWMGYELHPDKWTVQPIVLPEKDSWTVNDIQKLVGKLNWASQI
YPGIKVRQLCKLLRGTKALTEVIPLTEEALELAENREILKEPVH
GVYYDPSKDLIAEIQKQGQGWTYQIYQEPFKNLKTGKYARMRG
HTNDVKQLTEAVQKITTESIVIWGKTPKFKLPIQKETWETWTEY
WQATWIPEWEFVNTPLVLKWYQLEKEPIVGAETFYVDGAANRET
KLGKAGYVTNRGRQKVVTLTDTTNQKTELQAIYLALQDSGLEVNI
VTDSQYALGIIQAQPDQSESELVNQIIIEQLIKKEKVYLAWPAAK
GIGGNEOVDKLVSAGIRKVL

Residus conservats de:

- Finger domain

- Palm domain

- Thumb domain



HIV

TERT

Trp24

Trp24

Lys65

Lys443

Arg72

Arg450

Leu74

Ile452

Tyr115

Tyr717

Asp110

Asp740

Asp185

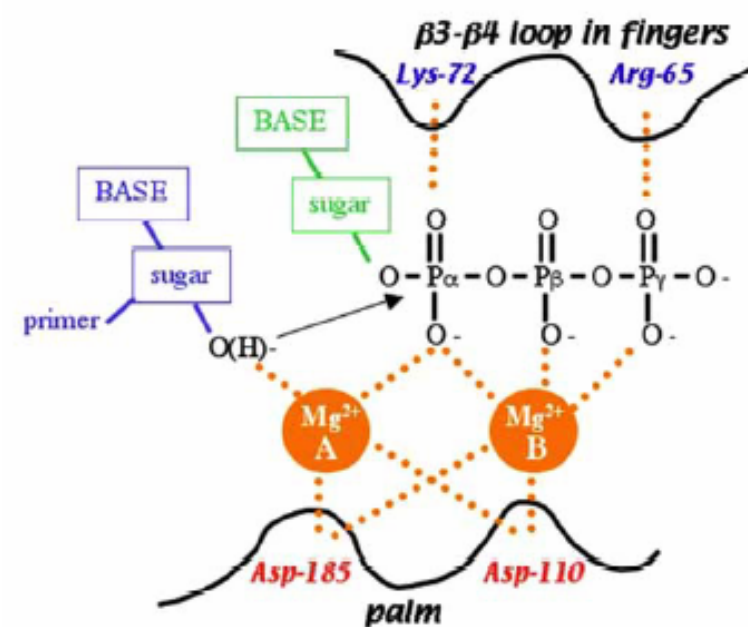
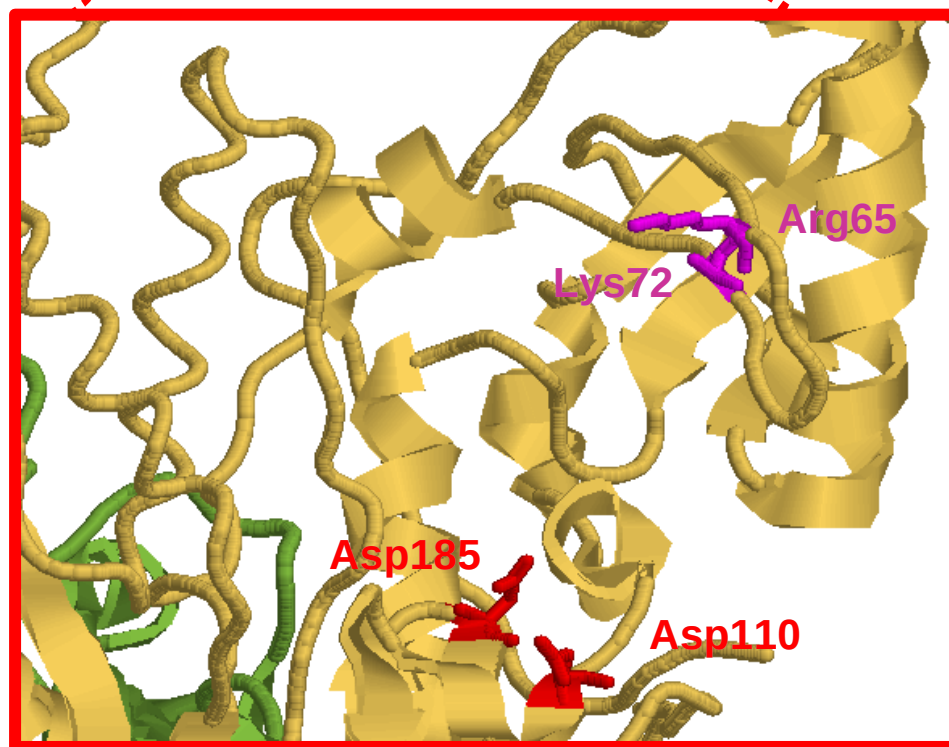
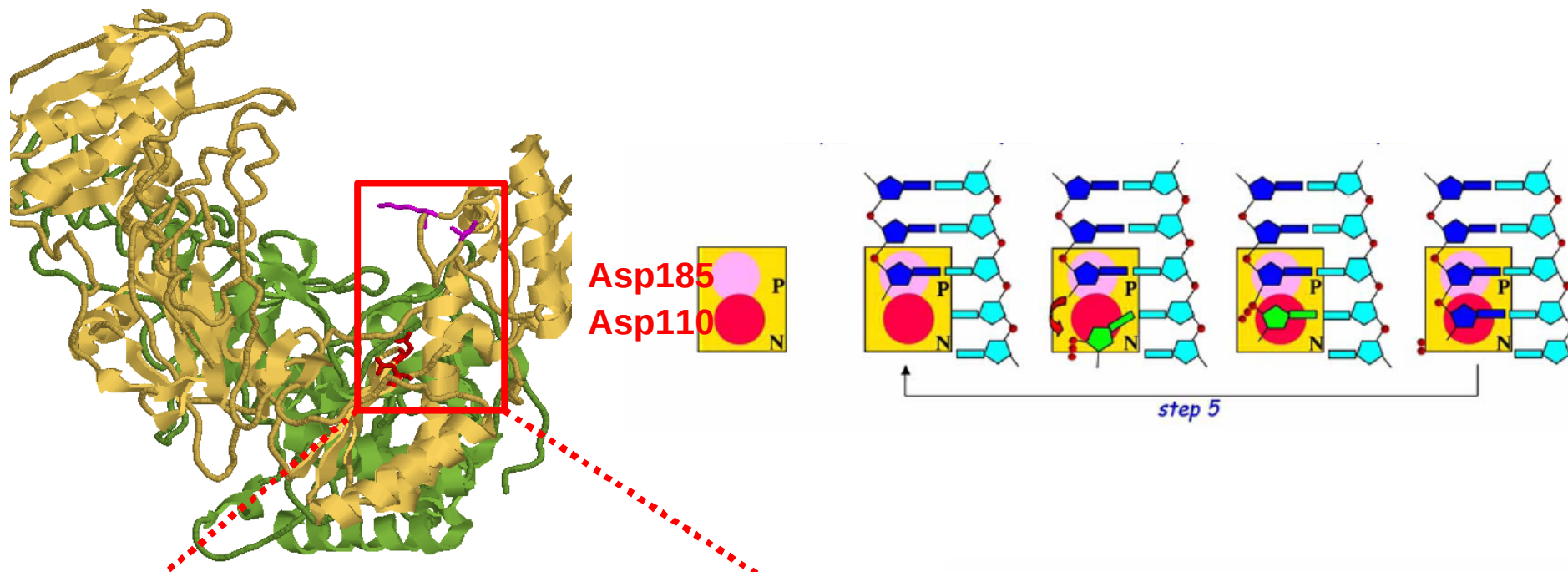
Asp856

Asp186

Asp857



Triada catalítica



Domini N i C terminal



- Dominis CP, QFP i T → reconeixement RNA-telomerasa
- Domini T → estabilitza el template
- Domini N-terminal i GQ → interacció amb DNA → *ANCHOR SITE* ¿?

C-terminal

- multimerització funcional amb altres molècules hTERT
- reclutament de telòmers per enzims
- localització nuclear
- possible implicació en el domini thumb

Informació disponible sobre la Telomerasa

- ✓ Pocs pdb's i cap per cristallografia
- ✓ Programes de modelatge no optimitzats per RNA (no STAMP)
- ✓ Seqüències molt divergents

PDB	Descripció	Any	Resolució
1OQ0	P6.1 stem loop	2003	---
1Z31	PJ6 Hairpin	2005	---
1LC6	U6 stem loop	2002	---
1QFQ	Bac BoxB	1999	---
1YMO	Pseudoknot	2005	---
1HVU	HIV-I RT	1998	4,75
1J50	HIV complexed	2002	2,8



RNA

Estructures de l'RNA

- ✓ Primària: cadena simple
- ✓ Secundària: interaccions intramoleculars
- ✓ Terciària: estructura global i local en 3D
- ✓ Quaternària: interacció entre varis RNA amb estructura terciària

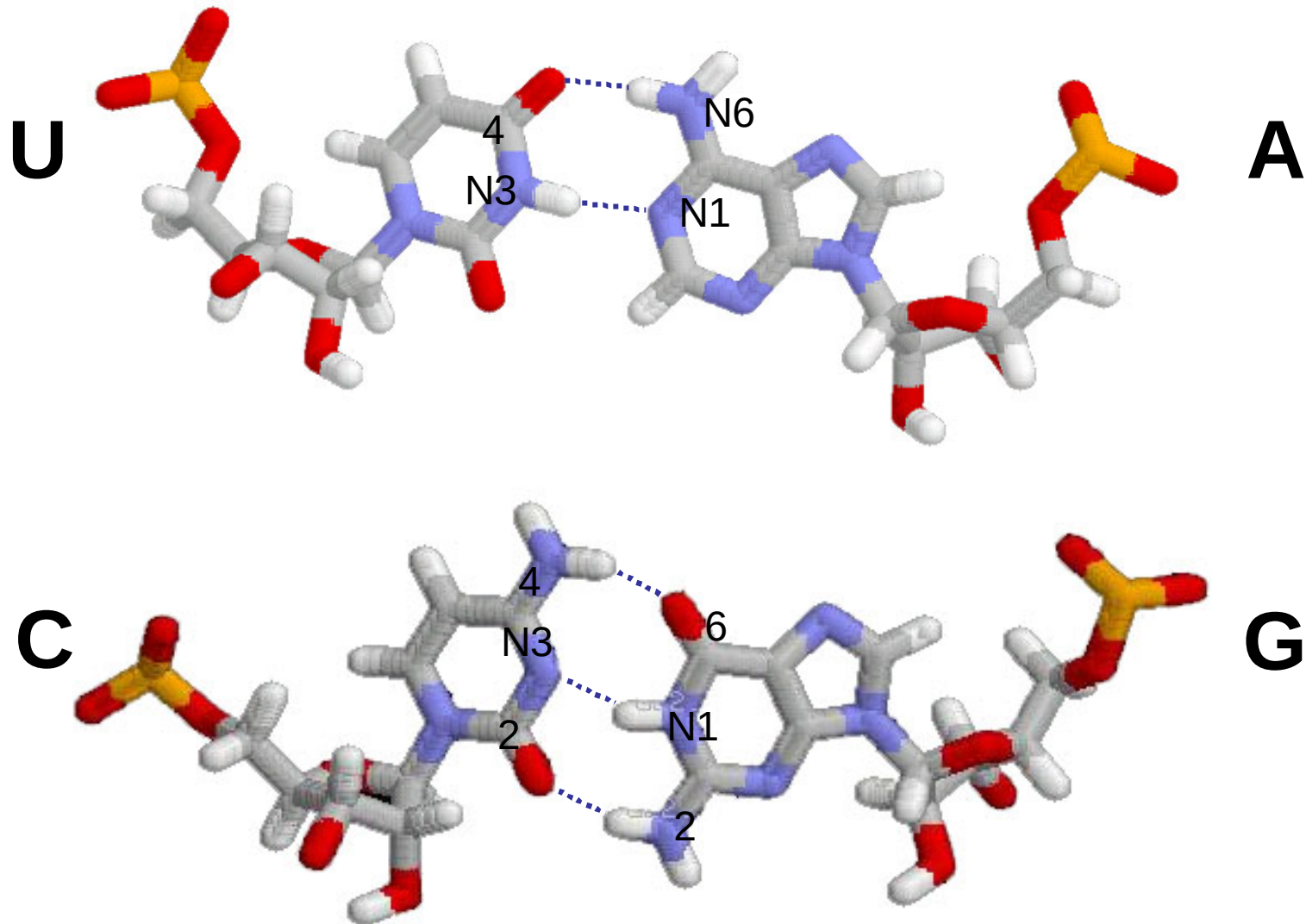
Per què es plega l'RNA?

Entropia desfavorable: en equilibri domina la doble hèlix

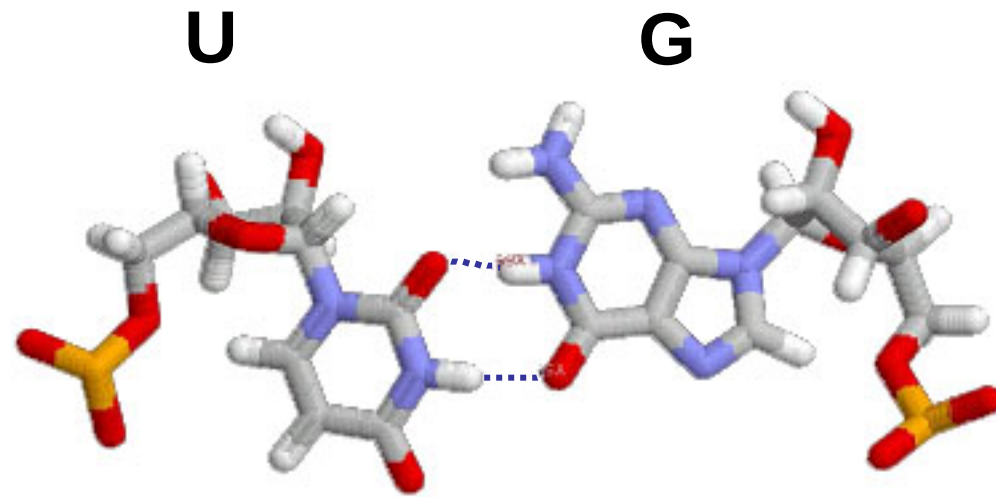
Forces que estableixen el plegament:

- ✓ interaccions Watson i Crick
- ✓ interaccions no-Watson i Crick
- ✓ interaccions de van der Waals
- ✓ unió a cations divalents

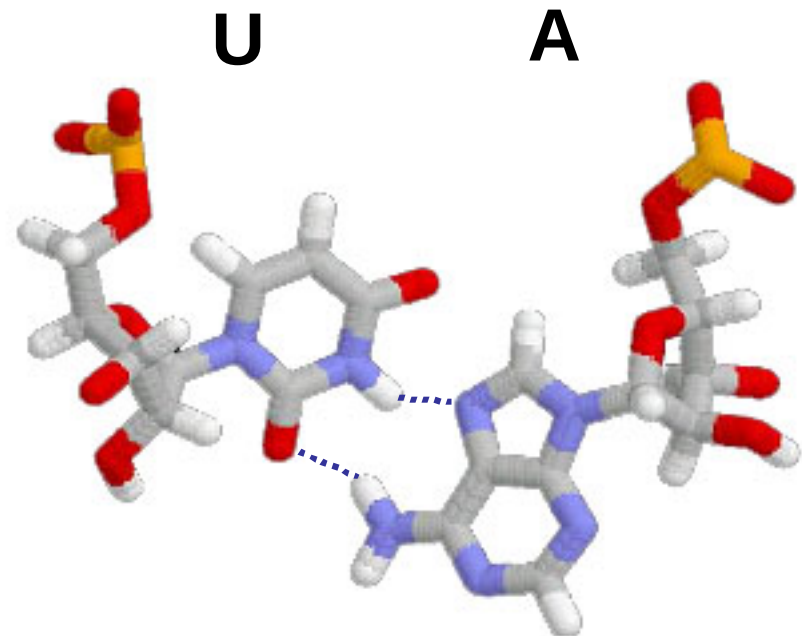
Parells de bases Watson i Crick



Parells de bases no-Watson i Crick

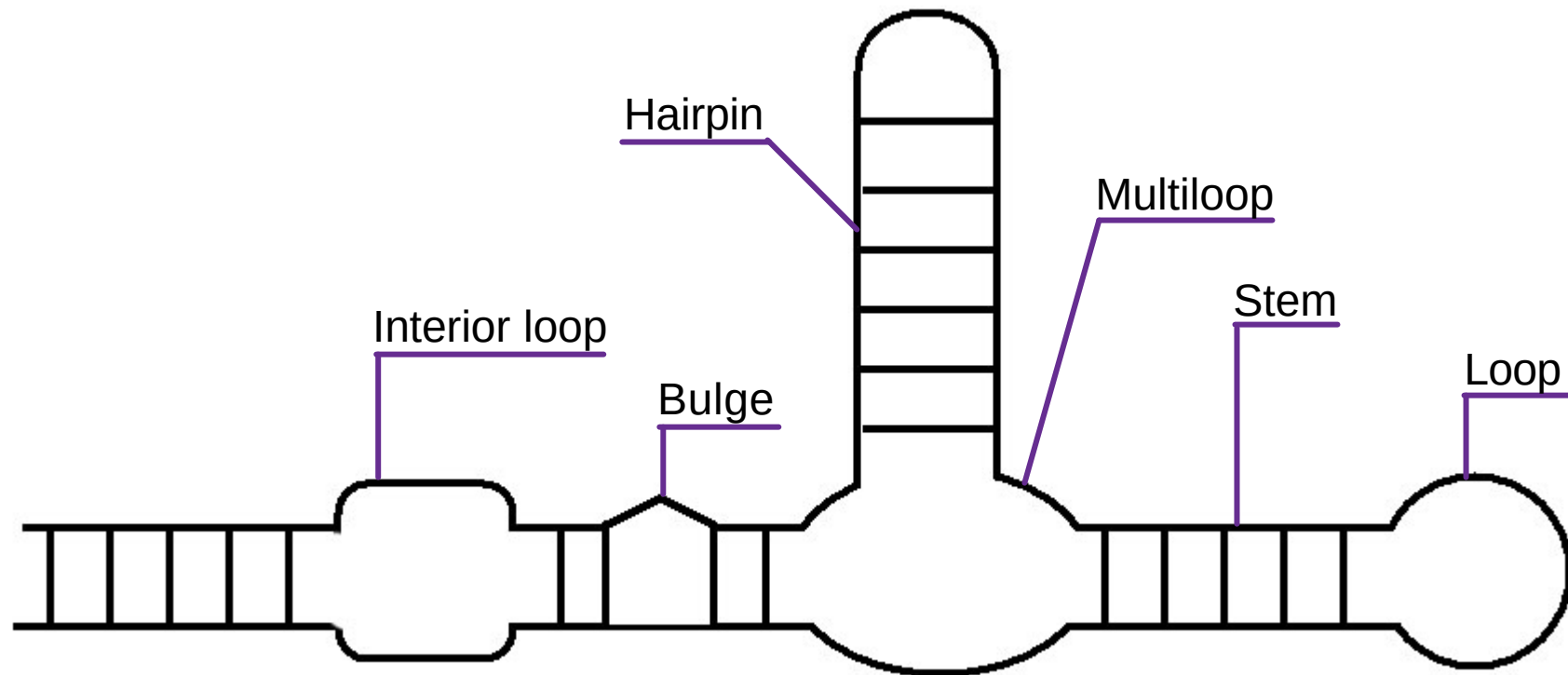


GU Wobble



Hoogsteen

Estructura Secundària



Telomerasa RNA

Alineament inicial (1-451)

CR1 CR2

```
Hom -----GGGTTGCGGAGGGTGGGC-CTGGGAGGGGTGGTGCCATTTTTG-TCTAACCTAAC-TGAGAA GG----GCGTAGGCGCCGTGCTTTTGCT-CCCCG-----CGCGCTGT
Ory TAAGACGACTCC---GGCCGGC---GCGCGCGGGCTGAGGAGGGTGGGC-TCGGGAGGGGCC-CGGTCATTTCTCA-TCTAACCTAAC-TGAGCA GG----GCGTAGGCGCCGCGCTTTTGTT-CCCCG-----CGCGCTGT
Bos TAAGGAGACGC---ACCCAGCG--GCGCGGCGGGTTGCGGAGGGTGGGC-CCCGGGTTGGTGCGAGCATTTCTCA-TCTAACCTAAC-TGAGAC AG----GCGTAGGCGCTGTGCTTTTGTT-TACCG-----CGCGCTGT
Sus TAGGGAGACGC---ATCCGCT--GATCGGCGGGTTGCGGAGGGTGGGC-CCAGGAGCGGTGGCGCCATTTTTAACTCTAACCTAAC-TGAAAG AG----GCGTAGGCGCTGCGCTTTTGCT-TCACG-----CGCGCTGT
Mus TAGGGAGACGC---GGCCGGGT--GCAGTTCGGGTGCGGAGGGTGGGC-TCGGGAGGGGTGGCGGTCATTTCTG-TCTAACCTAAC-TGAAAC GG----GCGTAGGCGCTGCGCTTTTGTT-CCCCG-----CACGCTGT
Pro TAGGGAGACGC---GGCGGGCT--GTAGCTCGGGTTGCGGAGGGTGGGC-CTGGGAGGGGTGGCGGTCGTTTATG-TCTAACCTAAC-TGAGAA GG----GCATAGGCGCTGCGCTTTTGTT-CCCCG-----CACGCTGT
Fel TAGGGAGCCGC---GGCGTTTT--GCACCTCGGGTTGTGGAGGGTGGGC-CTGGGAGGGGAAGCGGTGAGTTTTG-TCTAACCTAAC-TGAGAA GG----GCGTAGGCGCCGCGCTTTTGTT-TCCCG-----CACGCTGT
Equ TAAGGAGGTGC---GGCAGGC--ACGCGGCGGGTGGGGAGAGTGGGT-CTGGCGGGCGCGCGGTACGTTTTG-TCTAACCTAAC-TGAGCT GG----GCGGAGGCGCCGCGCTTTTGCT-CCCCG-----CGCGCTGT
Tri TAAGGAGACTTGGCGCGAGGCTTGGCGTGGAGGGTGAAGGATGGCGCC-CCGGGTGCGGCGAGTGGTCTTTTTGT-TCTAACCTAAC-TGGCAA GG----GCGTAGGCTGTGCTTTTGTT-CCCCG-----CGCGTTGT
Ele TAAAGAGGTGCGGCG-GCGCGGCT-GGTGCGGTGGGTGAGGAGGGTACGC-CCGGGA-GGGCGGTGGTCTGTTCTGT-TCTAACCTAAC-TGATAA GG----GCGTAGGCGCCGTGCTTTTGTT-CCCCG-----CGCGTTGT
Das TAAGGAGGCTGCGCGCGCCACG-----GGCGGTTGCGGAGGGAGGGC-CCGGGAGGGGTGAGCGTCCATTATCG-TCTAACCTAAC-TGAGAT GG----GCGTAGGCGCCGCGCTTTTGCT-TCCCG-----CGCGCTGT
Cav TAAGGAGCCTC-----TGCGAGCCGCTGGG-CCGGAGGGGGTGGTGGTC-TTCCCTG-TCTAACCTAAC-TGAAGAGG---ACGTGGGTGCGGTGTTTTTCGC--TCCCG-----CACGCTGT
Mic -AGGGCGTCCC-----GACGGGC---GGACGGGCGACGCGCGCTCTTC---TAACCTAAACTGTGG- AG----CTGTAGGTGTTGCTCTTTCAGC-GTC-G-----CCCGCTGT
Mus -AGGTCGA-----GGGC---GGCTAGGCCTCG-GCACCT-----AACCTGATTTCATT AG----CTGTGGGTCTGGTCTTTTGTT-CTCCG-----CCCGCTGT
Che GTGGAAGGTATATAAGACCCGCG-----CCAGGCGGGTCTGACCGCT---GCGGCGGAGGTGGGGGCTCAGTCT-TCTAACCTAACGCGA--A AT----GTGACCCCTCCCGCTGC-----AGCCG-----TCGCGTGT
Gal GAGGAGGCTACAAGACCCACG-----CGGGTTCCCGCGCACGC---GTGGCGGGTG-AAAGCTCCGCTGTCTCTAACCTAAC--GGGGA ATTGATGGTGTGTCGCCGCGCTCCCTCC--GCCG-----CCCGCTGT
Xen CTCTGACGTCAATGTAGTATATAAGCAGTTGCCAAGGTGATTAGCCTCAC-TCAATGTGAGCGGAGGTCTCTGTTTCG--CTAACCTAATA-CACTG6CT-----TCAGGCGATGGCTCTTCGCGG-CGGTG-----CTGTTGT
Rhi GCAGCTACTTTTTAGCCAGCGTCGGAAAGTCTTGAATCAGCGTTAAAG CATTGCTGCGGGGTGGAGGCGTTTTTAA--CTAACCTAATGCAGAGTAAGTGGCTGGGCTTCTCTCACACTGCTCCCGTGCGTGAAACCTCGCTGT
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CR2 CR3

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TTTTCTCGCTGACTTTACGCG-----CGTGGGAAAAGCCTT-----GGCCTA-CCGCCGTCACCGTTCATT-----TCGAGTAAGC-AAA-AA-TGTC--AGC-GCTGGCCGTTTCGCCCTCCCG-----
TTTTCTCGCTGACTTTACGCG-----GGCGG-AAAAGCCTC-----GGCCTA-CCGCCATCCACCATCCAGT-----CTGCAACAAAC-AAA-AA-TGTC--AGC-GCTGGCTCGCTCACCCTCCCG-----
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TTTTCTCGCTGACTTTACGCG-----GGCGG-AAAAGCCTC-----GGCCTA-CTGCCATCCACCATCCAGT-----TTGGAGCAAAAC-AAA-AA-TGTC--AGC-GCCGCGCTGCTCGCCCTCCCG-----
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TTTTCTCGCTGACTTTACGCG-----GGCGGGAAGAGCCCT-----GGCCTA-CCGCCGCTACCGATA-GT-----TTGGAGCAAAAC-AAA-AAATGTC--AGC-GCTGG-CCGCTACCCCTCCCG-----
TTTTCTCGCTGACTTTACGCG-----GGCGGGAAGAGCCTC-----GGTCTA-CCGCCGCTACCGATA-GC-----CTGGAGCAAAAC-AAA-AAATGTC--AGC-GCCG-CCGCTCGCCCTCCCG-----
TTTTCTCGCTGACTTTACGCG-----GGCGG-AAAAGCCTC-----GGCCTA-CTGCCGTCTACTGTCTAT-----CTGGAGCAAAAC-AAA-AA-TGTC--AGC-GCTGGTCCGCTCGCCCATCCG-----
TTTTCTCGCTGACTTTACGCG-----TGCAAG-AAAAGCCTT-----GGCCTA-CCGTCGGTTATTGTCTAAT-----TAGAAGCAAAAC-AAA-AA-TGTC--AGC--TGCCGGGCCGCCCTCCCG-----
TTTTCTCGCTGGCTTTACGCG-----GGCCAG-AAAGTTCA-----GACCTCTCAGCAGATCGTCGCGTCGT-----TCTCAACCACA-AAA--ATGCC--AGC-GCAAAG-----CGCGTACGCTAG-----
TTTTCTCGCTGACTTTACGCG-----GGCCAGGAAGTCCA-----GACCTG-CAGCGGGCCACCGCGGCTT-----CCCAGGCTCA-AAAACAAAGTC--AGC-GCAGGAGCTCCAAGTTTCGCCGG-----
TTTACTCGCTGACTTTACGCG-----GACGGGGGAGCGG-----GTGGAGACGCCAACAAAAACGTACG-----GAGGGGCCCTCCCTCCACGSC--GAC-TGGG-----CTGTGGTG-----
TTTACTCGCTGACTTTACGCG-----GGGAGAGAGAGCCGCCCGGGGGGAGGCGGCGGCGGAGGGGCC-----GGGCGCGCGCGCGGTGGGGGTC--GGGGGGGGGAGAGAAAGGGCCGAAAG-----
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CR5

CR6

CR7

CR8

CGGGGGCCAAGGGCG-----AGGCGCAGGCGGTCT-----GGCGCAGGAAGAG-GAACG--GA--CGAGTCCCCGCGC---CGGCGCAATCCCTGAGCTGTGGGAGGTGCACCCAGGACTGGCTCACACATC

CGGTGG-----GCC-----GAGGCATGGCTGT-----GGCGCAGGGAAGAG-GAACG--GA--CGGTCCCCAGCG---TGGTGCGATCCCTGAGCTGTGGGAGTTGCACCCGGGACTGGCTCAAAACAC

CGG-GG-----GCC-----AAGGCGAAGGCTCT-----AAGCGCAGGAAAG-GAACG--GA--T-GGGGTCCCCGCGC---CGGTGCGATCCCTGAGCTGTGGGAGTTGCACCCGGGACTGGCTCAGACATC

TGGGGG-----CCA-----AGGGCGAAGGCTCT-----GACGCGCAGGAAGAG-GAACG--GA--T-TGG-TCCCCGCGC---CTGTGCGATTCCTAAGCTGTGGGCTGTGCACCTGGGACTGGCTCAGACAC

TGGGGG-----CCA-----AGGGCGAAGGCTCT-----GGCGCAGGGAAGAG-AAA-C--GG-G-CGGGTCCCCTCGCG---CGGTGCGATTCCTGAGCTGTGGGAGTTGCACCCGGGACTGGCTCACACAC

TGGGGGG-----GCCG-----AGGGCGAAGGCTCT-----GGCGCAGGGAAGAG-AAAC--GG-G-CGGGTCCCCTTGCG---CGGTGCGATTCCTGAGCTGTGGGAGTTGCACCCGGGACTGGCTCACACAC

CGGGG-----CCA-----GGGACGAGGCTCT-----GACGCGCAGGGAAGAG-AAAC--GG-G-CAGGTCCCCGCGC---CGGTGCGATTCCTGAGCTGTGGGAGTTGCACCCGGGACTGGCTCACACAT

CGGGAACCAAGGGCG-----AGGCTTAGGCTCTCT-----GGCGCAGGGAAGAG-GAACG--GA--CGGGTCCCCGCGC---CGGTGCGATTCCTGAGCTGTGGGAGGTGCACCCGGGACTGGCTCAAAACAGT

CGGGAACCAAGGGCG-----AGGCTGGGGCCTCCT-----GAACGCGAGGAAGAG-AAATG--GA--CGATTCCCCAGTA---CG-TGTGATTCCTGAGTTGTGGGAGTGTGCTCCGGGACTGAGCTCCGACAGT

CGGGGGCCAAGGGTG-----AGGCTTAGGCCGCG-----GAACGCGAGGGAAGAG-AAACG--GA--CGGTTCCCCGCGTG---CG-TGCGATTCCTGAGTTGTGGGAGTGTGCTCGGGGCTGAGCTCCGACAC

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AGGGGCT--GGGGCC-----AGGCCCGGACAGC-----GGCGCAGGGAAGAG-AAACG--GA--CAGGTCTC--GCG---CGGTGCAATCCCTGAGCTGTGGGAGTGTGACC-GGGAC-GGCTCTACAA

GGGGGCT--GGGGCC-----AGGCCGGGCGAGC-----GTGCGCAGTACAG-TAACG--GA--CTGCTCT--TGTT---CGGTG-GATTCCTGAGCTGTAGGAAGTACACCCAGAGCTGGCTCTACAA

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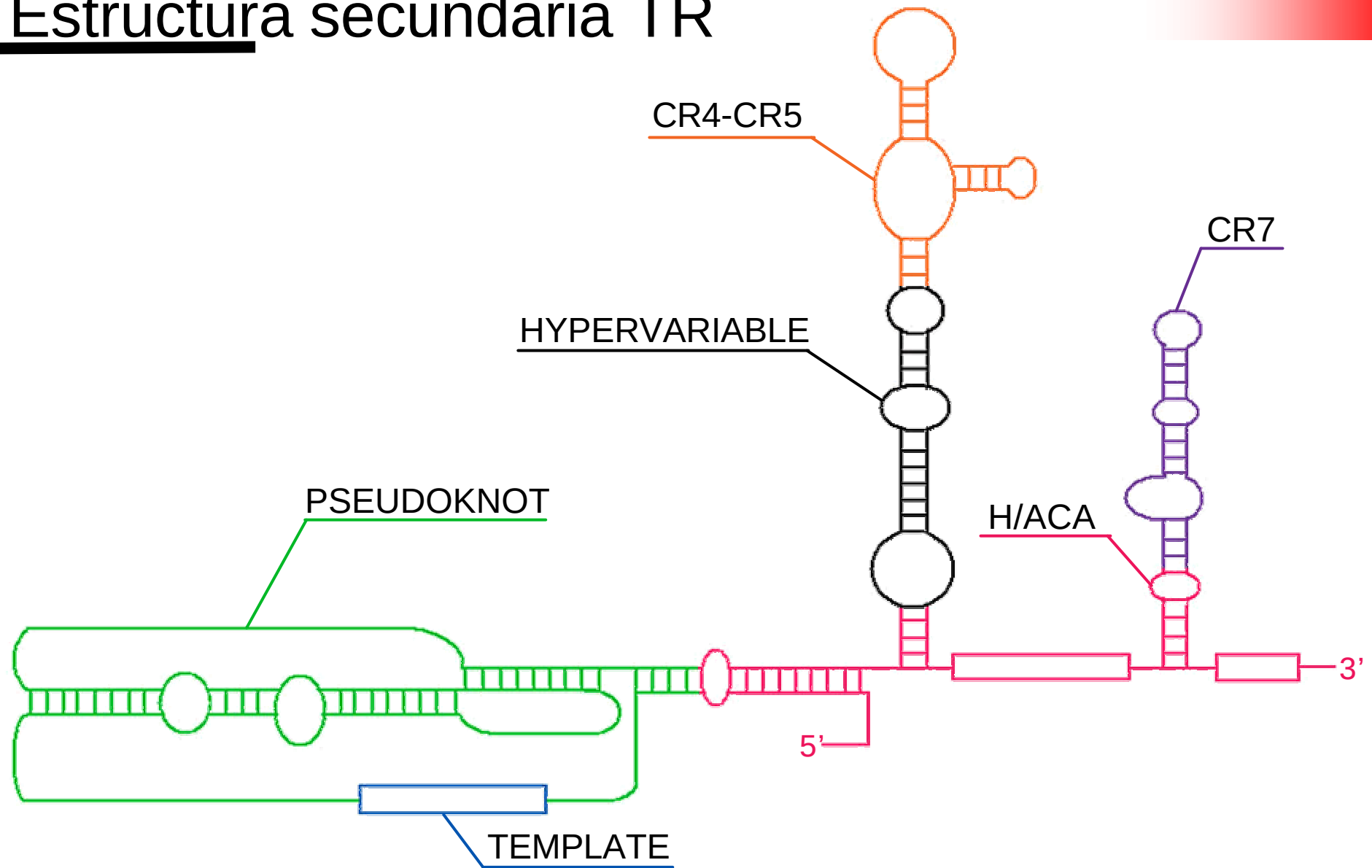
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GGTGGGGGCGGCACAGAGGGACACACCGGGCGGGGCGCCGAGGATAGCTACCGCCCGGAGTATGCAATGCAATATCCGTCACAGATGGCTCGGTG-----GCTGCGCTCCCGGCGCAATGGGAGCCGCAAG-GCTGCCCTGGTCTACAC

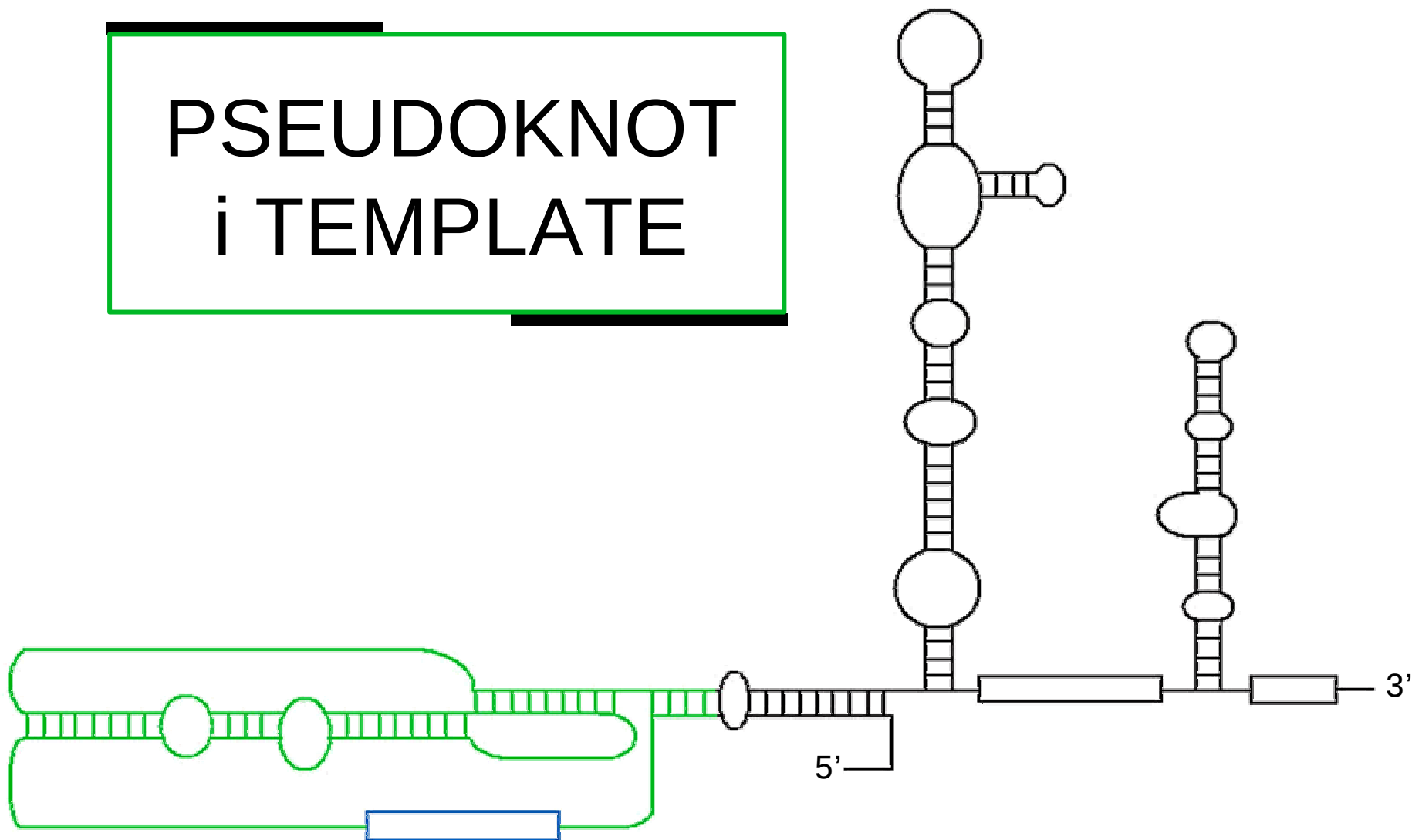
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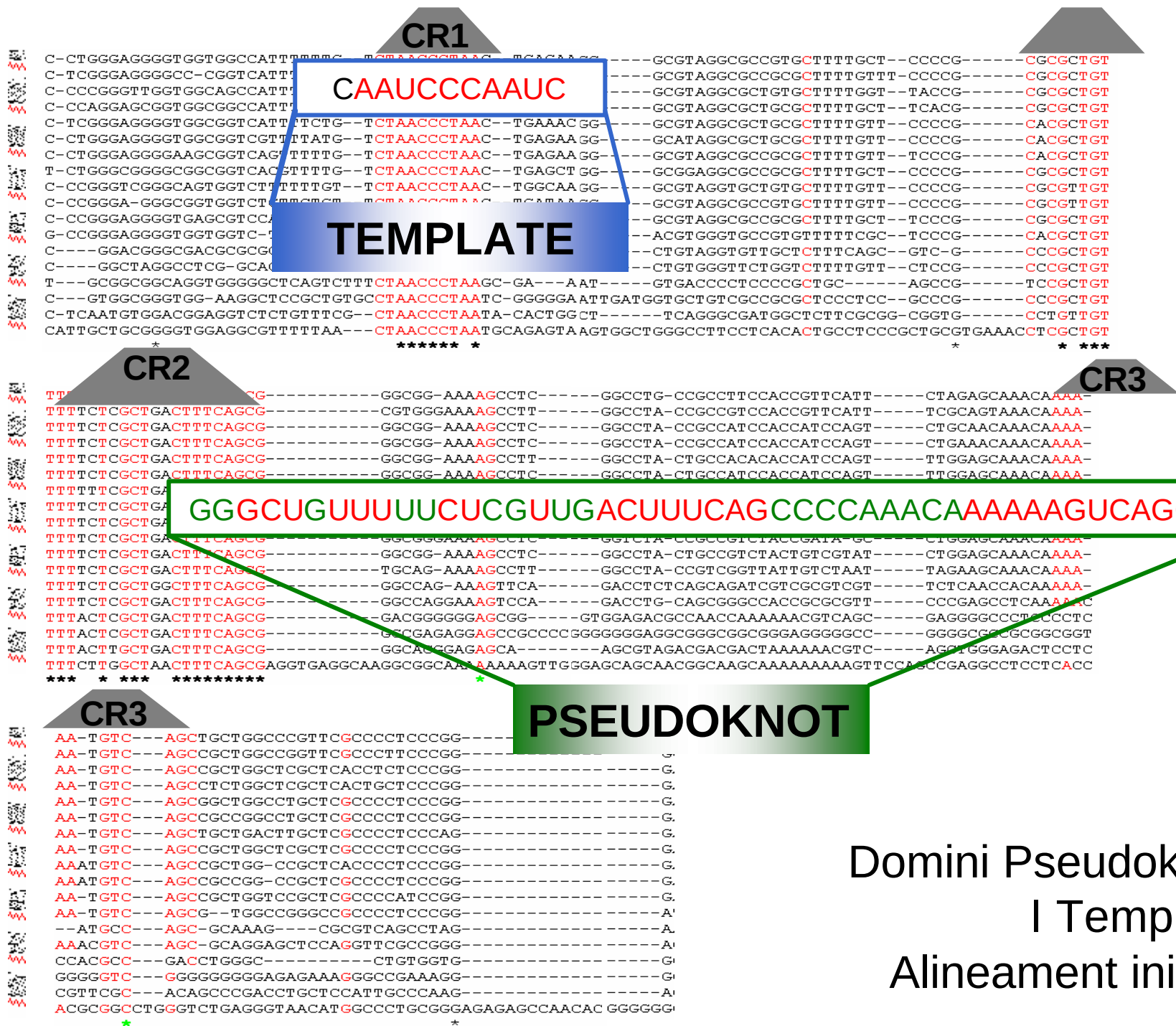
***** * * * *

Estructura secundària TR

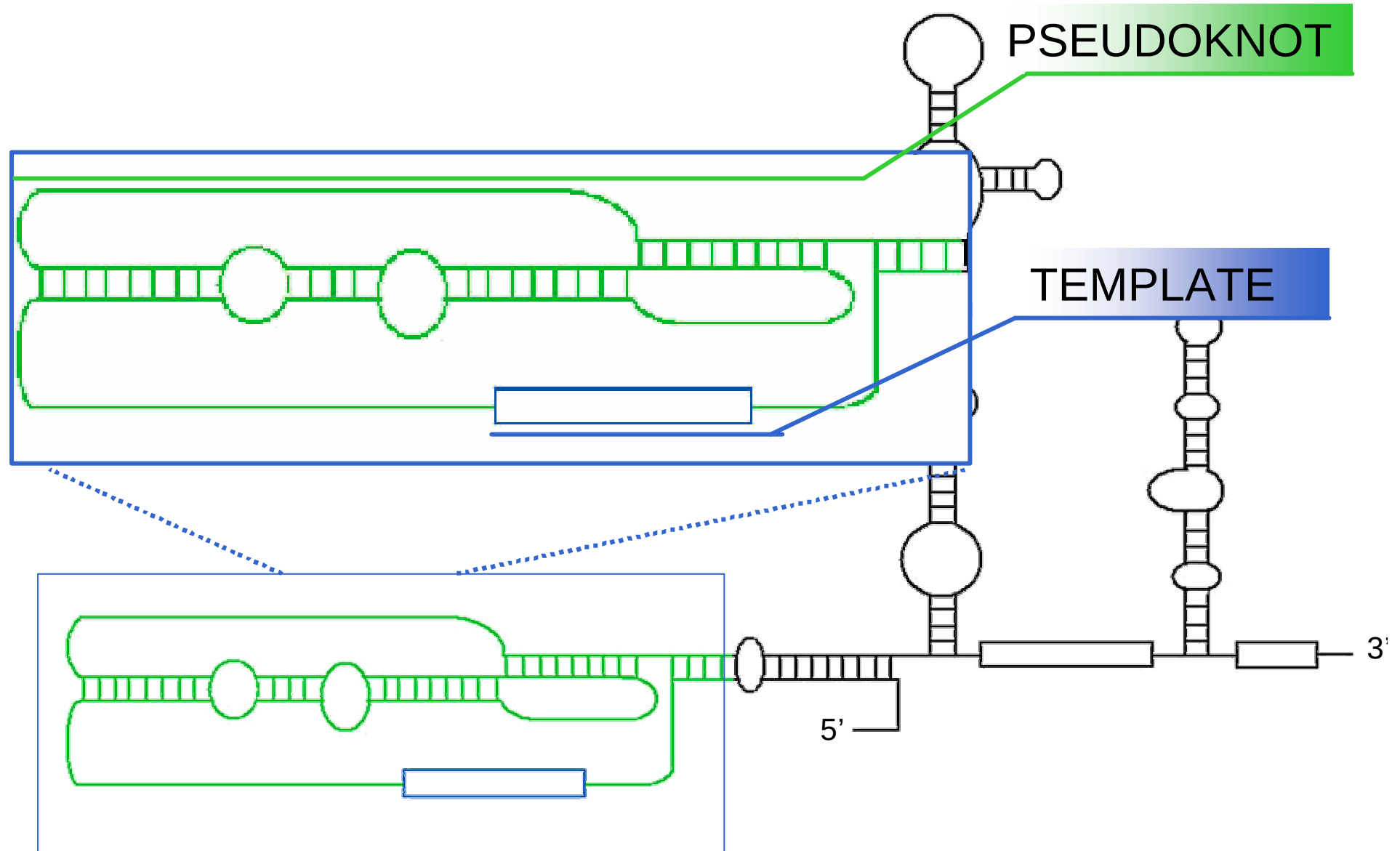


PSEUDOKNOT i TEMPLATE





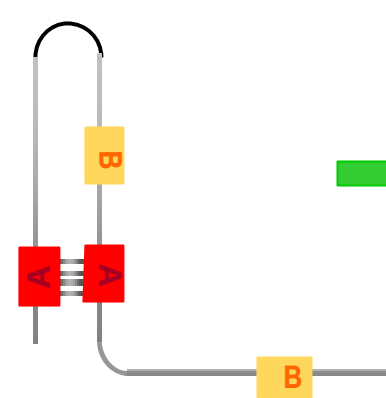
Domini Pseudoknot: domini d'activació



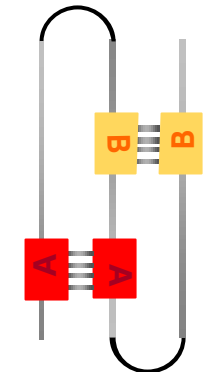
Formació del Pseudoknot



Seqüència lineal



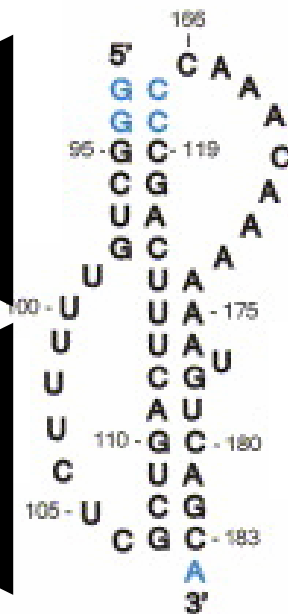
Hairpin



PSEUDOKNOT

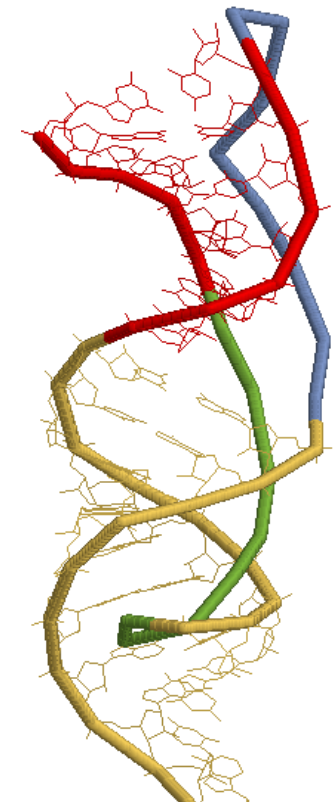
Stem 1:
6pb, ric e C-G

Loop 1:
8nt, ric en U

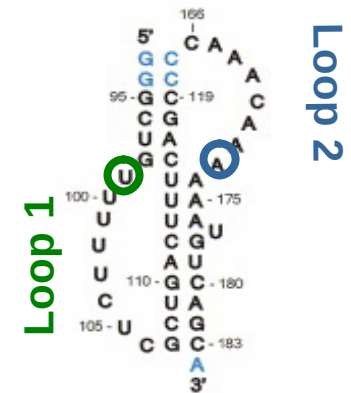
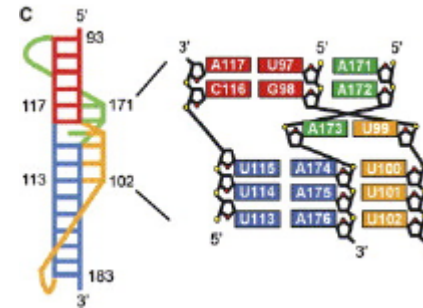
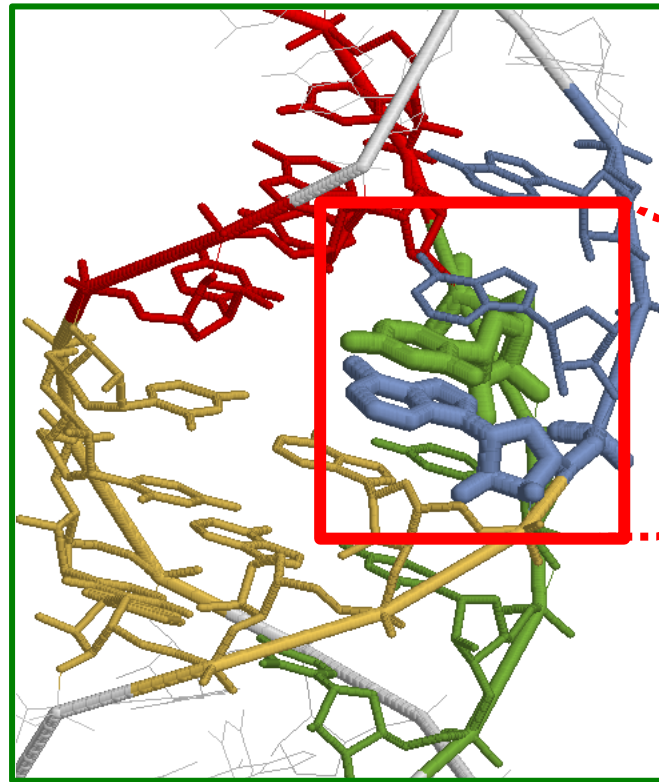


Loop 2:
8nt, ric en A

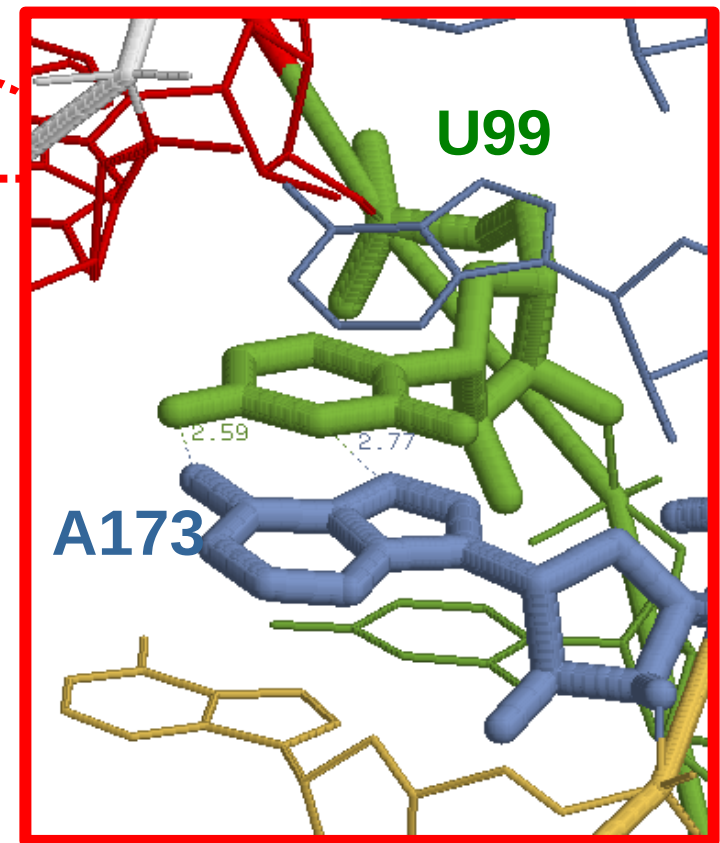
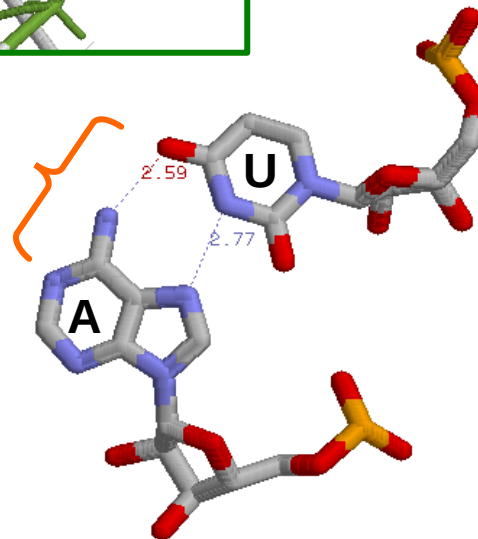
Stem 2:
9pb, ric en A-U



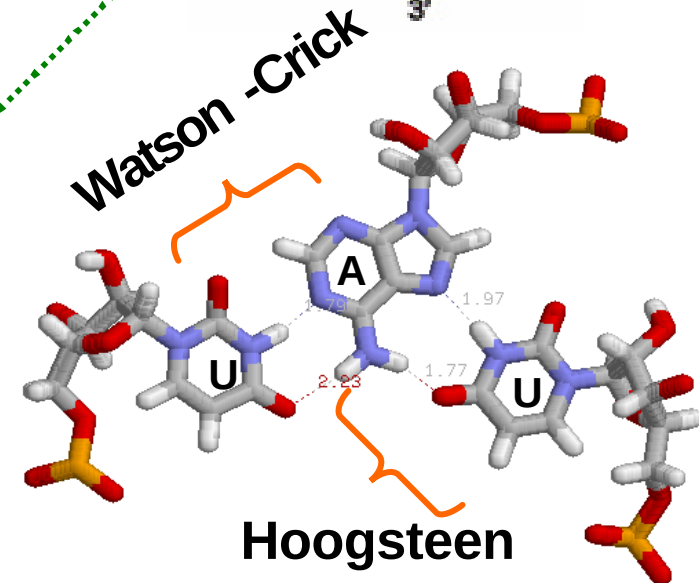
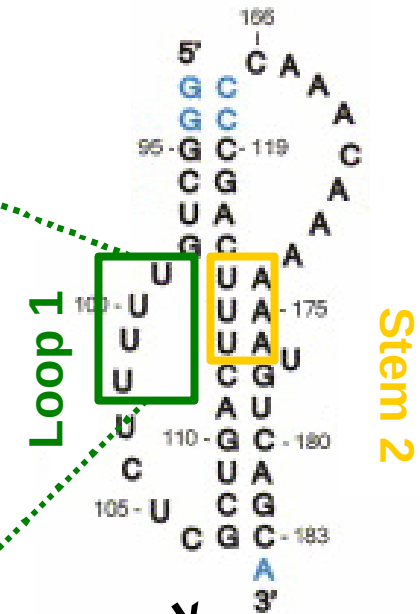
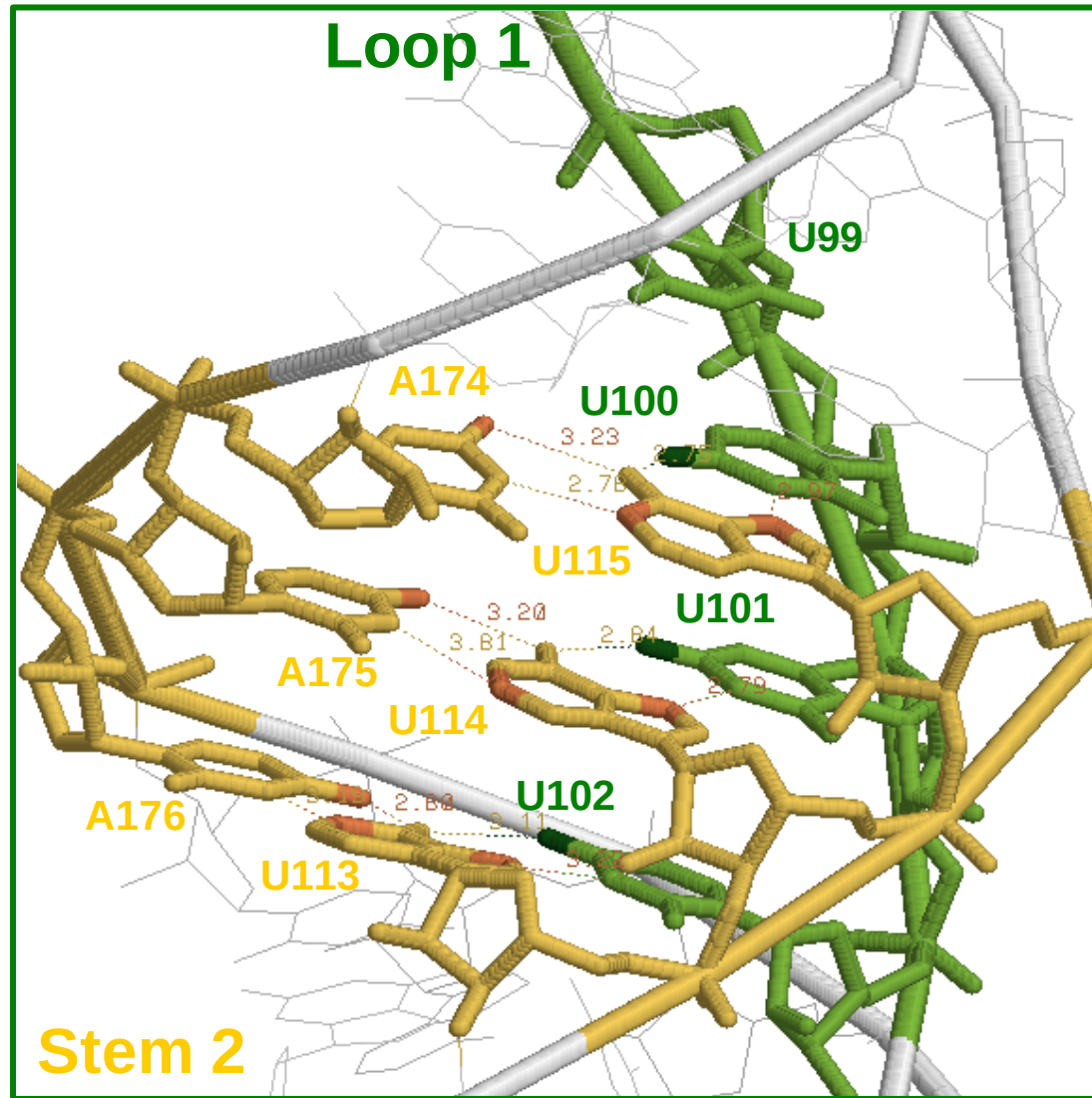
Pseudoknot – Loop1Loop2



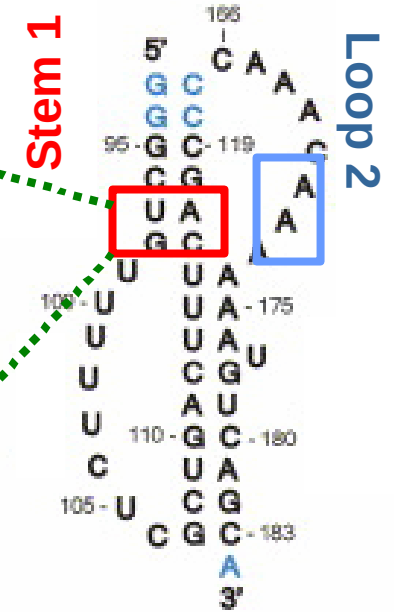
Hoogsteen



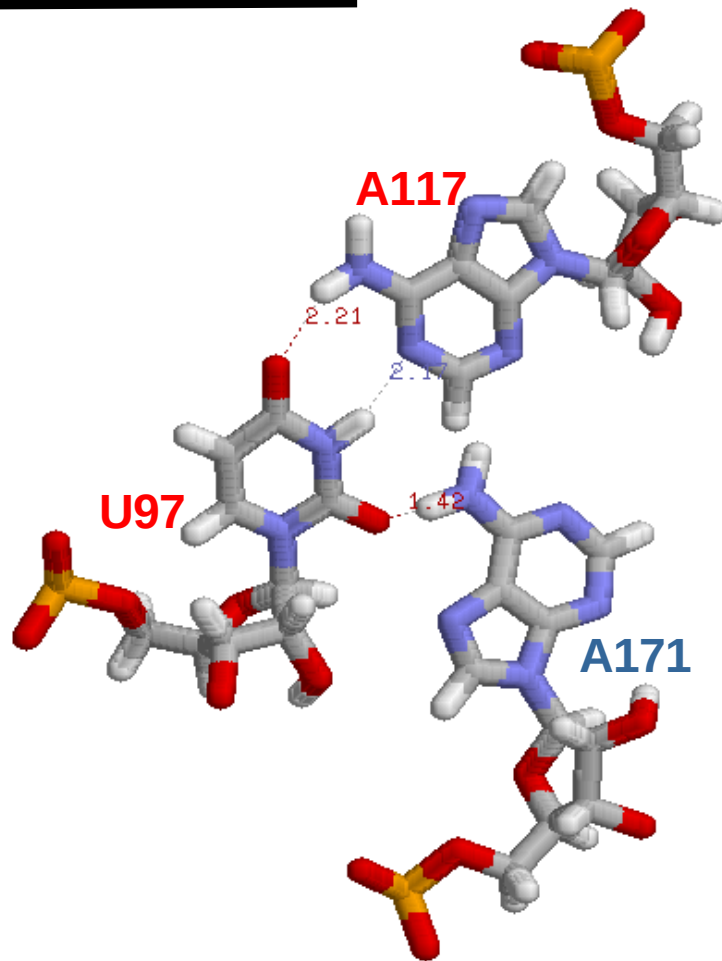
Pseudoknot – Loop1stem2



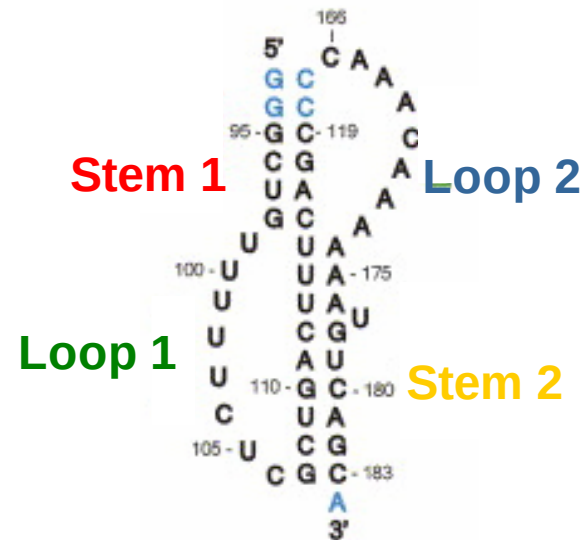
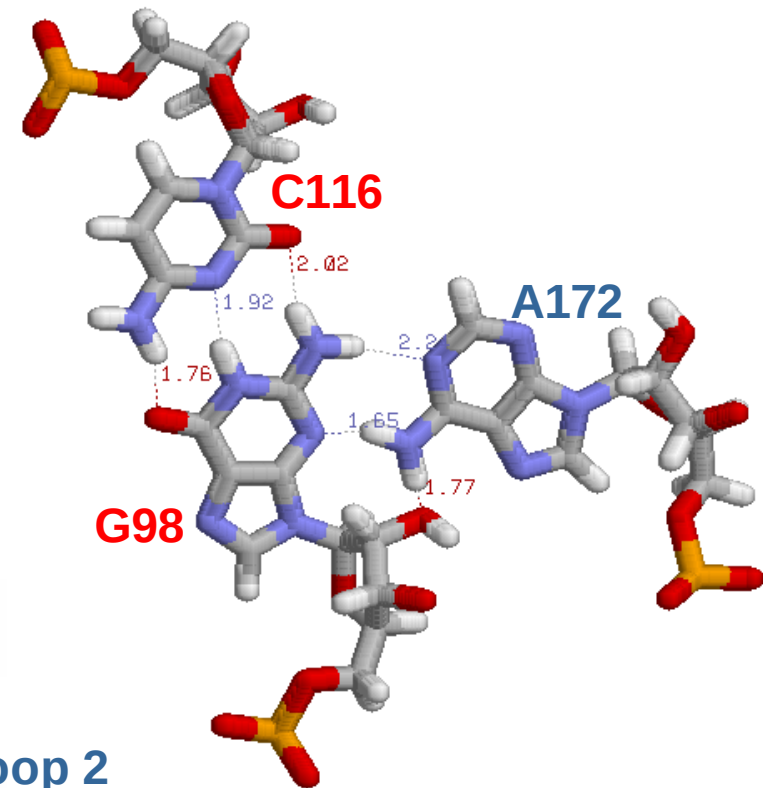
Abstract



Triples bases

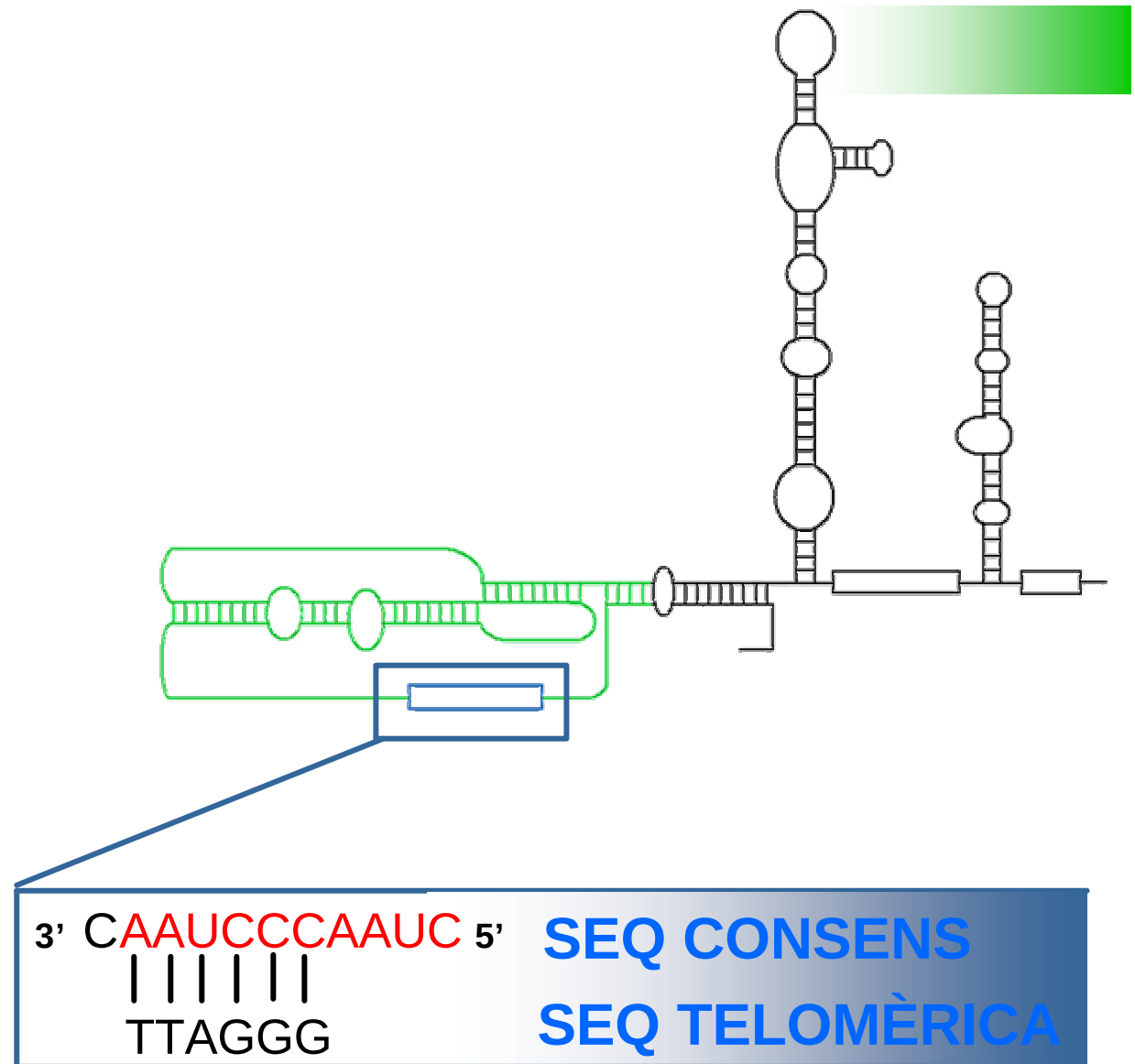


Triples bases

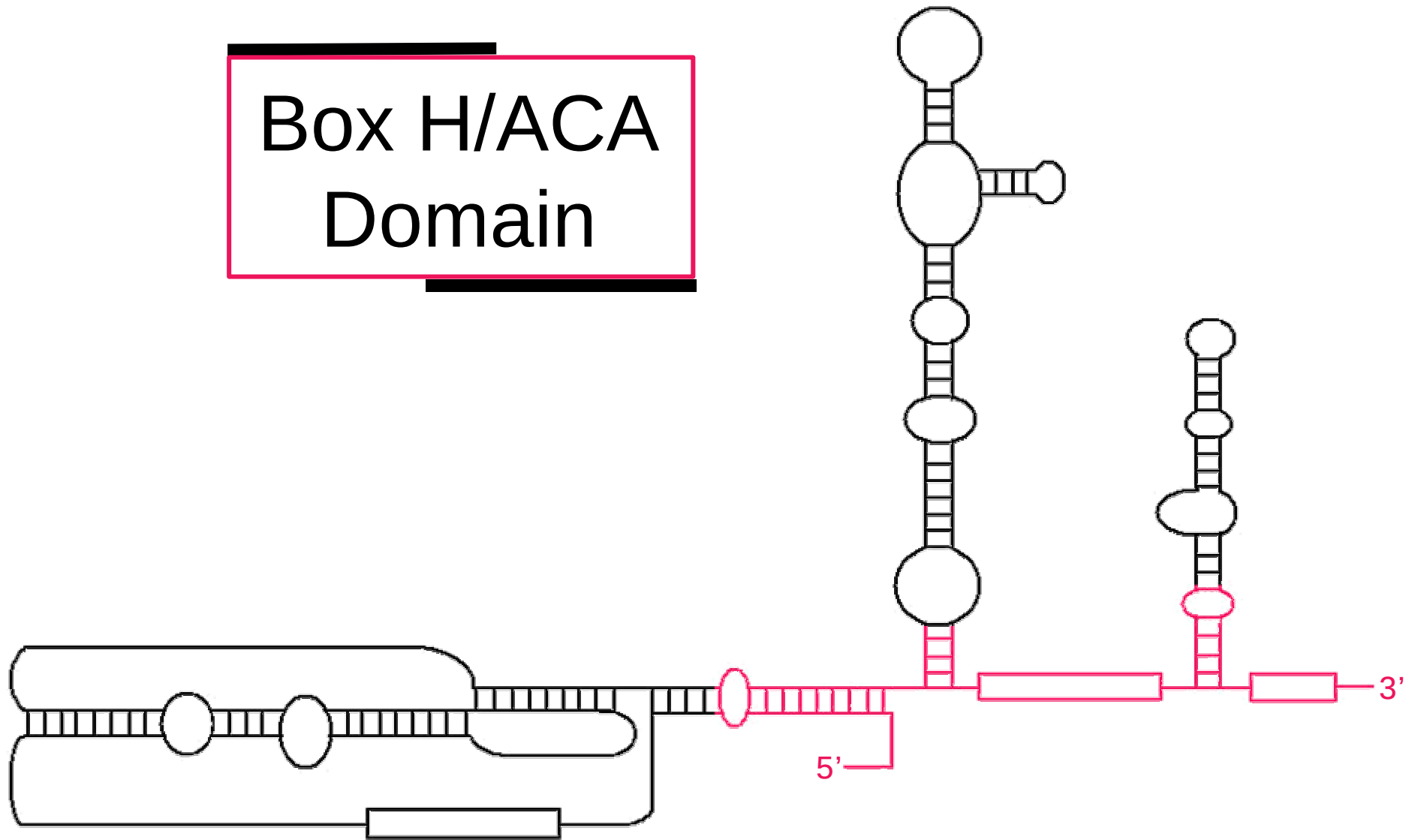


Template

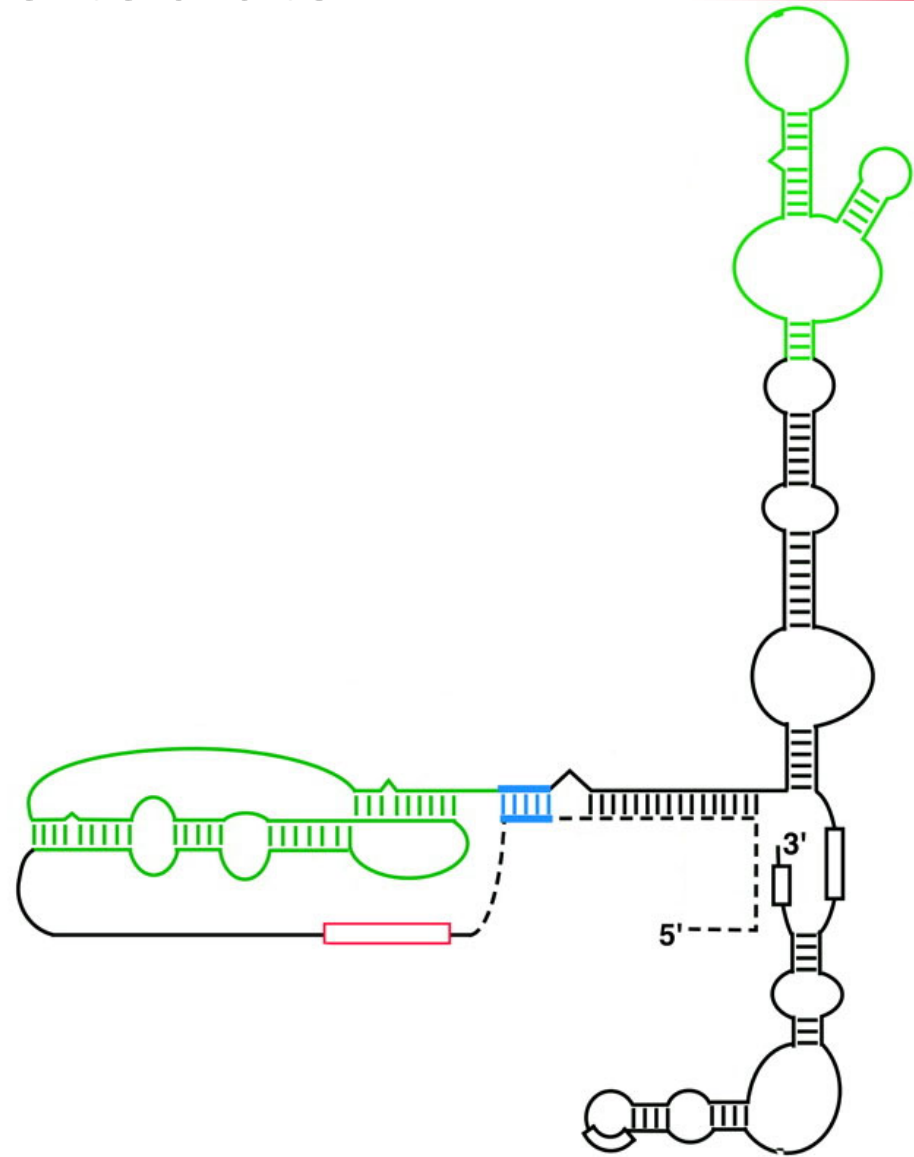
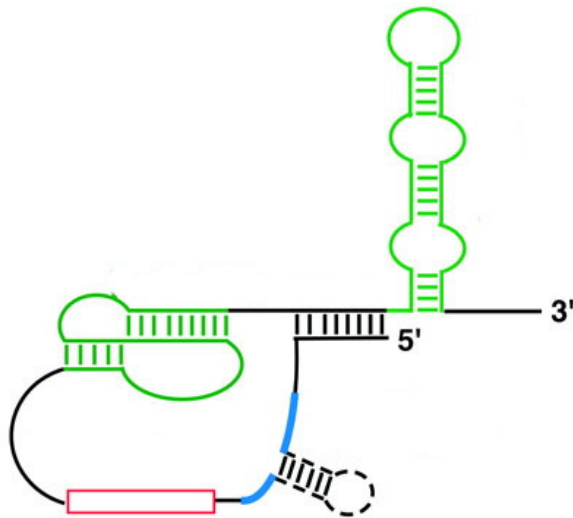
	5'	3'
Ho	CTAACCCTAA	
Or	CTAACCCTAA	
Bo	CTAACCCTAA	
Su	CTAACCCTAA	
Mu	CTAACCCTAA	
Pr	CTAACCCTAA	
Fe	CTAACCCTAA	
Eq	CTAACCCTAA	
Tr	CTAACCCTAA	
El	CTAACCCTAA	
Da	CTAACCCTAA	
Ca	CTAACCCTAA	
Mi	-TAACCCTAA	
Mu	--AACCCTGA	
Ch	CTAACCCTAA	
Ga	CTAACCCTAA	
Xe	CTAACCCTAA	
Rh	CTAACCCTAA	
	*****	*



Box H/ACA Domain



H/ACA Box: només a vertebrats



Vertebrats

Domini CR6-CR8 . Alineament inicial

CR6

Ho -GGCCG**CAGGAAGAG**-GAACG---GAG--CGAGTCCCCGCGCG---
 Or -GGCCG**CAGGGAGAG**-GAACG---GAG--CGGGTCCCCCAGCG---
 Bo -AACCG**CAGGGAAG**-GAACG---GAGT-GGGGTCCCCGCGCG---
 Su -GACCG**CAGGGAAG**-GAACG---GAGT-TGG-TCCCCGCGCG---
 Mu -GGCCG**CAGGGAGAG**-AAA-C---GGAG-CGGGTCCCCTCGCG---
 Pr -GGCCG**CAGGGAGAG**-AAAAC---GGAG-CGGGTCCCCTTGCG---
 Fe -GACCG**CAGGGAGAG**-AAACG---GGAG-CAGGTCCCCGCGCG---
 Eq -GGCCG**CAGGGAGAG**-GAACG---GAG--CGGGTCCCCGCGCG---
 Tr -GAACG**CAGGGAGAG**-AAATG---GAG--CGATTCCCCGAGTA---
 El -GAACG**CAGGGAGAG**-AAACG---GAG--CGGTTCCCCGCGTG---
 Da -GGCCG**CAGGAAGAA**-AAACC---GAG--CGAGTTCTCACGCG---
 Ca -GGCCG**CAGGGAGAG**-AAACG---GAG--CAGGTCCTC--GCG---
 Mi --GTCG**CAAGTACAG**-TAACG---GAG--CTGGTCCT--TGTT---
 Mu --GCCG**CGAGGACAG**-GAATG---GAA--CTGGTCCCCGTGTT---
 Ch ---CGG**CCGGAGAGCA**AAACG---TGAG-CGGCAGCCCCTGCG---
 Ga --GCCCC**AGCAGAGCA**AAACG---GGAG-CGGCGCCCCCGGGGTAA
 Xe -GGTCGGG**AGAACAAAA**AAGG---GCGCGCTGGTGCTCAGGCTCA-
 Rh CGCCCG**CAGGGATAGTA**AATATCCGTGACCAGTGGCCTCGGTG---

★ ★ ★ ★★

★ ★

CR8

TCG**GCTCACAC**ATGC 548
 TCG**GCTCAAAC**ACGC 547
 TCG**GCTCAGAC**ATCC 540
 TCG**GCTCAGAC**ACTT 541
 TAG**GCTCACAC**ACAC 541
 TAG**GCTCACAC**ACAT 542
 TGG**GCTCAGAC**ACAT 544
 TCG**GCTCAAAC**ACGT 540
 TCAG**CTCCGAC**AGGT 554
 TCAG**CTCCGAC**AGGT 549
 TCG**GCTCAGAC**ACGT 545
 -GG**GCTCCTACA**AGC 517
 TCG**GCTCCTACA**ACC 496
 TCG**GTCTCACA**ACC 490
 TGC**GCTCAGAC**ACGC 513
 CGCTCC**CACACAG**CG 569
 CAGTCC**CCGACAT**GT 584
 CCT**GGTCATACA**CGC 667

★ ★★

Alineament SnoRNA - TR

H box

Homo_sapie	ANANNAACG--GAGCGAGTCC
Bos_taurus	AAAGGAAACGG--AGTGGGGTCC
Sus_scrofa	AAAGGAAACGG--AGTTGG-TCC
Equus_caba	AGAGGAA-CG--GAGCGGGTCC
Felis_catu	AGAGAAACGG--GAGCAGGTCC
Mustela_pu	AGAGAAA-CG--GAGCGGGTCC
Procyon_lo	AGAGAAAACG--GAGCGGGTCC
Oryctolagu	AGAGGAA-CG--GAGCGGGTCC
Trichechus	AGAGAAA-TG--GAGCGATTCC
Dasypus_no	AGAAAAA-CC--GAGCGAGTTC
Elephas_ma	AGAGAAA-CG--GAGCGGTTCC
Xenopus_la	ACAAAAAGGGGCGCGCTGGTGC
Microtus_o	ACAGTAA-CG--GAGCTGGTCC
Chelydra_s	AGAGCAAACGT-GAGCGGCAGC
Mus_muscul	ACAGGAA-TG--GAACTGGTCC
Cavia_porc	AGAGAAA-CG--GAGCAGGTCC
Gallus_gal	AGAGCAAACGG-GAGCGGCGCC
gi 6041649	ATAAAAAGTTGTGGTTATAGTG
gi 5031301	AGAGCAAAGAAGGGGCTCTGGAG
gi 3860192	ACATTAACTGC-CTCACAACT
gi 5702104	AGAGTAAGAAAAAGCAAAAGAT
AJ310189.1	AGAGCAAAGCTTTGTCCCCGGCC
L16792.1/3	AGACAAACCATGCAGGAAACAT
AJ306560.1	AGAGCAAAGCCT-GTCTCTGGTT

* * **

Alineament SnoRNA - TR

ACA box

Homo_sapie	GGACTCGGCTCA'ACATGC
Bos_taurus	GGACTCGGCTCAGACATCC
Sus_scrofa	GGACTCGGCTCAGACACTT
Equus_caba	GGACTCGGCTCAAACACGT
Felis_catu	GGACTGGGCTCAGACACAT
Mustela_pu	GGACTAGGCTCACACACAC
Procyon_lo	GGACTAGGCTCACACACAT
Oryctolagu	GGACTCGGCTCAAACACGC
Trichechus	GGACTCAGCTCCGACAGGT
Dasypus_no	GGACTCGGCTCAGACACGT
Elephas_ma	GGGCTCAGCTCCGACAGGT
Xenopus_la	CAGCCAGTCCCCGACATGT
Microtus_o	GAGCTCGGCTCCTACAACC
Chelydra_s	GGGCTGCGCTCAGACACGC
Mus_muscul	GAACTCGGTTCTCACAAACC
Cavia_porc	GGGACGGGCTCCTACAAGC
Gallus_gal	CGGCGTCGCTCCCACACGC
gi 6041649	AACAACTTCTGGAACAACG
gi 6010124	GATTAGCACTCATACAGTC
gi 5031301	CTTGGTACGCATCACATCG
gi 4609203	CATAACTGTCACCACAATT
gi 3860192	TTGGTGATAAGGAACAGCT
gi 3860195	GATTCTGACTTGCAACAAGT
gi 5702104	TTTGAAGGCTGTAAACATTT
AJ310189.1	AACCATGCAGTGTACAACCT
L16792.1/3	AACCATGCAGGAAACATAT
AJ306560.1	AACCATGCAGGTTACAACCT
