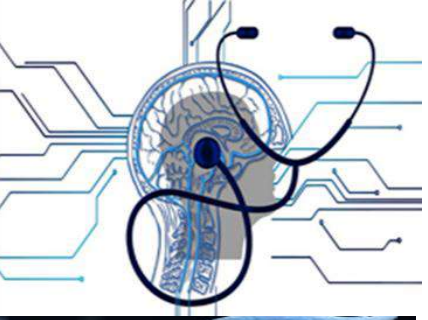
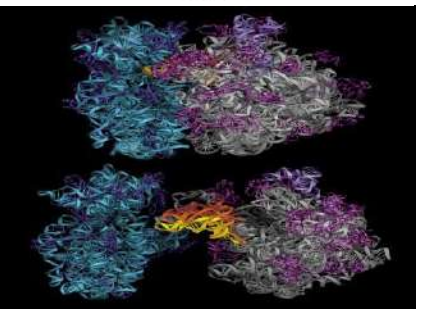






UNIVERSIDADE ESTADUAL DE RORAIMA

CURSO DE MEDICINA

Disciplina: Bioquímica

MÓDULO 1: Biomoléculas

AULA 3: ÁCIDOS NUCLÉICOS

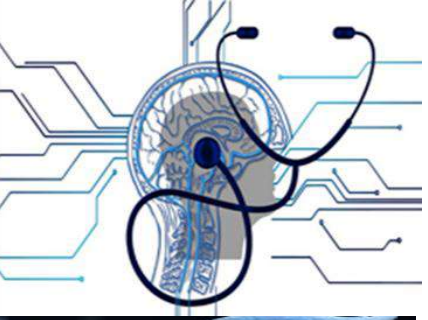
Prof. Higo Nasser S. Moreira

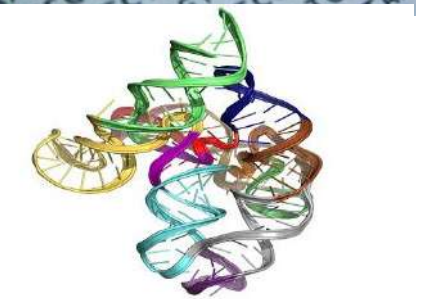
Doctor Scientiae em Bioquímica Aplicada

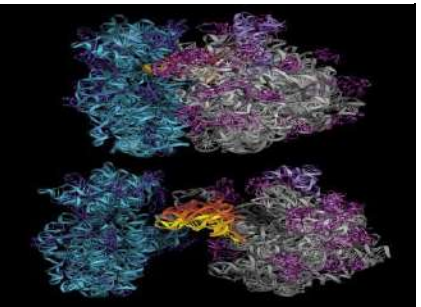
Universidade Federal de Viçosa – Brasil

Docente do Curso de Medicina da Universidade Estadual de Roraima

Boa Vista – Brasil







NUCLEOTÍDEOS: OS MONÔMEROS DOS ÁCIDOS NUCLÉICOS

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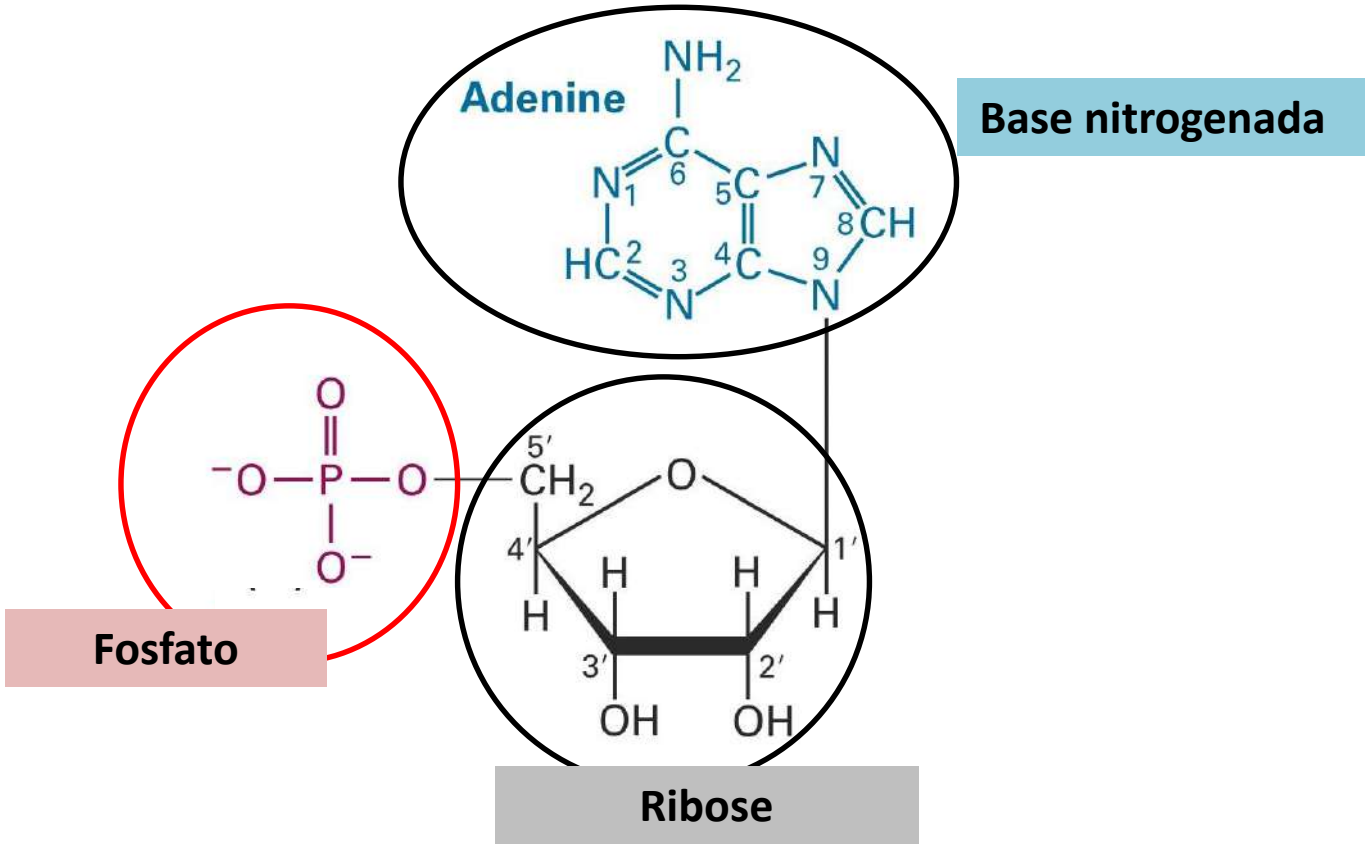

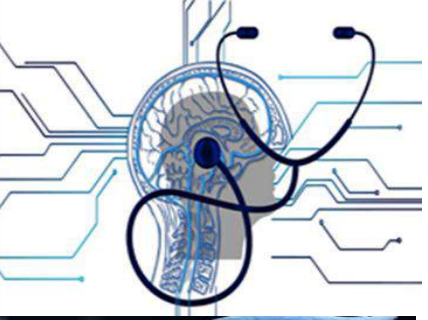

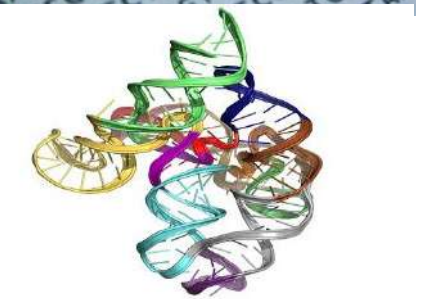

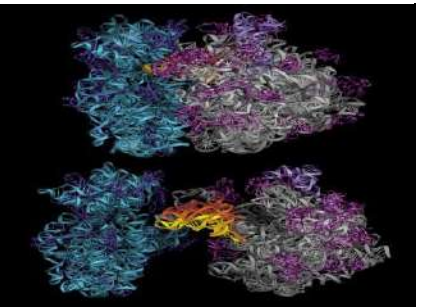

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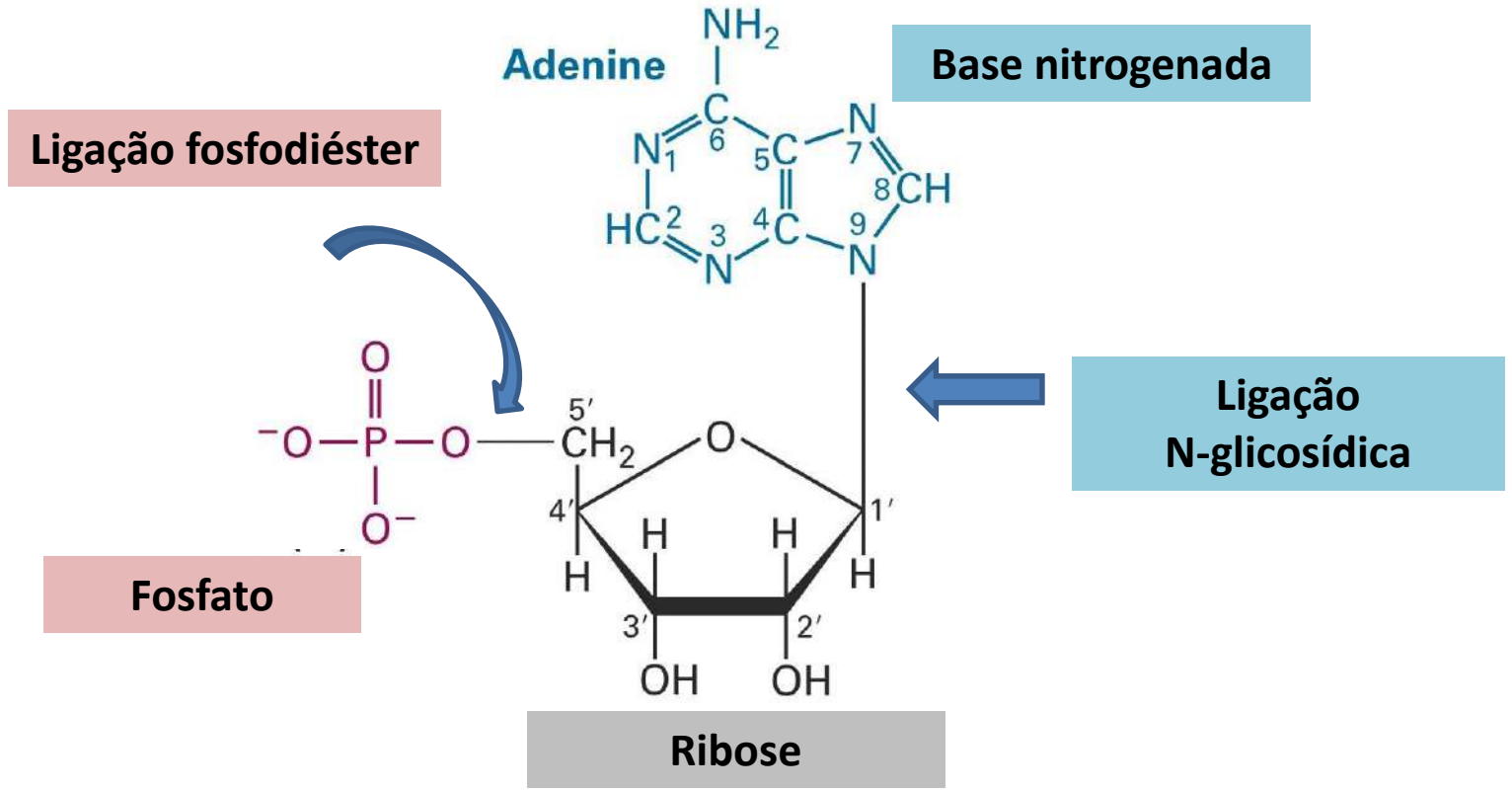
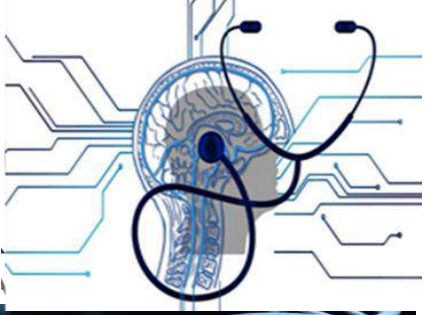
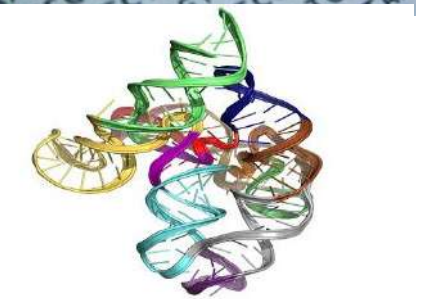
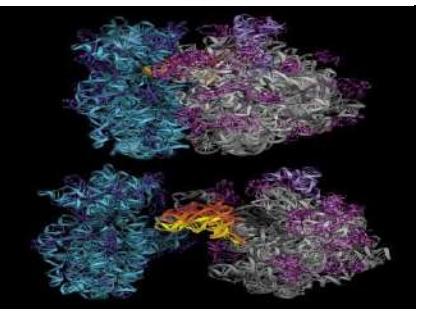


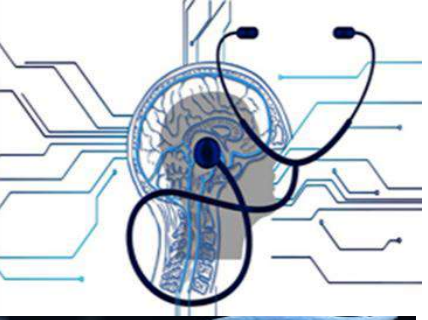


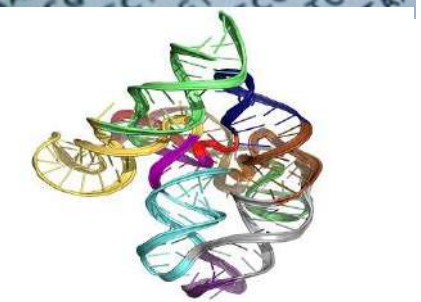


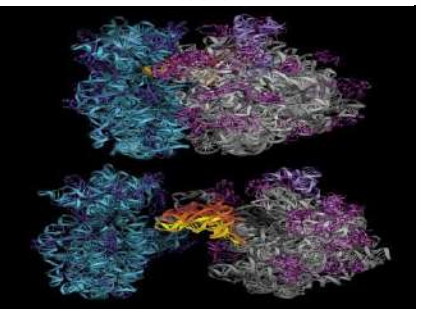


FUNÇÕES DOS NUCLEOTÍDEOS

- ✓ **Transportadores de energia química – ATP, GTP e CTP**
- ✓ **Molécula sinal em respostas celulares – cAMP, ppGpp**
- ✓ **Componentes estruturais de cofatores enzimáticos – NAD^+, FAD, coenzima A**
- ✓ **Constituintes dos ácidos nucléicos (DNA e RNA)**

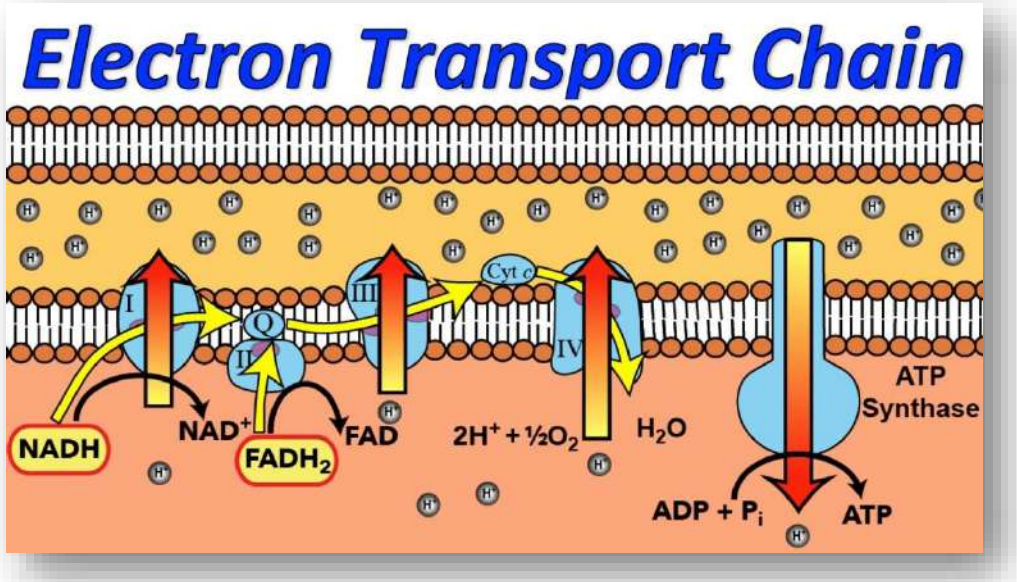


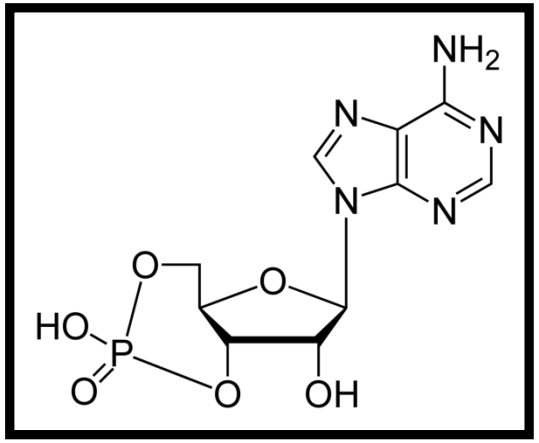




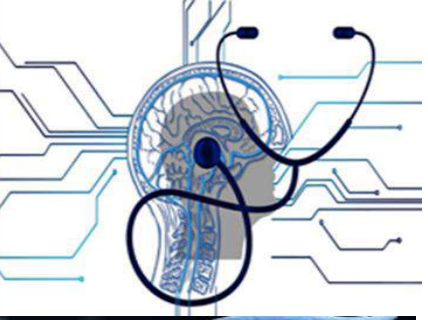
OUTRAS FUNÇÕES DOS NUCLEOTÍDEOS

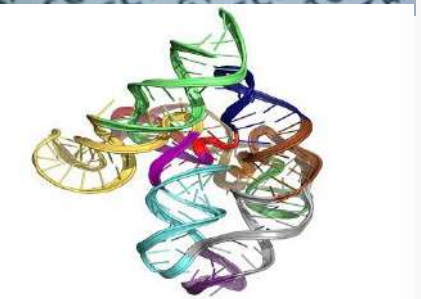
- ✓ **ATP é a moeda de energia da célula (molécula-chave nos processos de transferência de energia nas células)**
- ✓ **GTP desempenhar papel no metabolismo energético;**
- ✓ **O UTP é utilizado para ativar açúcares durante a síntese de polissacarídeos;**
- ✓ **AMP compõe da estrutura da coenzima A, NAD, NADP +,**
- ✓ **AMPc (AMP cíclico) é molécula chave nos processos de transdução de sinal.**

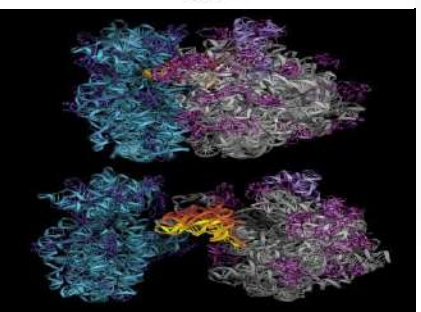




AMP cíclico:
Vias de sinalização

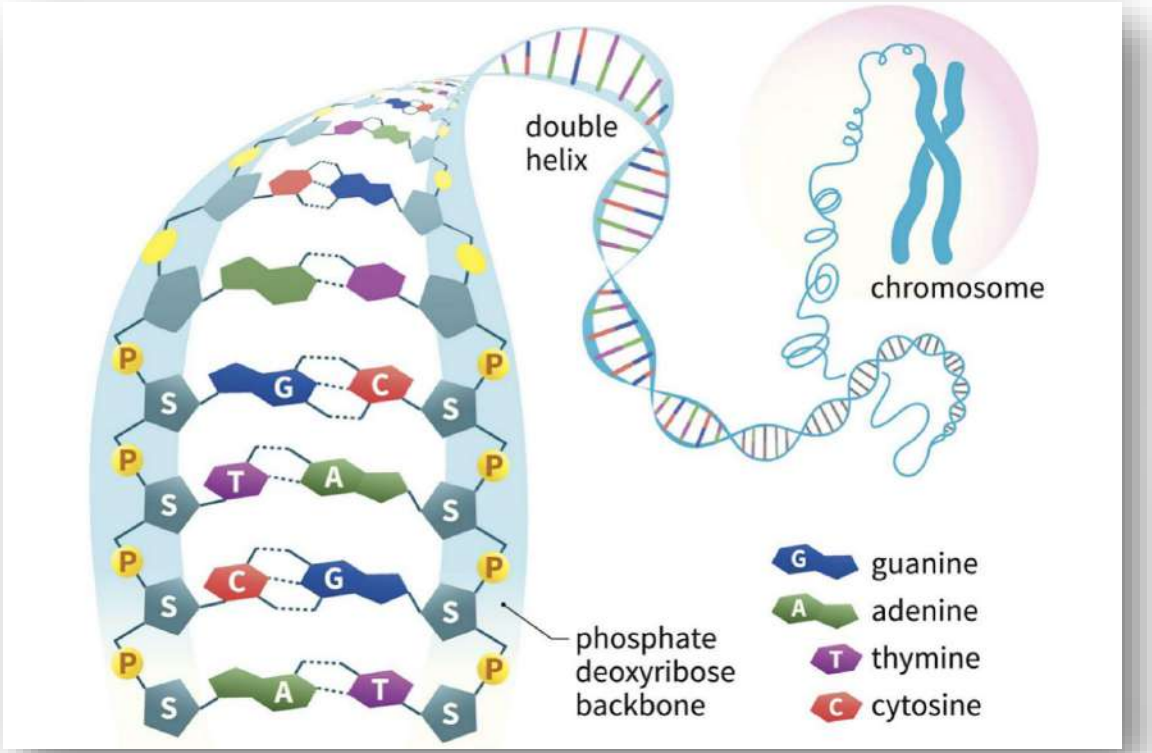


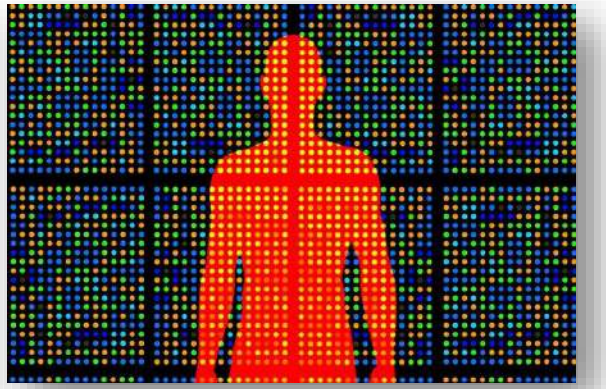


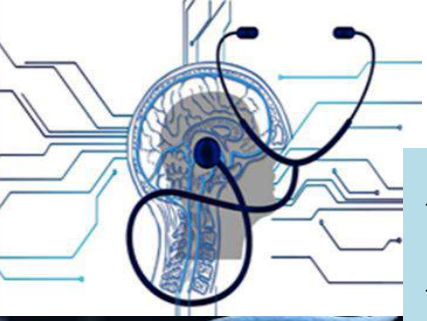


FUNÇÕES DO DNA

- ✓ **O DNA contém as instruções para todas as funções celulares e toda a síntese de proteínas;**
- ✓ **O DNA está presente no núcleo, porém pode ser encontrado nas mitocôndrias;**
- ✓ **Manutenção da integridade da informação genética e regulação da expressão gênica**



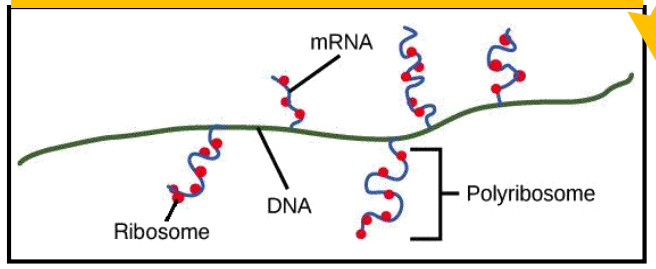


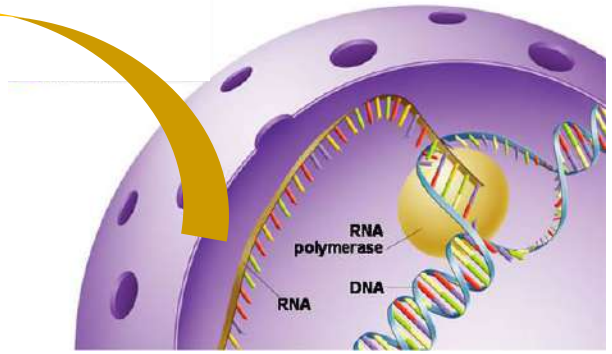


FUNÇÕES DO RNA

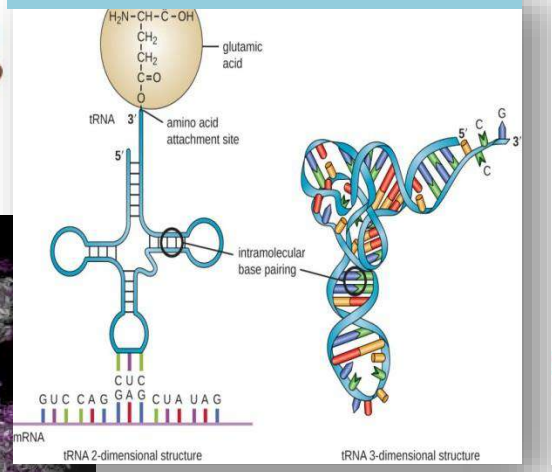
- ✓ **Transmissão de informação contida em genes (DNA) para a síntese de proteínas;**
- ✓ **Síntese proteica e regulação da síntese proteica;**

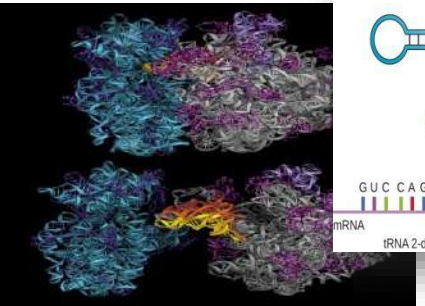
1. RNA mensageiro - mRNA



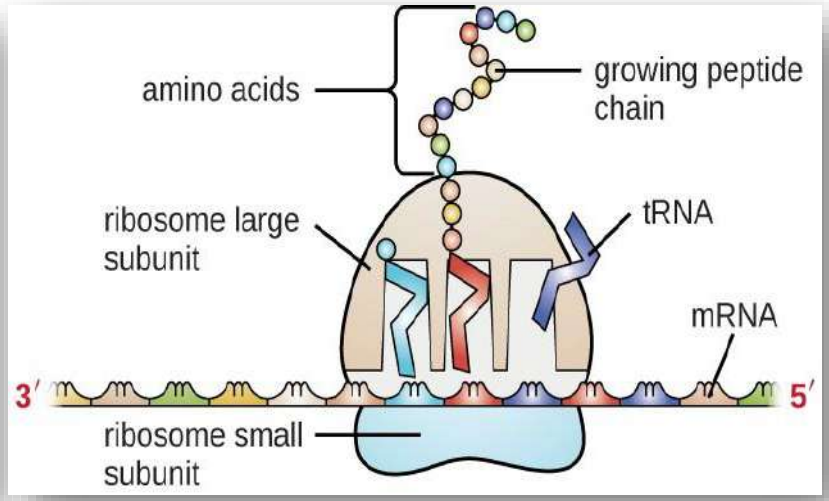


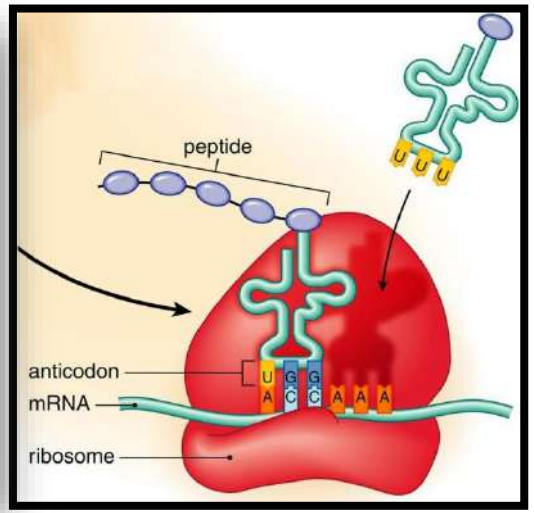
2. RNA transportador - tRNA

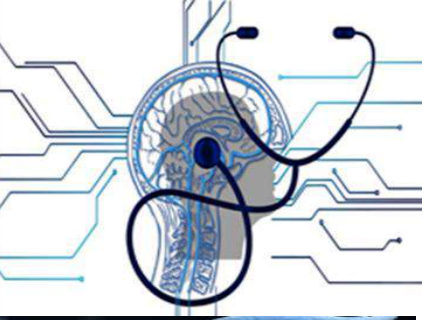


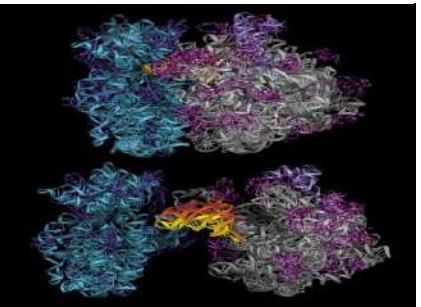


3. RNA ribossomal - rRNA



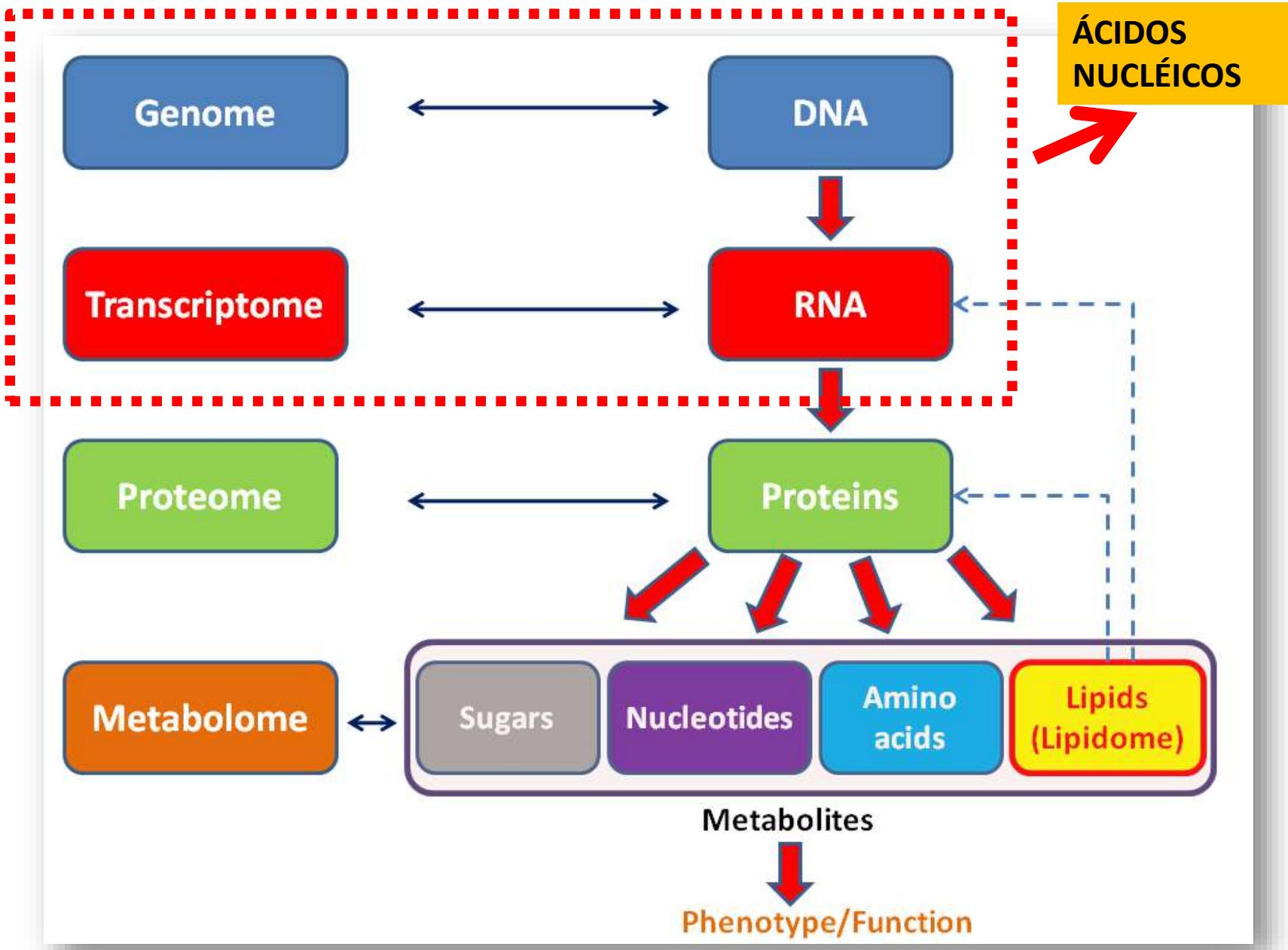


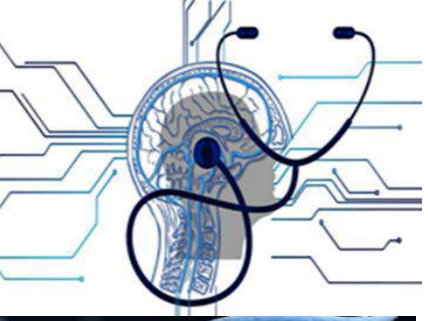


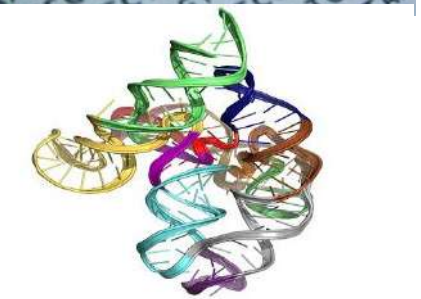


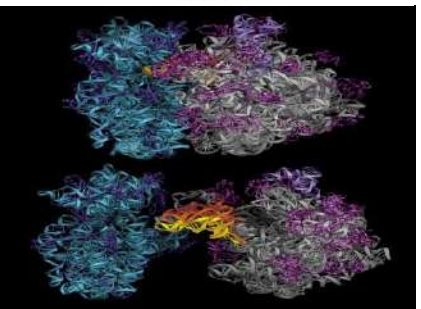
GENOMA, TRANSCRIPTOMA, PROTEOMA E METABOLOMA

ÁCIDOS NUCLÉICOS





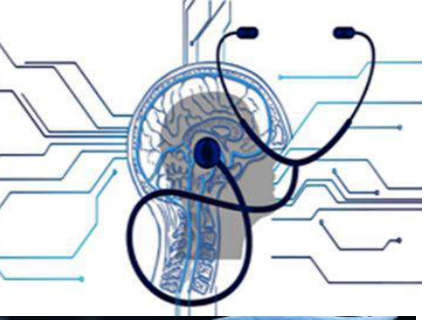


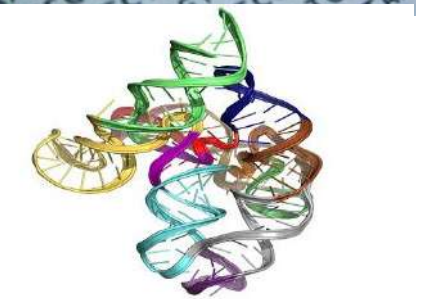


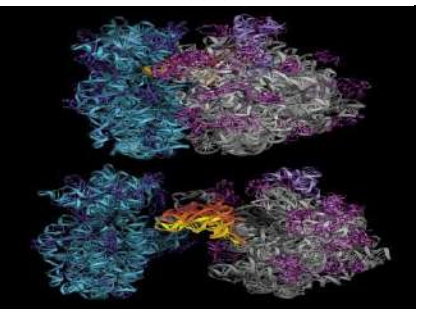
NUCLEOTÍDEOS: OS BLOCOS DE CONSTRUÇÃO DE ÁCIDOS NUCLÉICOS

ESTRUTURA QUÍMICA DOS NUCLEOTÍDEOS

DIFERENÇAS ENTRE DNA E RNA				
	DNA		RNA	
1. Pentose	2'-Deoxirribose		Ribose	
2. Purinas	Adenina	Guanina	Adenina	Guanina
3. Pirimidinas	Citosina	Timina	Citosina	Uracila
4. Estrutura	Hélice dupla		Hélice única	
5. Origem	Replicação		Transcrição	
6. Enzima sintétia	DNA-polmerase		RNA-polimerase	
7. Localização	Núcleo, mitocôndria		Núcleo, Citosol	
8. Função	Manutenção da informação genética		Síntese protéica	

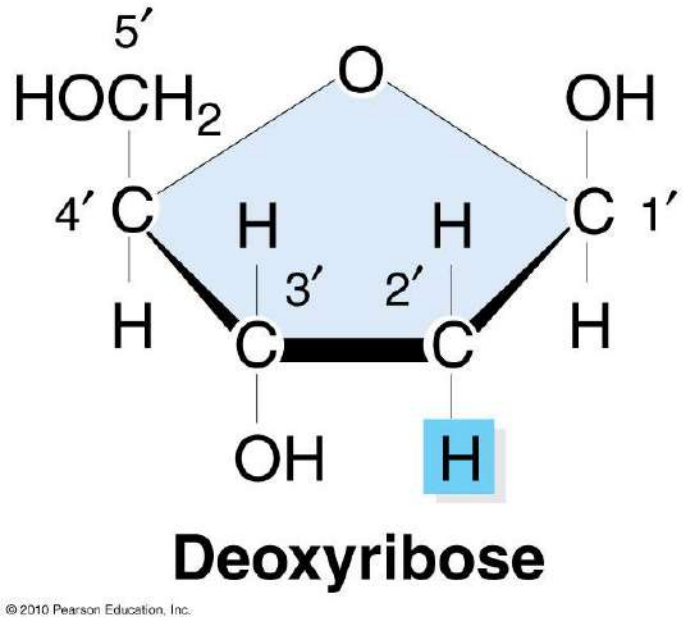






RIBOSE VERSUS 2'-DESOXIRRIBOSE

DNA:
ÁCIDO DESOXIRRIBONUCLÉICO



Deoxyribose

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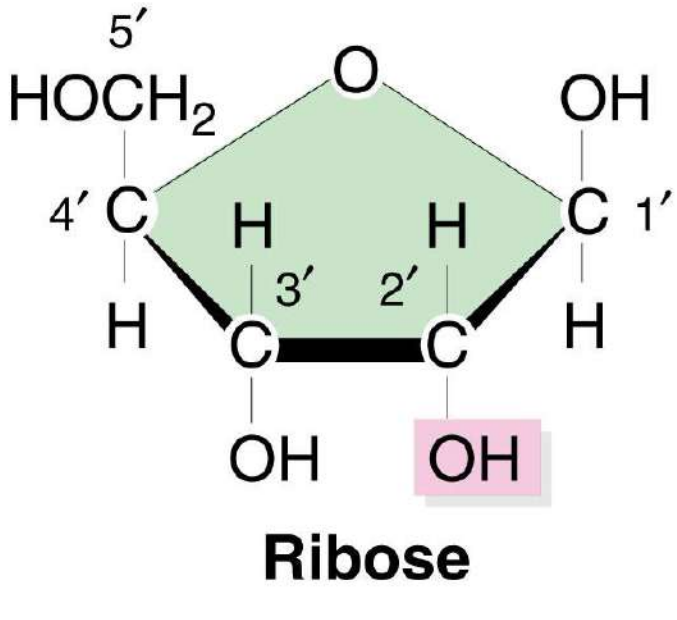
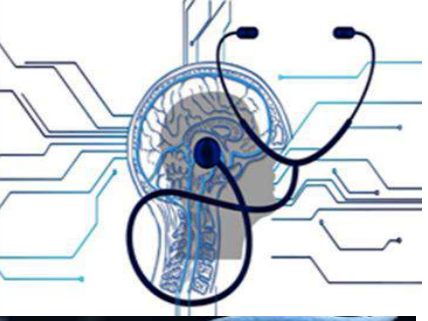
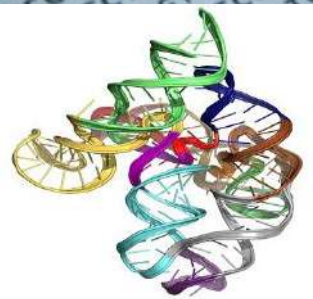
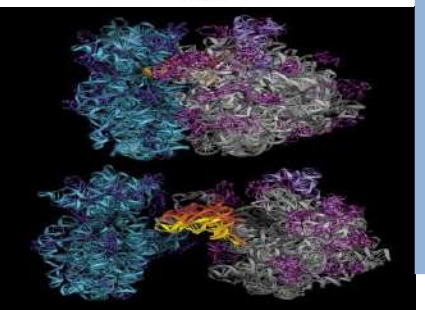
RNA:
ÁCIDO RIBONUCLÉICO



Ribose



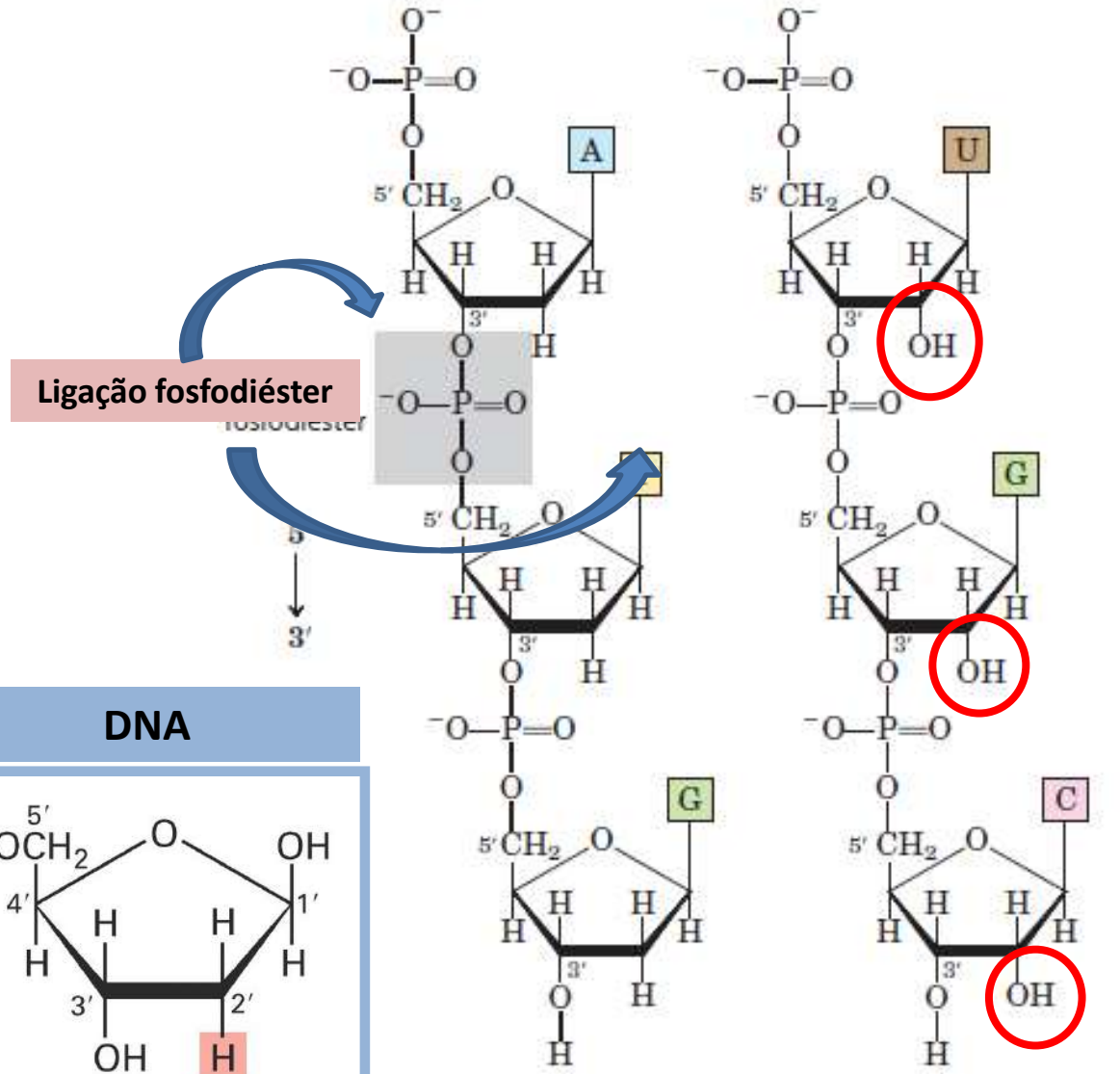




RIBOSE VERSUS 2‘-DEOXIRRIBOSE

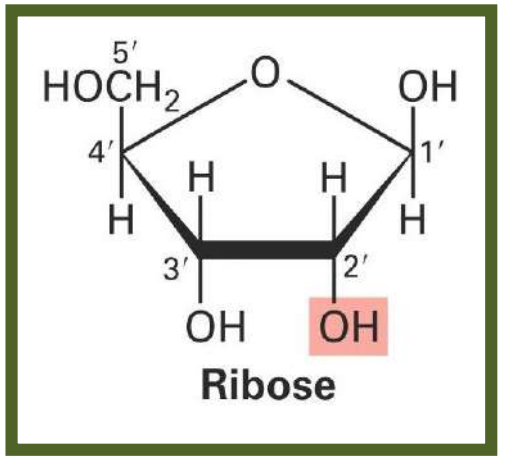
5‘ Terminal

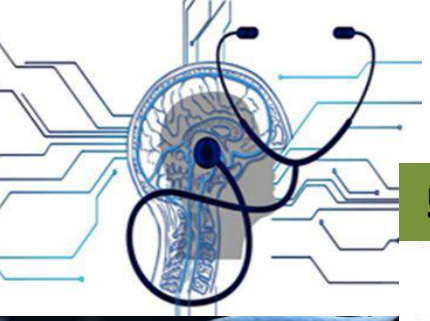
5‘ Terminal

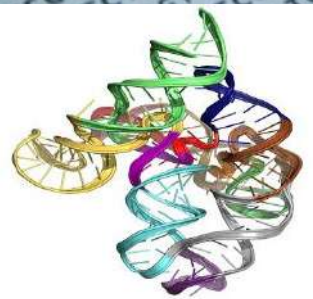


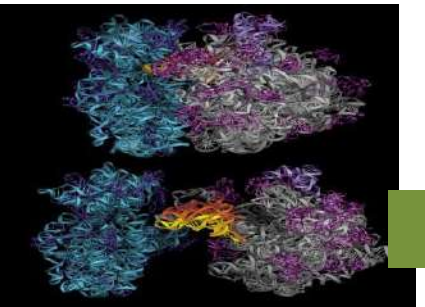
DNA

RNA



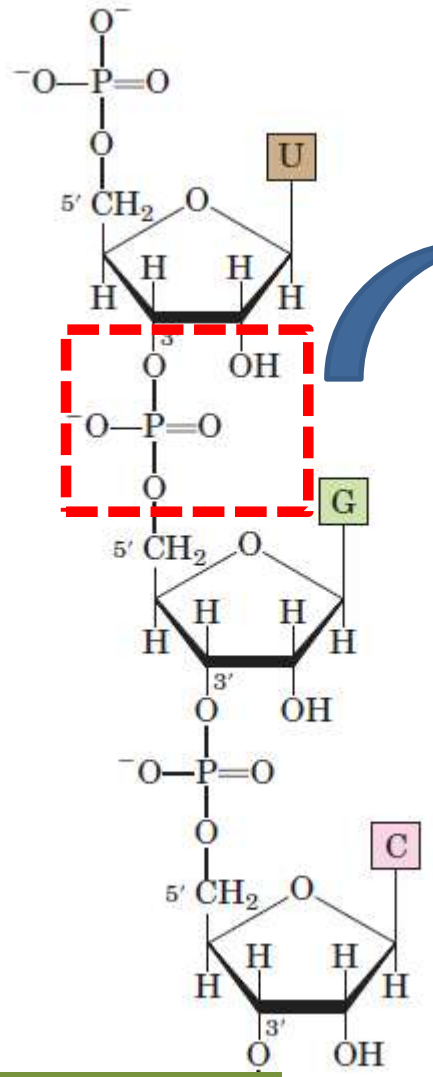






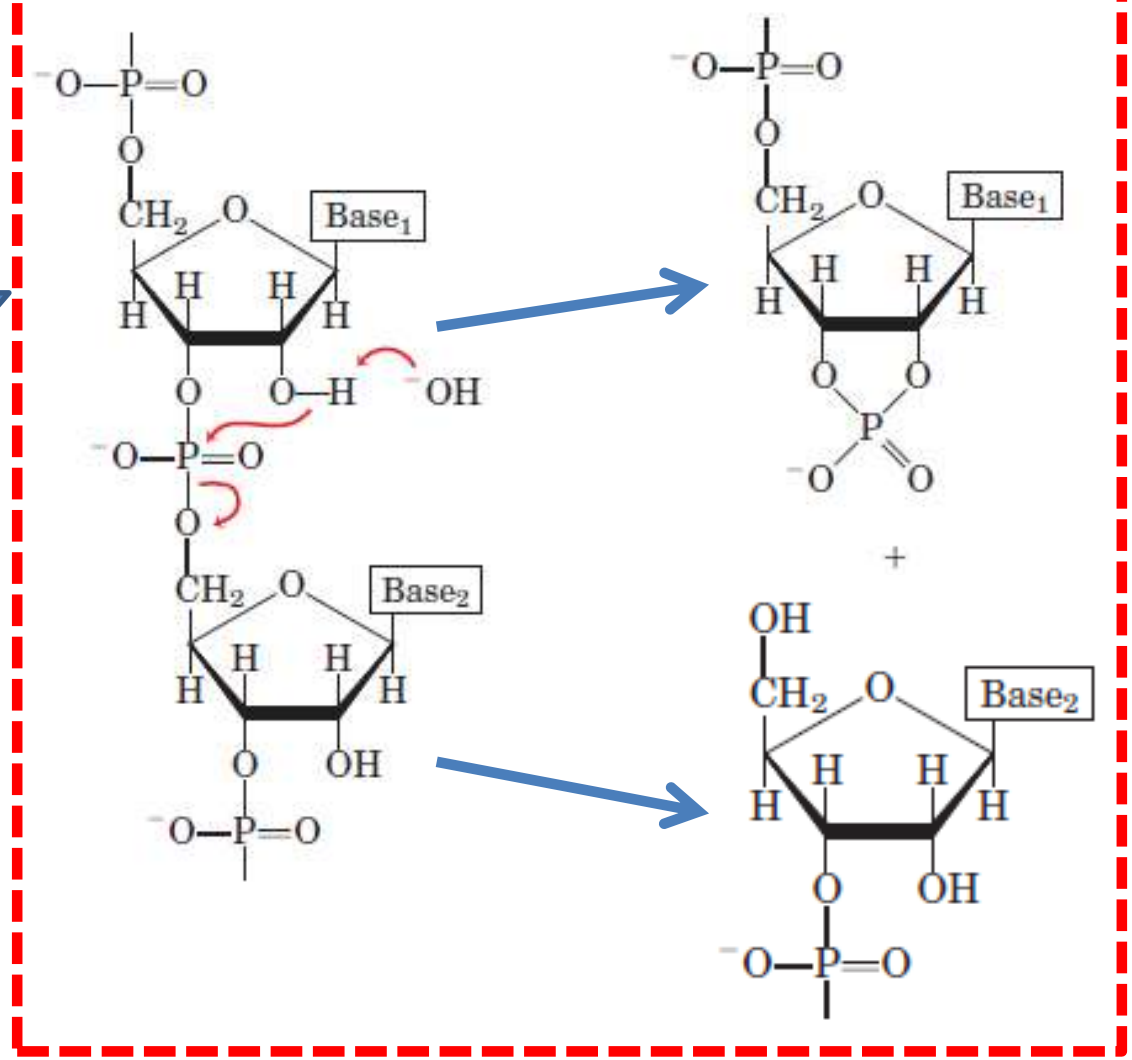
RNA É MUITO MAIS SUSCEPTÍVEL À DEGRADAÇÃO DEVIDO AO 2‘- OH

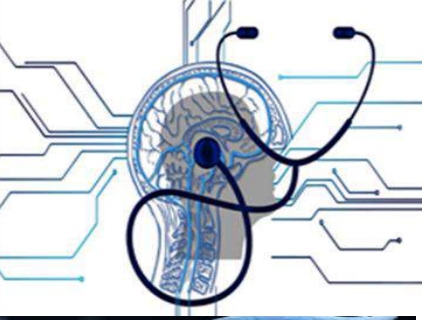
5‘ Terminal

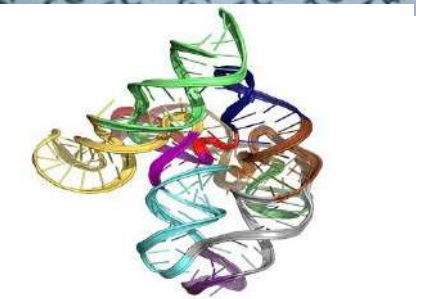


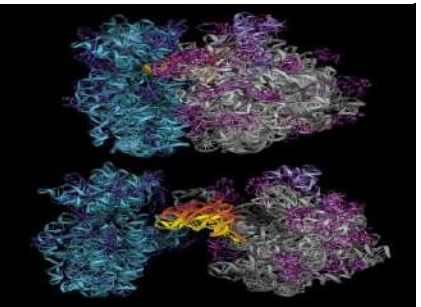
3‘ Terminal

Mecanismo de autólise do RNA





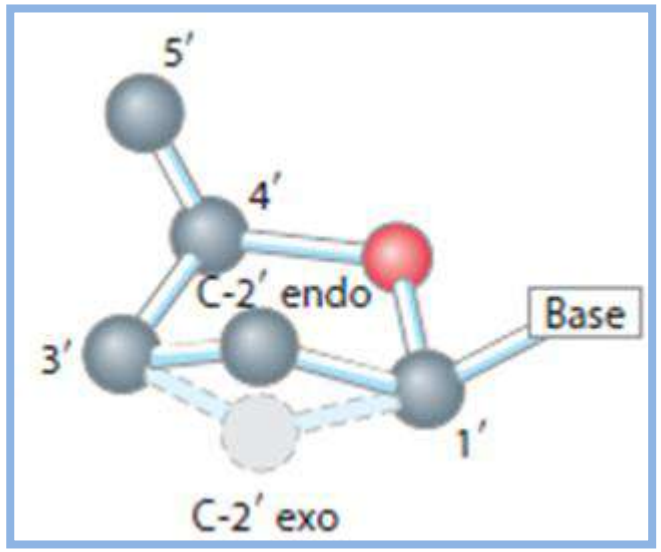




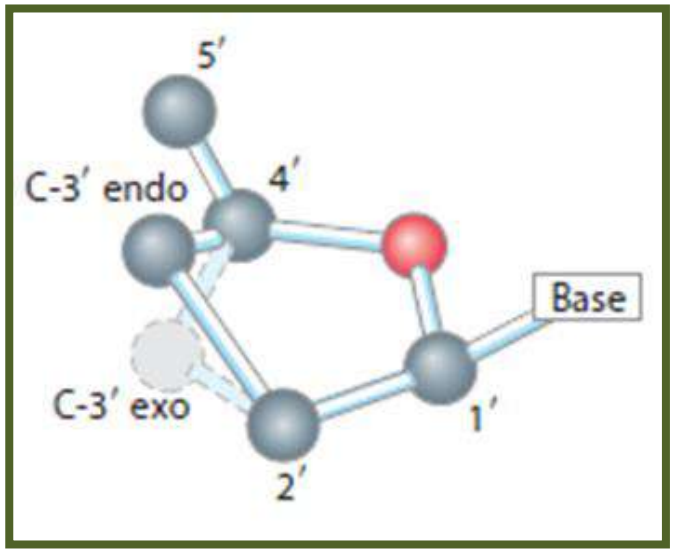
CONFORMAÇÃO DOS ANEIS DE RIBOSE E 2´DESOXIRRIBOSE

A ribose é um anel flexível que apresenta duas conformações preferenciais

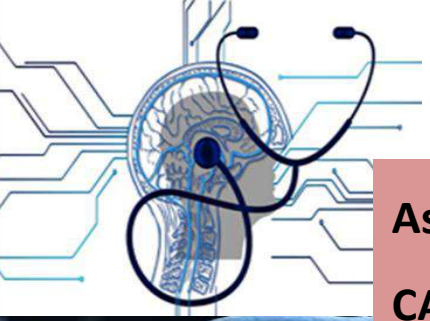
- ✓ **C3 '- endo encontrado principalmente em RNA e em fita simples de DNA**
- ✓ **C2´ - endo, encontrado principalmente em DNA**

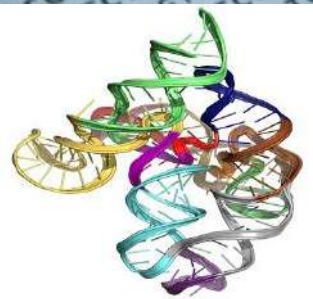


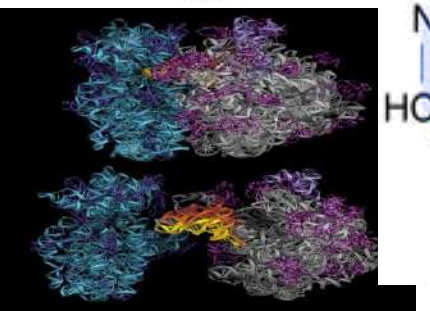
C2‘-endo: DNA



C3‘-endo: RNA

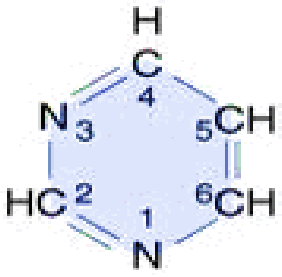


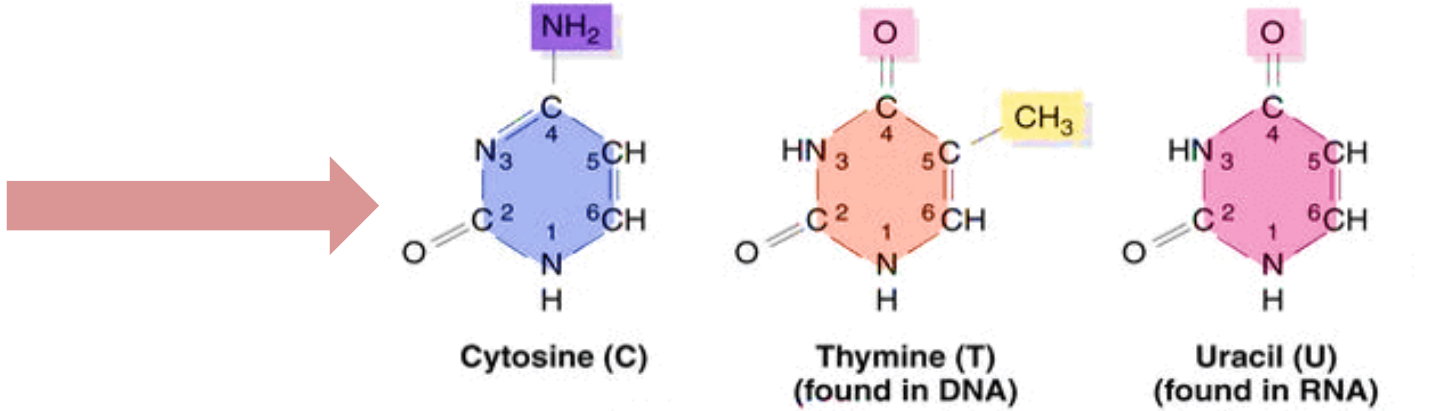




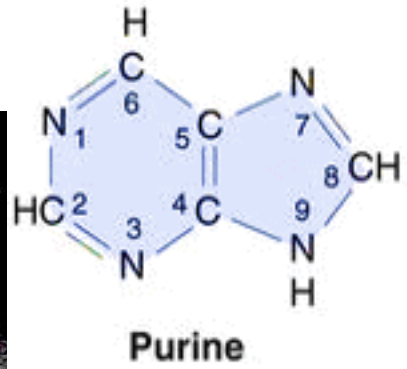
NUCLEOTÍDEOS: OS BLOCOS DE CONSTRUÇÃO DE ÁCIDOS NUCLÉICOS

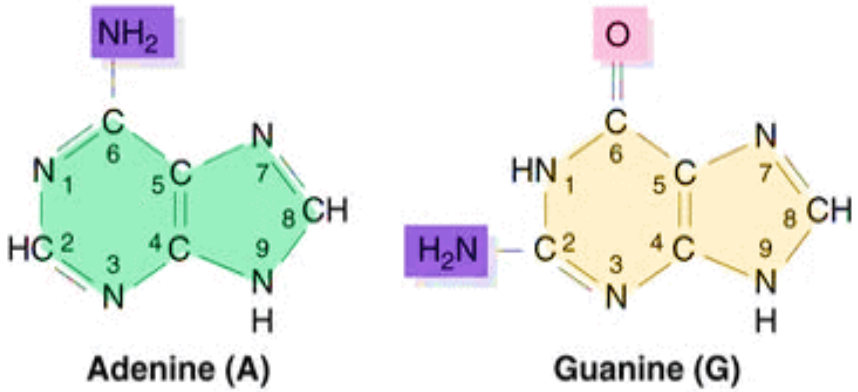
As BASES PIRIMÍDICAS são formadas por uma cadeia fechada com quatro átomos de CARBONO e dois de NITROGÊNIO: CITOSINA (C), TIMINA (T), URACIL (U).

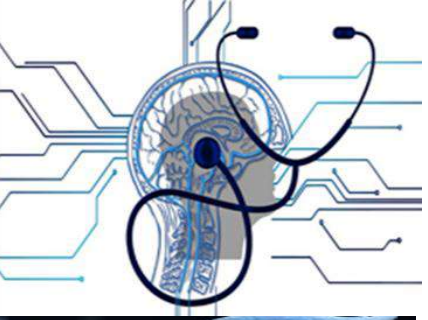


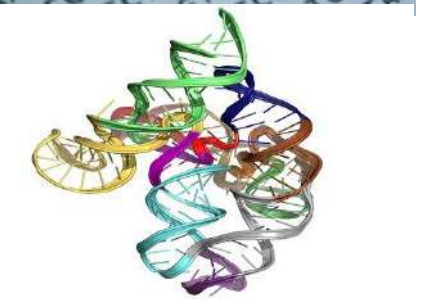


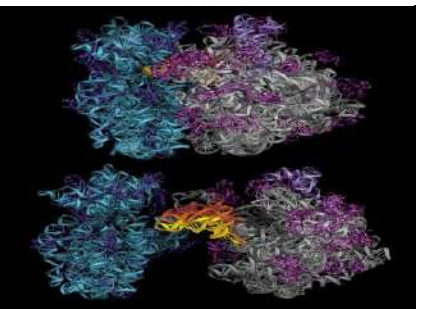
As PURINAS são formadas por duas cadeias fechadas: ADENINA (A) ou GUANINA (G).









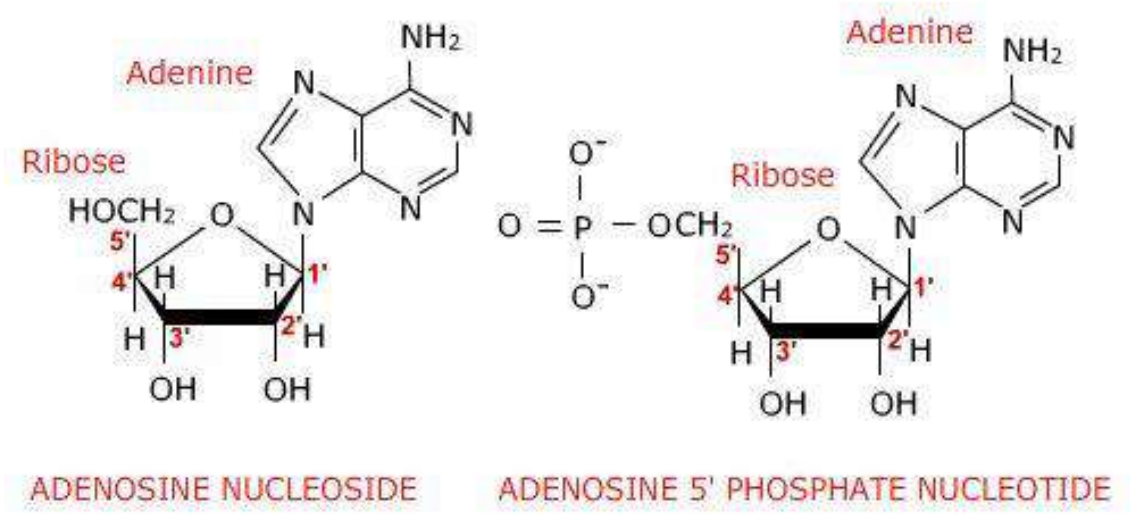


NUCLEOTÍDEOS E DESOXIRRIBONUCLEOTÍDEOS

BASE + PENTOSE → NUCLEOSÍDEO (SEM O FOSFATO)

ADENINA + RIBOSE = ADENOSINA

ADENINA + DEOXIRRIBOSE = DESOXIADENOSINA

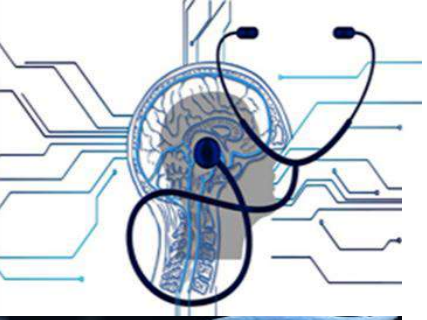


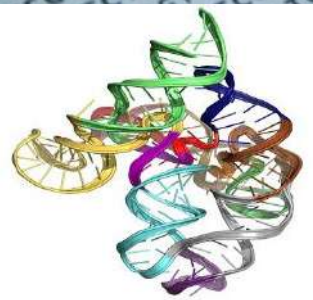
BASE + PENTOSE + FOSFATO → NUCLEOTÍDEO (COM O FOSFATO)

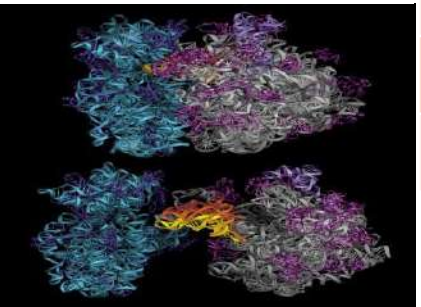
DEOSOXIADENOSINA MONOFOSFATO (dAMP)

DEOSOXIADENOSINA DIFOSFATO (dADP)

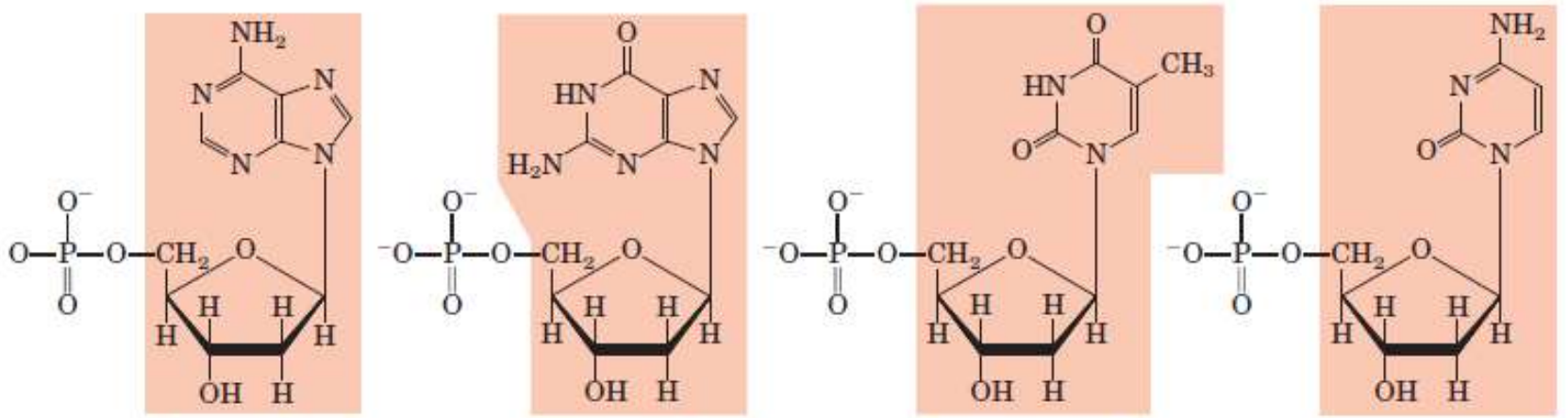
DEOSOXIADENOSINA TRIFOSFATO (dATP)



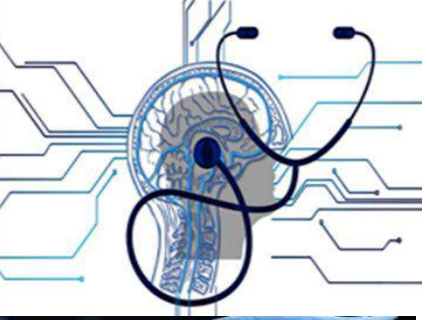


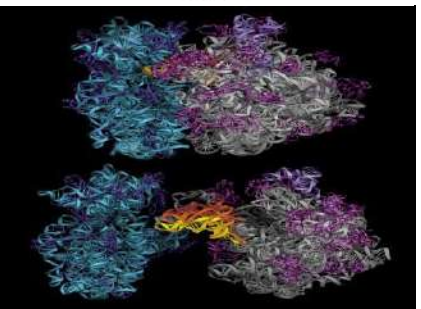


2´-DESOXINUCLEOTÍDEOS (DNA)

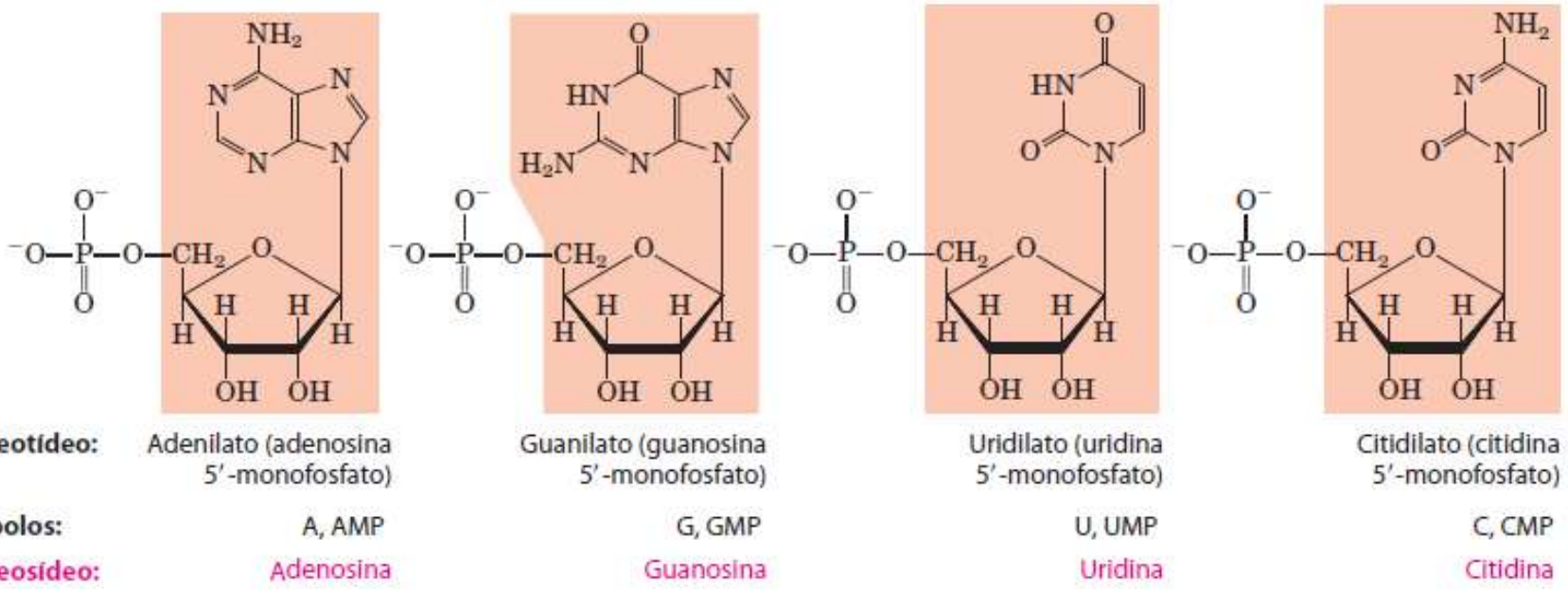


DNA	NUCLEOTÍDEOS (com fosfato)	NUCLEOSÍDEOS (sem fosfato)
ADENINA	DESOXIADENILATO - dAMP	DESOXIADENOSINA
GUANINA	DESOXIGUANILATO - dGMP	DESOXIGUANINA
CITOSINA	DESOXICITIDILATO - dCMP	DESOXICITINA
TIMINA	DESOXITIMIDILATO - dTMP	DESOXITIMIDINA

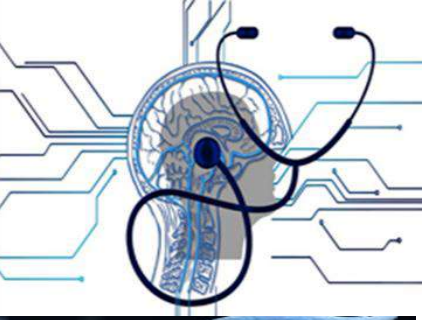


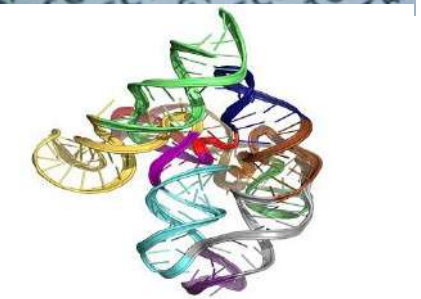


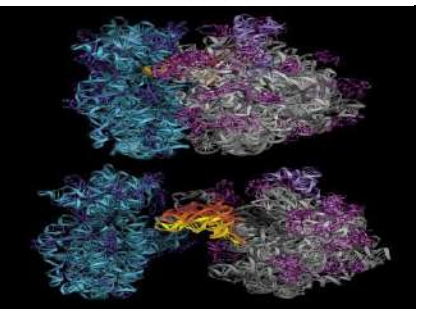
NUCLEOTÍDEOS (RNA)



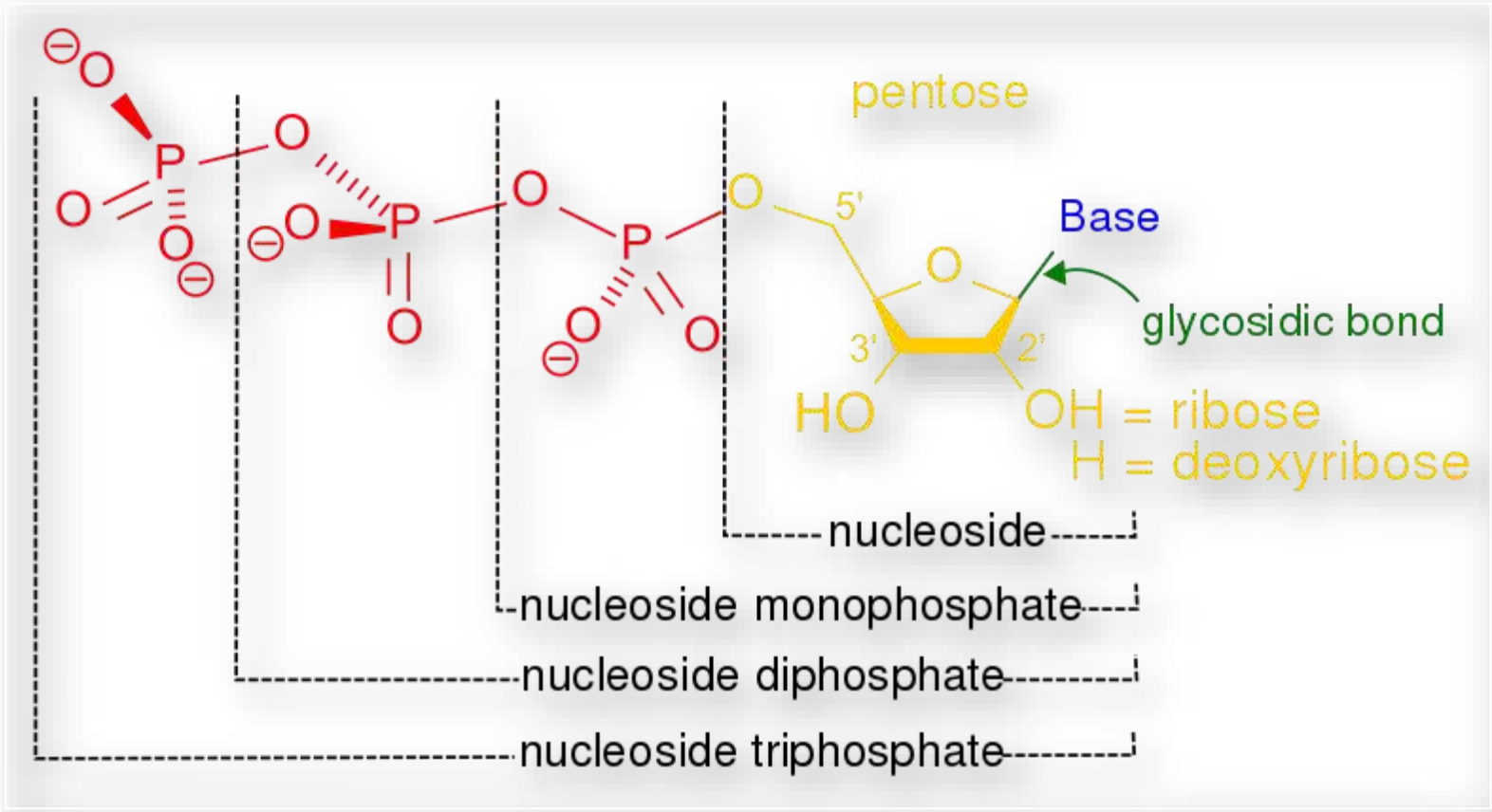
RNA	NUCLEOTIDES (with phosphate)	NUCLEOSIDES (without phosphate)
ADENINA	ADENILATO - AMP	ADENOSINA
GUANINA	GUANILATO - GMP	GUANOSINA
CITOSINA	CITIDILATO - CMP	CITIDINA
URACILA	URIDILATO - UMP	URIDINA

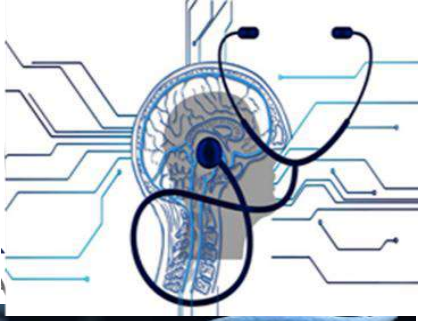


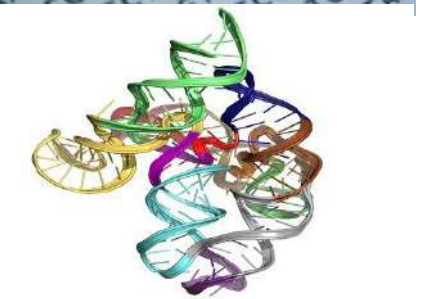


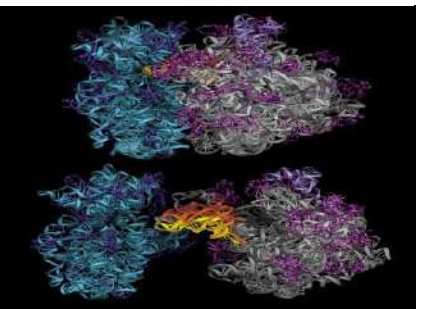


NUCLEOTÍDEOS (MONÔMEROS DE RNA)



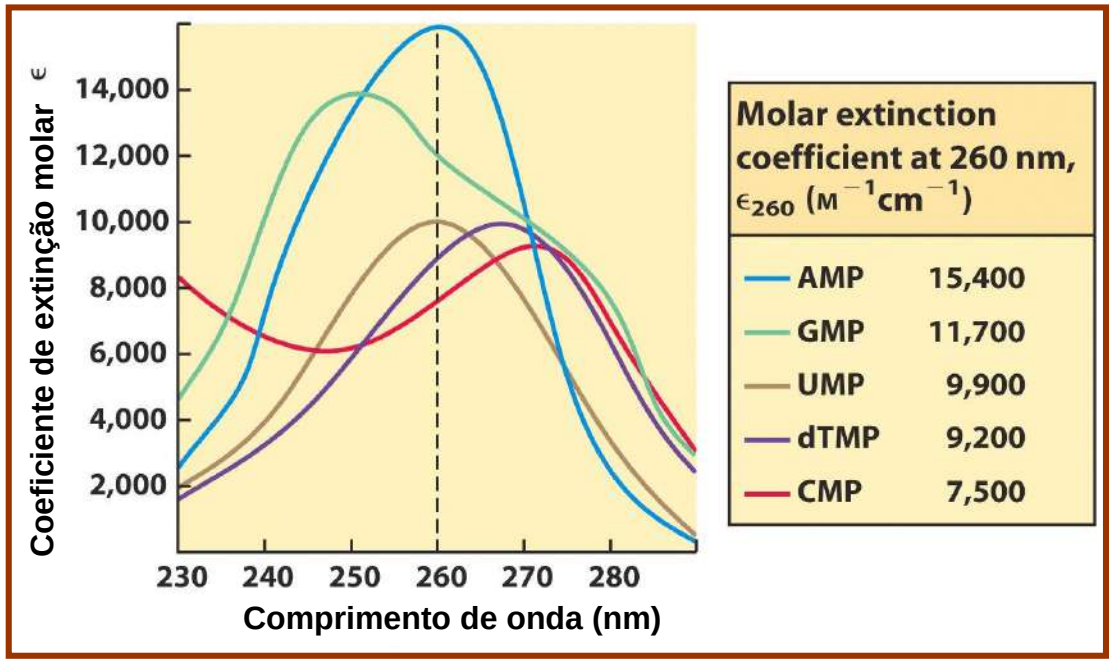


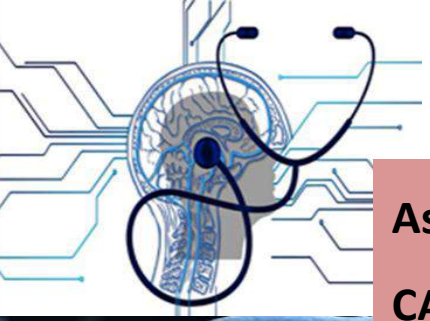


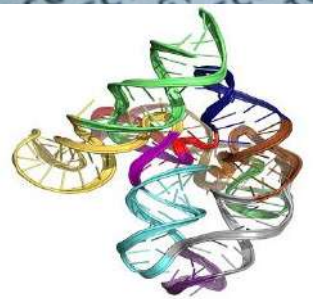


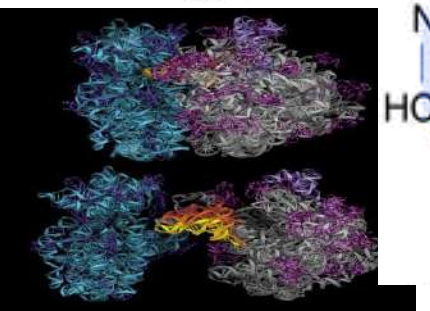
PROPRIEDADES DOS NUCLEOTÍDEOS

- ✓ **Moléculas altamente conjugadas afetando estrutura, distribuição de elétrons e absorção de luz UV**
- ✓ **Moléculas planas (pirimidina) ou quase (purina)**
- ✓ **Absorbância máxima - cerca 260 nm**









NUCLEOTÍDEOS: OS BLOCOS DE CONSTRUÇÃO DE ÁCIDOS NUCLÉICOS

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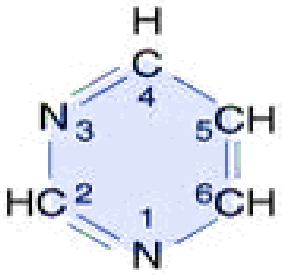

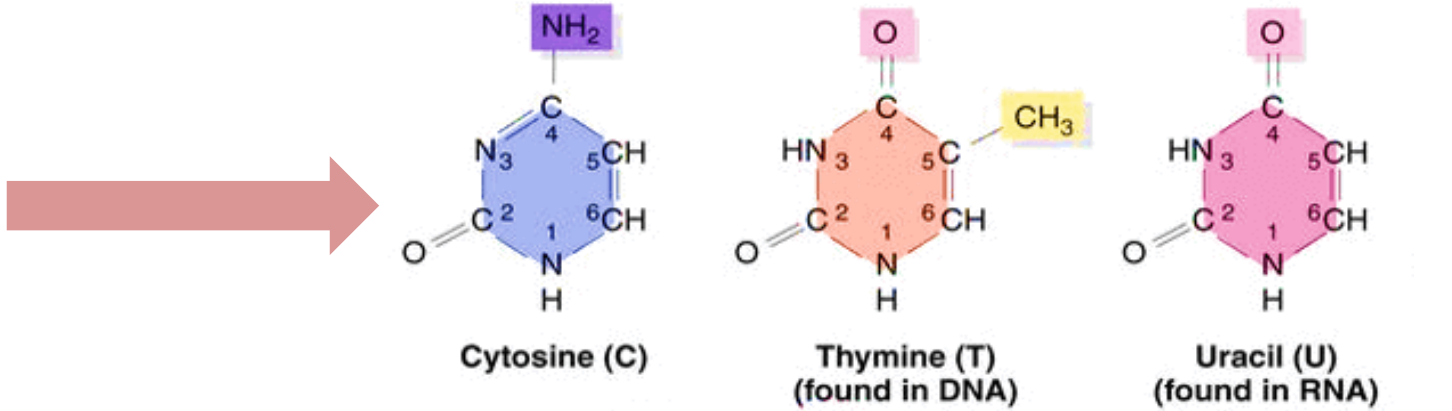

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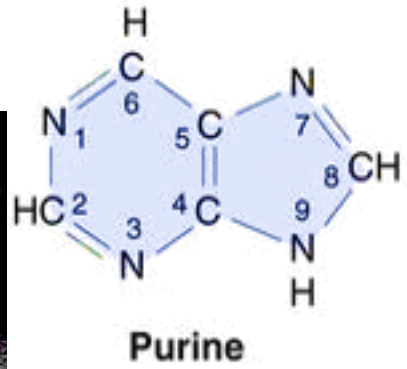
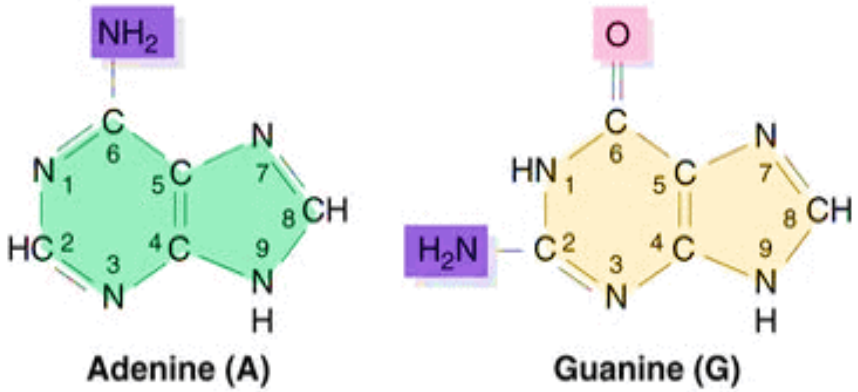
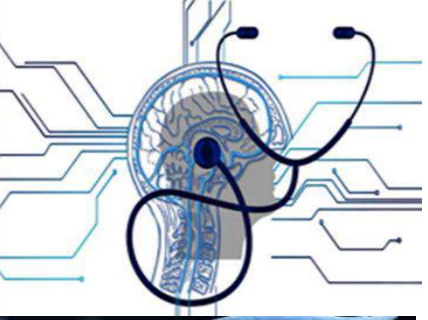
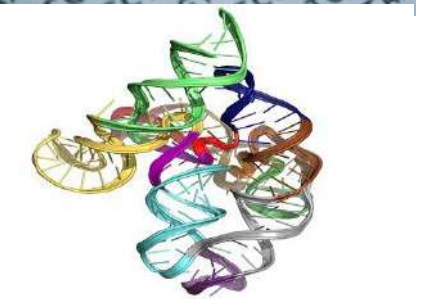
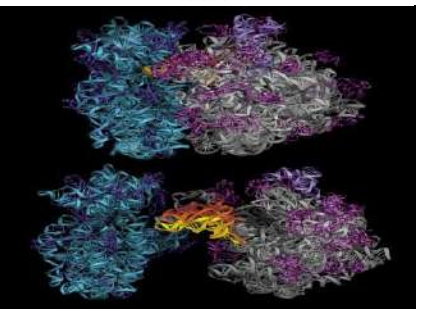




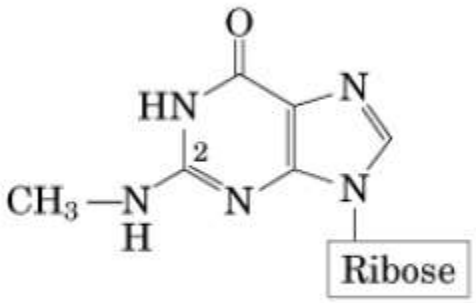




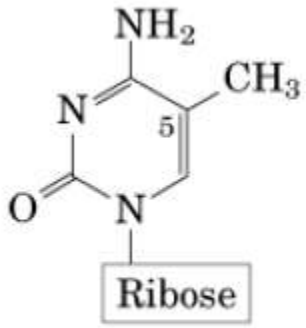


MUDANÇAS NAS ESTRUTURAS DAS BASES NITROGENADAS

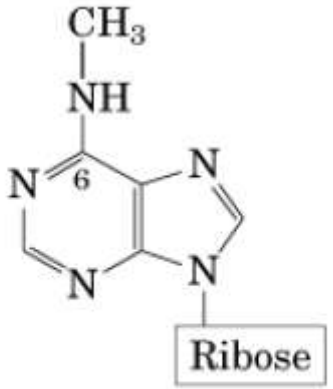
- ✓ **As bases nitrogenadas do DNA podem sofrer metilação.**
- ✓ **Reconhecimento de DNA celular em comparação com DNA exógeno não-metilado.**
- ✓ **Mecanismo de defesa: importante no reparo do DNA em caso de erro de replicação**



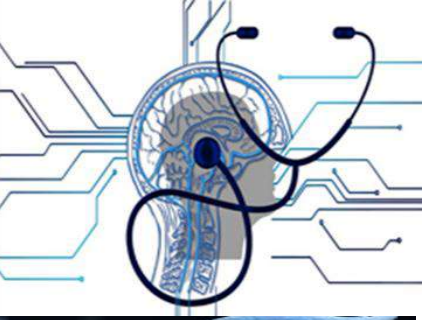
N^2-Methylguanosine

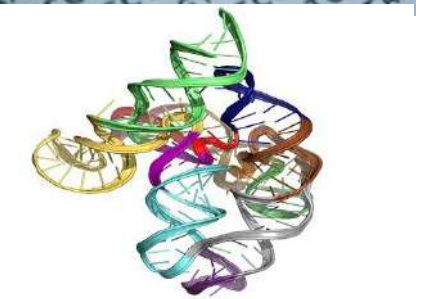


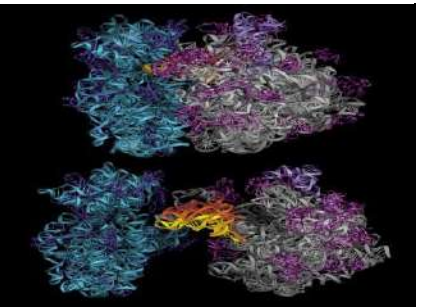
5-Methylcytidine



N^6-Methyladenosine





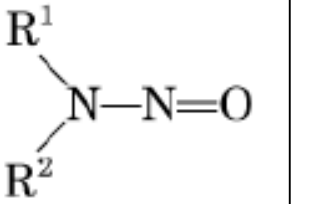


MUDANÇAS NAS ESTRUTURAS DAS BASES NITROGENADAS

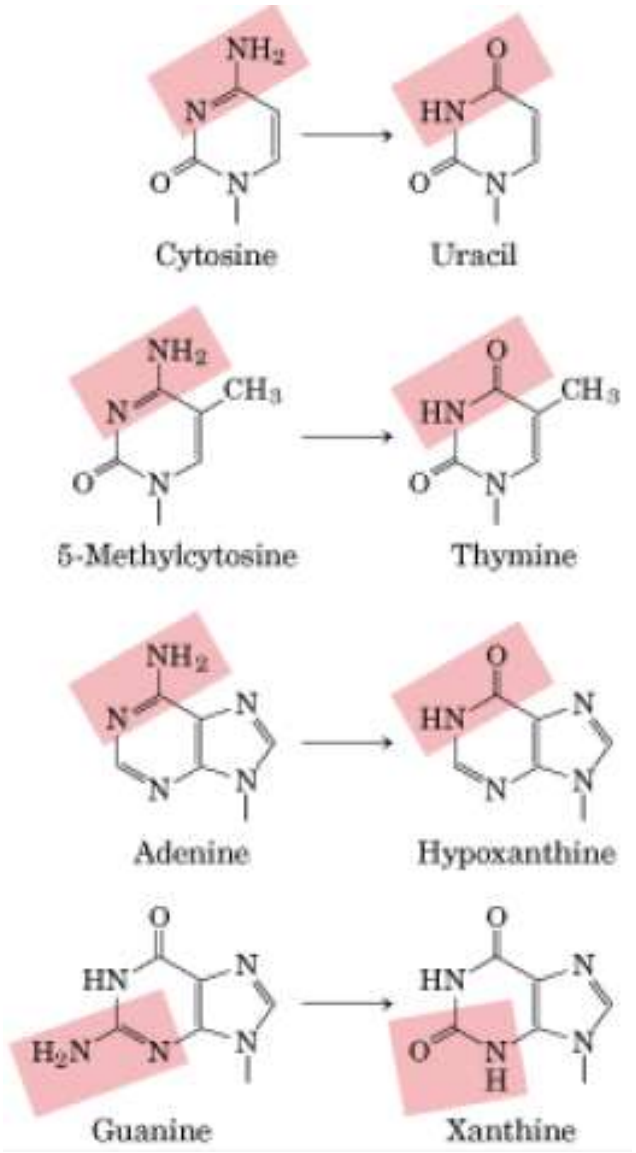
✓ **Bases nitrogenadas podem sofrer desaminação**

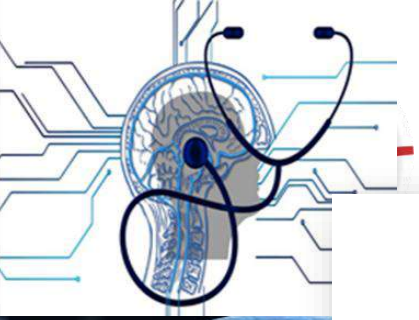
$NaNO_2$
Sodium nitrite

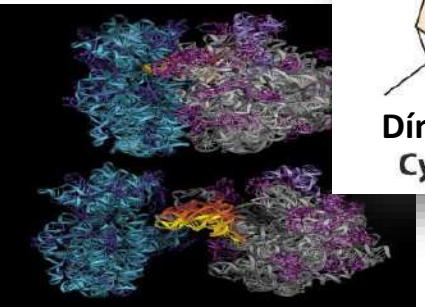
$NaNO_3$
Sodium nitrate



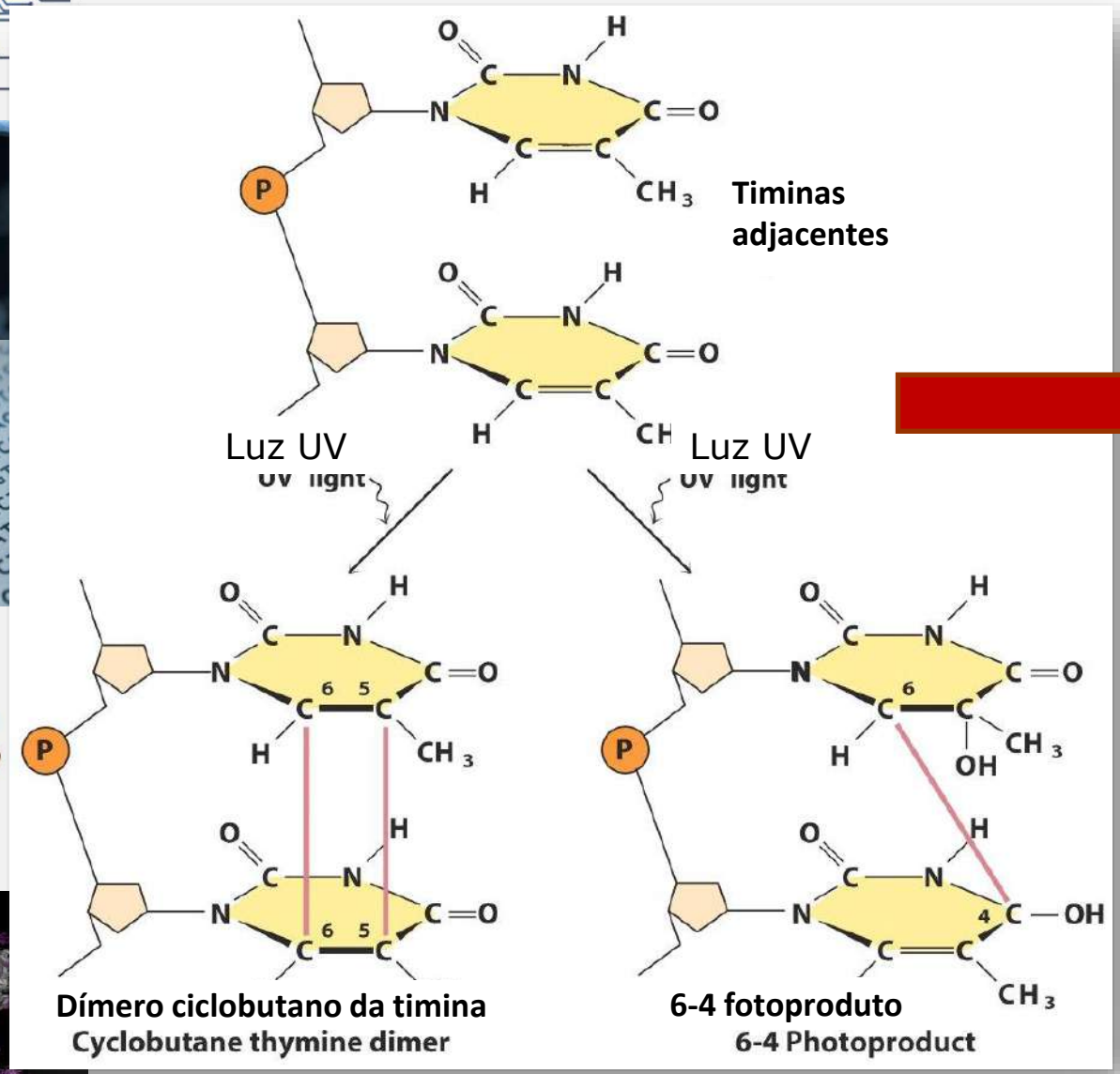
Nitrosamine

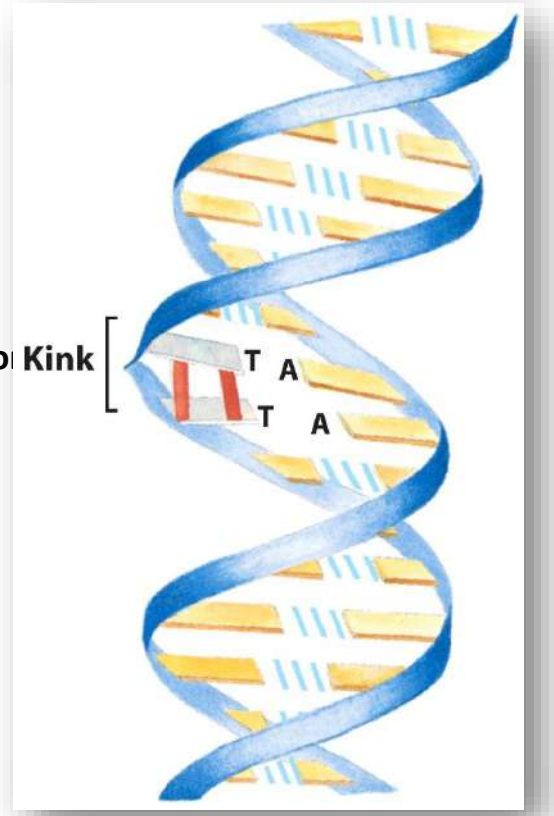


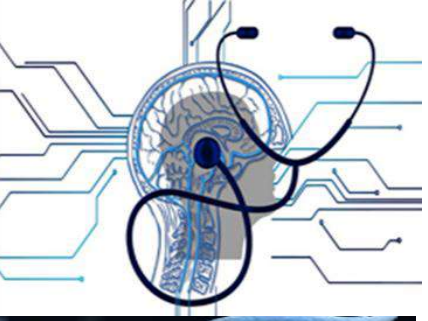


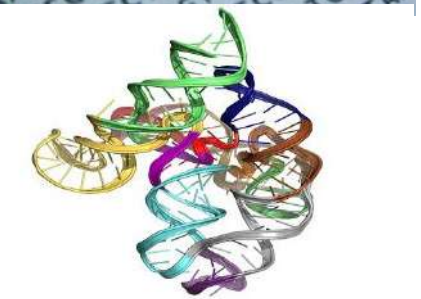


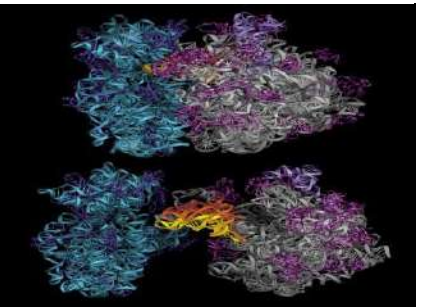
MUDANÇAS NAS ESTRUTURAS DAS BASES NITROGENADAS
LUZ UV





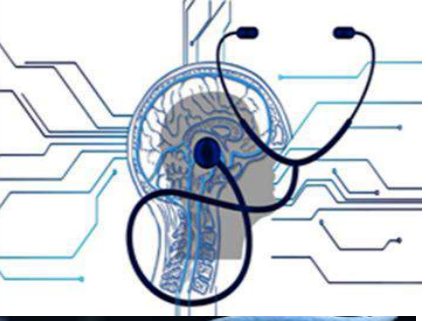


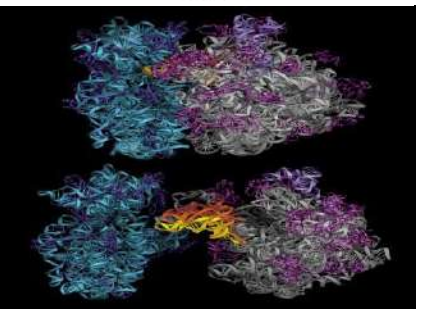




ALGUNS PRINCIPAIS EVENTOS QUE LEVARAM À DESCOBERTA DO DNA

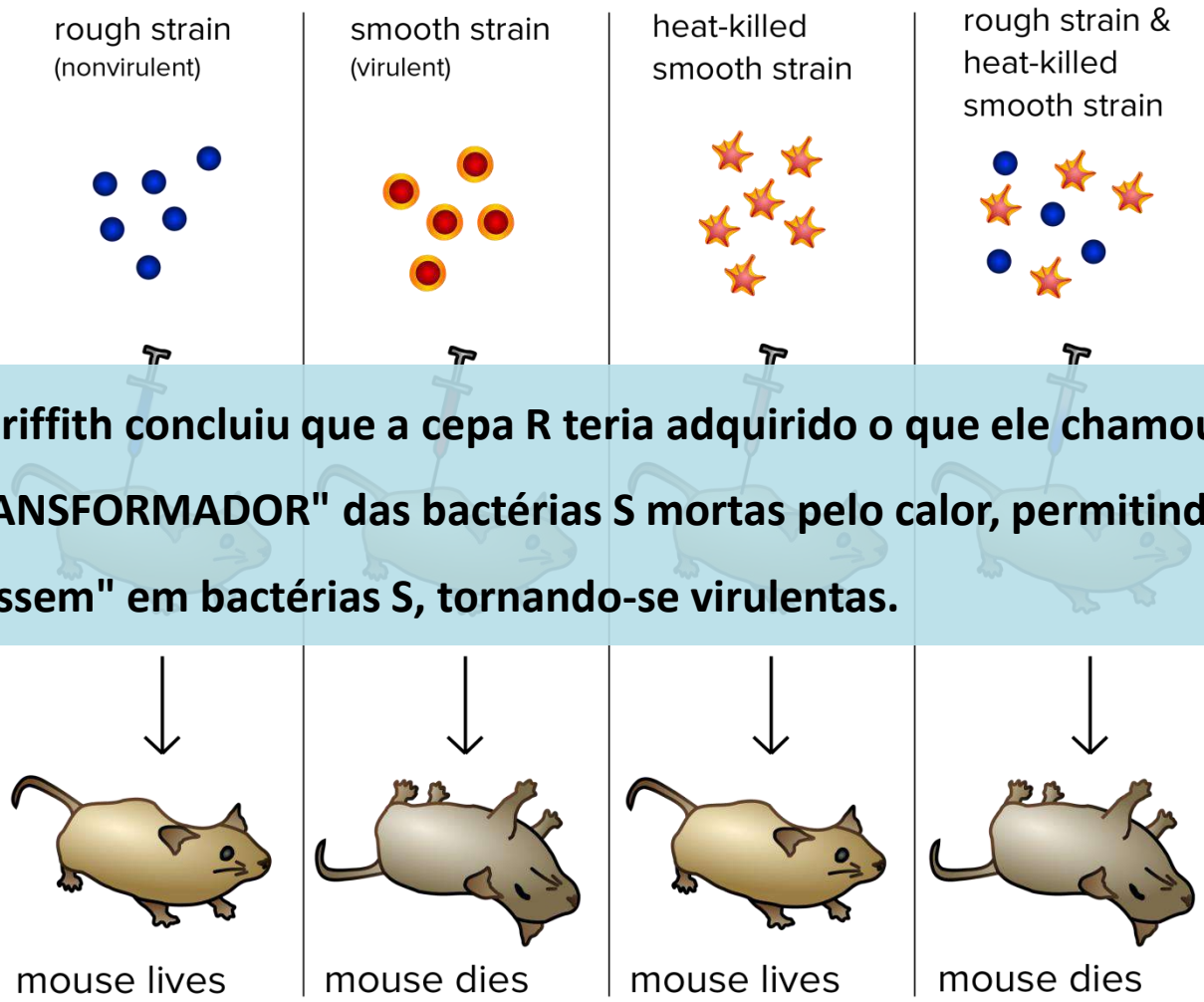
- ✓ **Friedrich Miescher, em 1868, descobre uma substância ácida extraída de glóbulos brancos amostras de pus de pacientes;**
- ✓ **A molécula é diferente das proteínas (contêm C, O, N, H e P)**
- ✓ **Miescher acreditava que as proteínas eram as moléculas responsáveis transmissão da hereditariedade**
- ✓ **Uma vez que as moléculas foram extraídas do núcleo, ele a chamou NUCLEINA (DNA)**



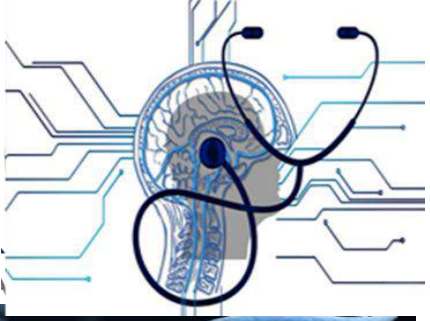


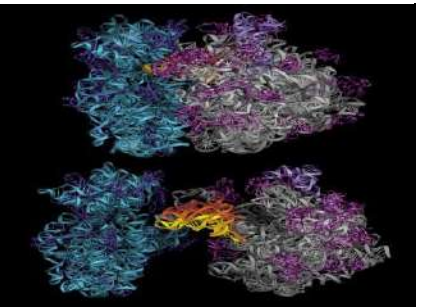
O EXPERIMENTO DE GRIFFITH (1928)

- ✓ **Uma série de experimentos utilizando a bactéria *Streptococcus pneumoniae* (cepa R ou rugosa - não virulenta e cepa S ou liso-virulenta) e ratos.**

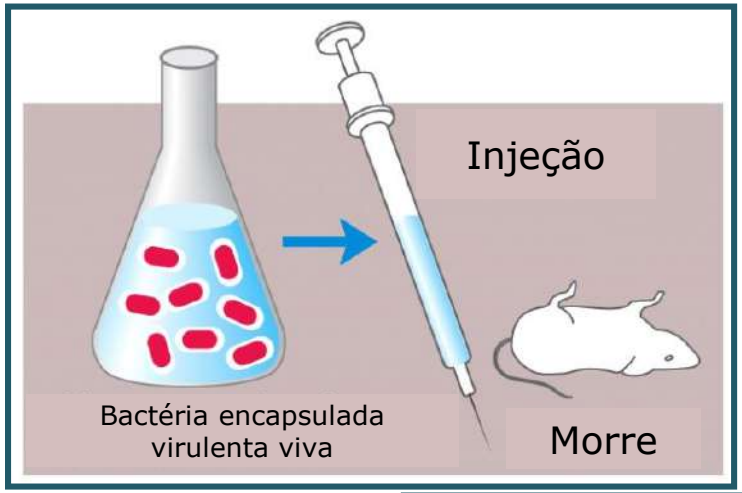


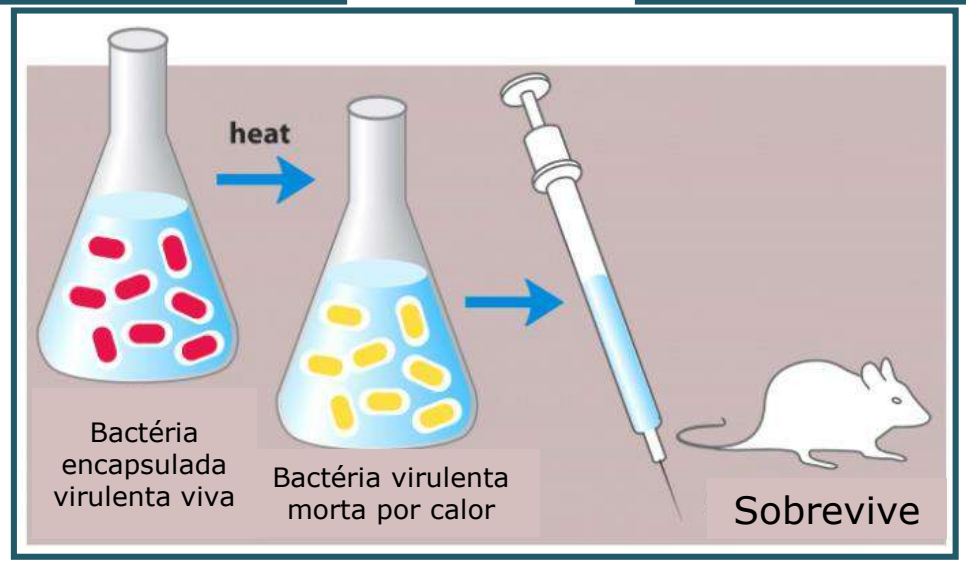
CONCLUSÃO: Griffith concluiu que a cepa R teria adquirido o que ele chamou de "PRINCÍPIO TRANSFORMADOR" das bactérias S mortas pelo calor, permitindo que elas "se transformassem" em bactérias S, tornando-se virulentas.

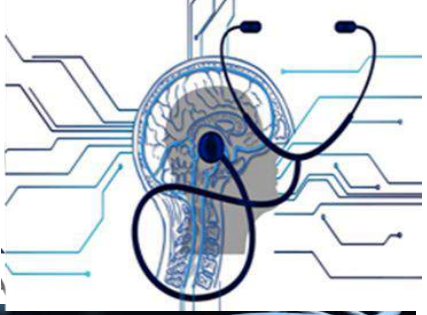


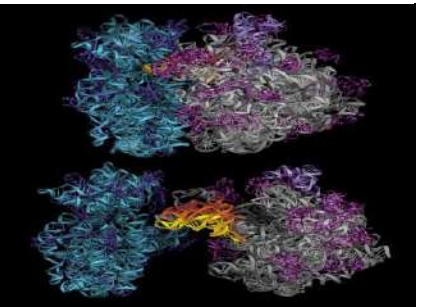


EXPERIMENTO DE AVERY-MACLEOD-MCCARTHY

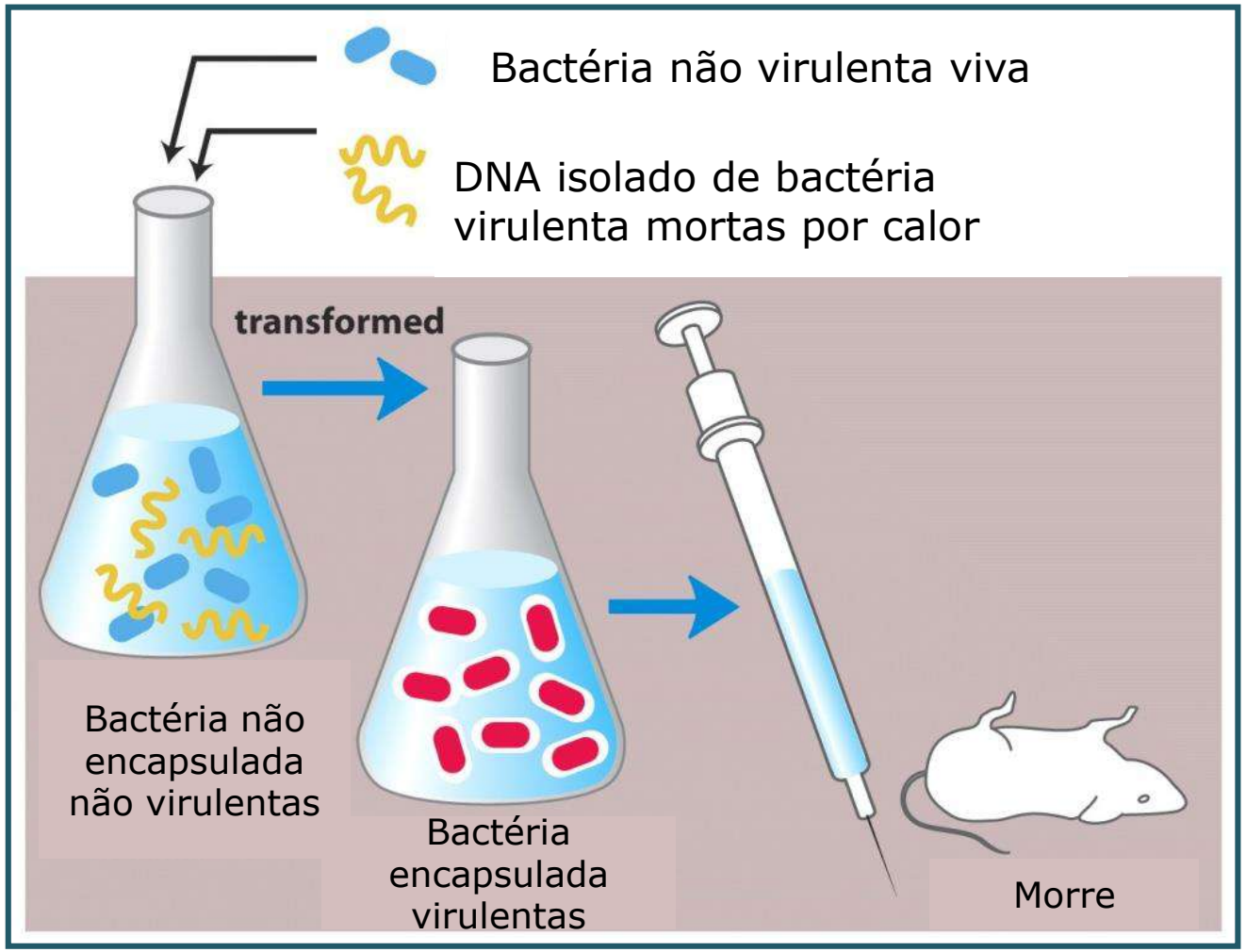


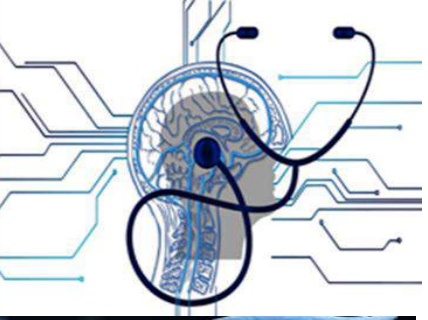


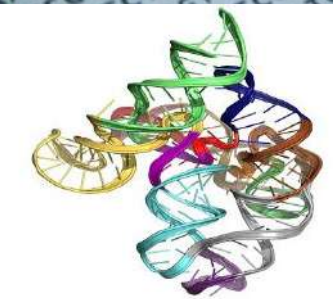


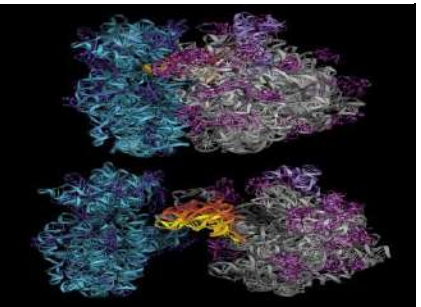


EXPERIMENTO DE AVERY-MACLEOD-MCCARTHY



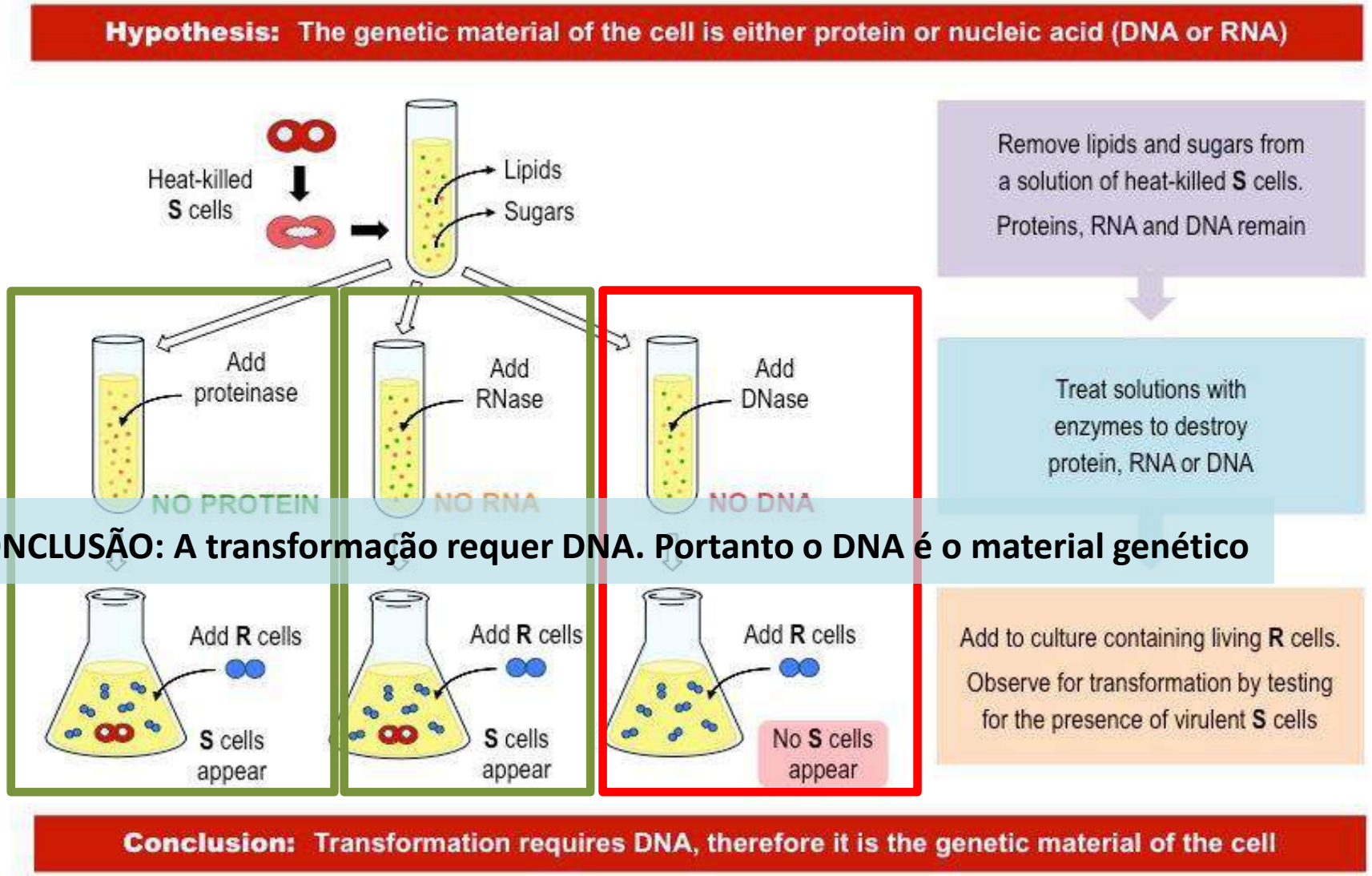




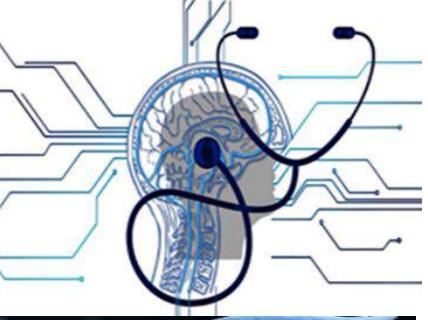


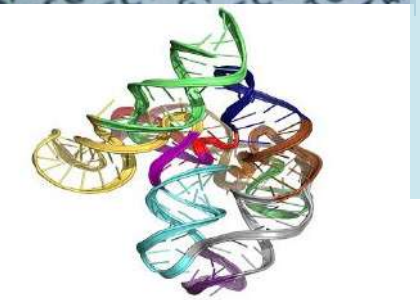
EXPERIMENTO DE AVERY, MACLEOD E MCCARTHY

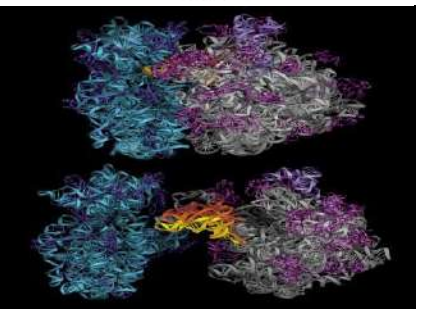
✓ ***Streptococcus pneumoniae (S cells - virulent e R cells-non-virulent)*** **e ratos.**



CONCLUSÃO: A transformação requer DNA. Portanto o DNA é o material genético



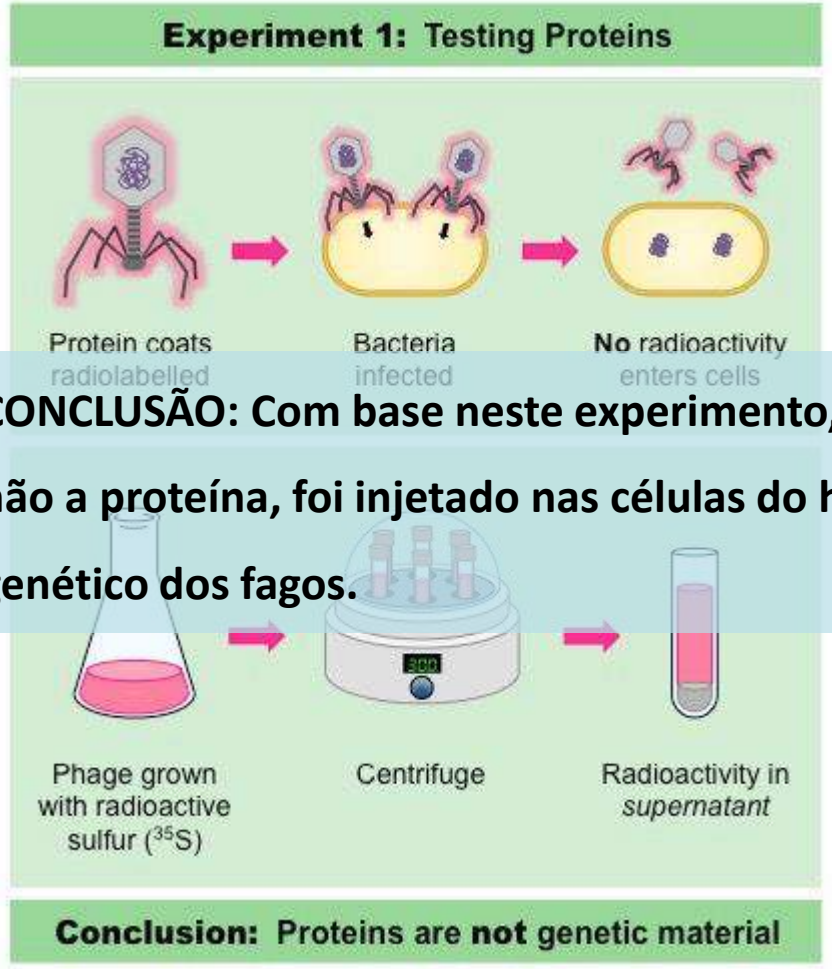




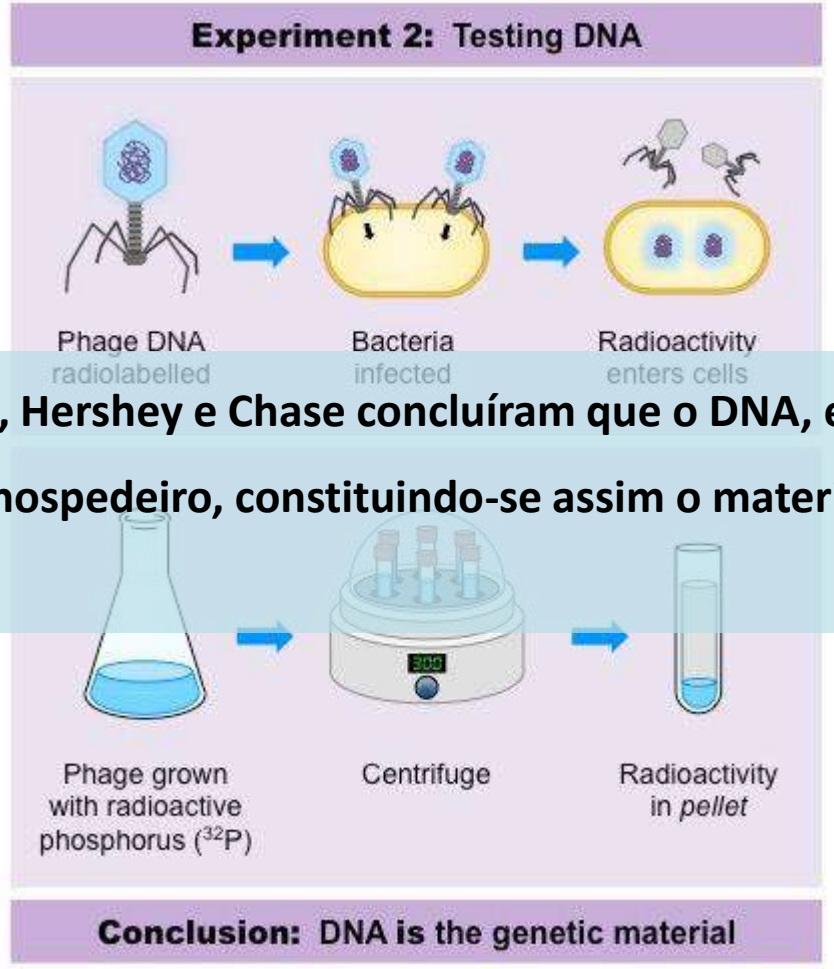
EXPERIMENTO DE HERSHEY E CHASE

✓ **Descobrir se o fago injeta proteína ou DNA dentro da célula hospederia**

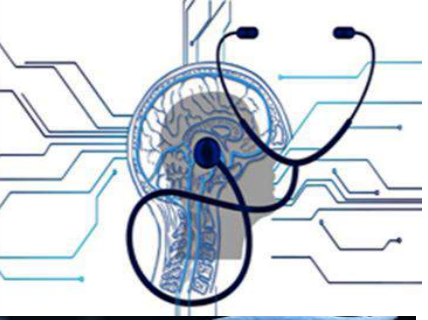
Teste 1: Proteína marcada (S^{32})

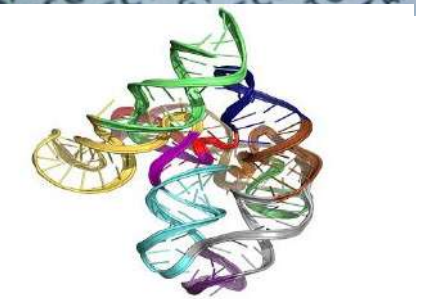


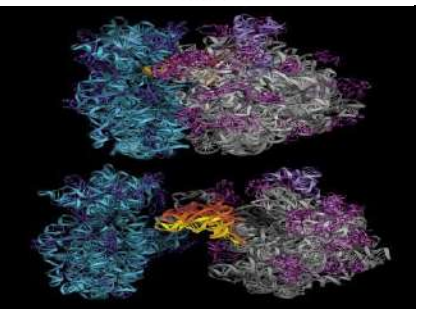
Teste 2: DNA marcado (P^{35})



CONCLUSÃO: Com base neste experimento, Hershey e Chase concluíram que o DNA, e não a proteína, foi injetado nas células do hospedeiro, constituindo-se assim o material genético dos fagos.





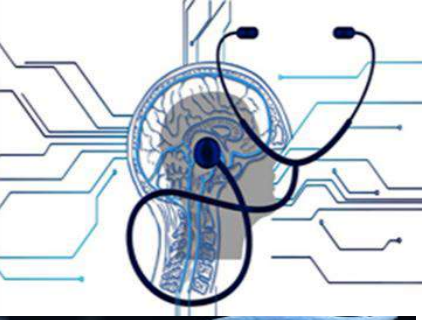


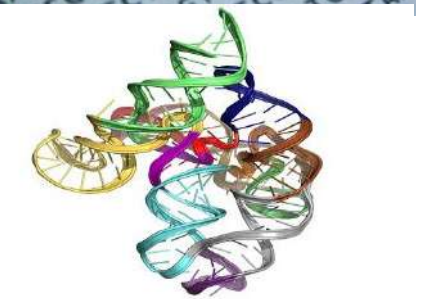
EXPERIMENTO DE ERWIN CHARGAFF BASES COMPLEMENTARES

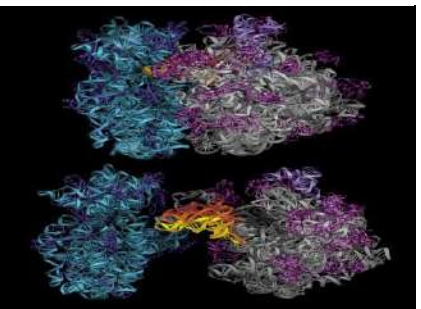
- ✓ **Chargaff melhorou muitas das técnicas bioquímicas para isolamento, purificação e quantificação de DNA de células vivas;**
- ✓ **Sabia-se que o DNA continha as quatro bases: A, G, C e T;**
- ✓ **Chargaff analisou a composição do DNA de muitas espécies diferentes.**

Composição de bases do DNA de vários organismos

ORGANISMO	% ADENINA	% TIMINA	% GUANINA	% CITOSINA
Streptococcus pneumoniae	29.8	31.6	20.5	18.0
Levedura	31.7	32.6	18.3	17.4
Células de salmão	29.7	29.1	20.8	20.4
Hemáceas de galinha	28.0	28.4	22.0	21.6
Hepatócito humano	30.3	30.3	19.5	19.9







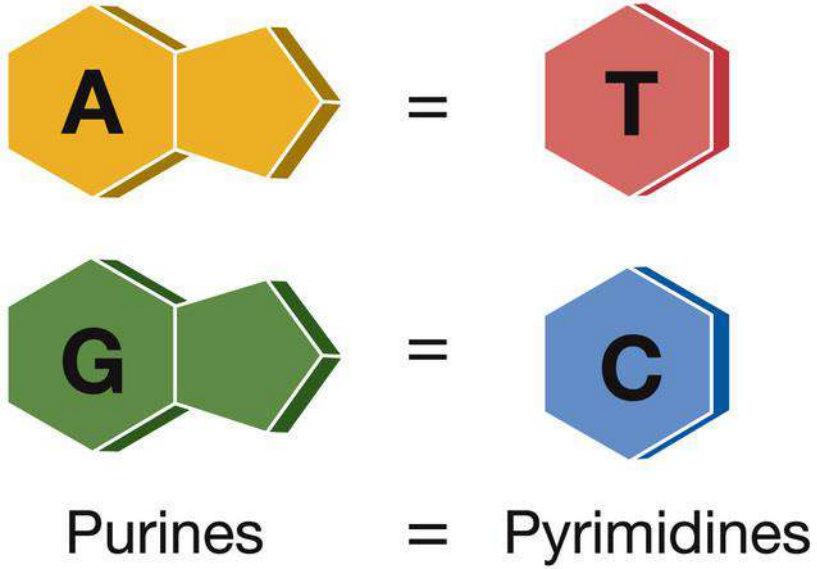
EXPERIMENTO DE ERWIN CHARGAFF : COMPLEMENTARIEDADE DE BASES

INTERPRETAÇÃO DO DADOS: REGRA DE CHARGAFF

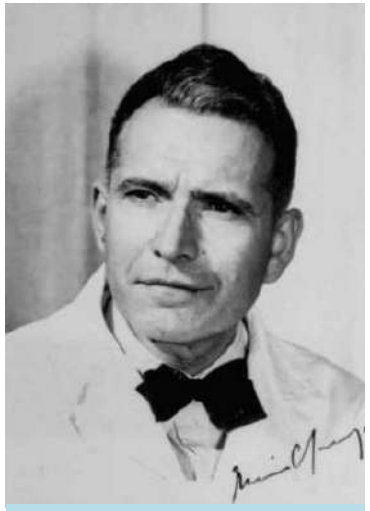
✓ **Observação final**

Porcentagem de Adenina (%A) = Porcentagem de Timina (%T)

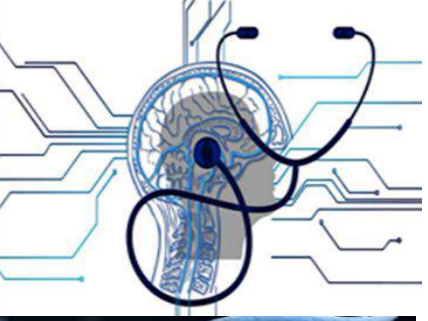
Porcentagem de Citosina (%C) = Porcentagem de Guanina (%G)

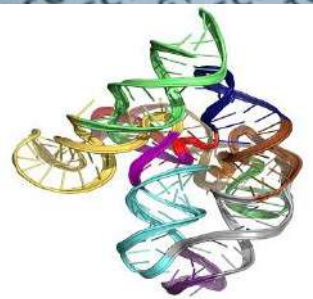


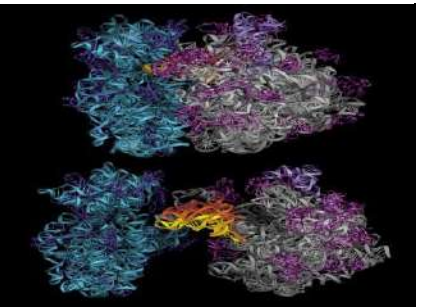
A + G = T + C = 50%



Erwin Chargaff (1905-2002)

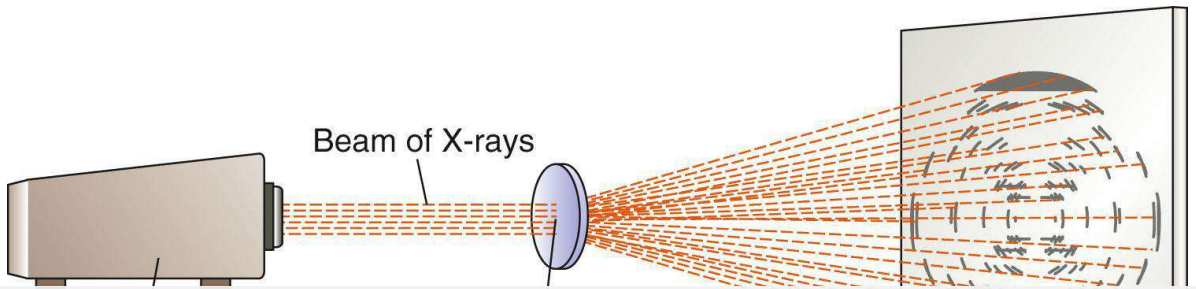


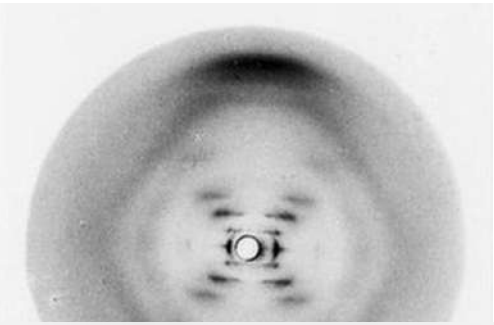




ROSALIND FRANKLIN (DULPA HÉLICE DO DNA)

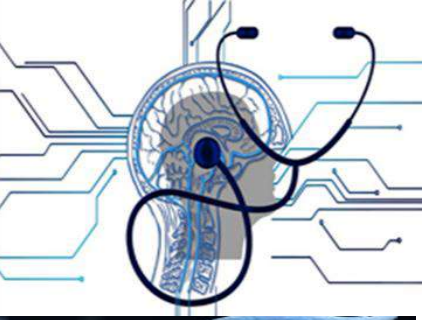
- ✓ **Trabalhava no laboratório de Maurice Wilkins.**
- ✓ **Avanços no uso da difração de raios X como técnica para estudo do DNA**

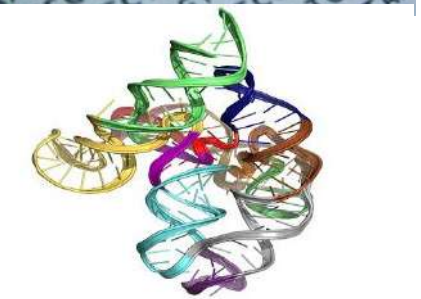


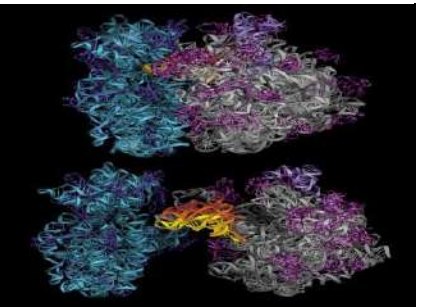


O padrão de difração sugeriu várias características estruturais do DNA:

- ✓ **Formato helicoidal;**
- ✓ **Mais de 1 fita**
- ✓ **10 pares de bases por volta na hélice**
- ✓ **Moléculas helicoidais com duas periodicidades ao longo de seu maior eixo (3,4 nm e 34 nm)**

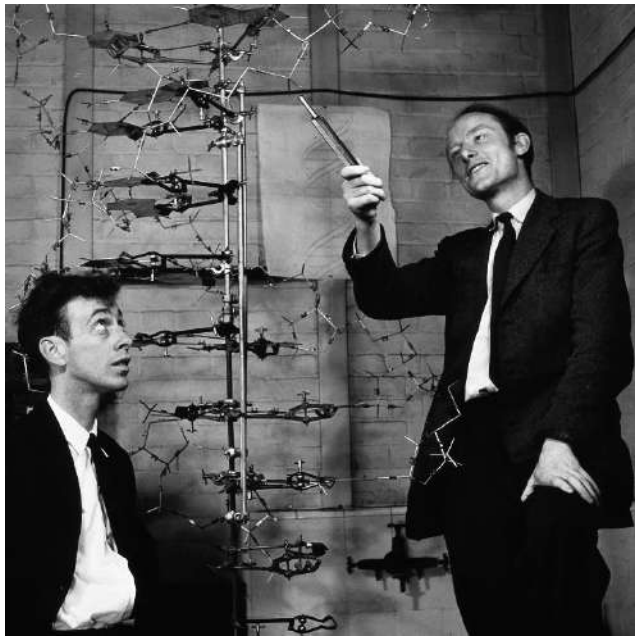


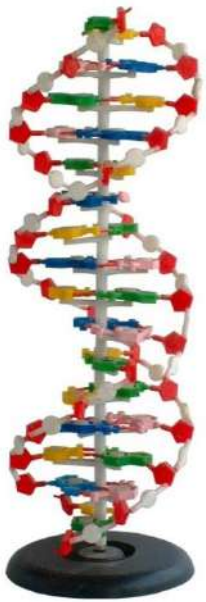


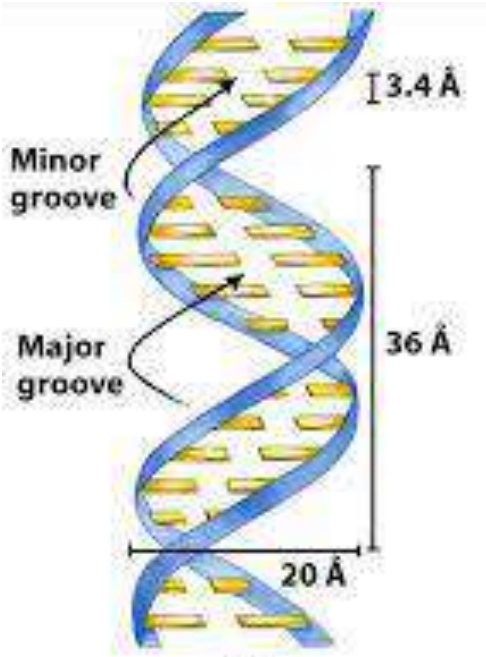


WATSON & CRICK: O MODELO DE DUPLA HÉLICE DO DNA (1953)

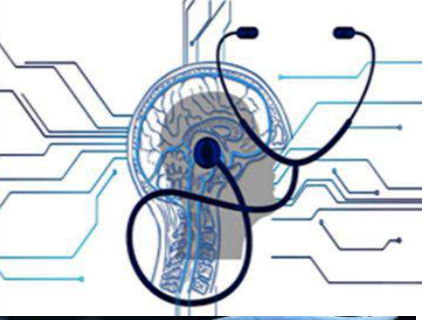
James Watson e Francis Crick, deduziram a estrutura tridimensional da molécula de DNA à partir dos resultados de Chargaff e Franklin e Wilkins.

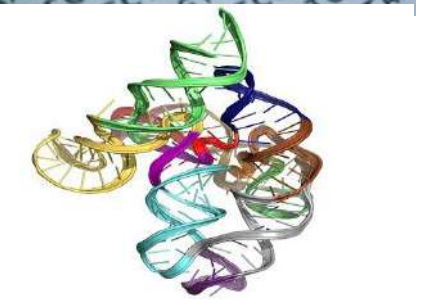


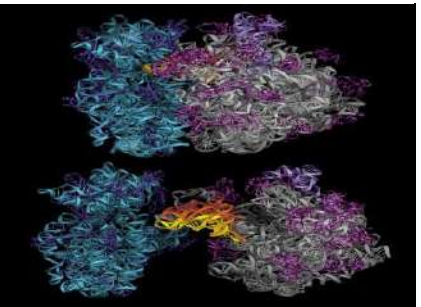




Eles deduziram a estrutura do DNA através de modelos moleculares, levando em conta os resultados de pesquisas anteriores. Receberam o Prêmio Nobel de 1962 por descobrir a estrutura molecular do DNA.

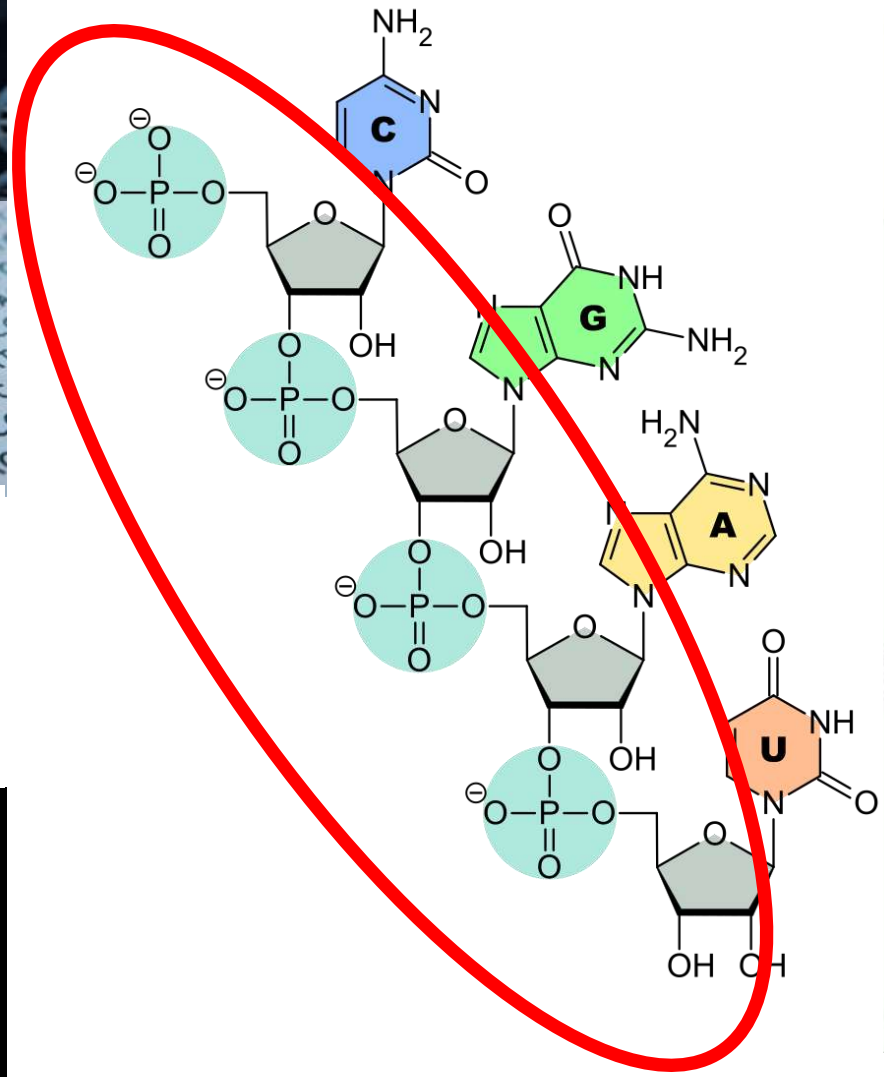


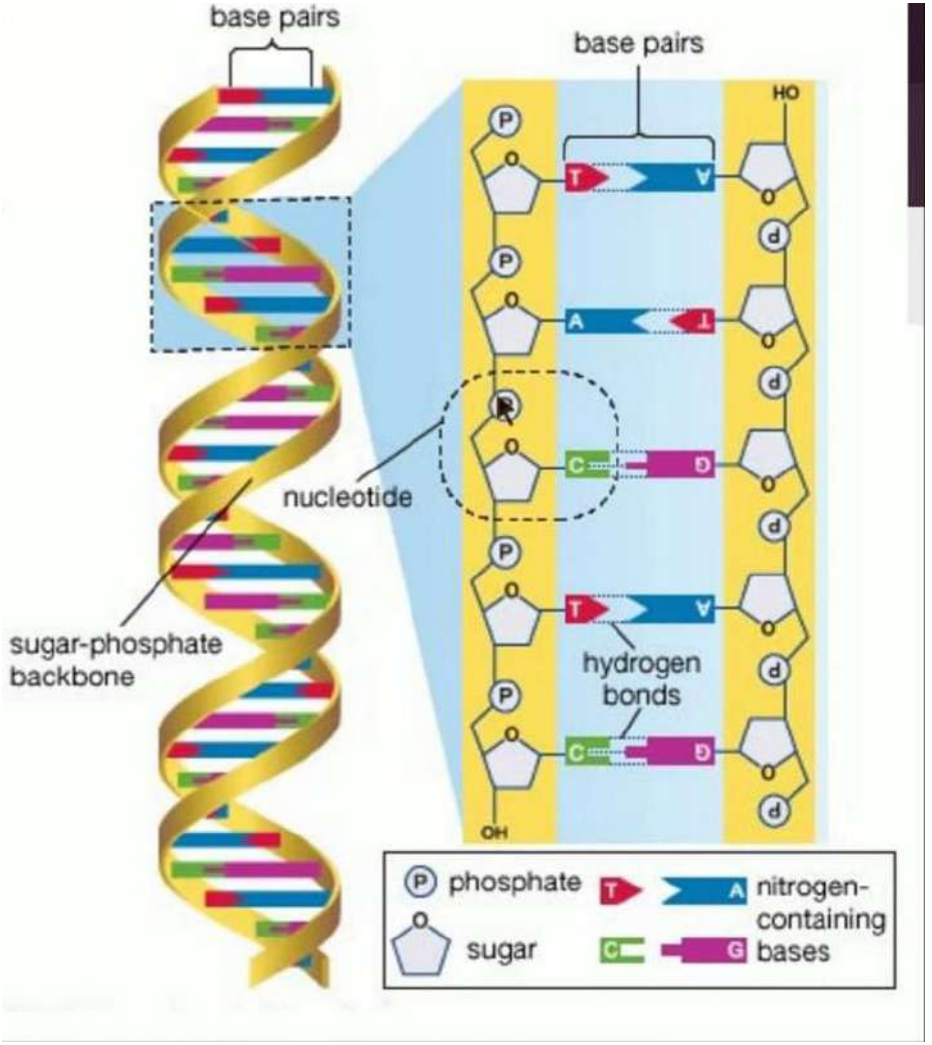


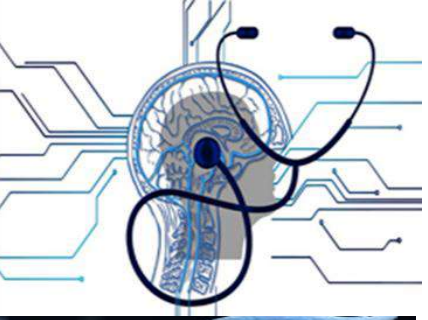


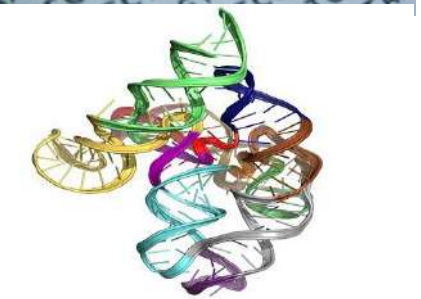
PRINCIPAIS CARACTERÍSTICAS DA DUPLA HÉLICE DO DNA

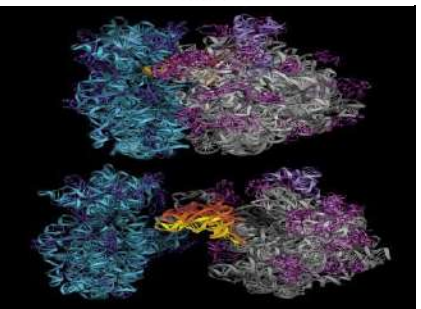
1. Cadeia alternada de pentose-fosfato ligados por ligações fosfodiéster





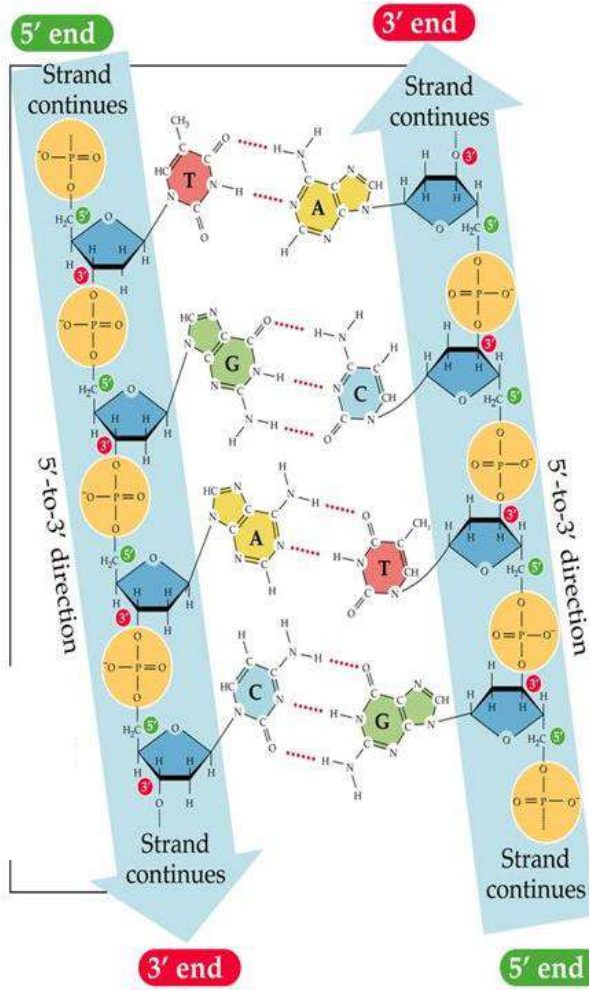


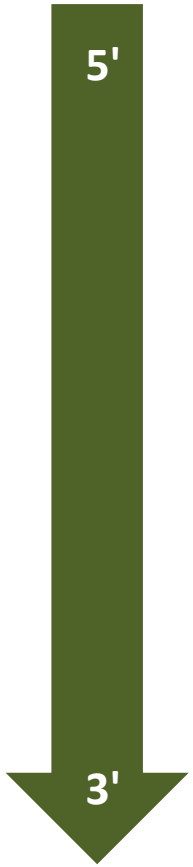


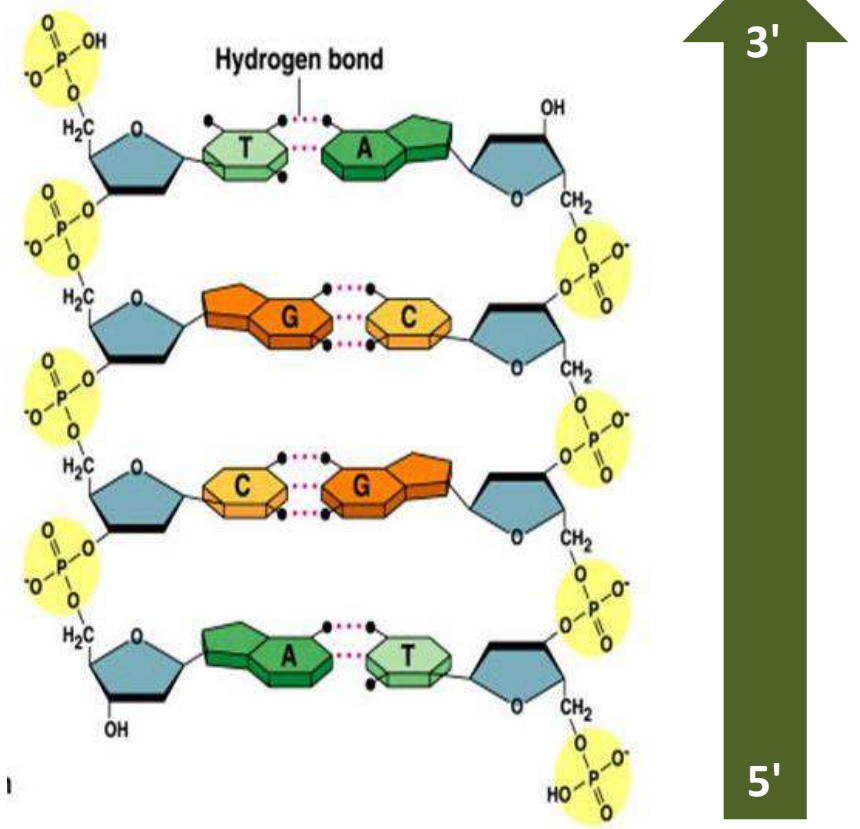


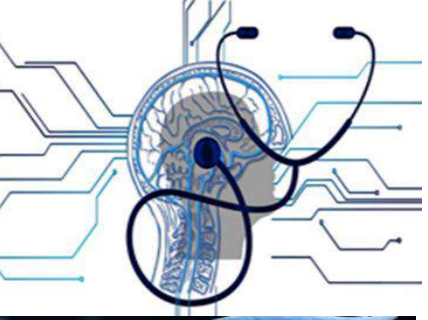
PRINCIPAIS CARACTERÍSTICAS DA DUPLA HÉLICE DO DNA

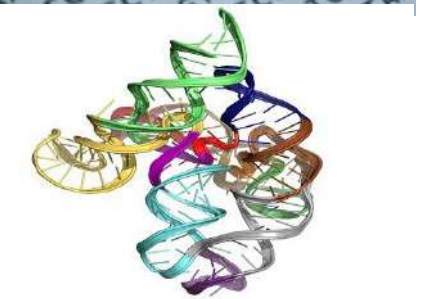
2. As duas cadeias são anti-paralelas. Um apresentada polaridade 5'→3 e a outra 3'→5‘.

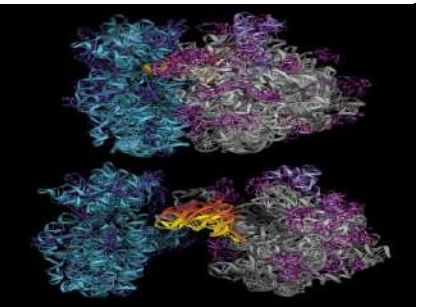










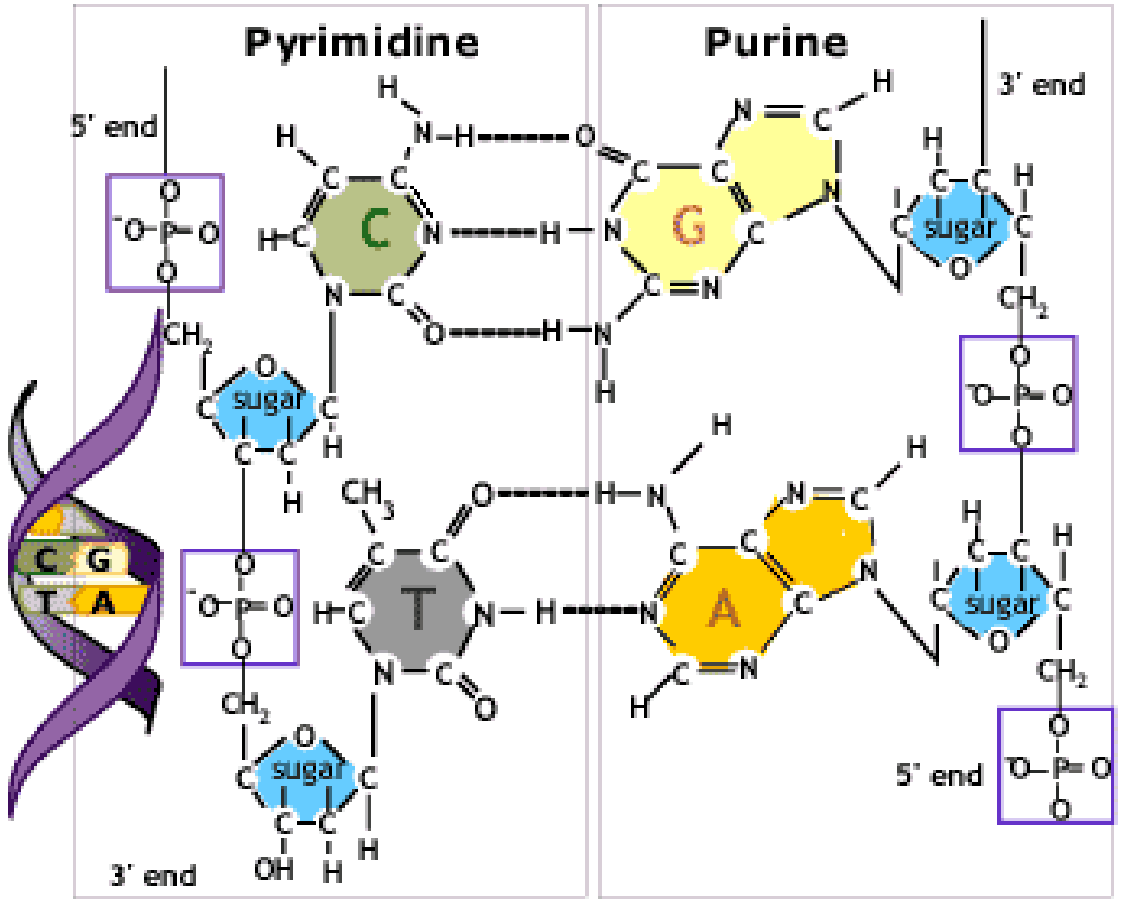


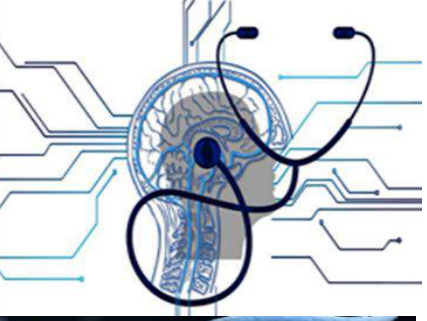
PRINCIPAIS CARACTERÍSTICAS DA DUPLA HÉLICE DO DNA

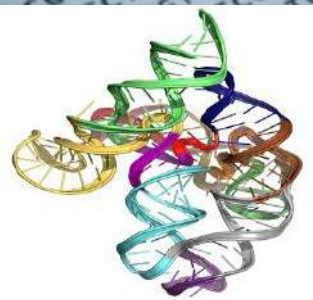
3. Ligações de hidrogênio entre as bases mantêm as duas cadeias juntas

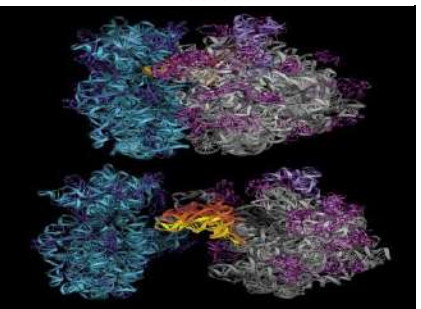
A – T : 2 ligações de hidrogênio

G – C: 3 ligações de hidrogênio



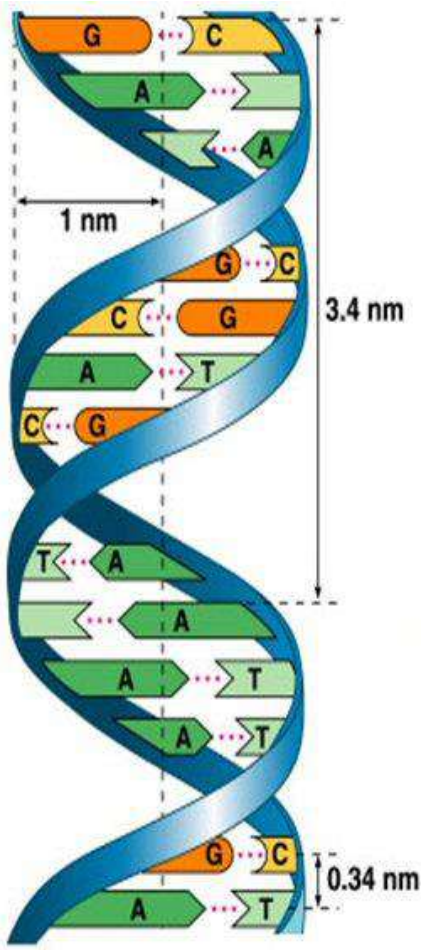


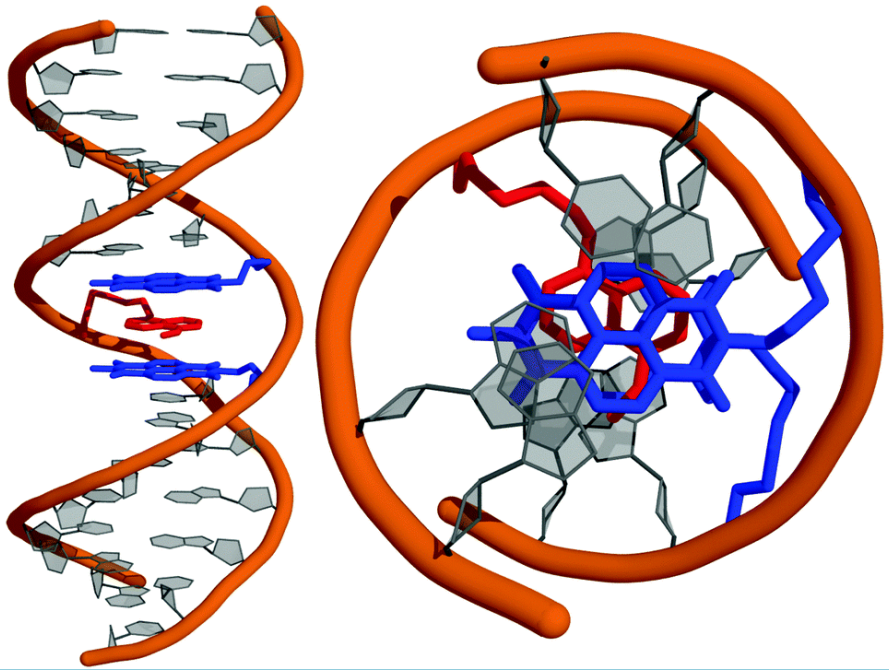




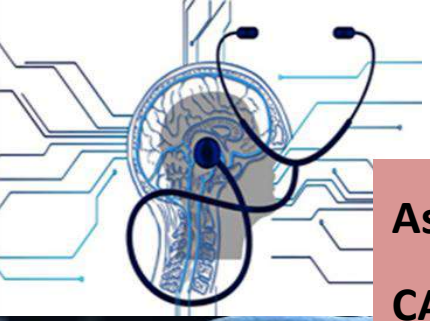
PRINCIPAIS CARACTERÍSTICAS DA DUPLA HÉLICE DO DNA

4. As duas cadeias são orientadas para direita no sentido horário. O passo da hélice é de 3,4 nm e há aproximadamente 10 pb em cada volta. Consequentemente, a distância entre pb em uma hélice é de aproximadamente 0.34nm



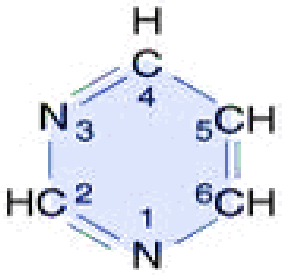


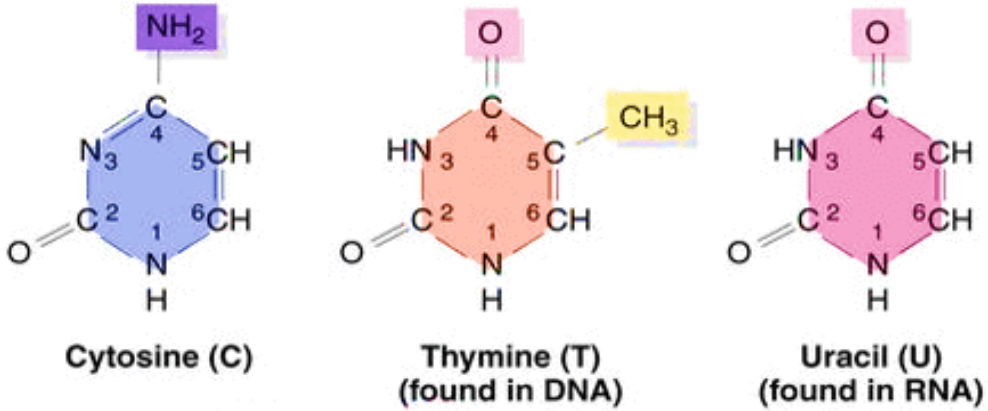
Forças de empilhamento das bases são as principais forças estabilizadoras da dupla hélice do DNA

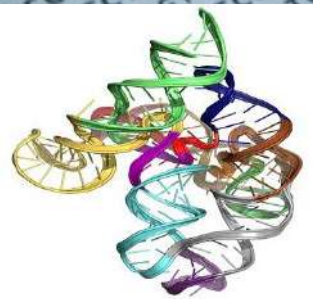


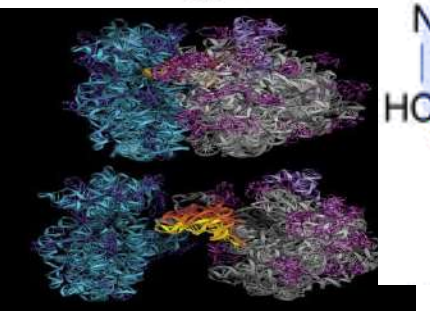
HIDROFOBICIDADE E O EMPILHAMENTO DAS BASES

As BASES PIRIMÍDICAS são formadas por uma cadeia fechada com quatro átomos de CARBONO e dois de NITROGÊNIO: CITOSINA (C), TIMINA (T), URACIL (U).

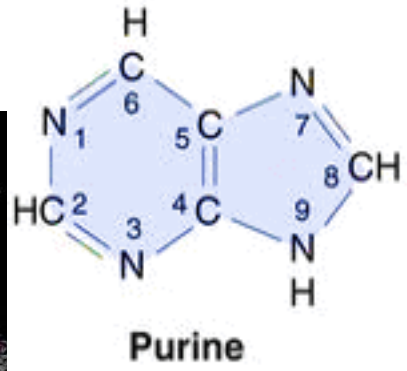


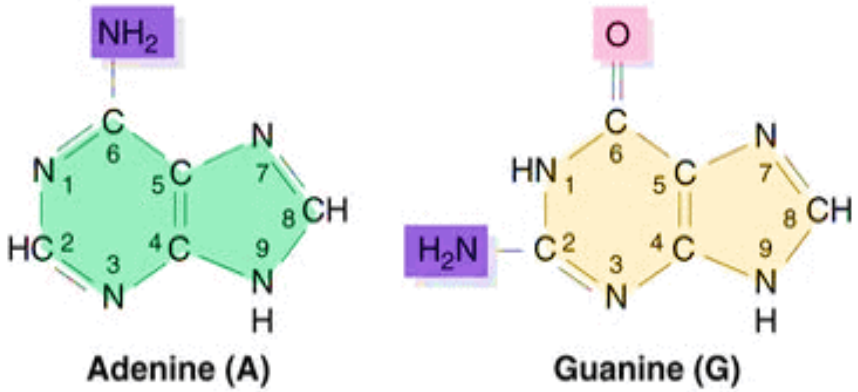


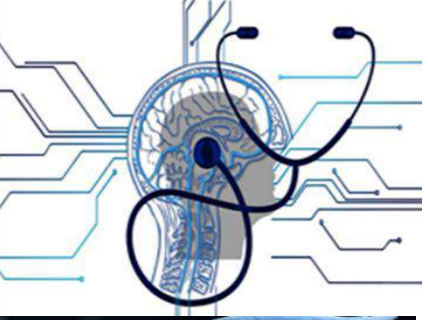


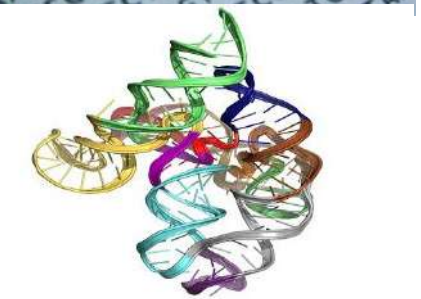


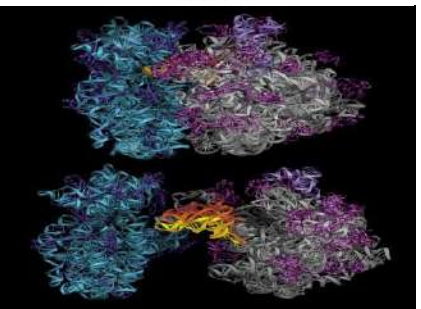
As PURINAS são formadas por duas cadeias fechadas: ADENINA (A) ou GUANINA (G).







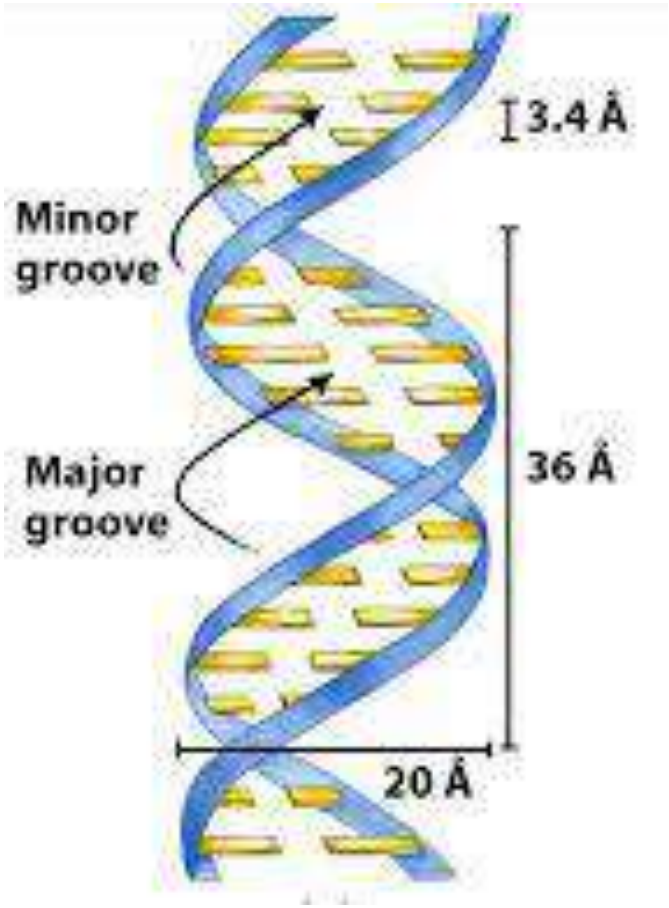


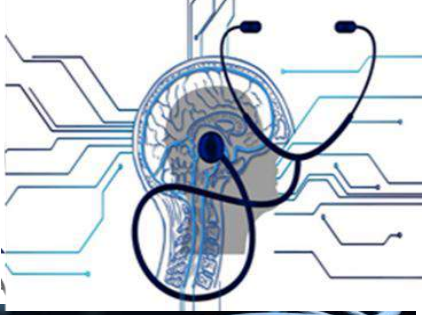


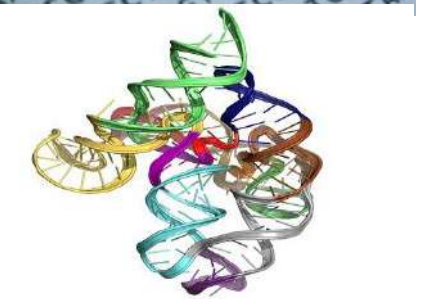
PRINCIPAIS CARACTERÍSTICAS DA DUPLA HÉLICE DO DNA

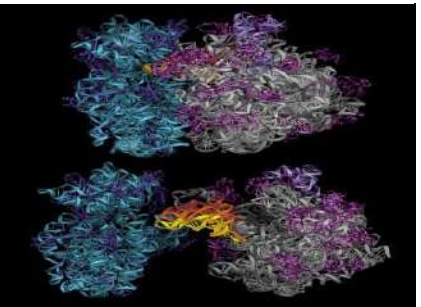
5. Presença de 2 sulcos assimétricos na hélice dupla do DNA

✓ **Sulcos atual como sítios para o reconhecimento por proteínas;**

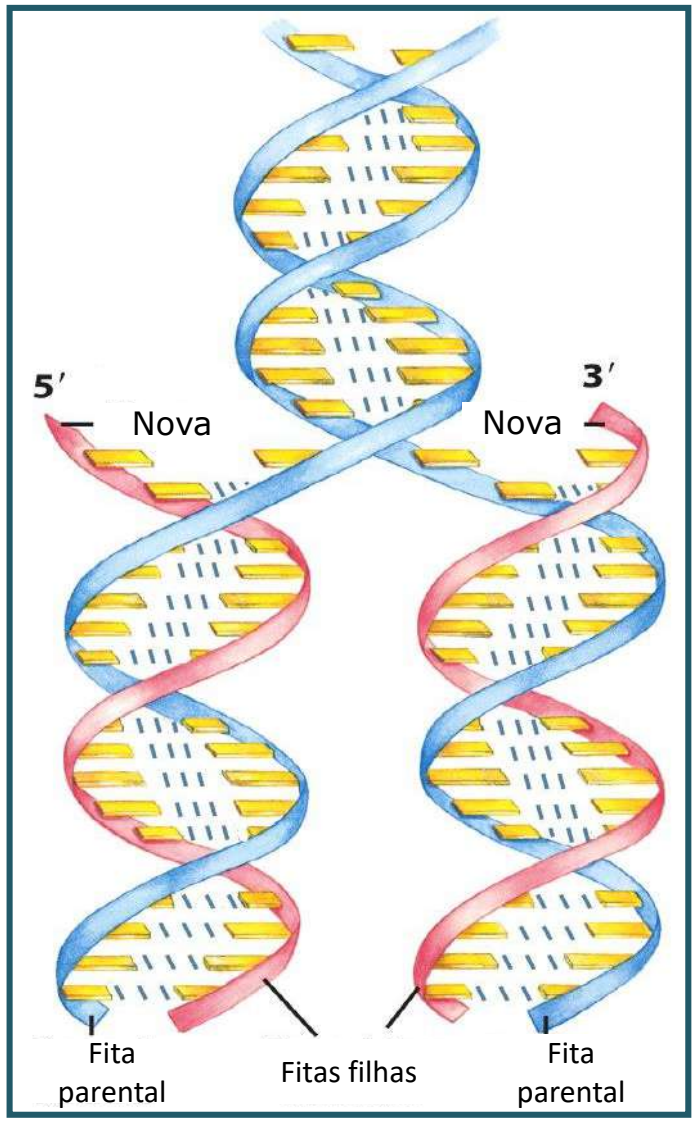


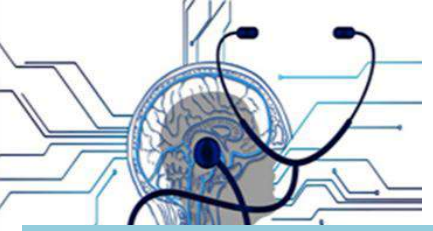






REPLICAÇÃO DO DNA É SEMICONSERVATIVA

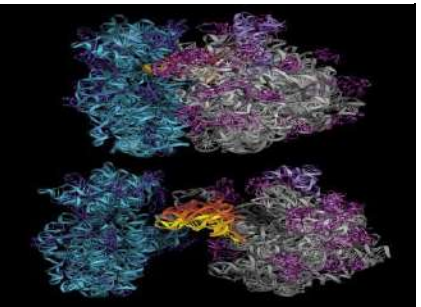


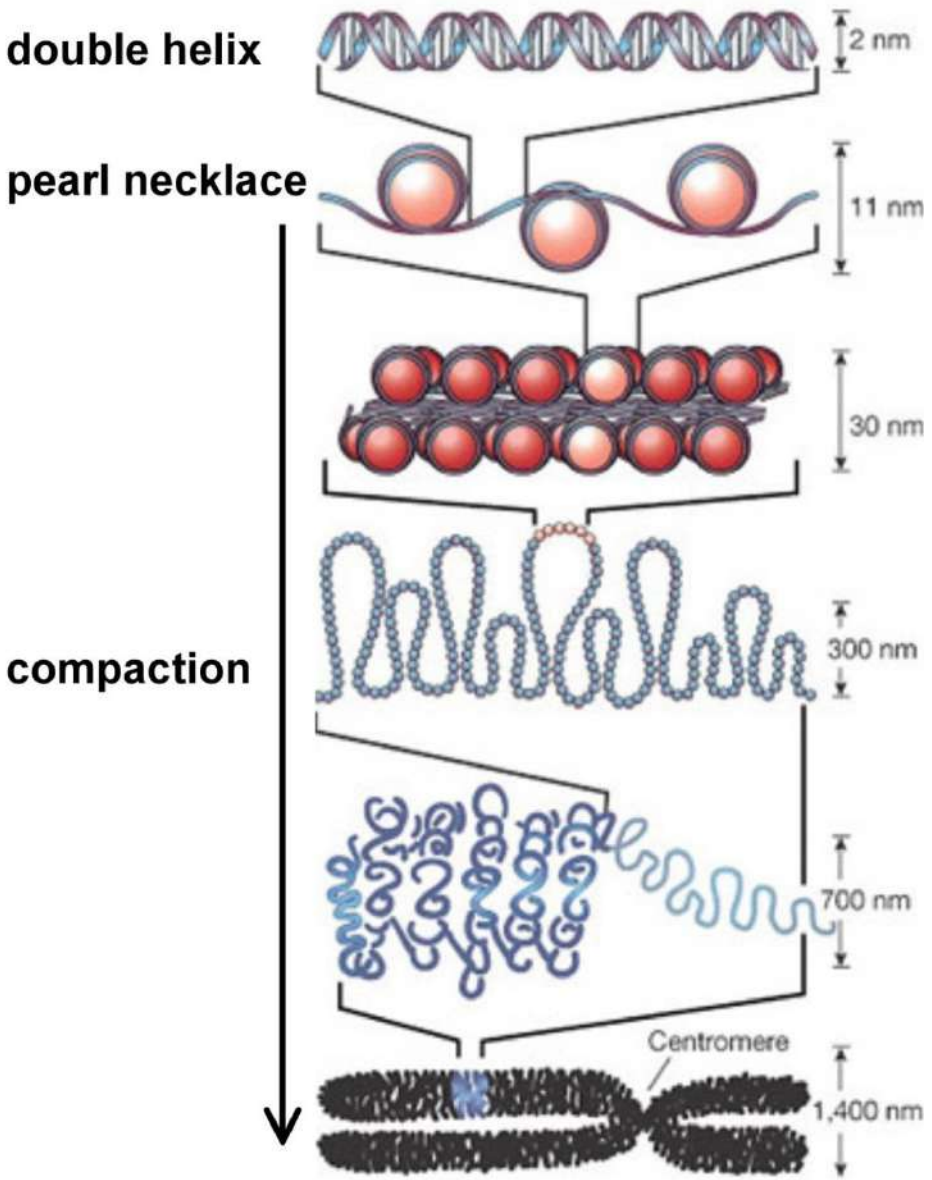


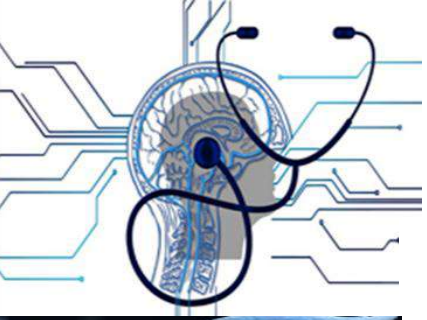
ESTRUTURA DA CROMATINA: COMPACTAÇÃO DO DNA

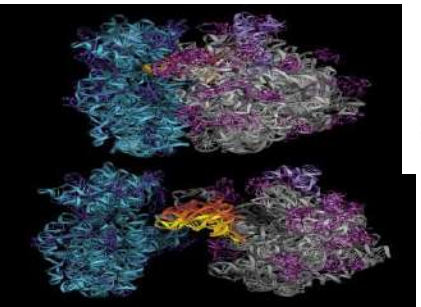
- ✓ **Genoma humano: 3 metros!!!**
- ✓ **Nucleosomo: unidade organizacional básica da cromatinva;**
- ✓ **Eucariotos: DNA associado à histonas;**
- ✓ **Histonas: abundância de Lis e Arg**

1. **H1**
2. **H2A**
3. **H2B**
4. **H3**
5. **H4**

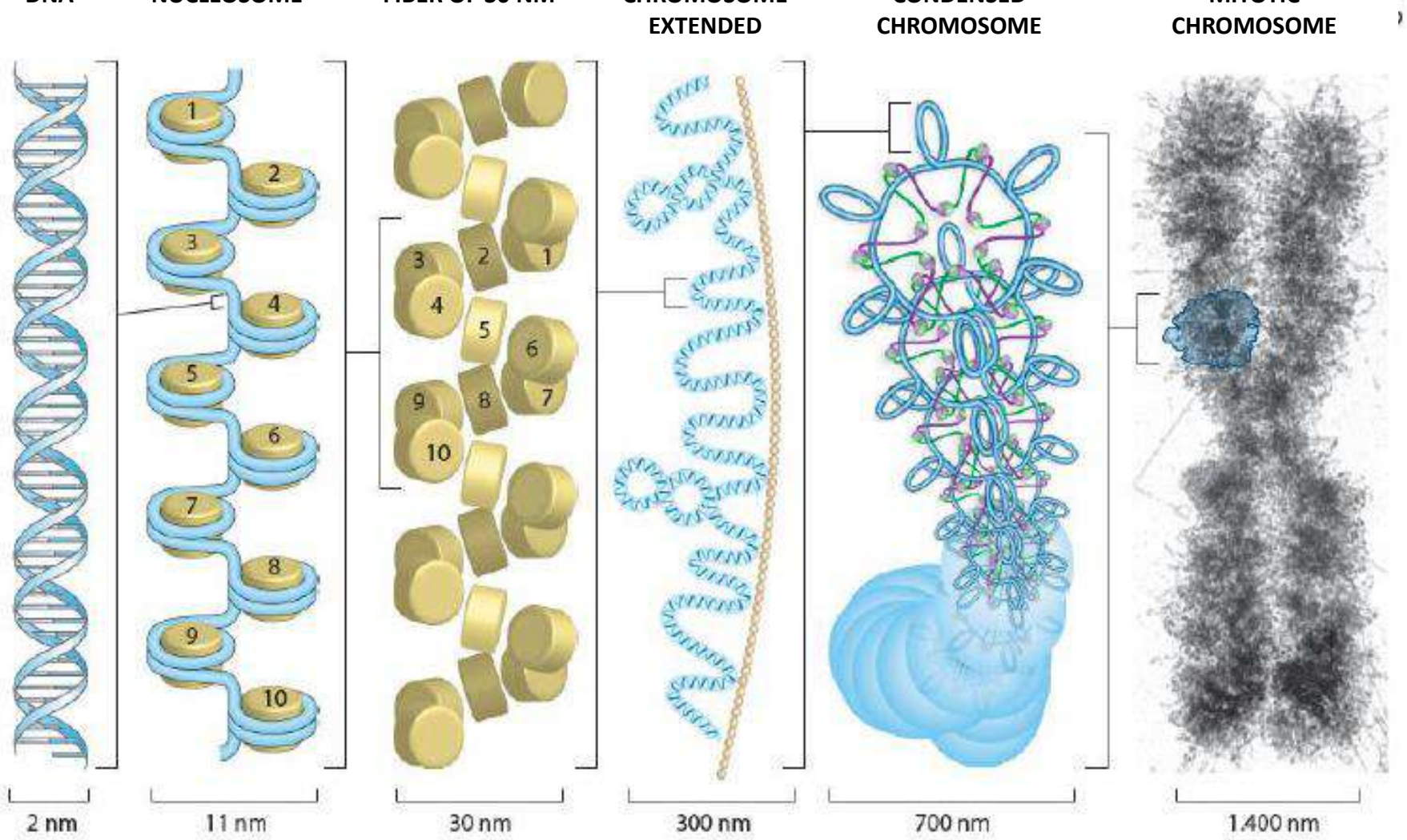


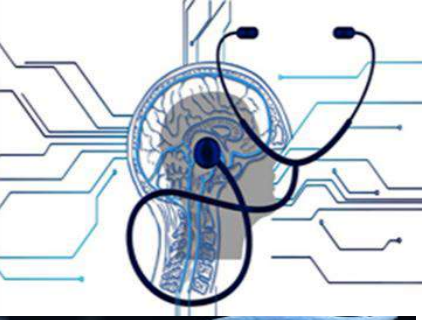


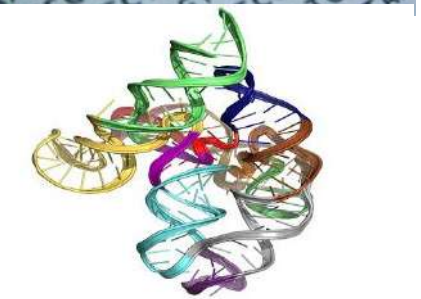


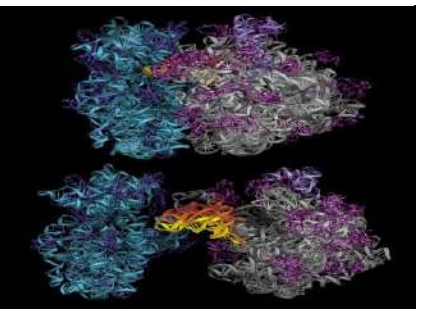


DNA EM CÉLULAS EUCARIÓTICAS



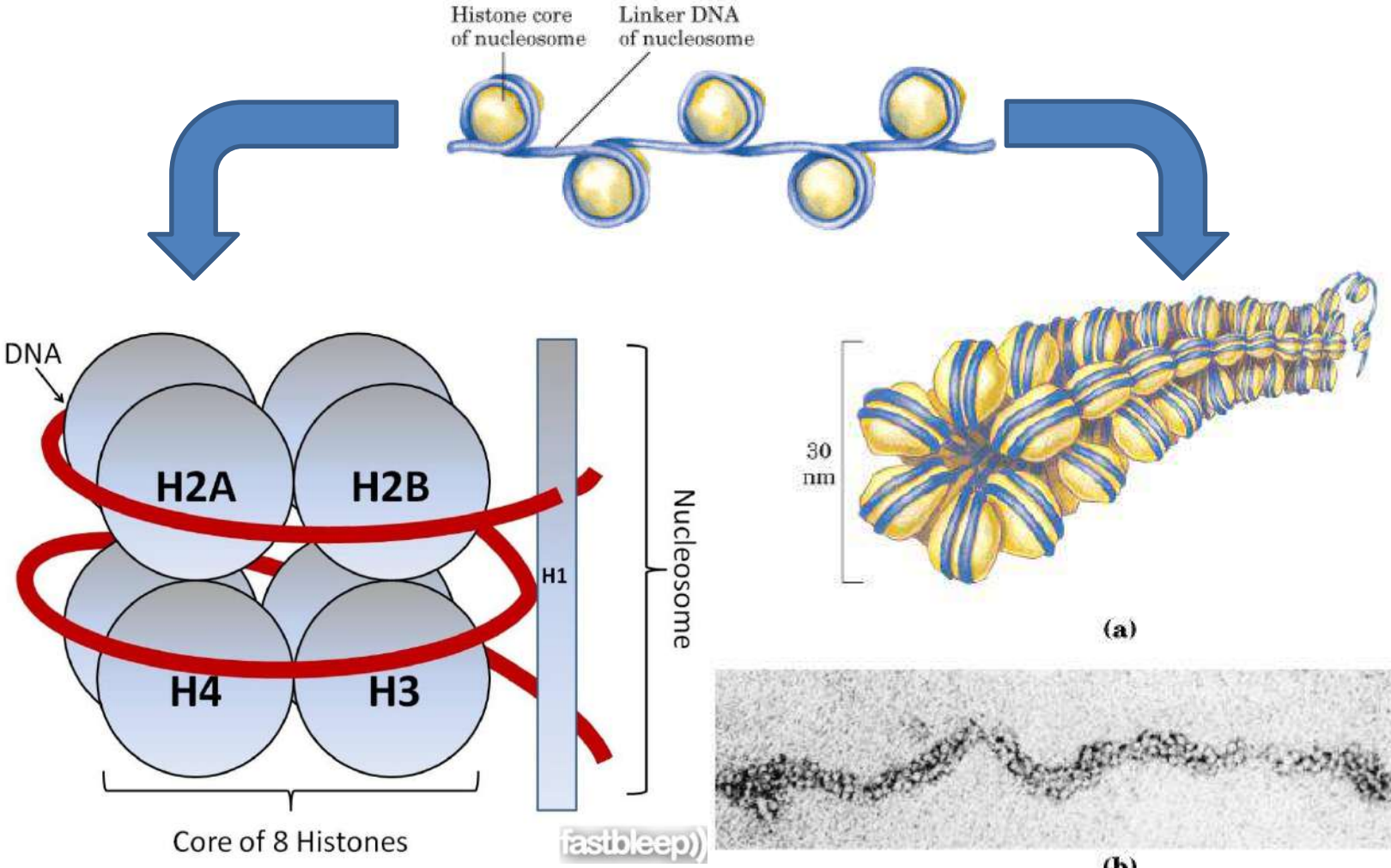


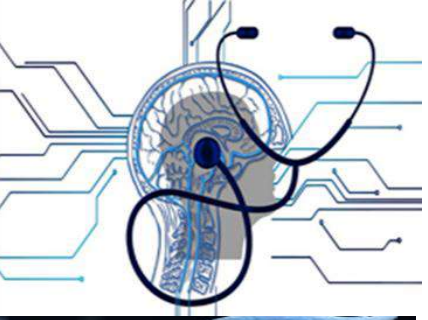


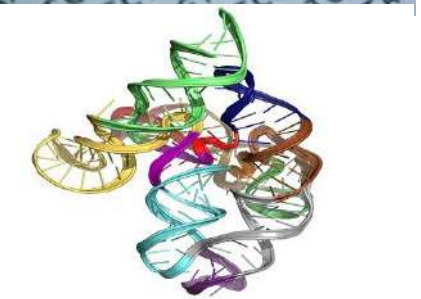


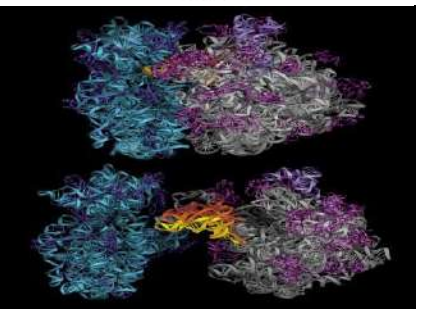
DNA EM CÉLULAS EUCARIÓTICAS

- ✓ **Histonas H1, H2A, H2B, H3 e H4 empacotam o DNA formando o NUCLEOSSOMO e a FIBRA de 30 nm.**



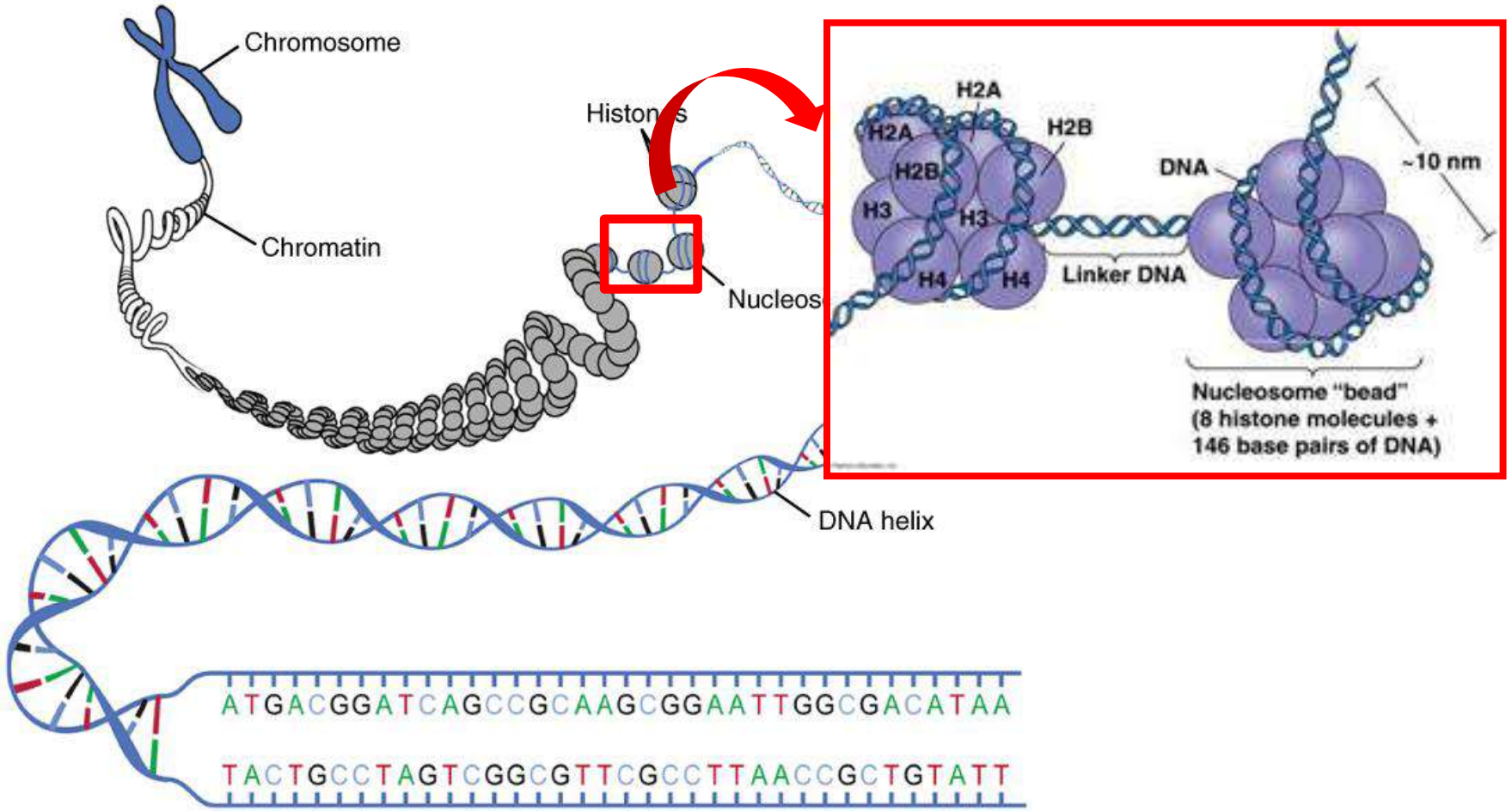


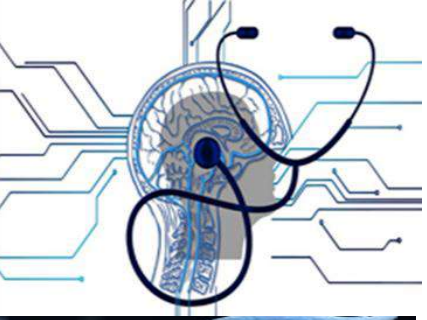


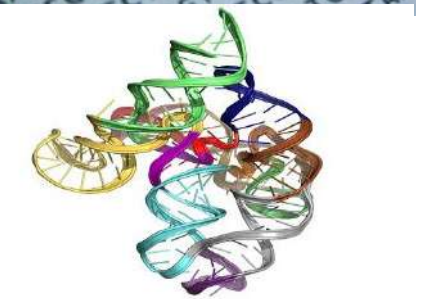


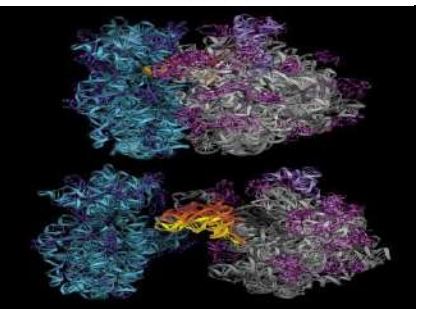
HISTONAS DO DNA

NUCLEOSOMO: Unidade básica de compactação do DNA composta por segmento dupla fita enrolada em torno de um núcleo protéico (2 cópias de cada 4 tipos de histonas).

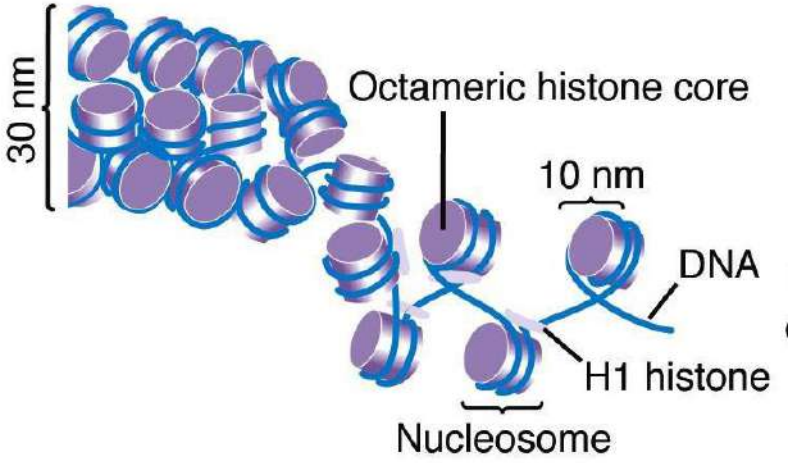




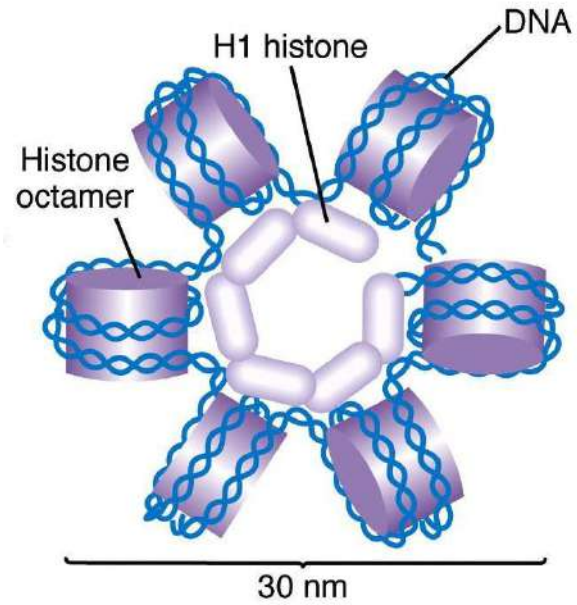


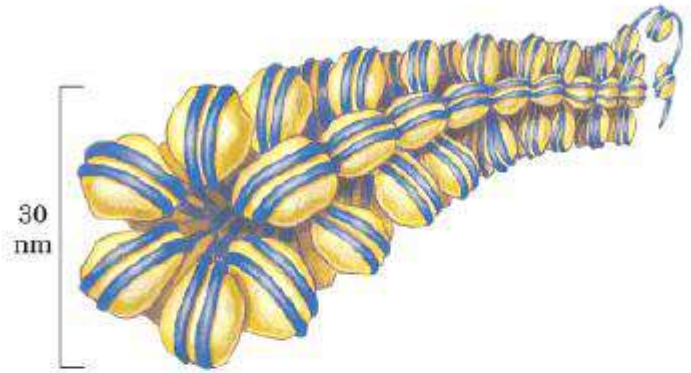


DNA EM CÉLULAS EUCARIÓTICAS

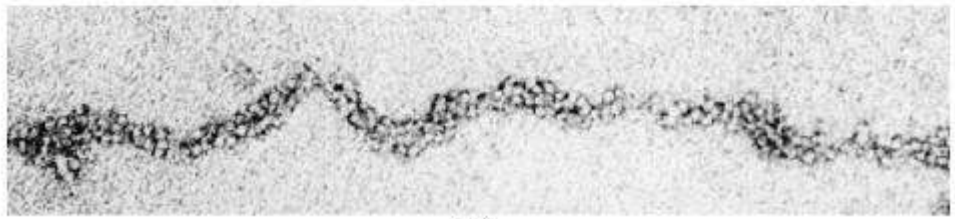


>HistonA H2B
MPPQPSGKAIKKAGKAQKAVRTTDKKKKKRRRKE
SFSIIKVLKQVHPDTGVSSKAMSIMNSFVNDIFERIA
AEASRLAHNKRSTITSREVQTAVRLLLPGELAKHAVS
EGTKAVTKiTSSK

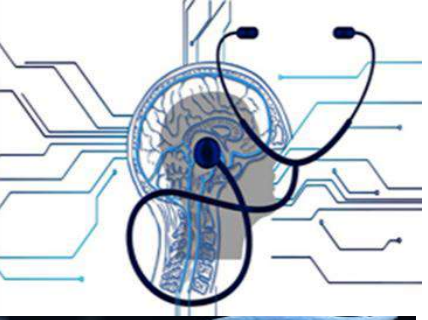


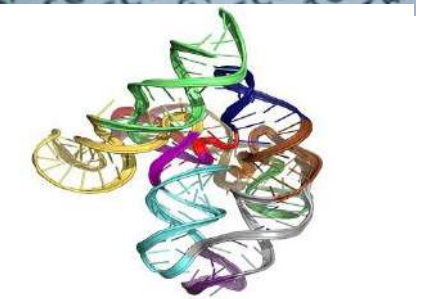


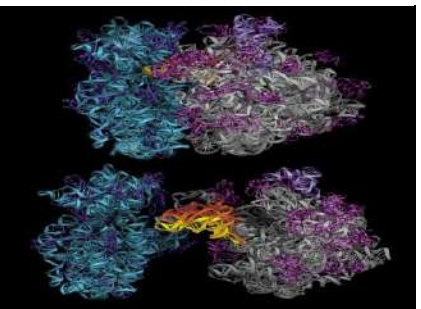
(a)



(b)

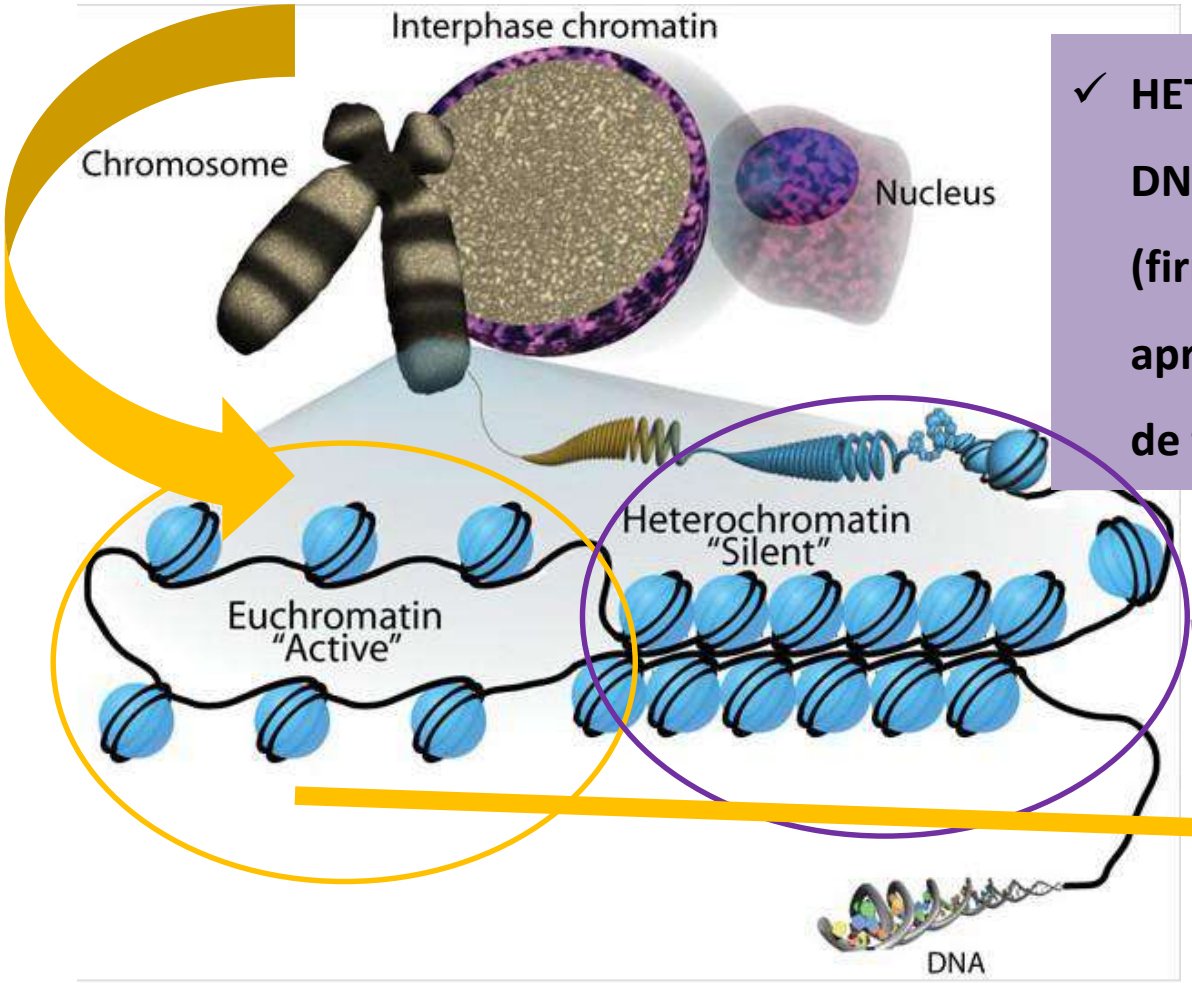




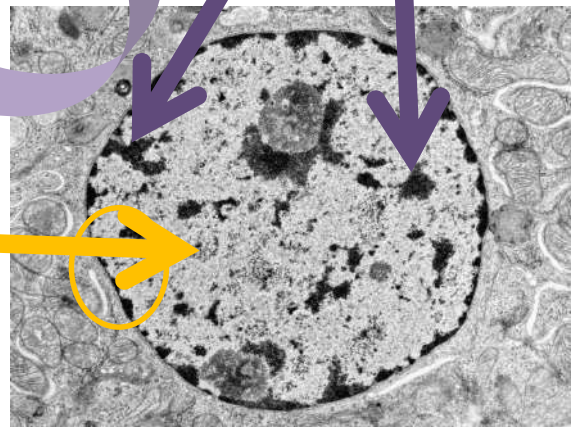


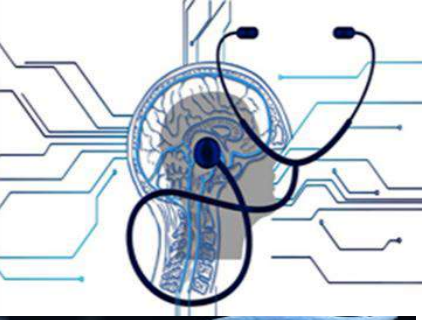
CROMATINA: EUCROMATINA E HETEROCROMATINA

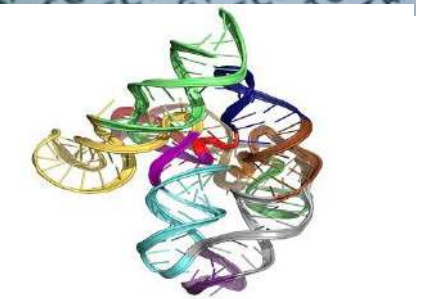
✓ **EUCROMATINA: região altamente descompactaa (DNA livre de histonas) que apresenta alta taxa de transcrição**

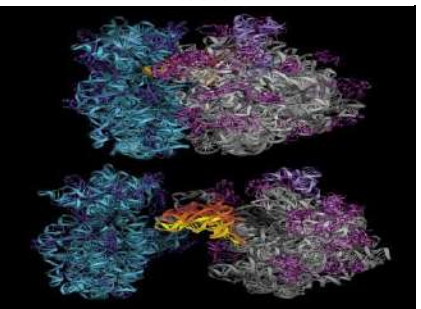


✓ **HETEROCROMATINA: região de DNA altamente compactado (firmemente ligado a histonas) que apresenta baixa ou nenhuma taxa de transcriçã**









DNA PODE ASSUMIR FORMAS NÃO USUAIS

✓ **Sequencias específicas levam à variações estruturais no DNA**

1. Sequência palindrômica

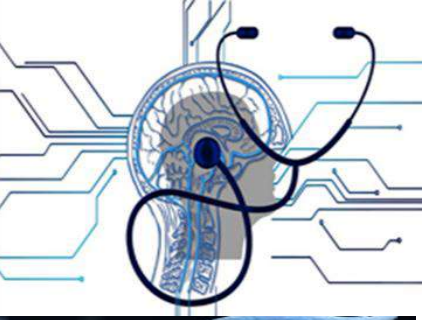
T T A G C A C G T G C T A A

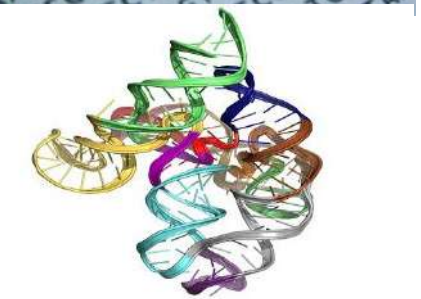
A A T C G T G C A C G A T T

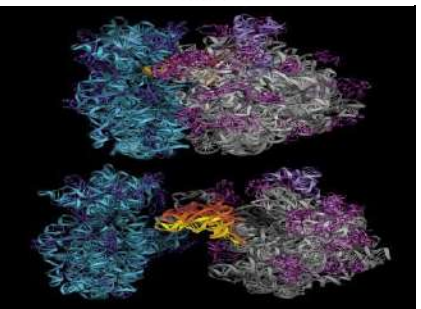
2. Repetição em espelho

T T A G C A C C A C G A T T

A A T C G T G G T G C T A A



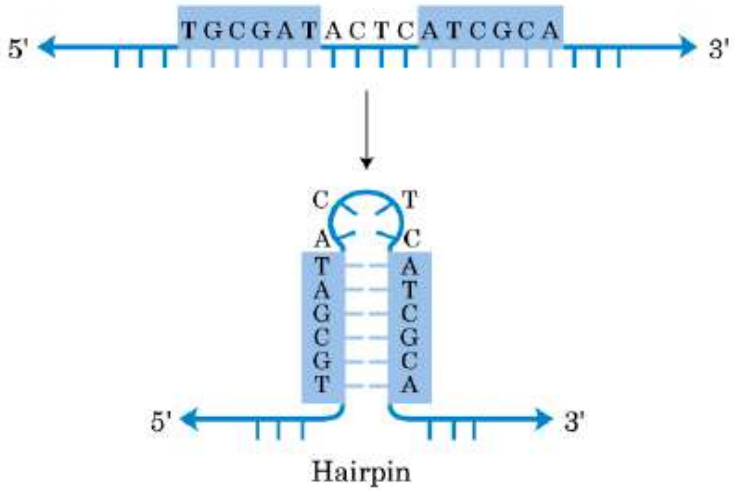




DNA PODE ASSUMIR FORMAS NÃO USUAIS

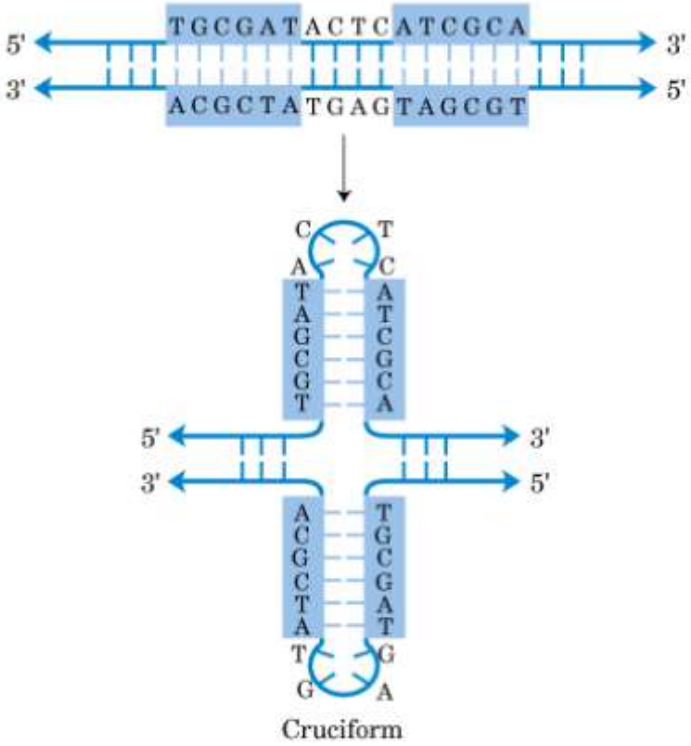
✓ **Sequencias palindrômicas podem forma estruturas**

Grampos

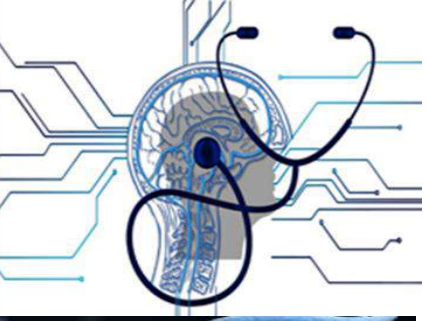


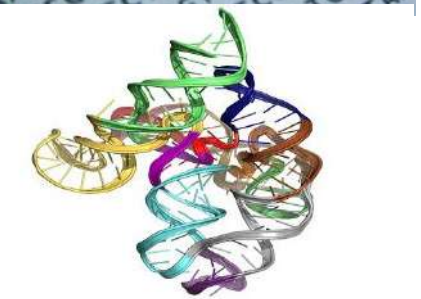
Hairpin

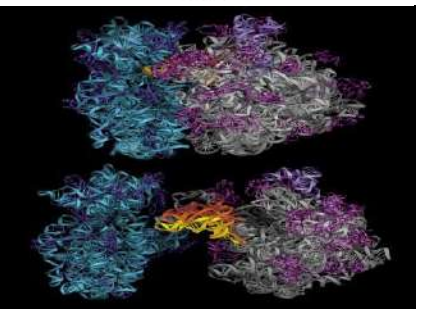
Cruciforme



Cruciform

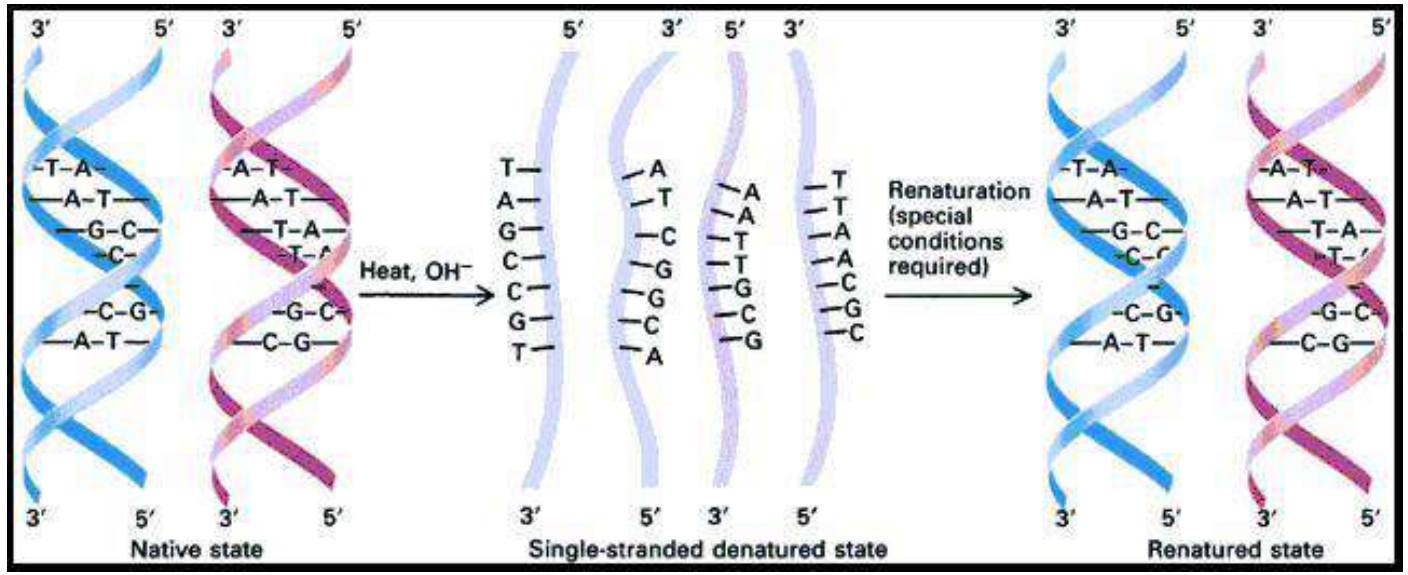




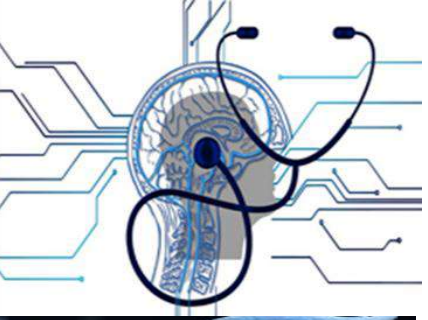


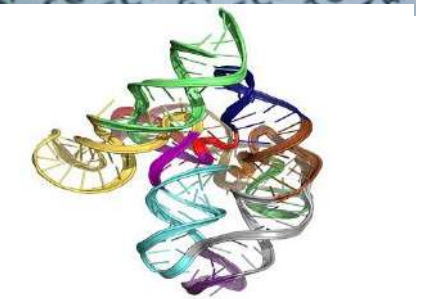
PROPRIEDADES FISICO-QUÍMICAS DO DNA

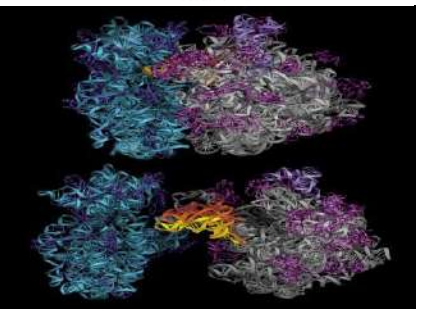
- ✓ **DESNATURAÇÃO: As ligações de hidrogênio presentes no DNA da fita dupla (dsDNA) podem ser quebradas pelo calor ou altas concentrações de íons;**
- ✓ **RENATURAÇÃO: as ligações de hidrogênio entre DNAs de fita simples (ssDNA) podem ser estabelecidas novamente**



- ✓ **Temperatura de Desnaturação: 50% DNA fita simples + 50% DNA fita dupla**

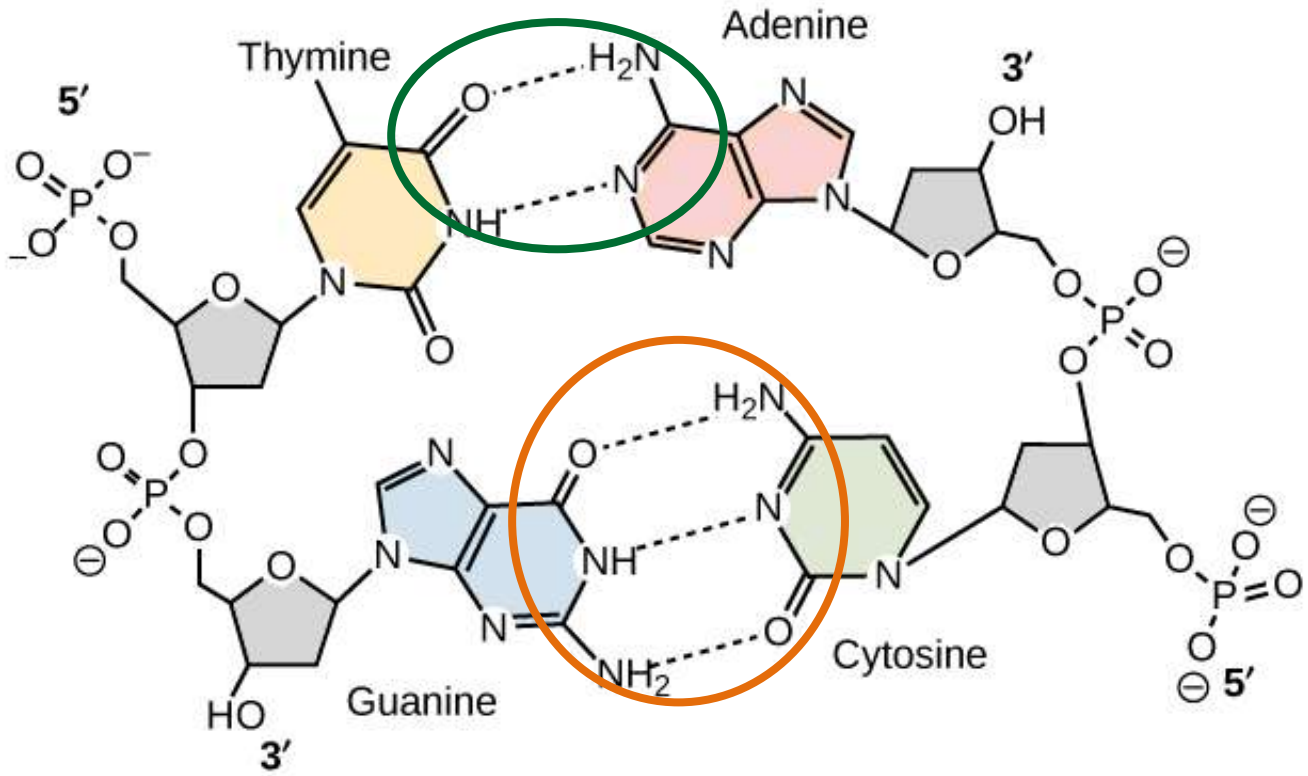


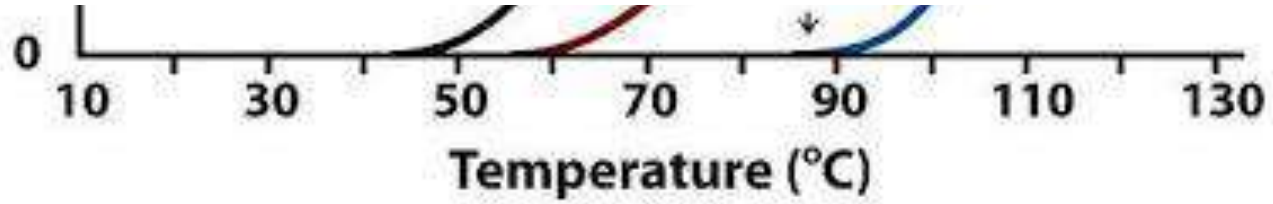


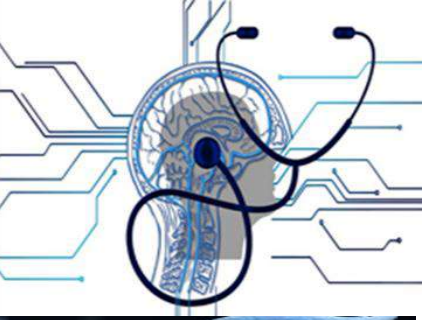


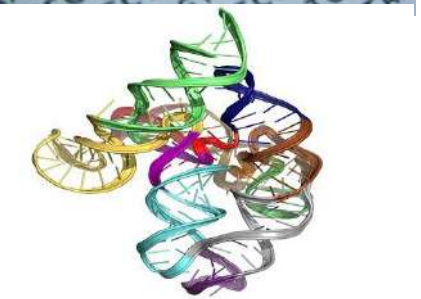
PROPRIEDADES FISICO-QUÍMICAS DO DNA

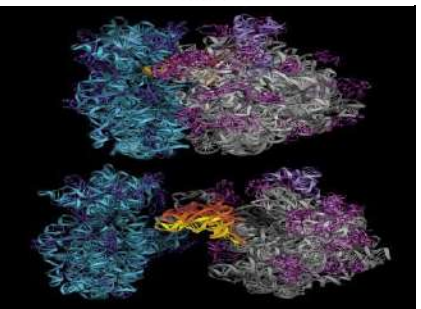
✓ **MELTING TEMPERATURE IS A FUNCTION OF BASES COMPOSITION (% A-T and % G-C)**





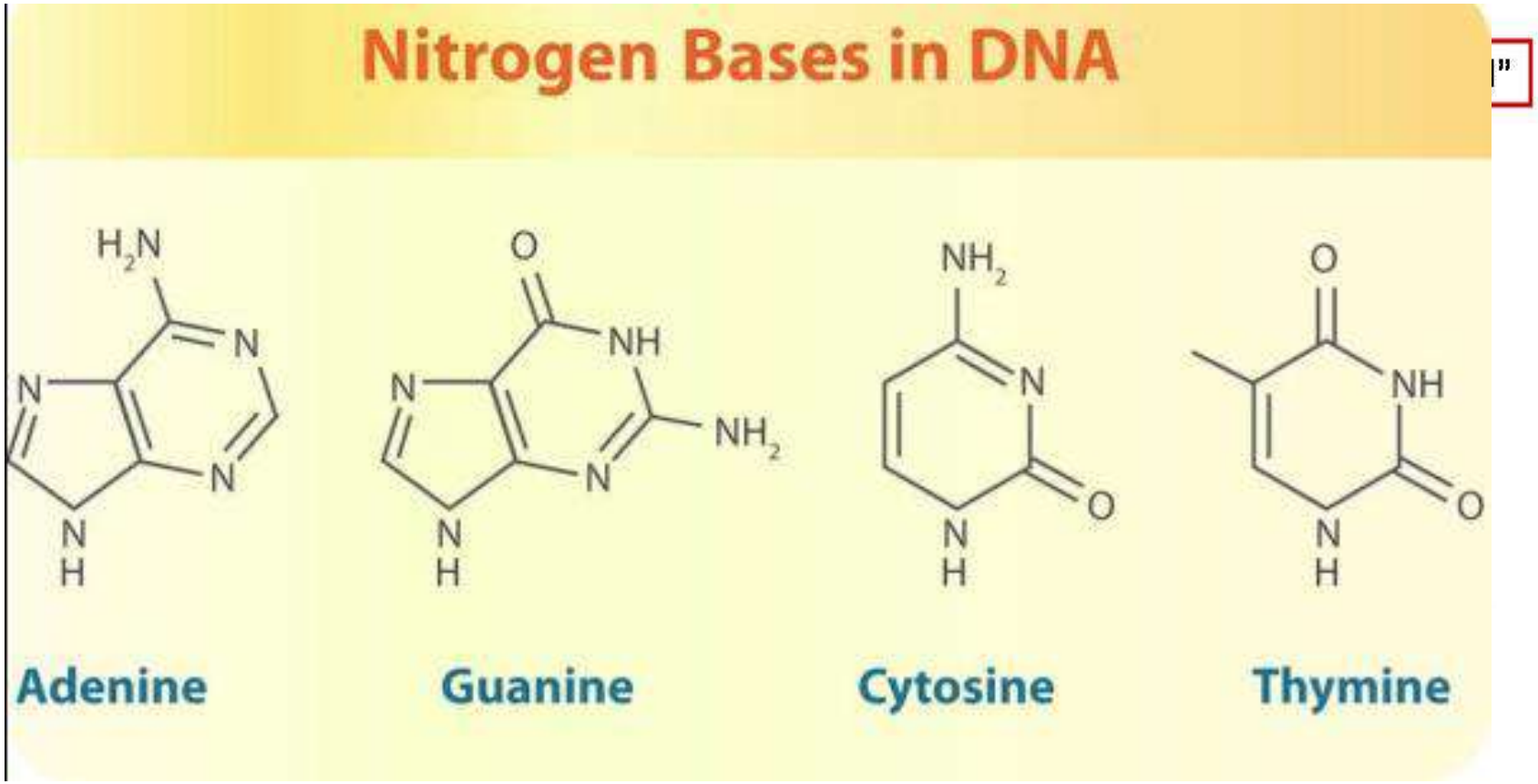




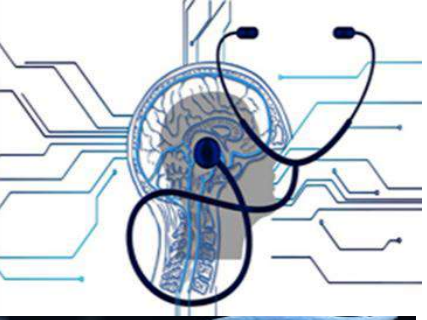


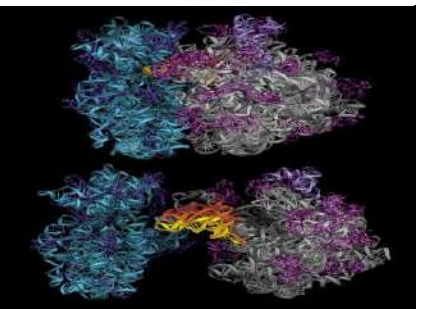
A desnaturação do dsDNA

- ✓ **O pH de uma solução de DNA é alterado**
- ✓ **A solução é aquecida (temperatura de desnaturação)**

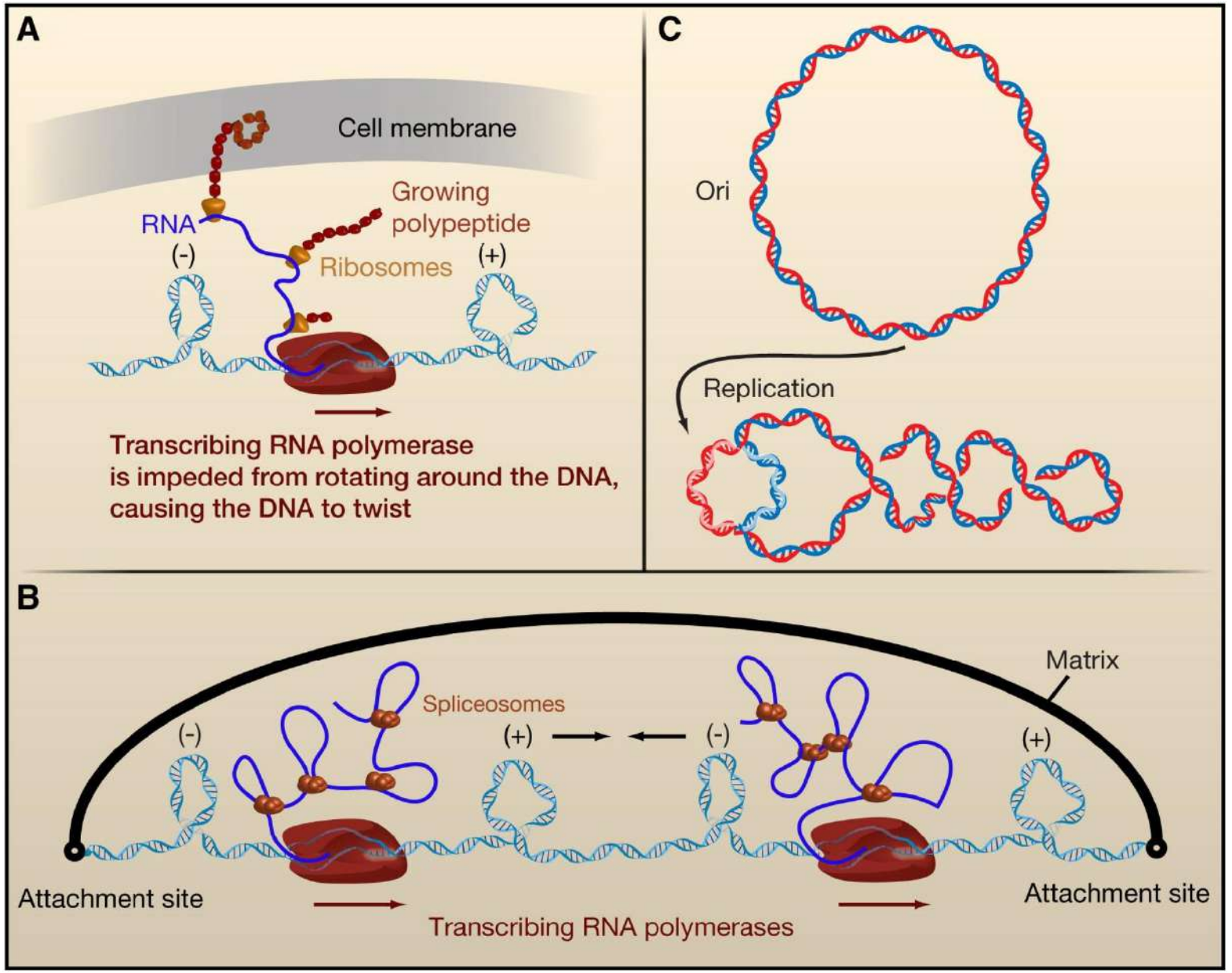


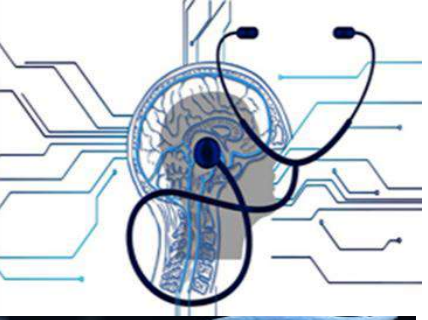
ANÉIS AROMÁTICOS: Absorção de luz UV à 260 nm

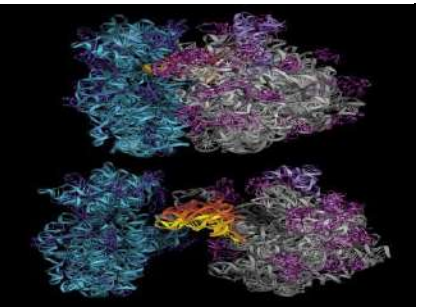




PROPRIEDADES FISICO-QUÍMICAS DO DNA



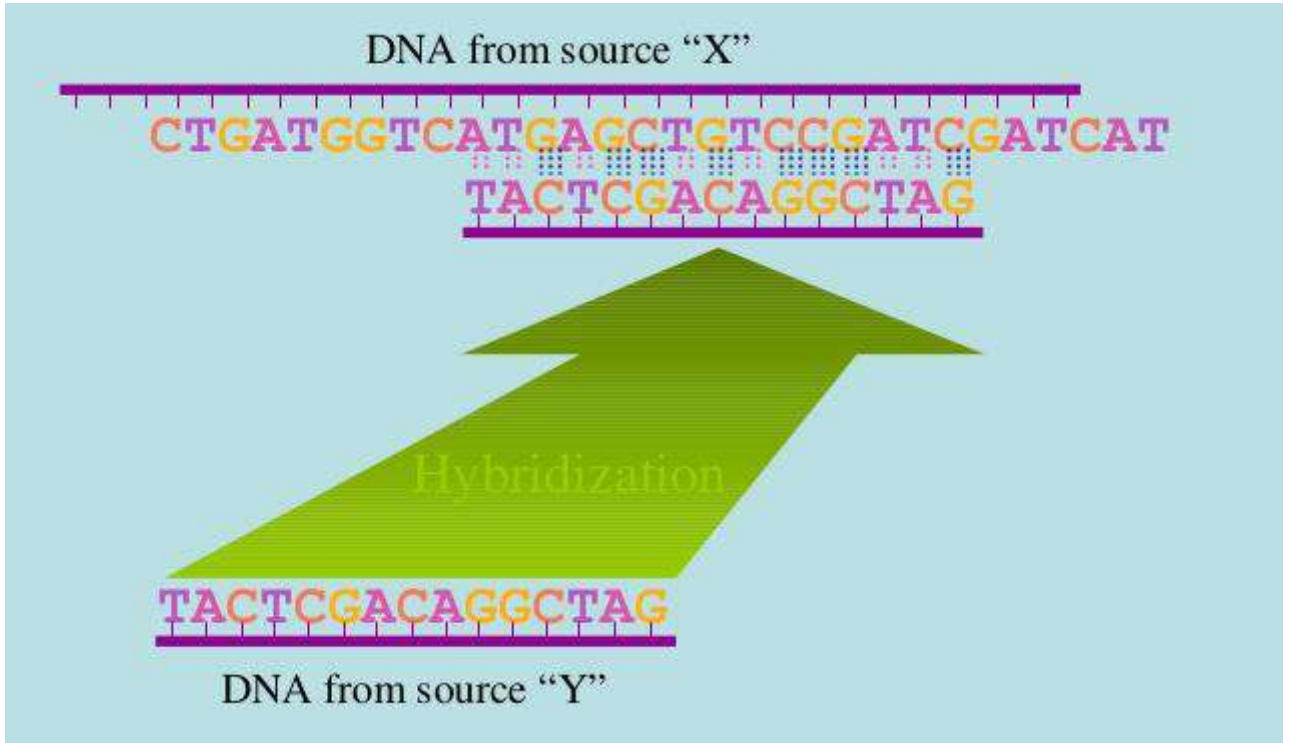


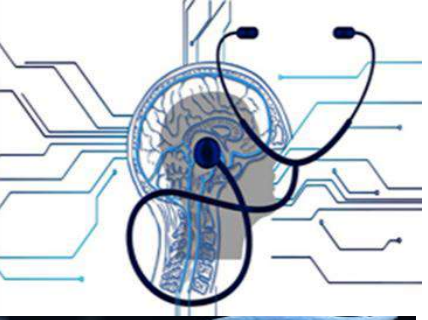


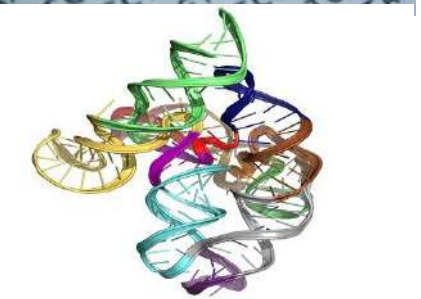
PROPRIEDADES FISICO-QUÍMICAS DO DNA

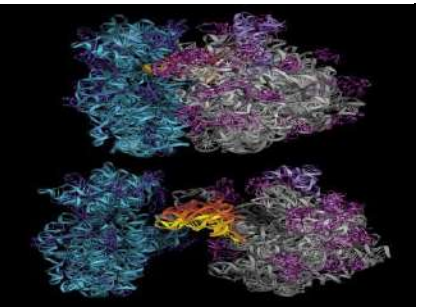
DNA e RNA podem hibridizar

- ✓ **Pareamento de bases de duas fitas, uma de DNA e outra de RNA .**
- ✓ **Pareamentos podem DNA-DNA e DNA-RNA.**
- ✓ **Sondas fluorescentes**









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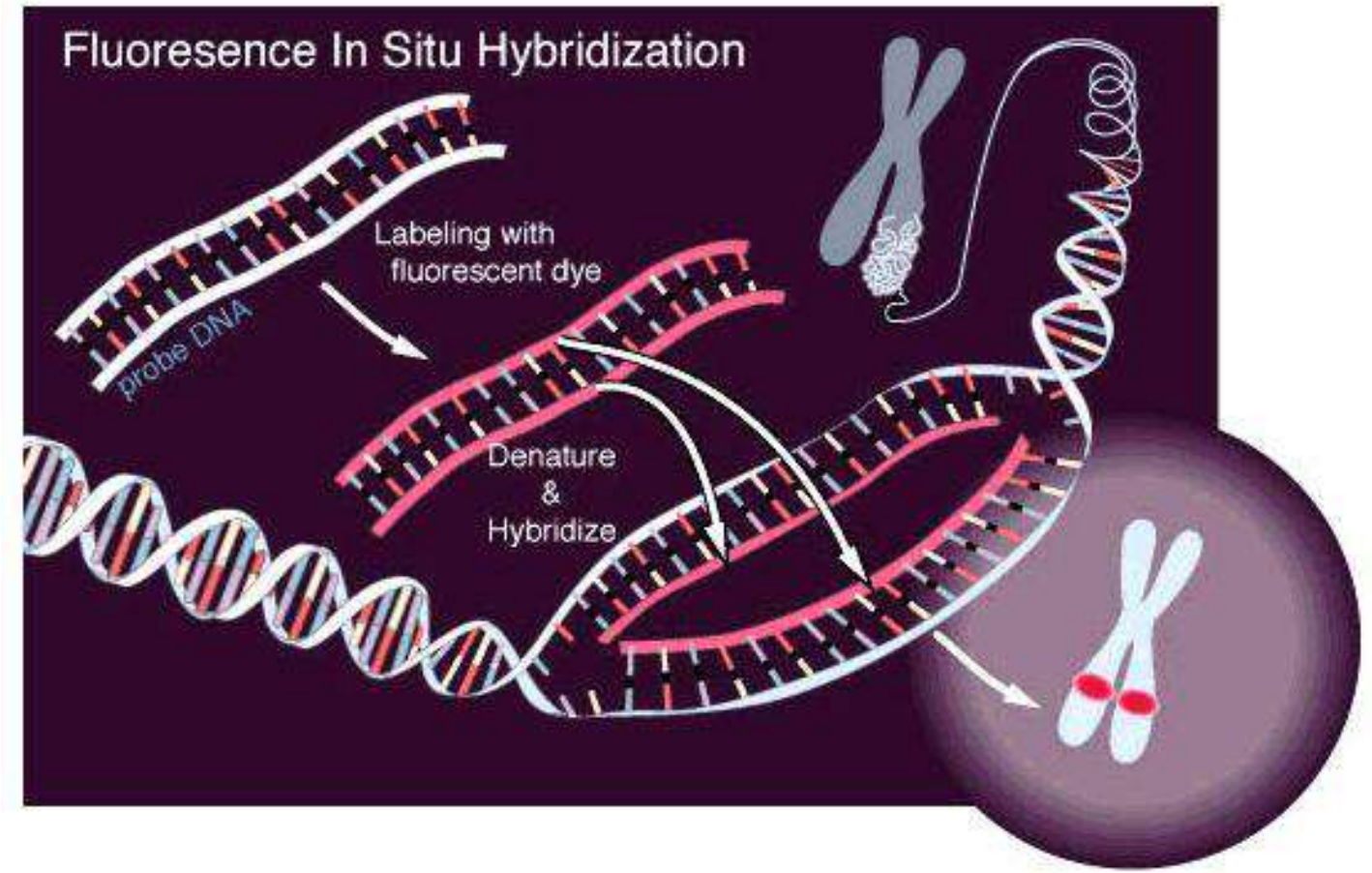
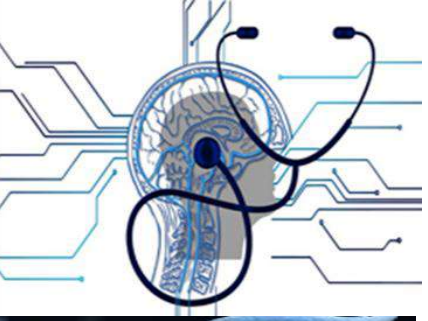
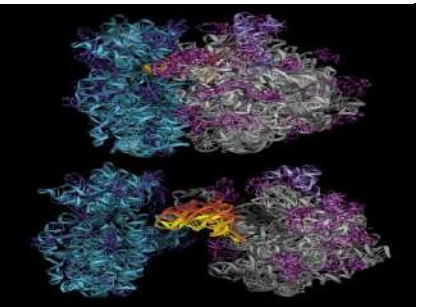
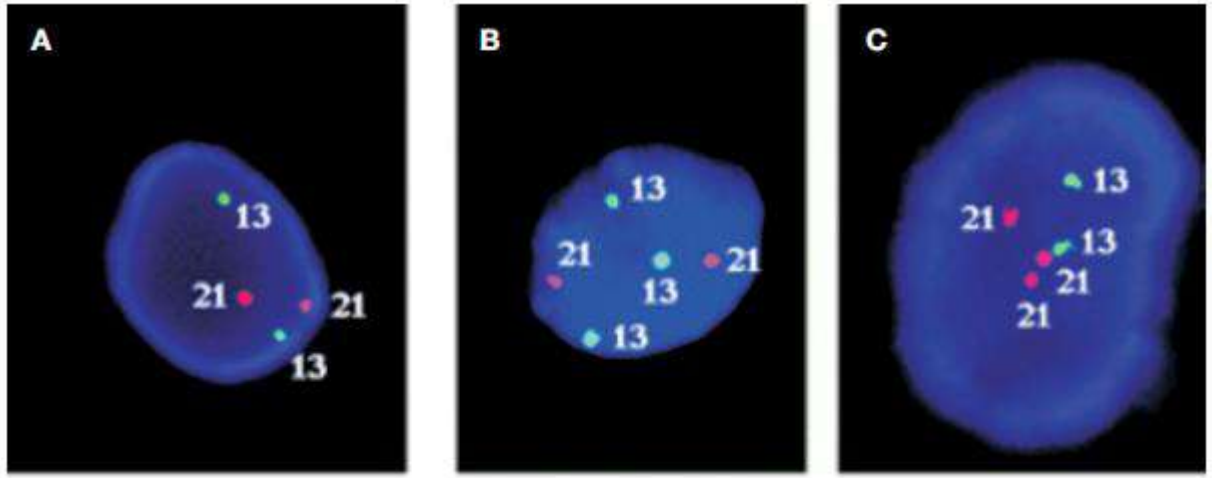






TÉCNICAS CITOGENÉTICA MOLECULAR
Hibridização por Fluorescência in Situ (FISH)

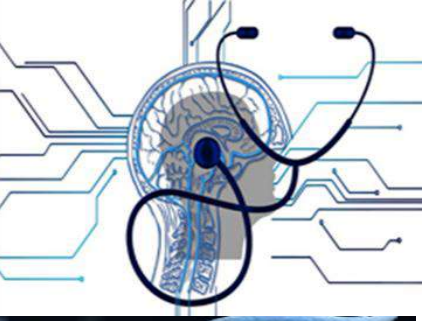
2-SONDAS CROMOSSOMO-ESPECÍFICAS

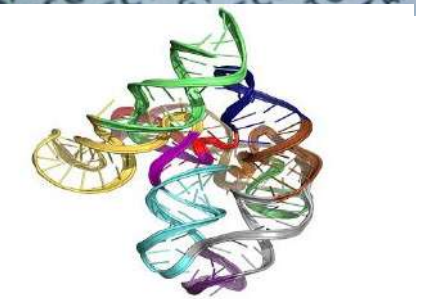


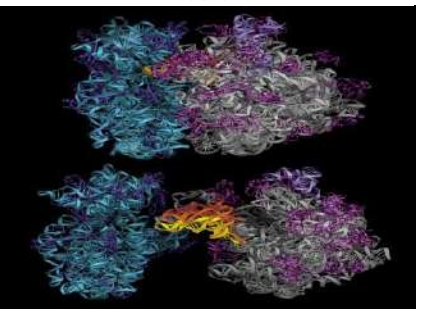
A: Célula normal com 2 sinais para os cromossomos 13 e 21

B: Três sinais verdes indicando Trisssomia do cromossomo 13

C: Três sinais vermelhos indicando Trisssomia do cromossomo 21

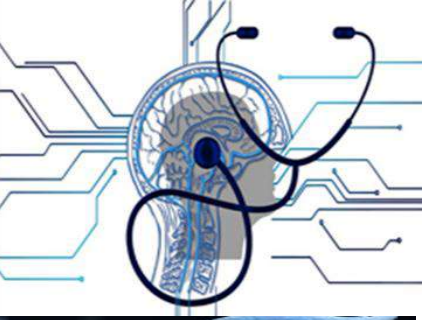


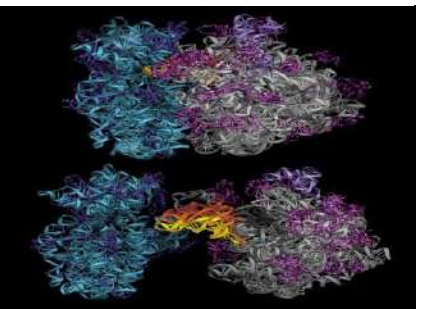




DNA VS RNA

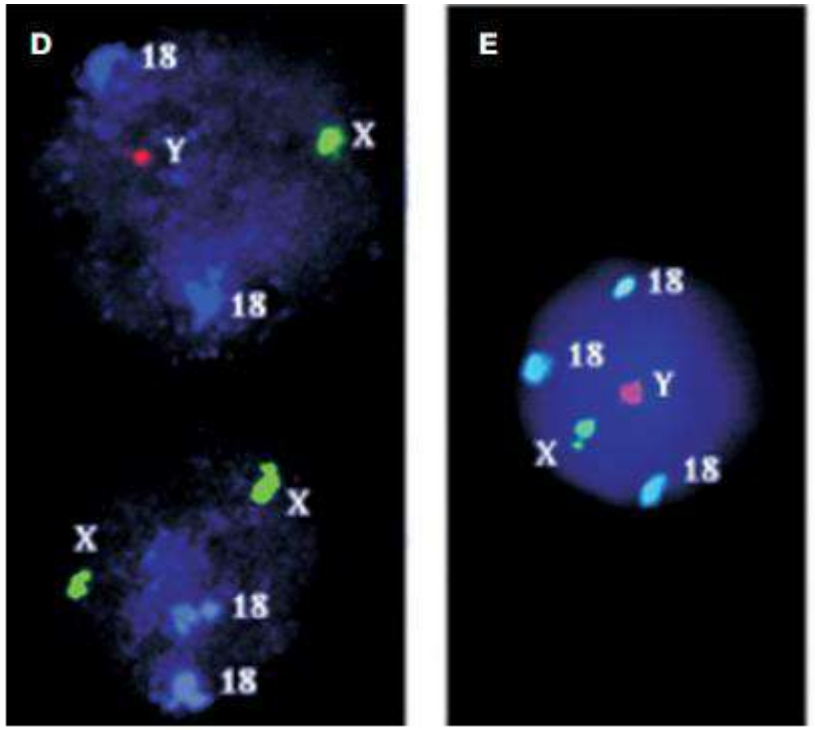
DNA	RNA
Fita dupla	Fita simples
Pentose: Desoxirribose	Pentose: Ribose
C, G, A, T	C, G, A, U
Replicação própria	Não pode se replicar
Informação genética mantida no DNA	Síntese de proteínas ✓ RNA mensageiro (mRNA) ✓ RNA ribossomal (rRNA) ✓ RNA transportador (tRNA)





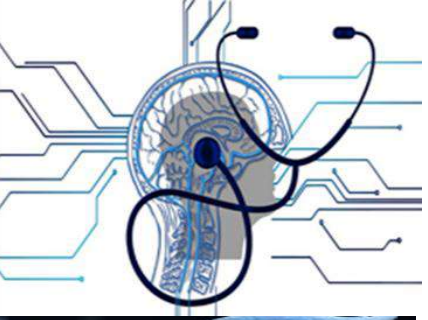
TÉCNICAS CITOGENÉTICA MOLECULAR
Hibridização por Fluorescência in Situ (FISH)

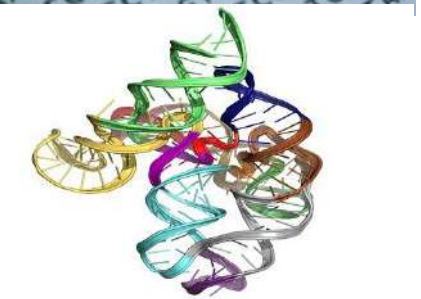
2-SONDAS CROMOSSOMO-ESPECÍFICAS

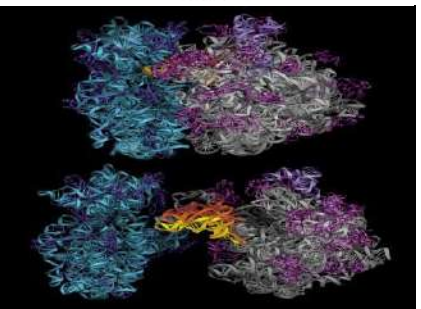


D: Células masculina (XY) e feminina (XX) com marcação no cromossomo 18

E: Trissomia do cromossomo 18 em uma célula masculina







TIPOS RNA E FUNÇÕES

mRNA

in cytoplasm & nucleus

Messenger RNA (mRNA)

- **Involved in transcription (1st stage of protein synthesis)**
- "Photocopies" the DNA and carries message from DNA in nucleus to ribosome in cytoplasm

tRNA & rRNA

- In cytoplasm only

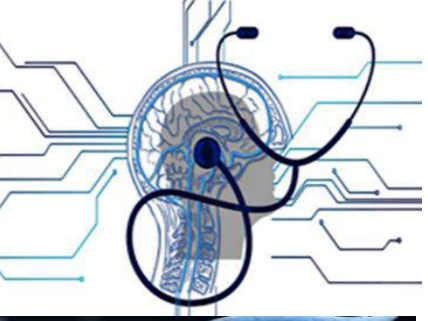
Ribosomal RNA (rRNA)

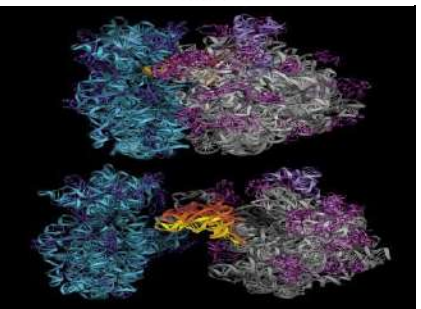
- **Makes up the ribosomes**

Transfer RNA (tRNA)

- **carries amino acids to mRNA**

All RNA produced in nucleolus.





- ✓ 30.000 genes codificam RNAs
- ✓ 3.000 genes codificam RNA e tRNAs
- ✓ 27.000 genes codificam mRNA

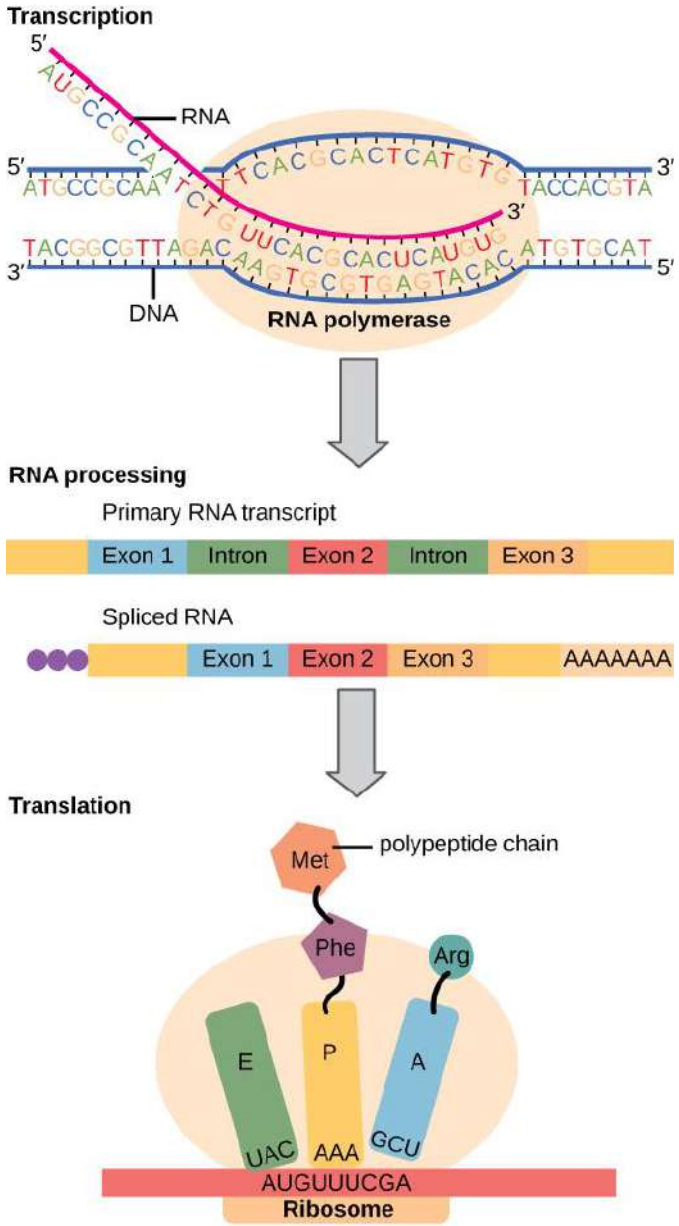
RNA mensageiro (mRNA) contém a informação genética para a sequência de resíduos AA da proteína

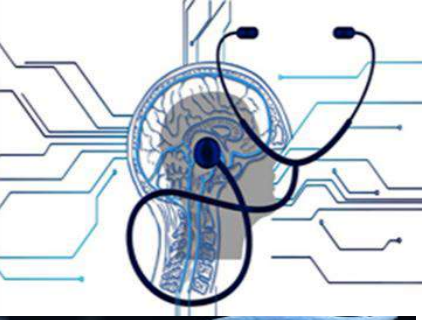
RNA transportador (tRNA) identifica e transporta AA para o ribossomo (sítio da síntese protéica)

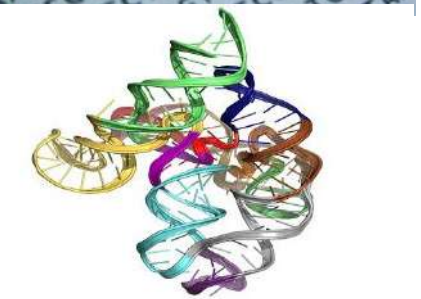
RNA ribossomal (rRNA) sítio da síntese protéica

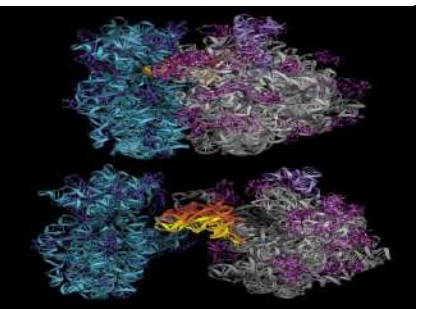
TRANSCRIPTOMA: total de genes (mRNA) expressos em um dado momento e tipo celular

PRINCIPAIS FUNÇÕES DO RNA

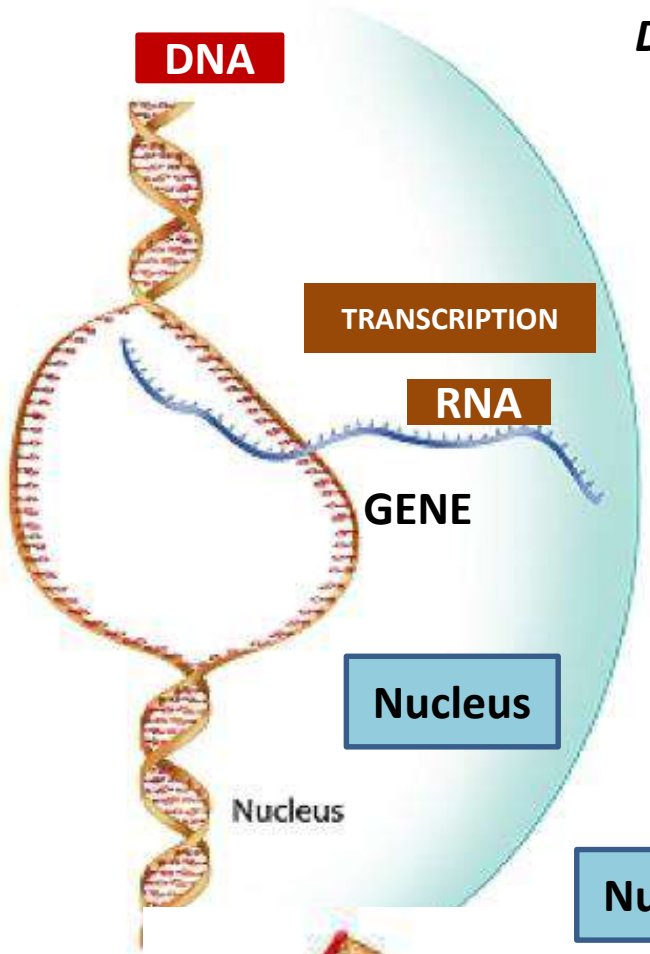


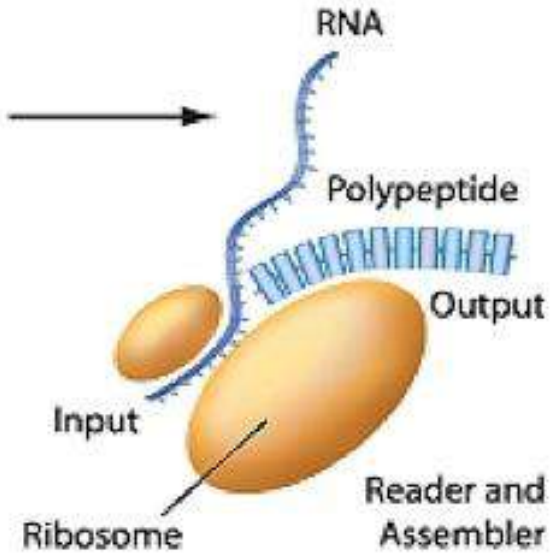






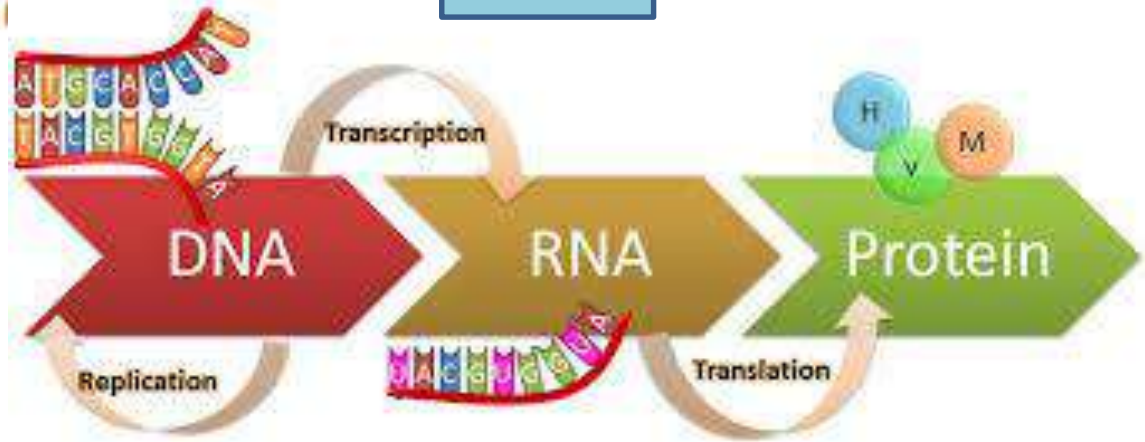
DOGMA CENTRAL DA BIOLOGIA MOLECULAR
RNA MENSAGEIRO (MRNA)

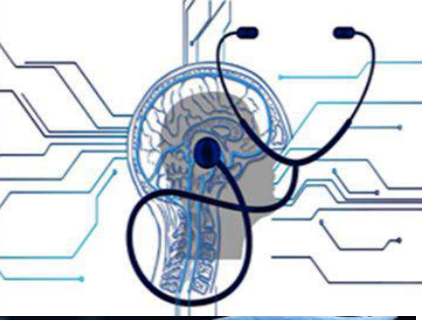


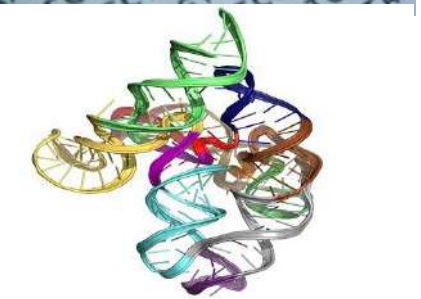


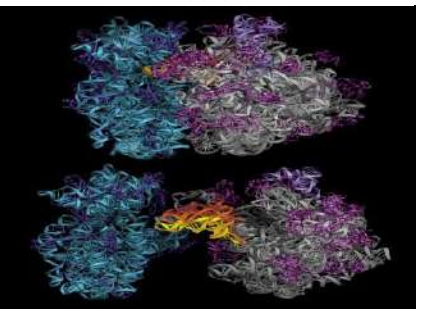
Nucleus

TRANSLATION

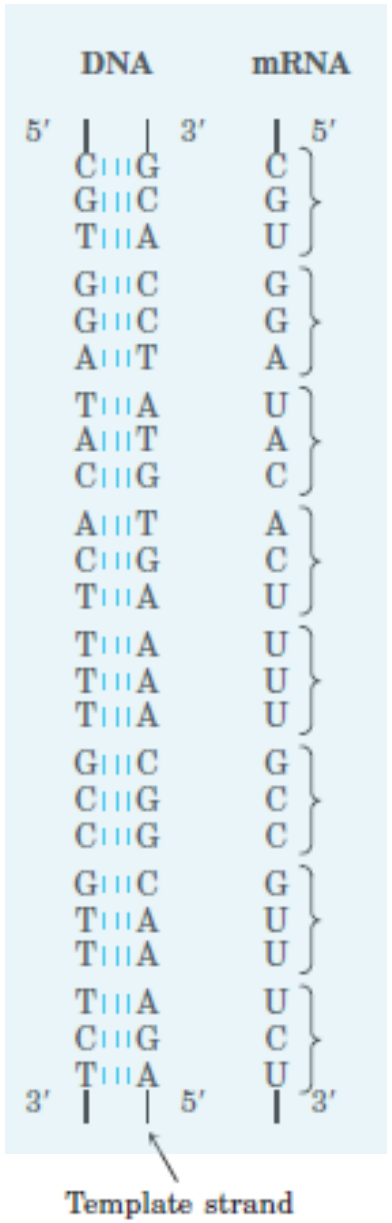


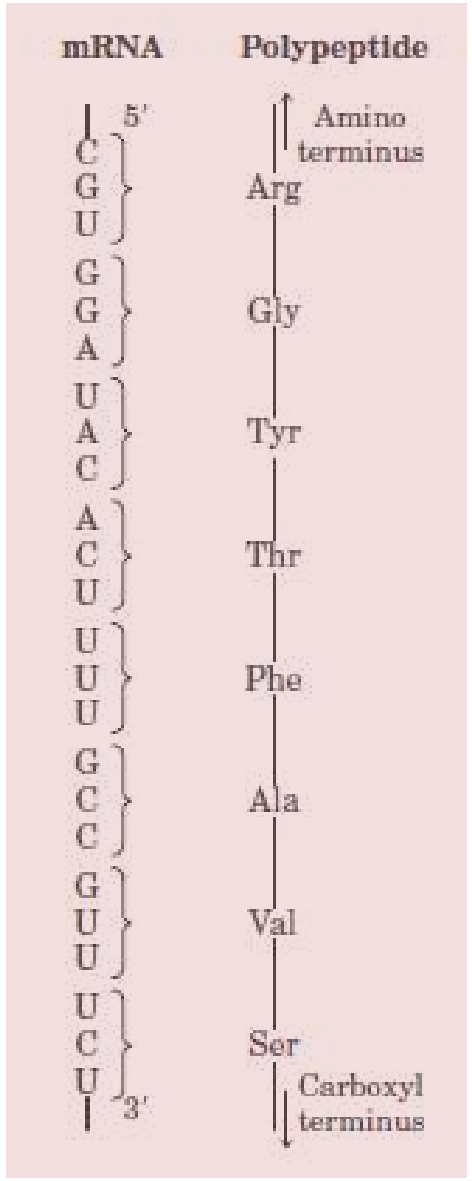






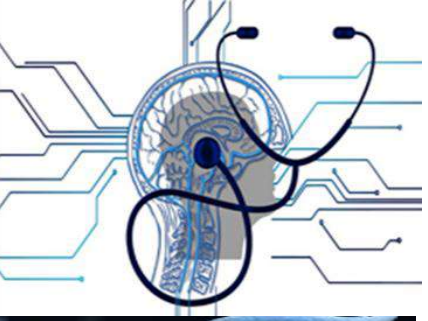
RNA MENSAGEIRO (mRNA)

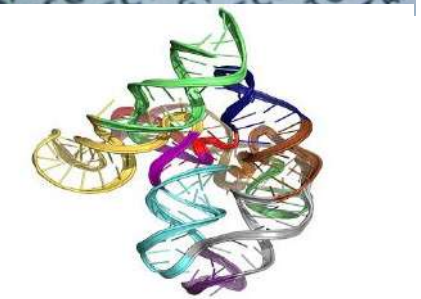


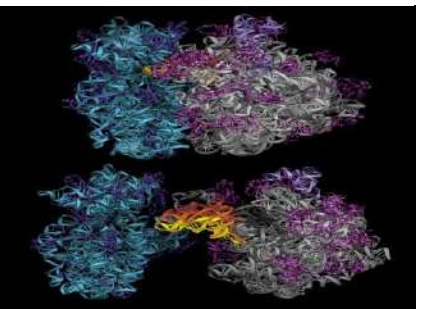


TRADUÇÃO: Transferência da informação genética de mRNA para Proteína.

TRANSCRIÇÃO: Transferência da informação genética do gene (DNA) para mRNA.





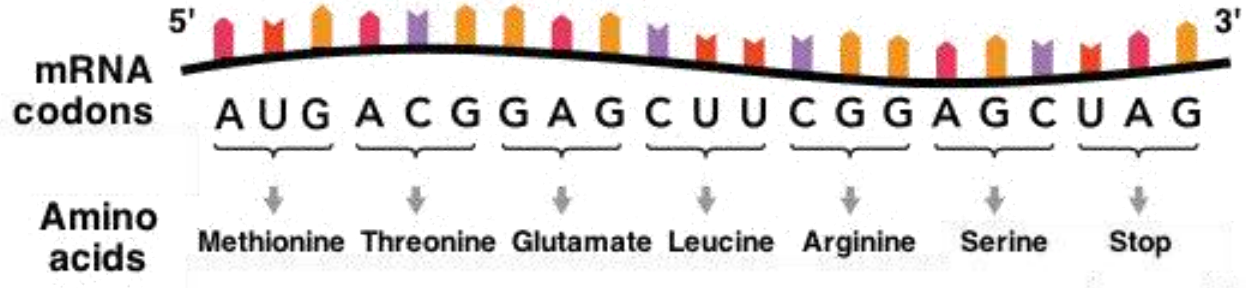


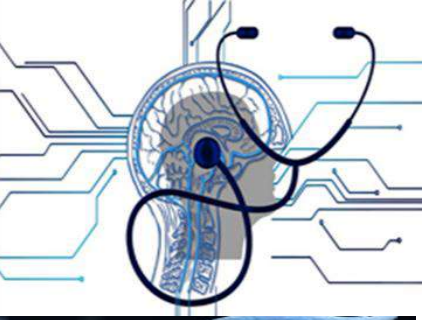
RNA MENSAGEIRO (MRNA)

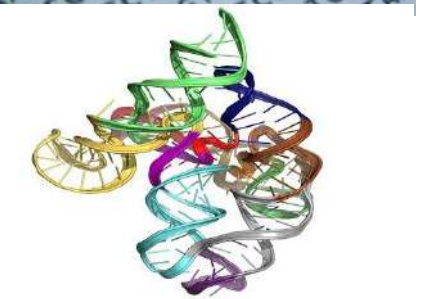
✓ **Genes são constituídos por códons (trincas) de bases, codificam aminoácidos específicos. O DNA no núcleo é transcrito para mRNA usando por meio da complementariedade de bases complementares para converter os tripletes de bases do DNA nos códons do mRNA.**

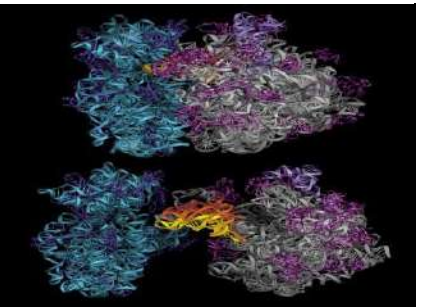
1st letter	Second Letter: U	Second Letter: C	Second Letter: A	Second Letter: G	3rd letter
U	UUU Phe UUC UUA Leu UUG	UCU UCC UCA Ser UCG	UAU Tyr UAC UAA Stop UAG Stop	UGU Cys UGC UGA Stop UGG Trp	U C A G
C	CUU CUC CUA Leu CUG	CCU CCC CCA Pro CCG	CAU His CAC CAA Gln CAG	CGU CGC CGA Arg CGG	U C A G
A	AUU AUC AUA Ile AUG Met	ACU ACC ACA Thr ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
G	GUU GUC GUA Val GUG	GCU GCC GCA Ala GCG	GAU Asp GAC GAA Glu GAG	GGU GGC GGA Gly GGG	U C A G

O código genético é degenerado: 63 códons para 20 aminonoácidos



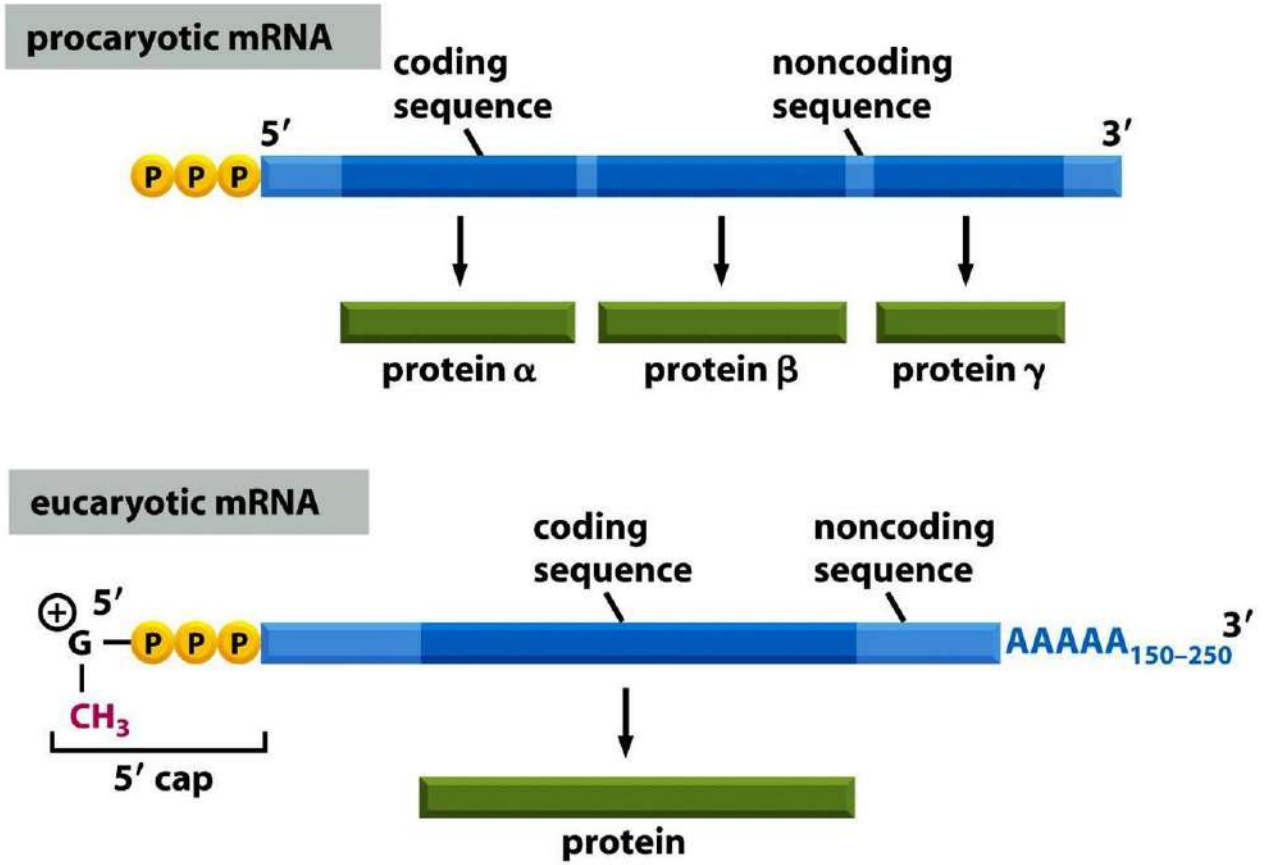


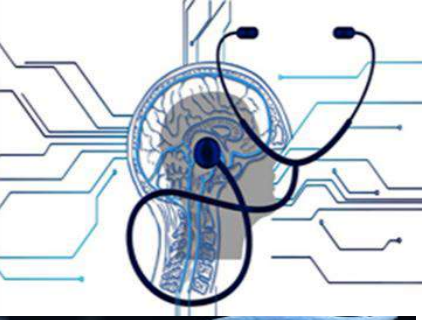


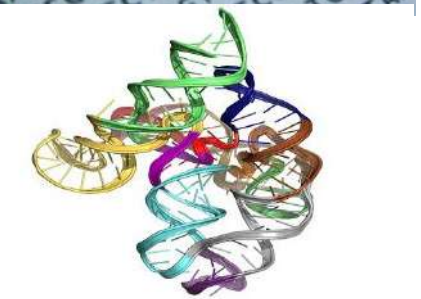


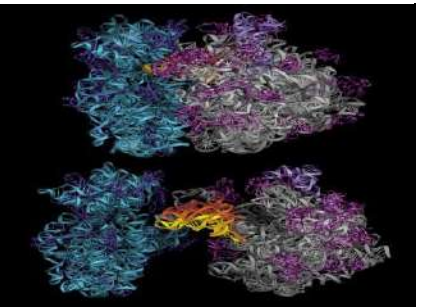
RNA MENSAGEIRO (MRNA)

- ✓ **mRNA contém a informação codificada do DNA, que será traduzida em proteína**
- ✓ **O RNA pode ser monocistrônico e policistrônico**



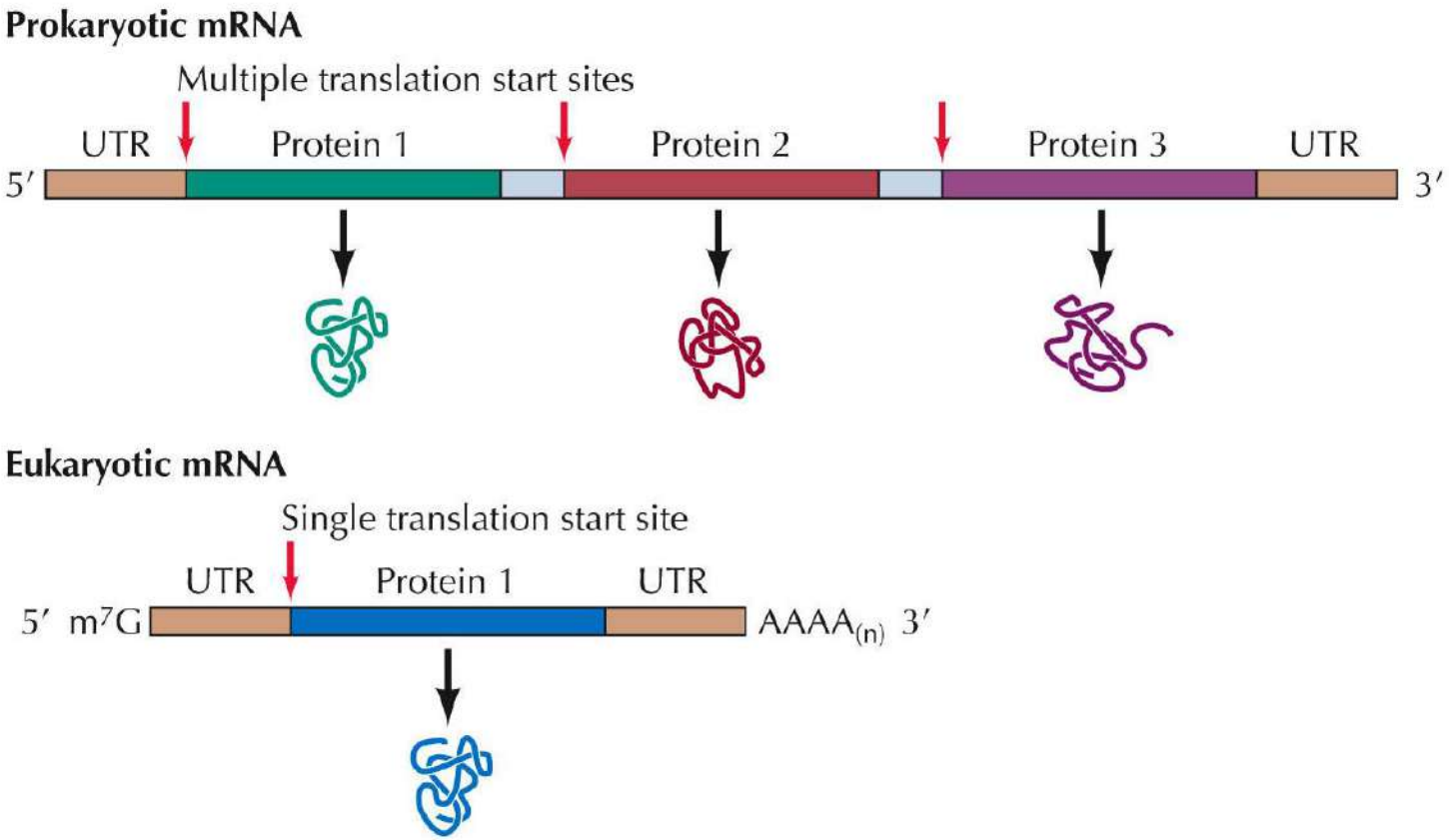


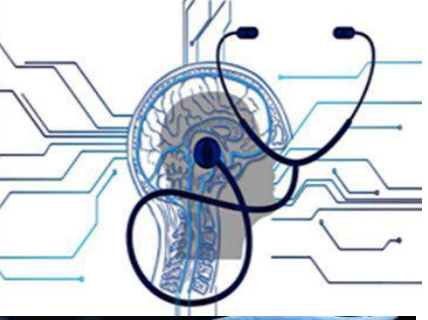


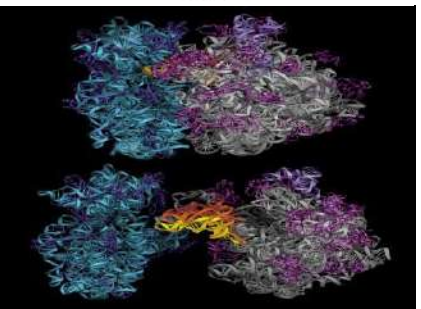


RNA MENSAGEIRO (MRNA)

- ✓ **RNA mensageiro pode ser monocistrônico e policistrônico**
- ✓ **mRNA EUCARIOTICO: Monocistrônico**
- ✓ **mRNA PROCARIÓTICO : Policistrônico**

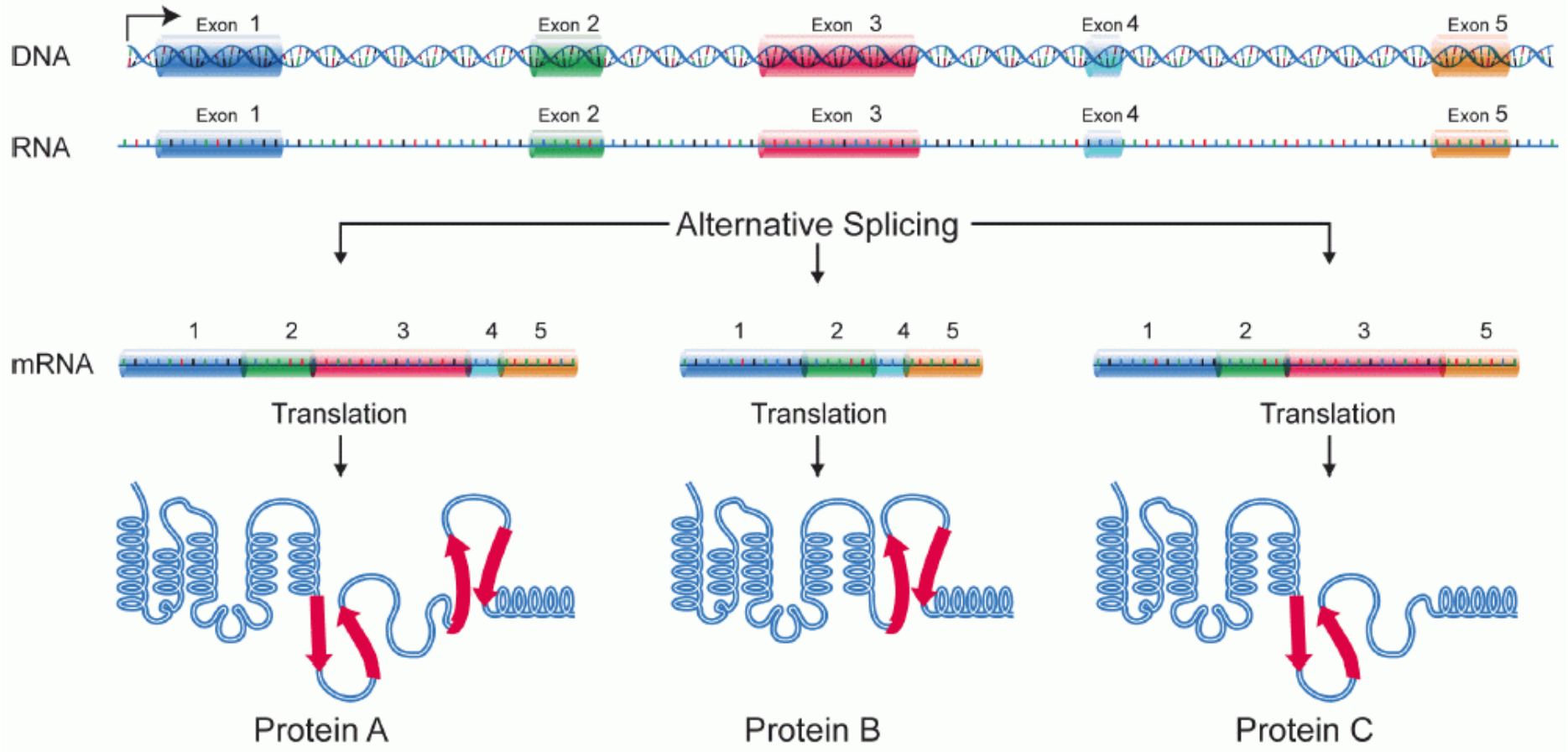


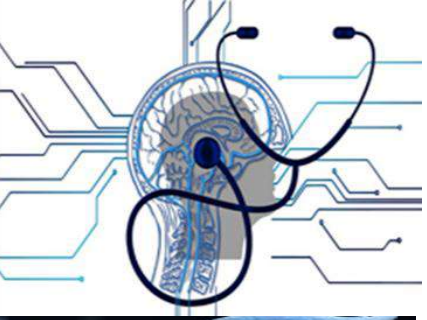


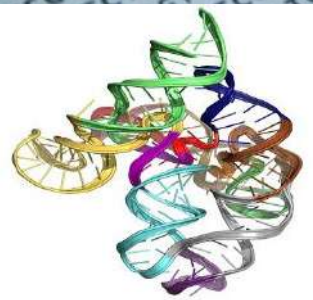


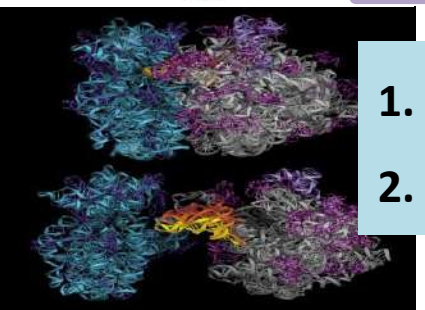
RNA MENSAGEIRO (MRNA) - EUCARIOTOS

EM EUCARIOTOS, VÁRIAS PROTEÍNAS PODEM SER SINTETIZADAS DE UM ÚNICO GENE ATRAVÉS DO PROCESSO DE SPLICING ALTERNATIVO

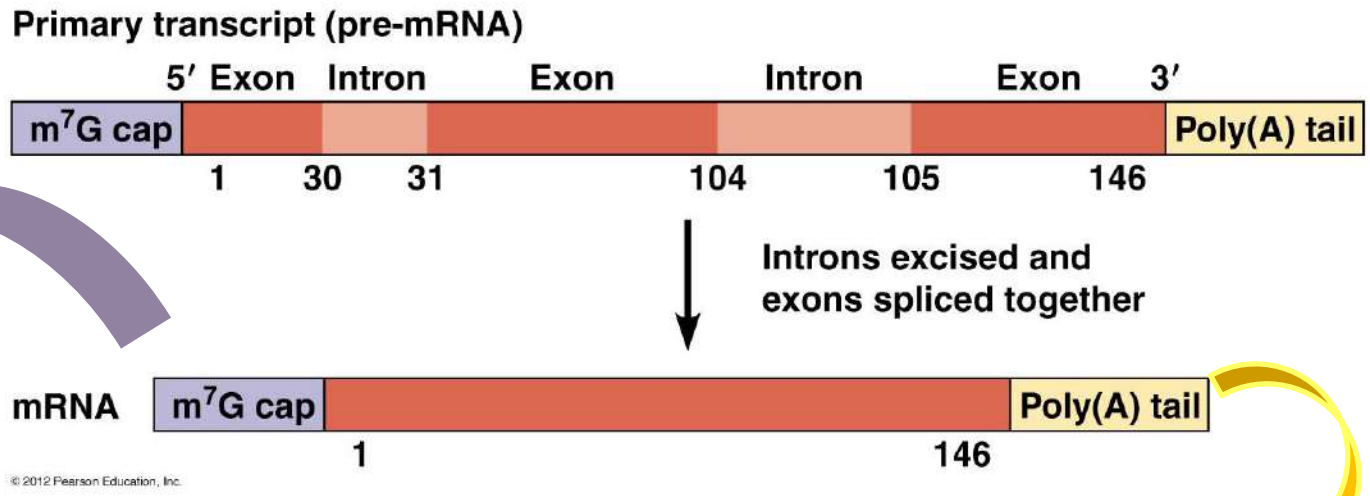


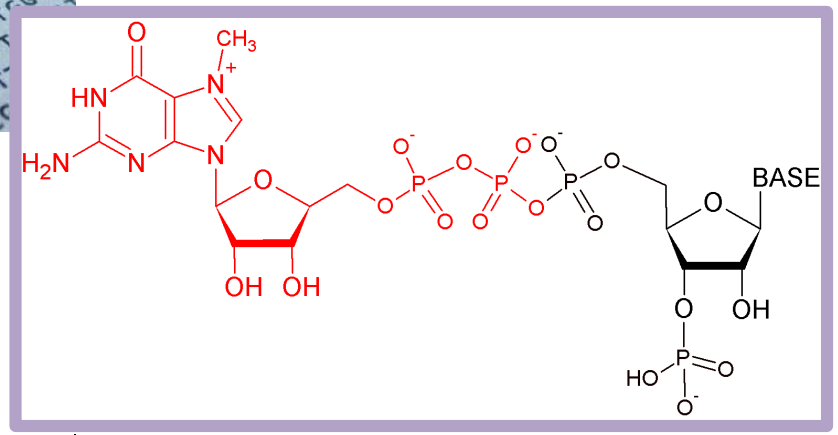




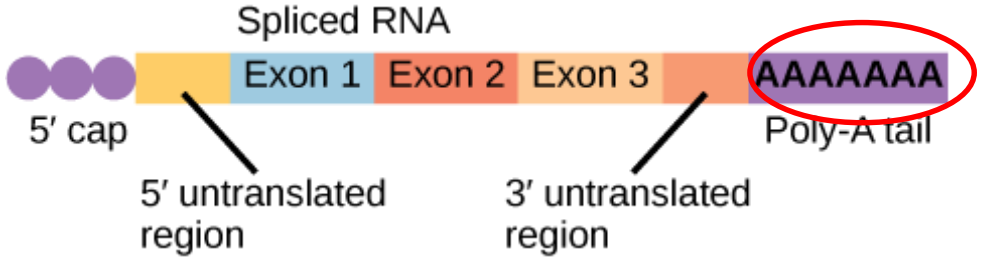


RNA MENSAGEIRO (MRNA) - EUCARIOTOS

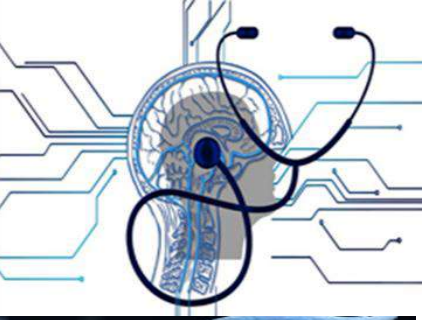


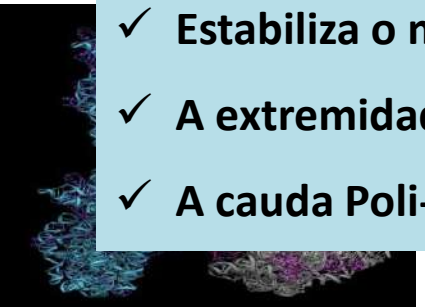


5‘-AAAAAAA-‘3

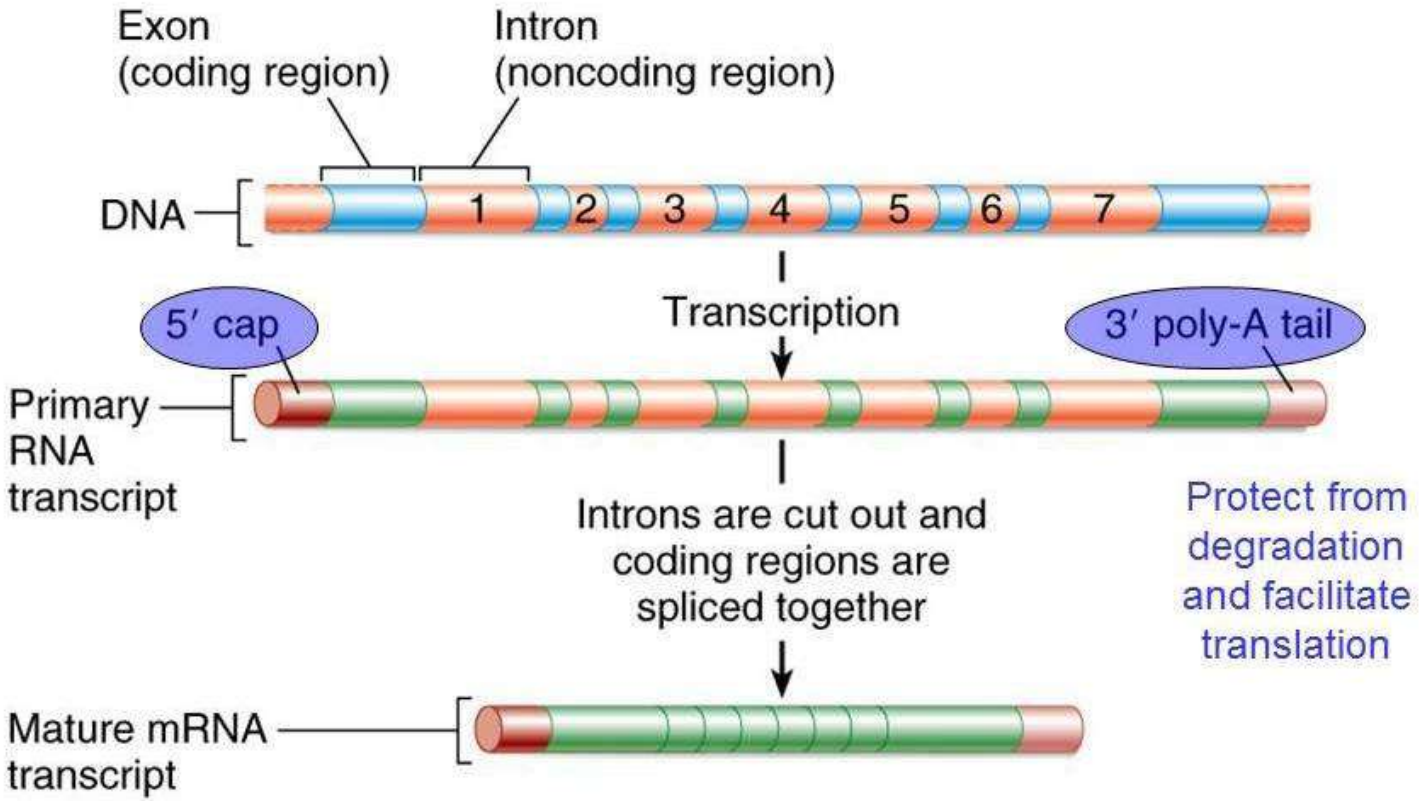


1. **7 - METIL GUANOSINA TRIFOSFATO CAP (m^{7}G cap) na extremidade 5‘ ;**
2. **Cauda POLI-A na extremidade 3‘ (20-250 adeninas).**

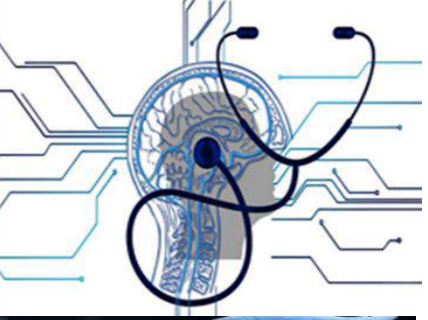


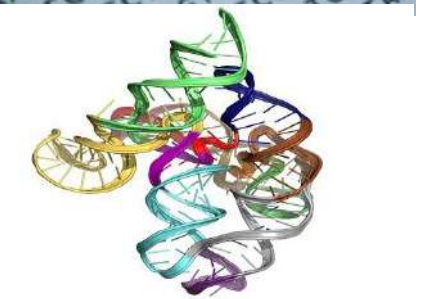


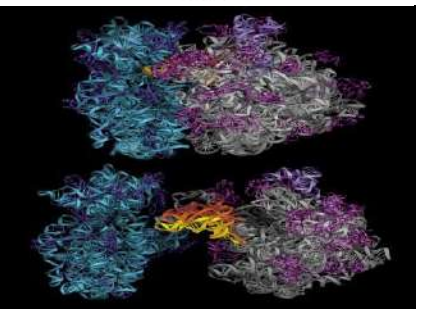
RNA MENSAGEIRO (MRNA) - EUCARIOTOS



- ✓ **O CAP está envolvido no reconhecimento de mRNA pela maquinaria de tradução;**
- ✓ **Estabiliza o mRNA protegendo-o de <u>5 'EXONUCLEASES</u>**
- ✓ **A extremidade 3` da maioria dos mRNAs possuem um polímero de resíduos de adenilato (20-250) - cauda poli-A;**
- ✓ **A cauda Poli-A impede a degradação por <u>3 '-EXONUCLEASES</u>;**



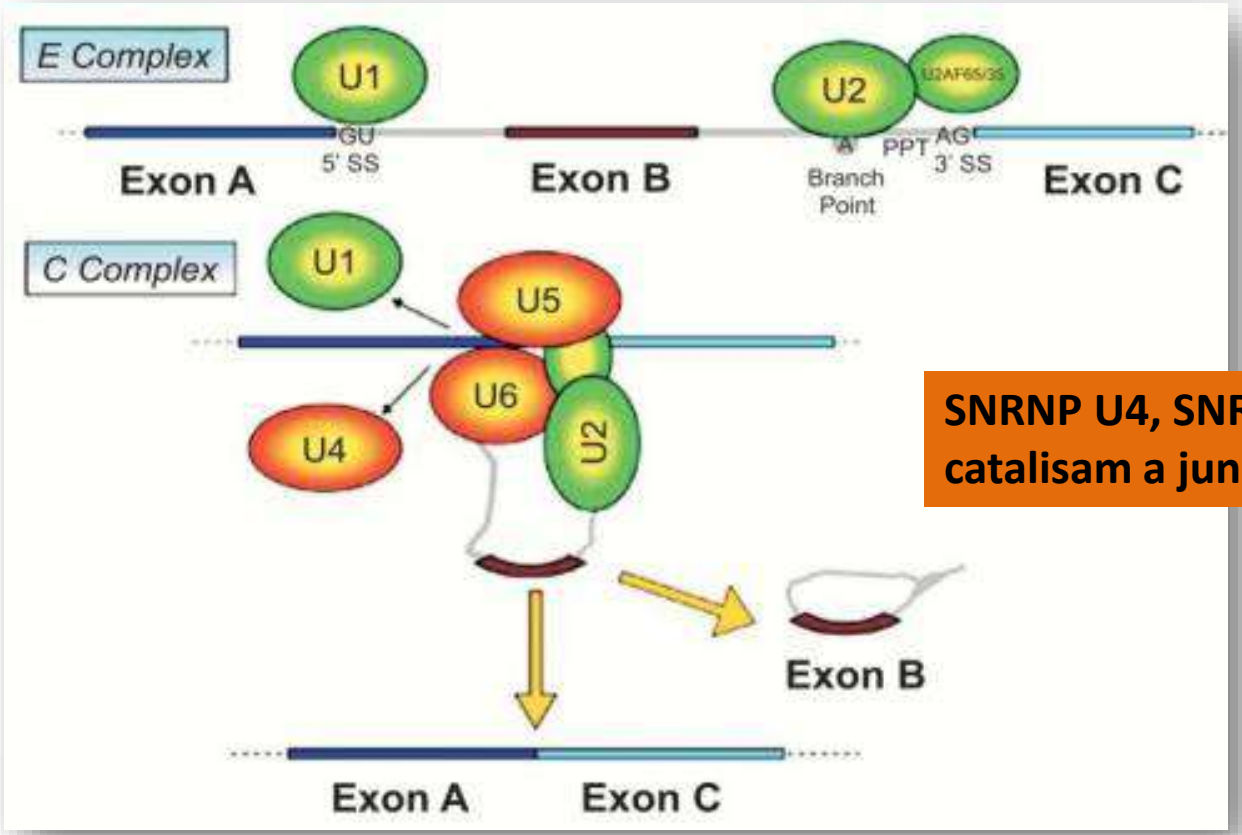




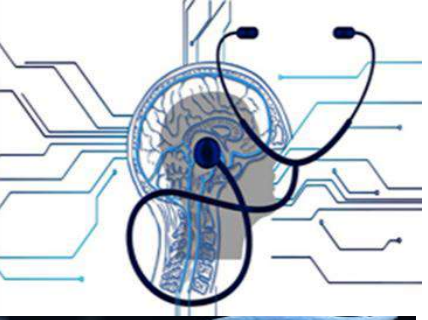
RNA MENSAGEIRO (MRNA) – SPLICING ALTERNATIVO

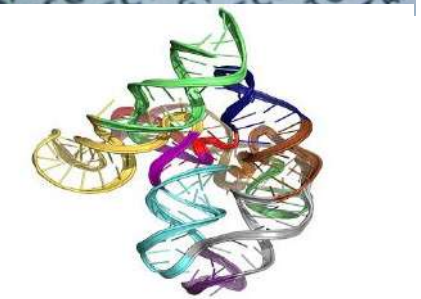
SNRNP – Small Ribonuclear Protein

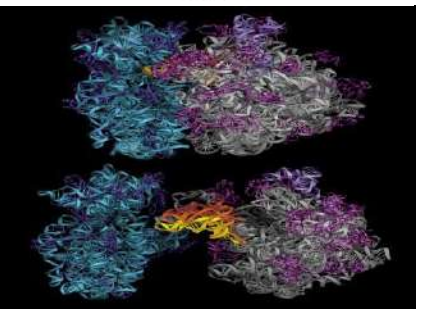
SNRNP U1 – reconhece o sítio GU
SNRNP U2 – liga as regiões A e AG



SNRNP U4, SNRNP U5 e SNRNP U6 catalisam a junção do Exon A com o Exon C



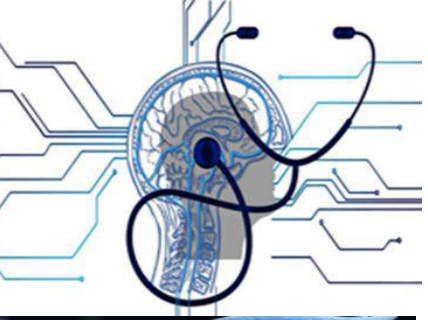


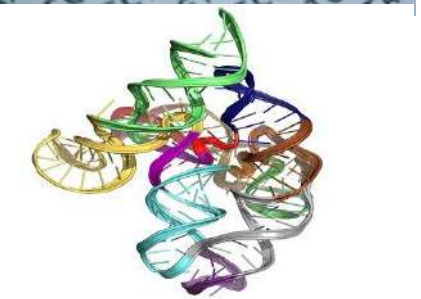


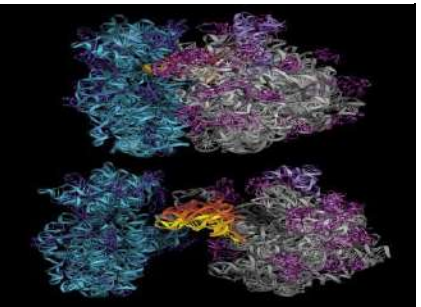
RNA TRANSPORTADOR (T-RNA)

De onde vem a informação necessária para determinar a sequência de resíduos de aminoácidos de uma proteína?

1st letter	Second Letter: U	Second Letter: C	Second Letter: A	Second Letter: G	3rd letter
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC	UCC	UAC	UGC	C
	UUA Leu	UCA	UAA Stop	UGA Stop	A
	UUG	UCG	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC	CCC	CAC	CGC	C
	CUA	CCA	CAA Gln	CGA	A
	CUG	CCG	CAG	CGG	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC	ACC	AAC	AGC	C
	AUA	ACA	AAA Lys	AGA Arg	A
	AUG Met	ACG	AAG	AGG	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC	GCC	GAC	GGC	C
	GUA	GCA	GAA Glu	GGA	A
	GUG	GCG	GAG	GGG	G





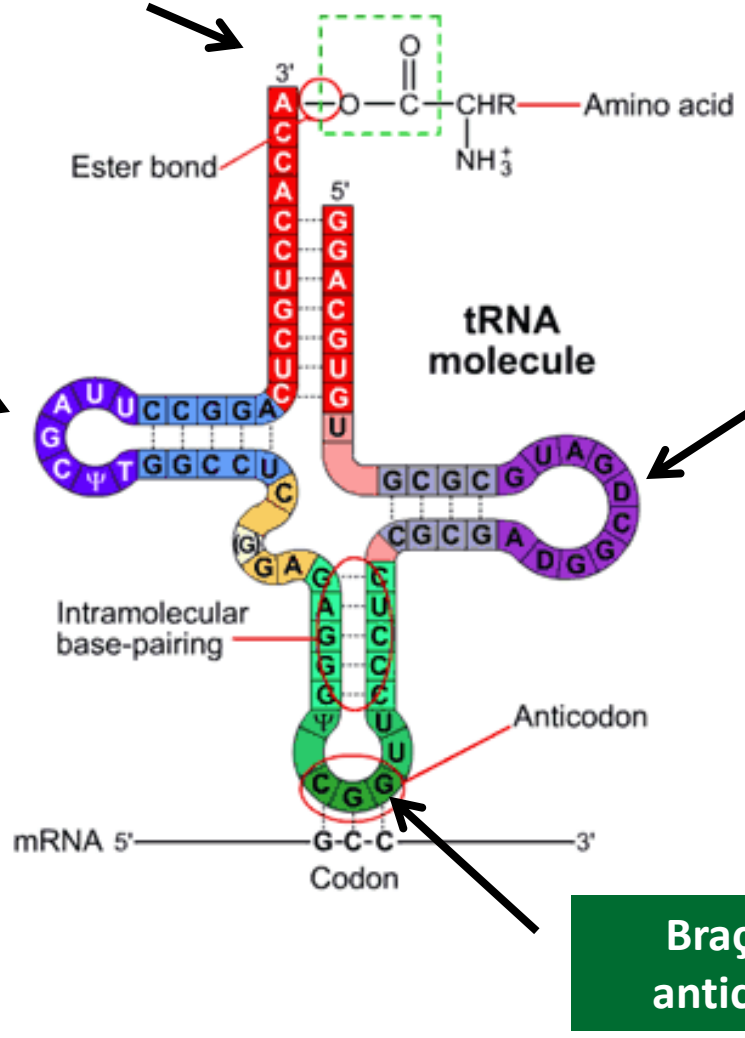


RNA TRANSPORTADOR (TRNA)

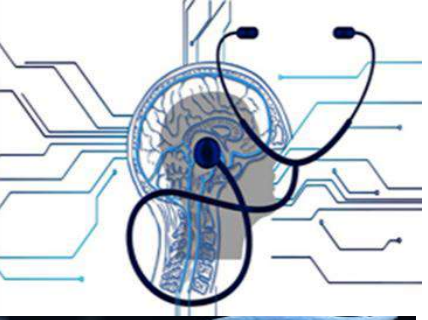
Braço aceptor de AA

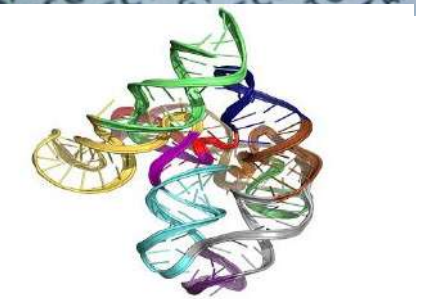
Sítio de ligação ao ribossomo

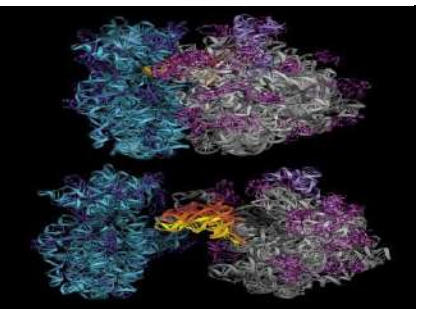
Reconhecimento da enzima específica



Braço do anticódon

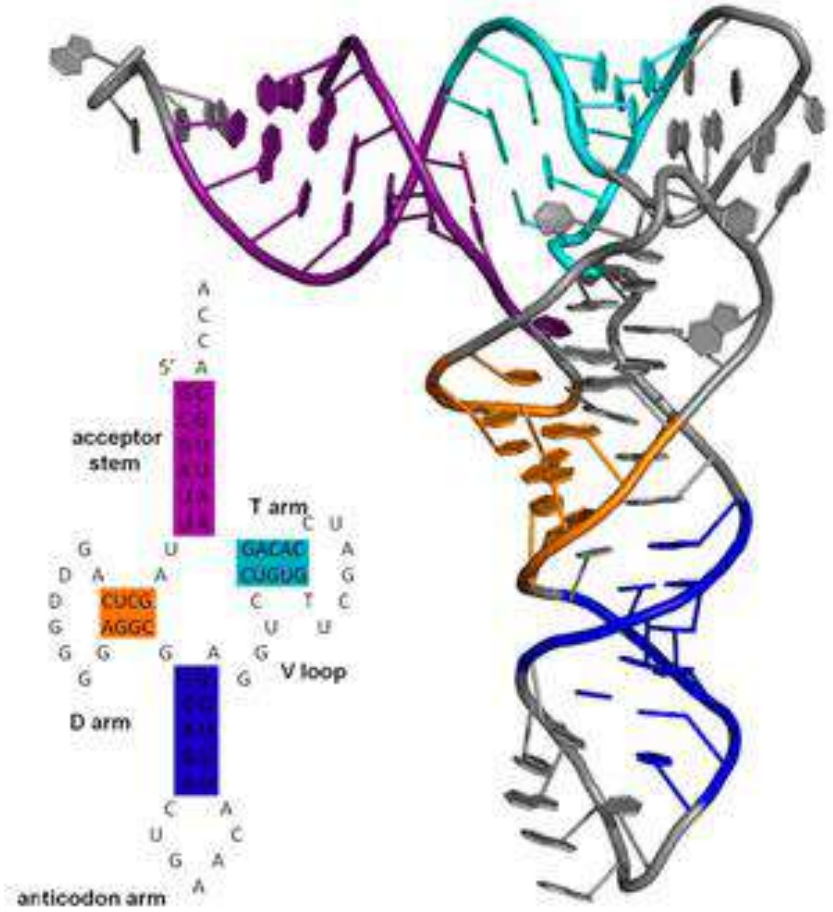


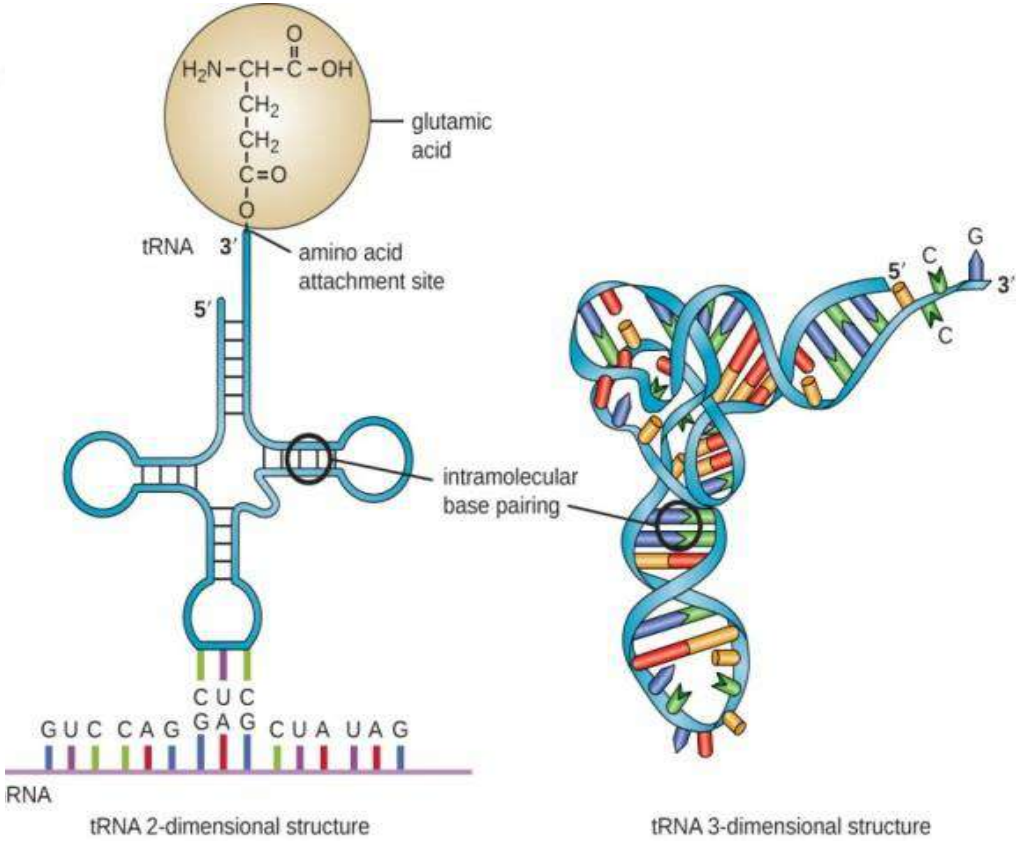


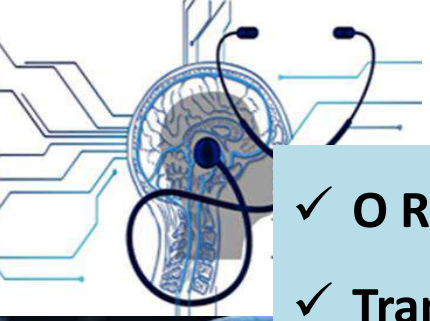


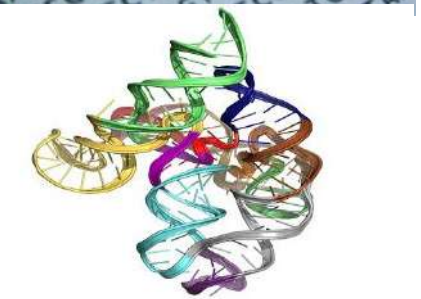
RNA TRANSPORTADOR (TRNA) - BASES MODIFICADAS

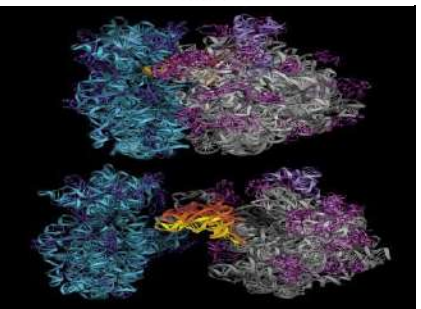
- ✓ **tRNA podem apresentar estrutura terciária em dupla hélice**





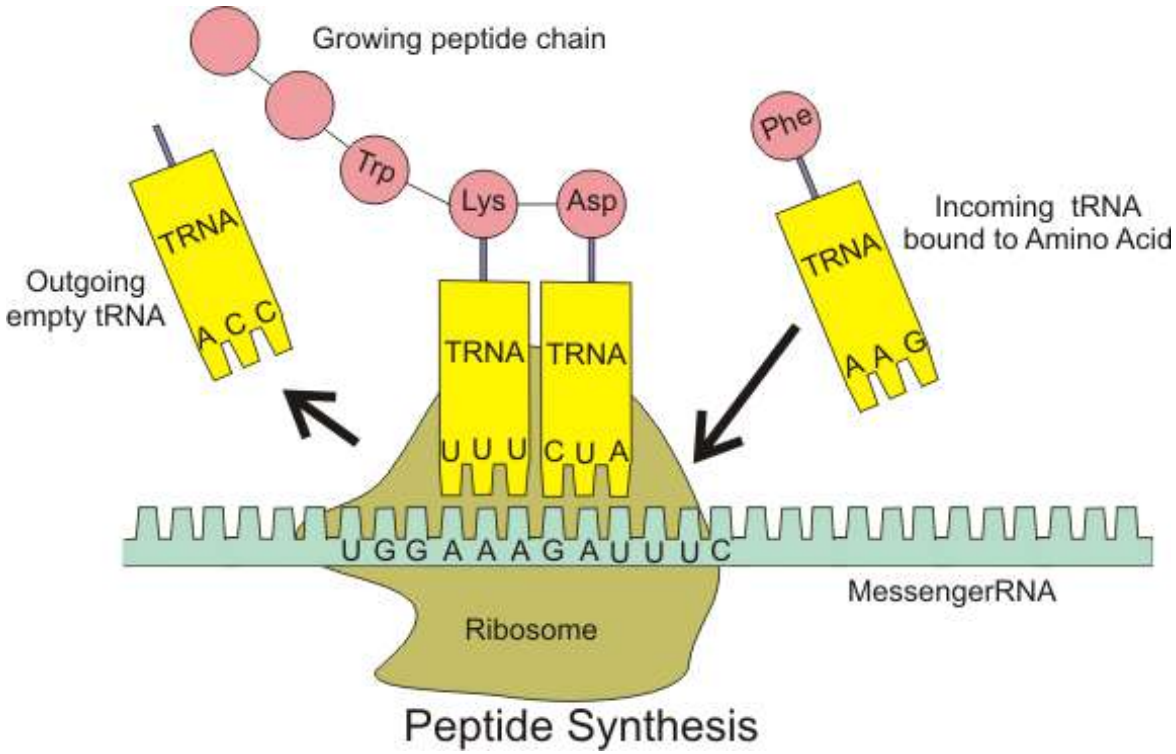


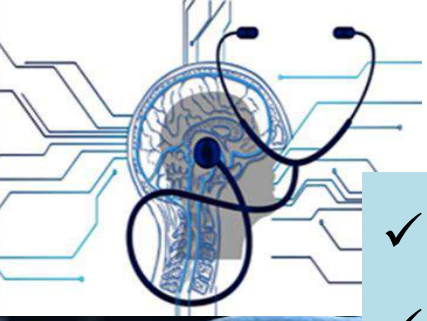


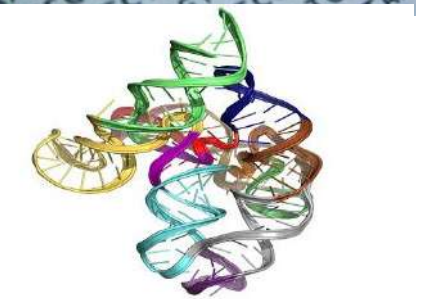


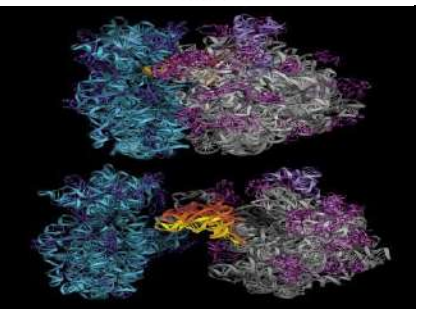
RNA TRANSPORTADOR

- ✓ **O RNA transportador é a menor das três principais espécies de RNAs (74-95 nucleotídeos);**
- ✓ **Transferência de aminoácidos do citoplasma para a maquinaria de síntese de proteínas;**
- ✓ **Existem pelo menos 20 espécies de tRNA, uma correspondente a cada um dos 20 aminoácidos necessários para a síntese de proteínas.**



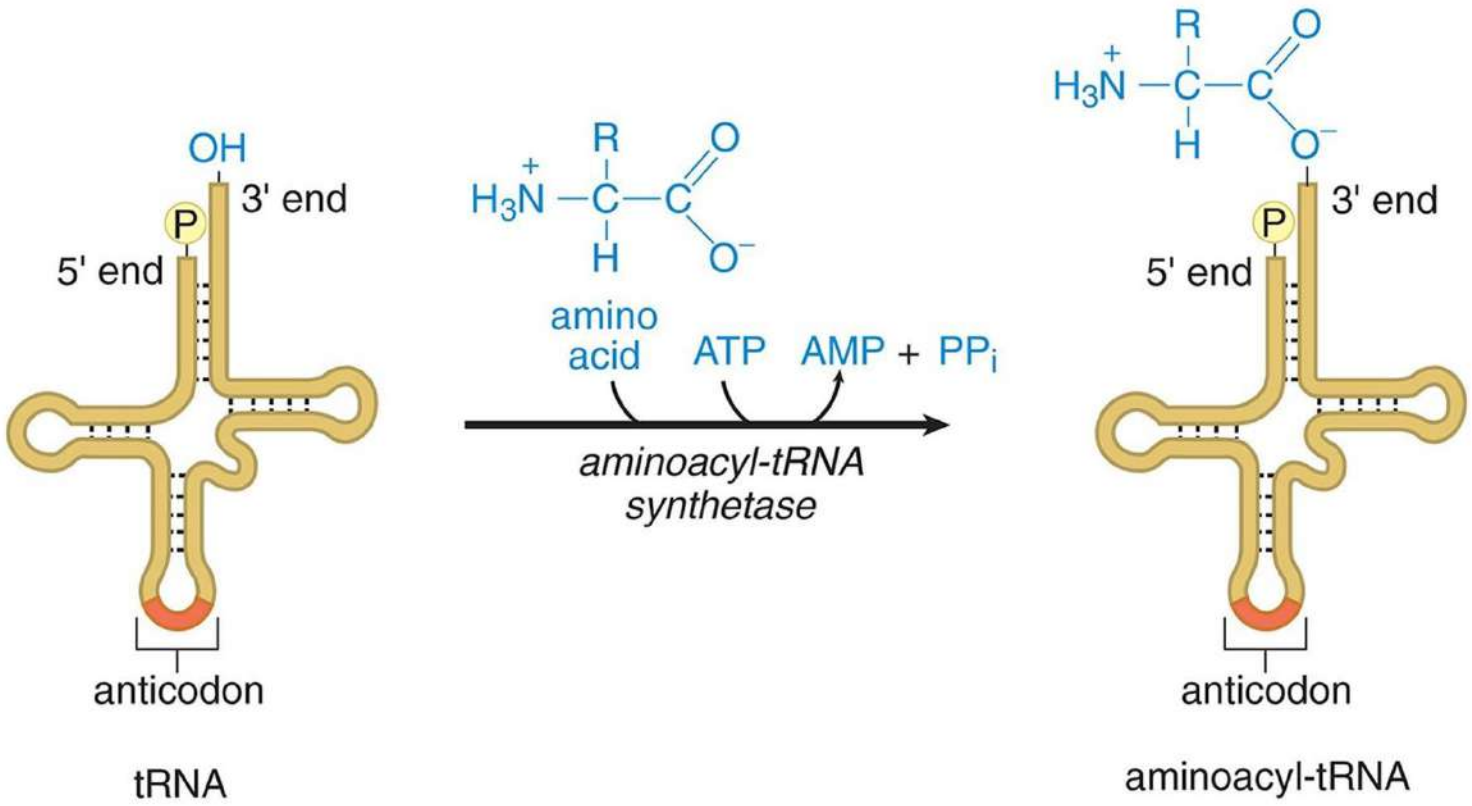




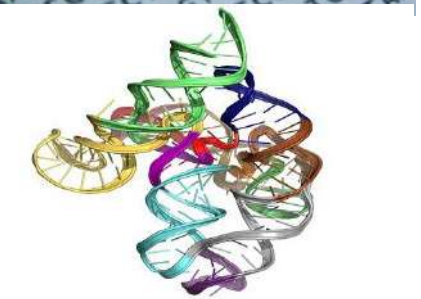


AMINOACIL-TRNA SINTETASES

- ✓ **Classe de enzimas necessárias para ligação do AA ao seu tRNA correspondente**
- ✓ **A sintetase tem revisão ou edição de atividade podendo remover AA da enzima ou tRNA**



EXISTEM PELO MENOS 20 DIFERENTES TIPOS DE tRNAs, UM CORRESPONDENTE PARA CADA UM DOS 20 AMINOÁCIDOS PROTEINOGÊNICOS



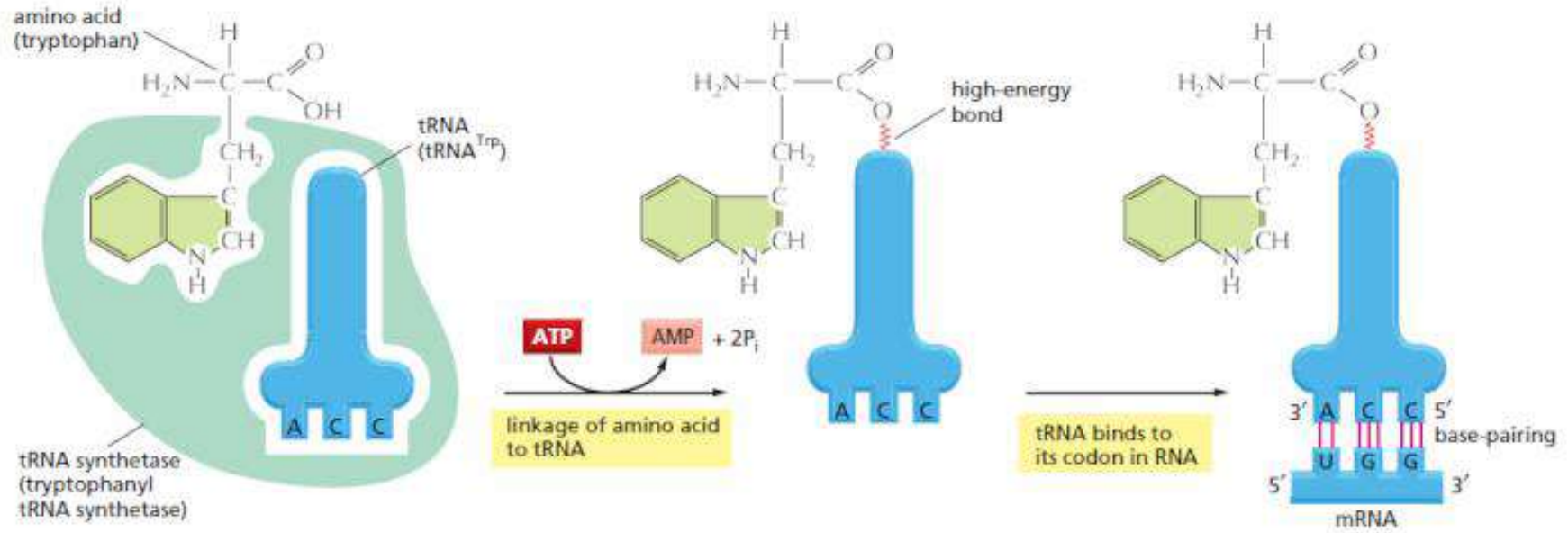
1. Glicil tRNA sintetase
2. Alanil tRNA sintetase
3. Valil tRNA sintetase
4. Leucil tRNA sintetase
5. Isoleucil tRNA sintetase
6. Metionil tRNA sintetase
7. Prolil tRNA sintetase

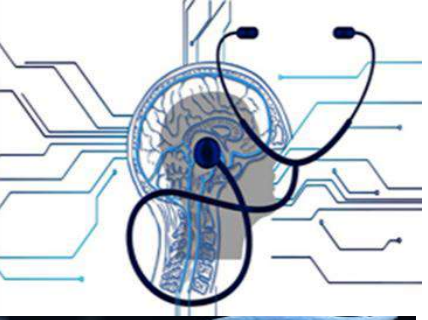
8. Seril tRNA sintetase
9. treonil tRNA sintetase
10. Cisteinil tRNA sintetase
11. Glutamil tRA sintetase
12. Asparaginil tRNA sintetase

13. Lisil tRNA sintetase
14. HistidiniltRNA sintetase
15. Arginil tRNA sintetase

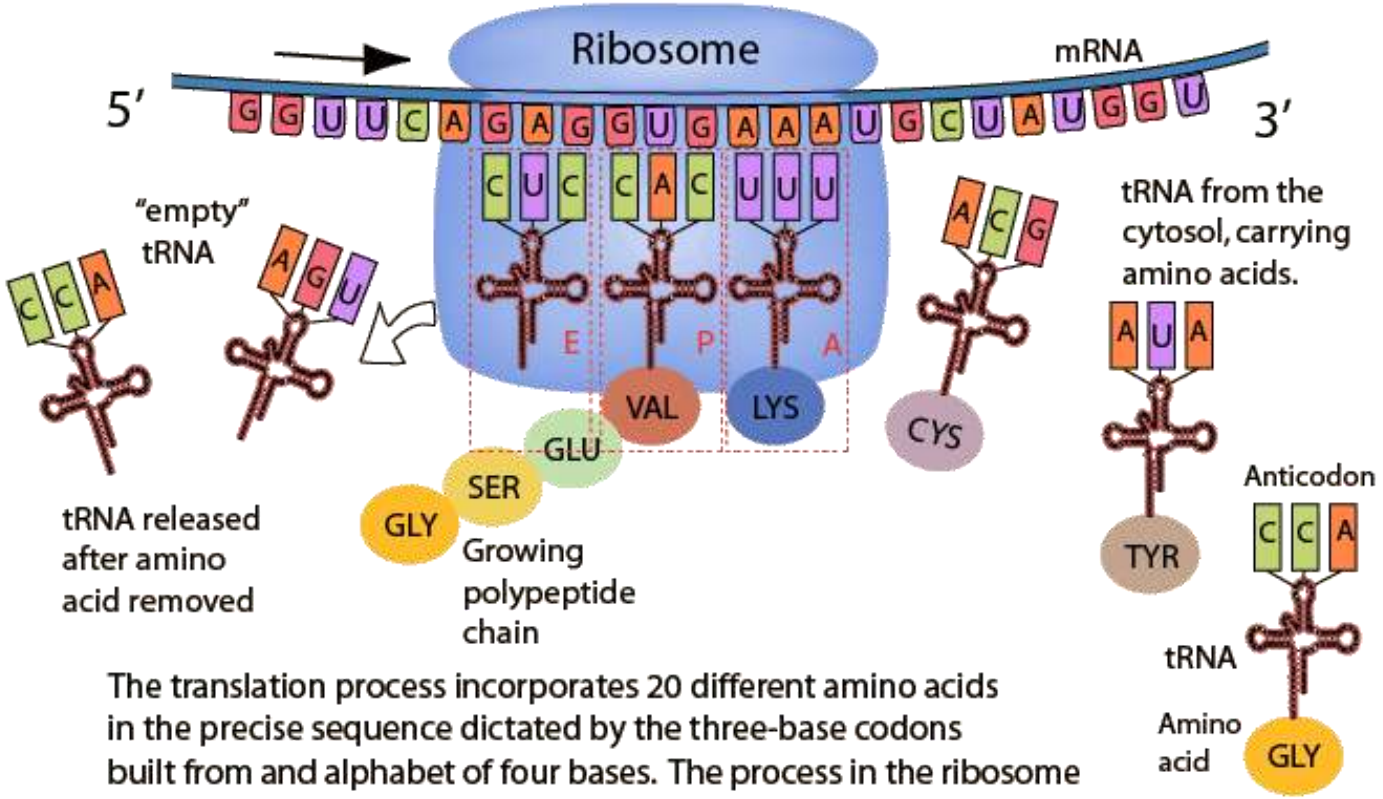
16. Aspartil tRNA sintetase
17. Glutamil tRNA sintetase

18. Phenilalanil tRNA sintetase
19. Tirosinil tRNA sintetase
20. Triptofanil tRNA sintetase



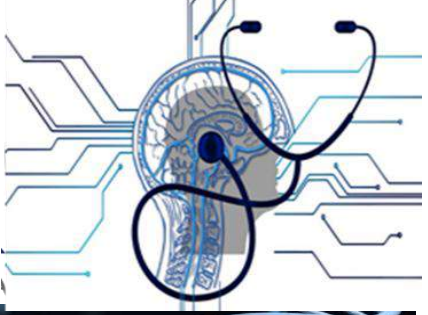


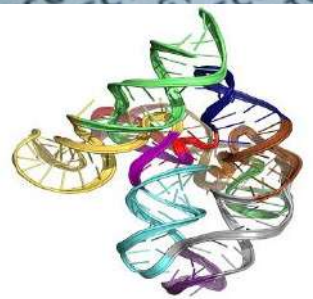
AMINOACIL-TRNA SINTETASES

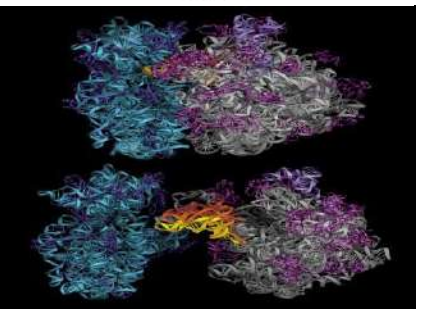


The translation process incorporates 20 different amino acids in the precise sequence dictated by the three-base codons built from and alphabet of four bases. The process in the ribosome builds the polypeptide chains tha will become proteins.

- ✓ **No citosol, os ribossomos se movem ao longo do mRNA, traduzindo-o em um polipeptídeo. Os anticódons do tRNA ligam-se aos códons do mRNA, por complementariedade de bases, transportando o seu aminoácido específico. Uma reação de condensação une os aminoácidos vizinhos (LIGAÇÃO PEPTÍDICA), formando uma cadeia polipeptídica.**

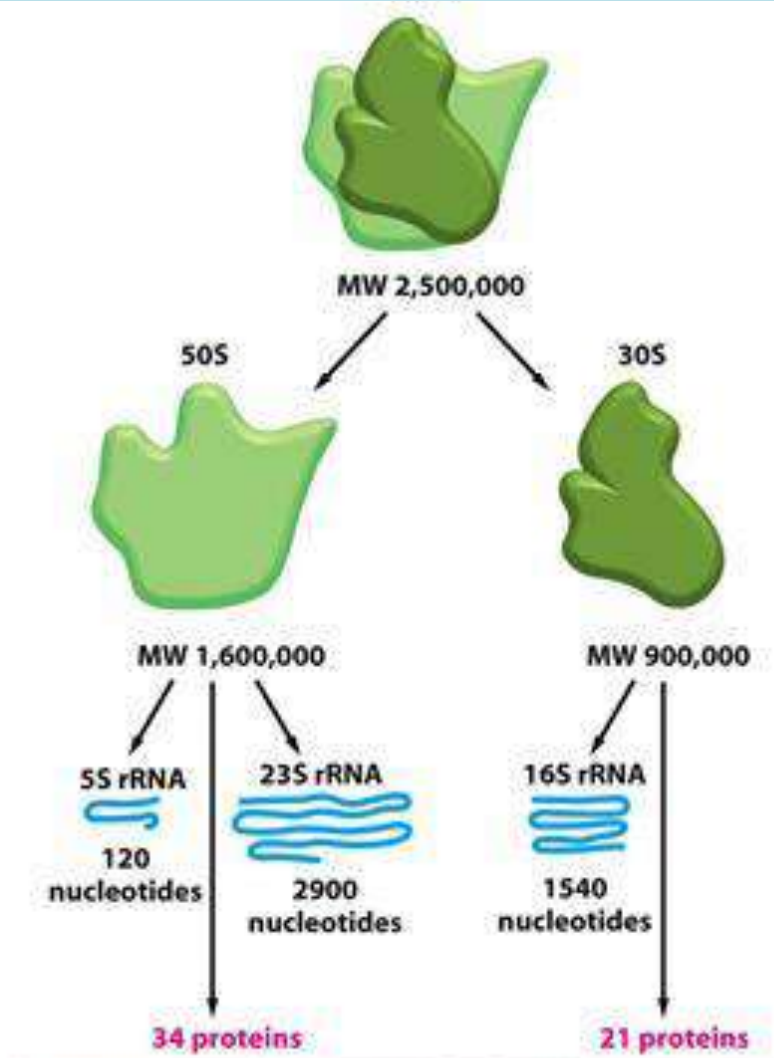




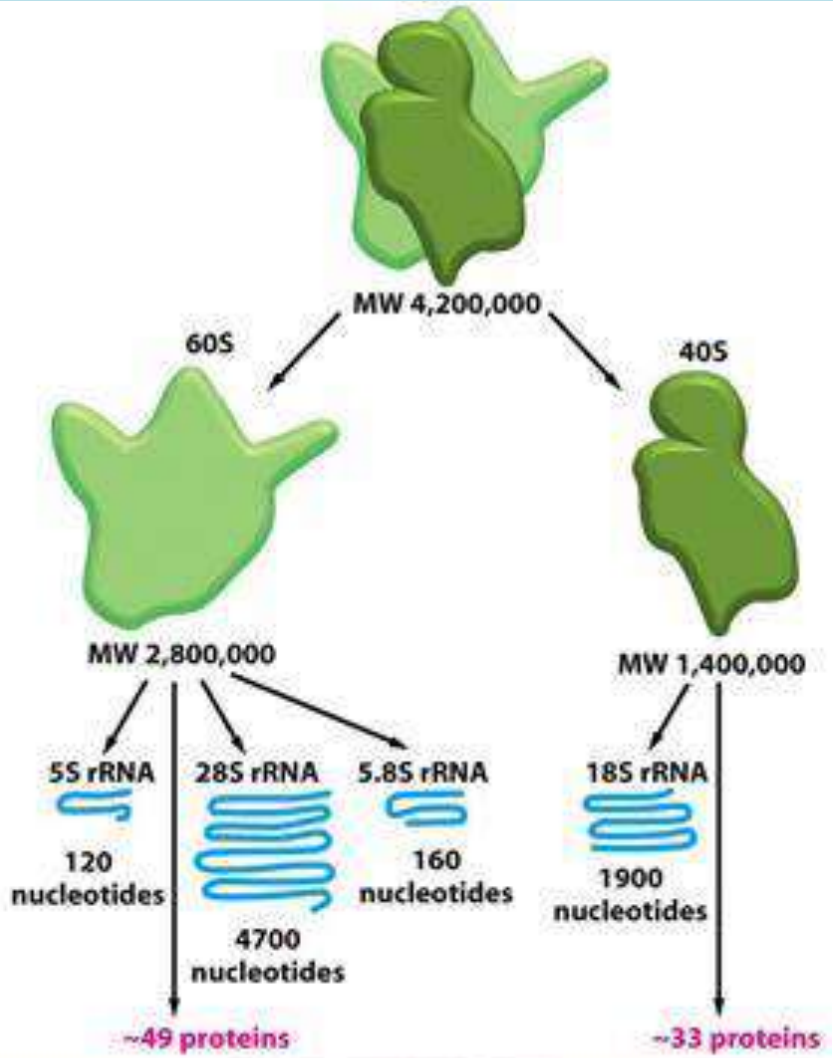


RNA RIBOSSOMAL (rRNA)

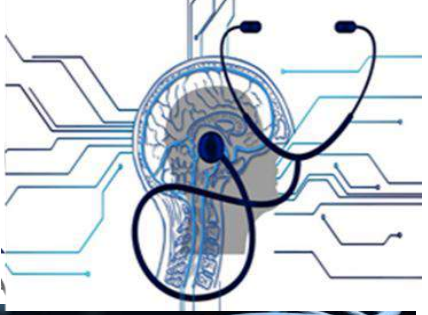
✓ **Compõe a estrutura dos ribossomos (procariotos e eucariotos)**

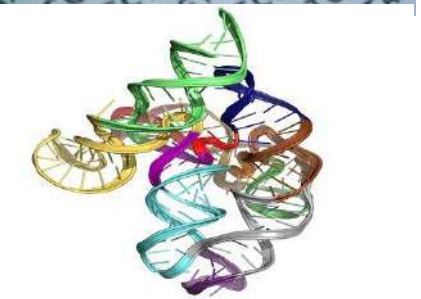


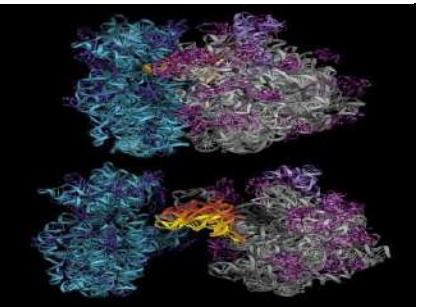
RIBOSSOMO PROCARIOTO



RIBOSSOMO EUCARIOTO

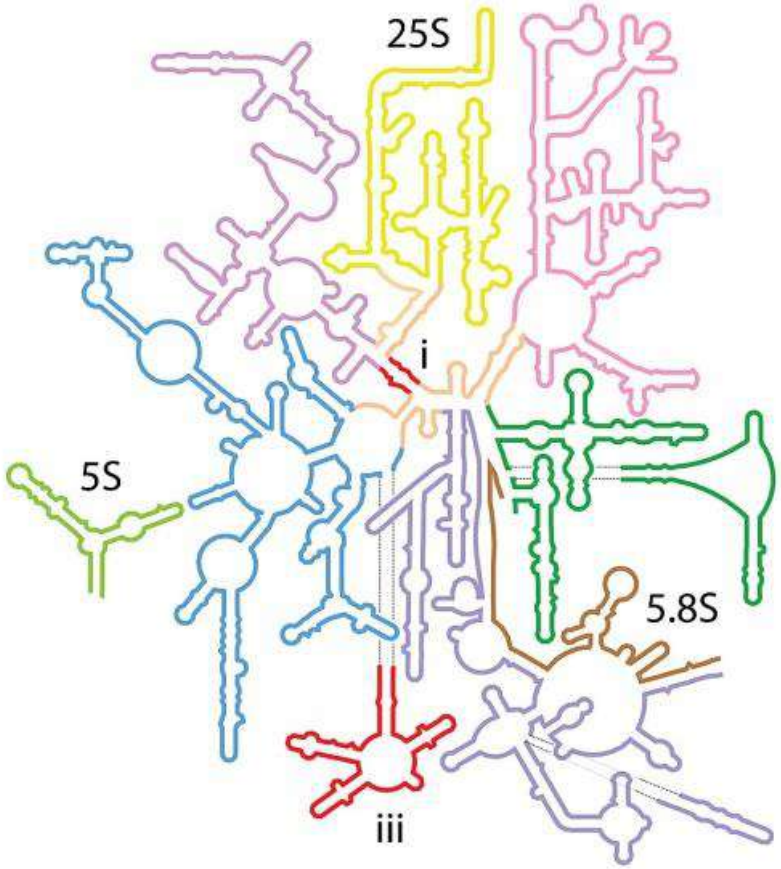




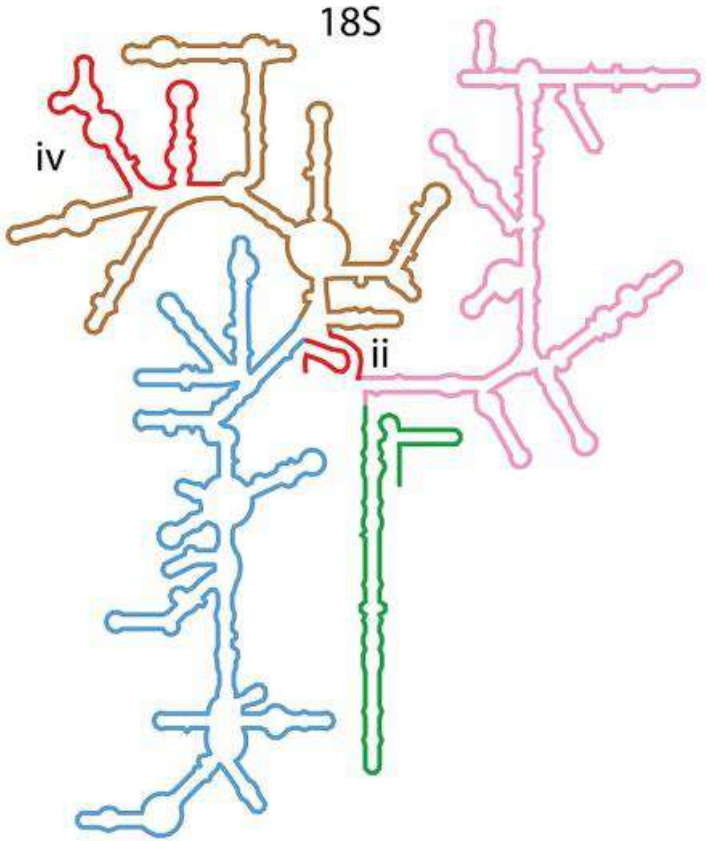


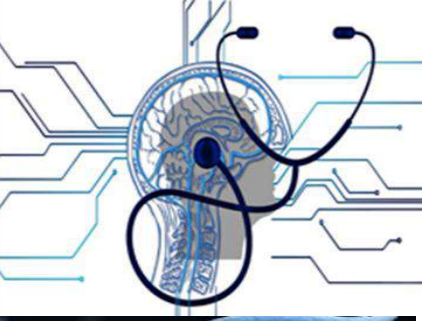
ESTRUTURA TRIDIMENSIONAL DO rRNA EUCARIOTOS

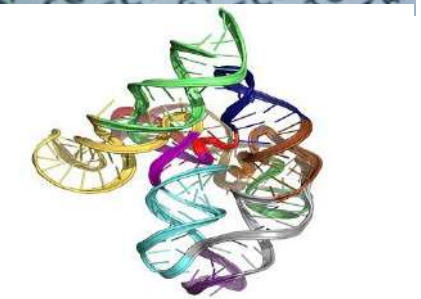
a) *S. cerevisiae* LSU

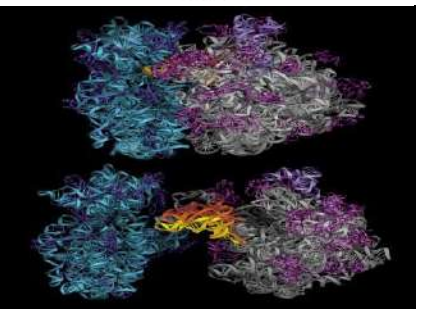


b) *S. cerevisiae* SSU









GENOMA, TRANSCRIPTOMA, PROTEOMA E METABOLOMA