Universidad Autónoma de Baja California

Facultad de Ciencias Marinas CURSO: BIOQUÍMICA

Unidad 2

2.7. Nucleótidos y ácidos nucleicos : Estructura y función biológica



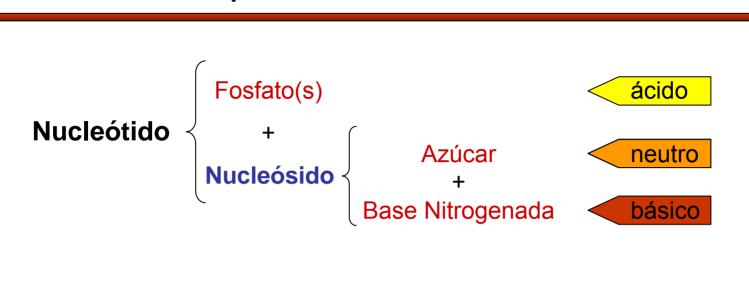
Profesor:

Dr. Eduardo Durazo Beltrán

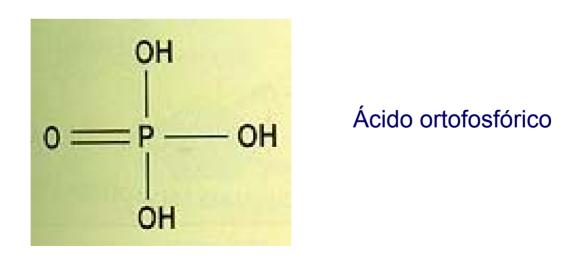


Textos de apoyo subtema 2.7

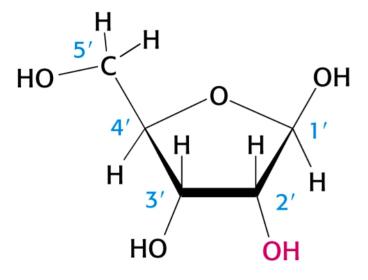
- ➤ Garrett, R.H., Grishman, C.M., 2002. Principles of Biochemistry. Capítulo 8. Hartcourt College Publishers, Fort Worth.
- ➢ Nelson, D.L., Cox, M.M., 2006. Lehninger Principios de Bioquímica. 4ª edición, capítulo 8. Ediciones Omega, Barcelona.
- ➤ Voet, D., Voet, J., 2002. Fundamentals of Biochemistry Upgrade. Capítulo 13. John Wiley & Sons, New York.



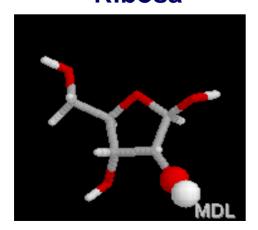
Componente ácido: Fosfatos

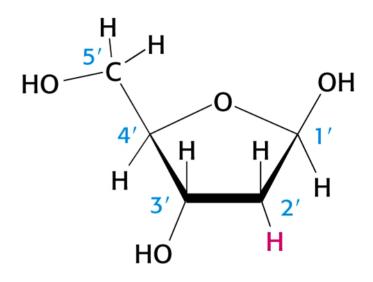


Componente neutro: Azúcares

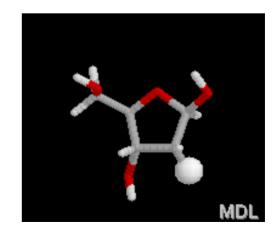


Ribosa

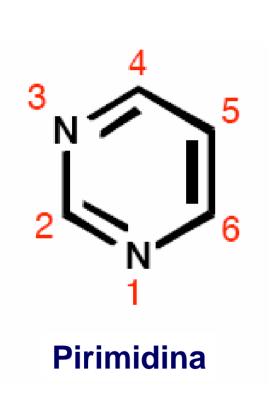


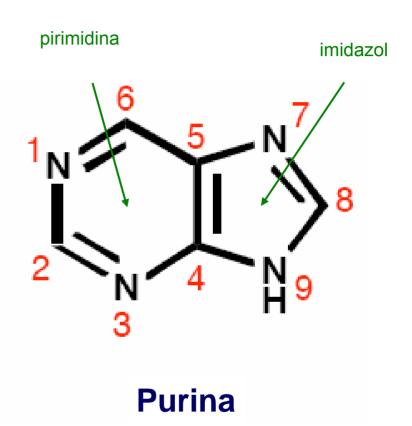


Desoxirribosa



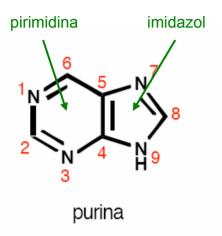
Componente básico: Bases Nitrogenadas

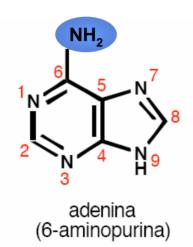




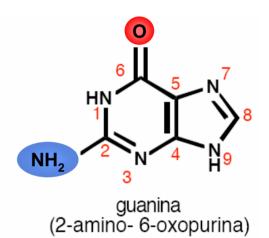
Componente básico: Bases Nitrogenadas

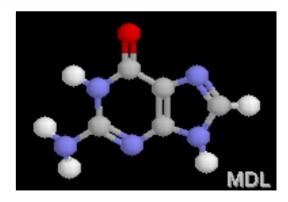
Bases Purínicas (o Púricas)





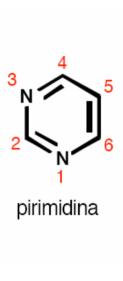


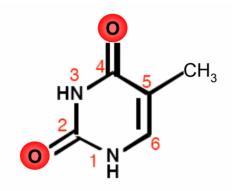




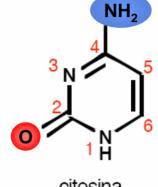
Componente básico: Bases Nitrogenadas

Bases Pirimidínicas

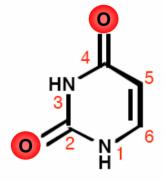




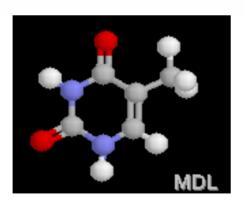
timina (2,4-dioxo-5metilpirimidina)

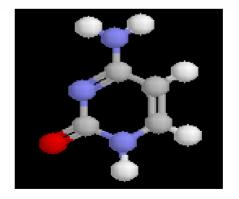


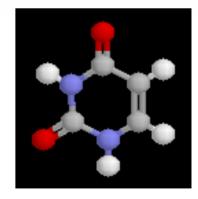
citosina (2-oxo-4-aminopirimidina)



uracilo (2,4-dioxopirimidina)







Propiedades fisicoquímicas de las bases nitrogenadas

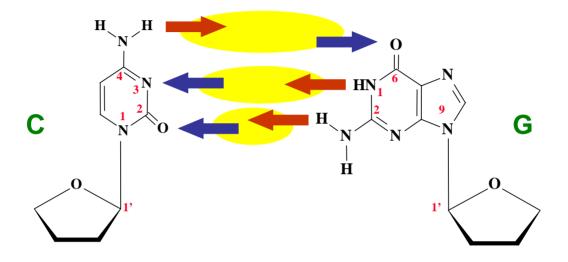
- Existencia de dipolos
- Hidrofobicidad
- Disposición coplanar de los enlaces de cada anillo (C-N y C-C)

Tautomería o isomería dinámica

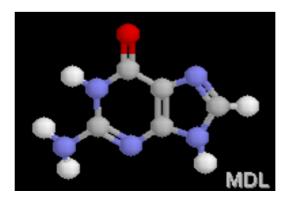
- Carácter básico
- Absorción de la luz en el ultravioleta

Propiedades fisicoquímicas de las bases nitrogenadas

Existencia de dipolos



- Hidrofobicidad y disposición coplanar de los enlaces de cada anillo (C-N y C-C)
- La naturaleza aromática de los anillos influye en la solubilidad en agua



Propiedades fisicoquímicas de las bases nitrogenadas

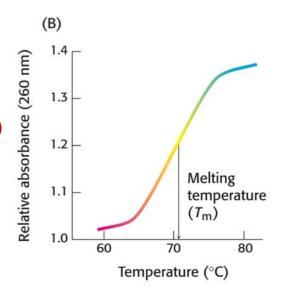
- Tautomería o isomería dinámica
 - Isomería de grupos funcionales

Forma ceto o lactama Forma enol o lactima

Forma ceto o lactama

Forma enol o lactima

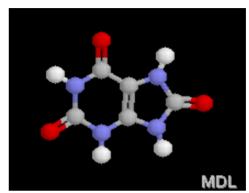
- Carácter débilmente básico
- Absorción de la luz en el ultravioleta
 - Debido a su carácter aromático (resonancia)
 - Máxima absorción cerca de 260 nm



Otras bases nitrogenadas de interés biológico y clínico

Las bases nitrogenadas tienen poco interés bioquímico como sustancias libres, salvo en las vías biosintéticas y degradativas de los ácidos nucleicos.

El **ácido úrico** es un derivado púrico que constituye el producto final de la degradación de purinas.



Cafeína

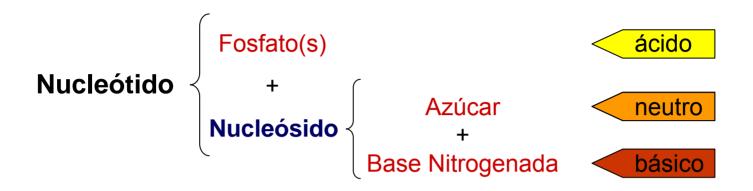
Teofilina

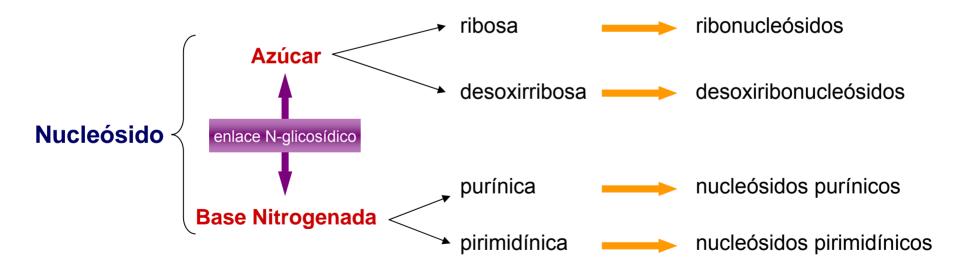
Análogos sintéticos, terapia antiviral

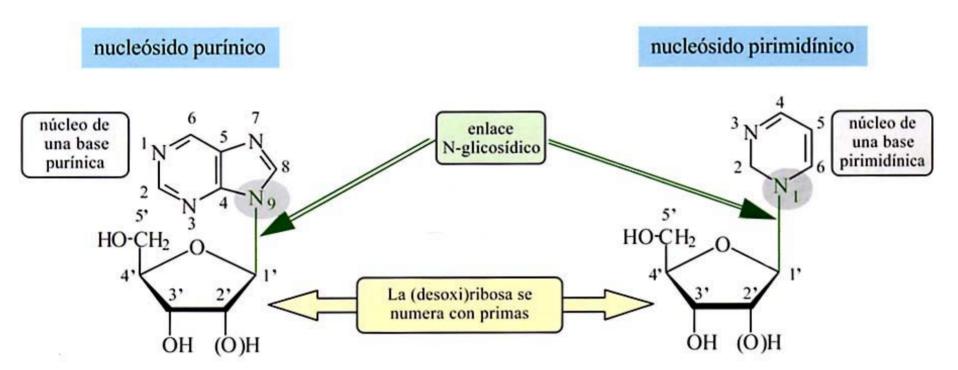
- Aciclovir (9-(2-hidroximetil)guanina
- Ganciclovir (9-(1,3-dihidroxi-2-proposimetil)guanina

Antitumorales sintéticos

5-fluorouracilo





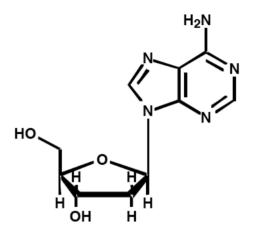


Nucleósidos purínicos

adenosina

guanosina

Ribonucleósidos

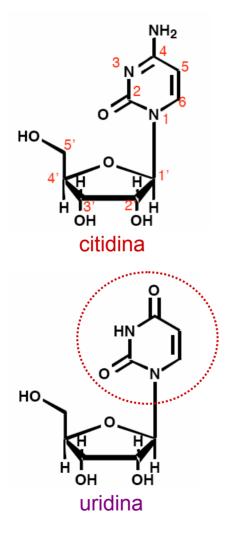


desoxiadenosina

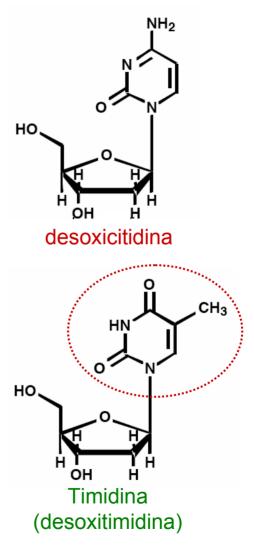
desoxiguanosina

Desoxirronucleósidos

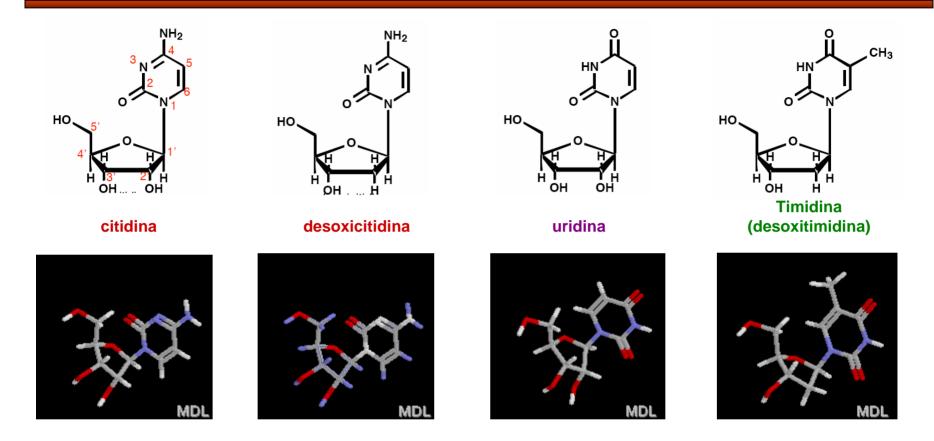
Nucleósidos pirimidínicos



Ribonucleósidos



Desoxirronucleósidos



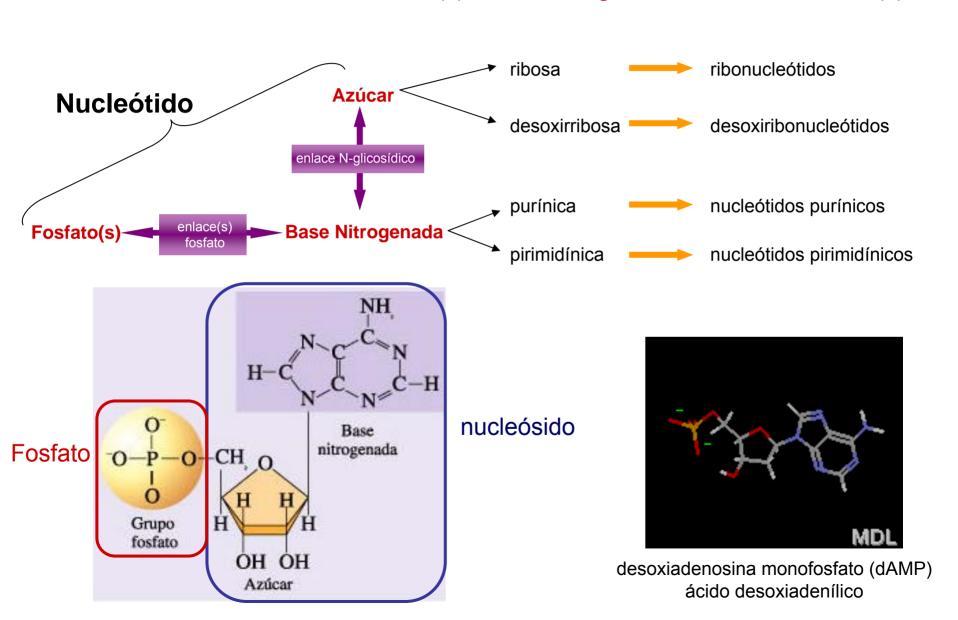
Otros nucleósidos de interés biológico y clínico

puromicina (antibiótico)

arabinosiladenina (antiviral y anticancerígeno)

AZT - derivado de timina (antirretroviral)

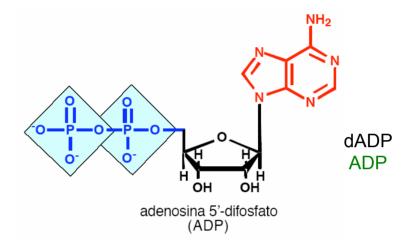
Nucleótido = nucleósido + fosfato(s) = base nitrogenada + azúcar + fosfato(s)



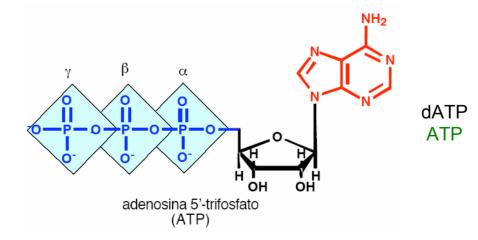
Nucleósidos-Monofosfato: NMP

dAMP AMP adenosina 5'-monofosfato (AMP)

Nucleósidos-Difosfato: NDP

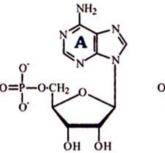


Nucleósidos-Trifosfato: NTP



Nucleósidos-monofosfato componentes del ARN (ribonucleótidos)

Purínicos

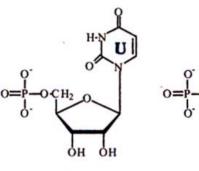


adenilato, AMP, 5'-AMP, A, adenosina-5'-fosfato

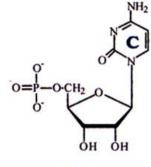
$$O = P - O \cdot CH_2 O OH OH$$

guanilato, GMP, 5'-GMP, G, guanosina-5'-fosfato

Pirimidínicos



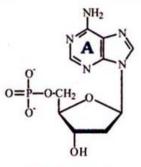
uridilato, UMP, 5'-UMP, U, uridina-5'-fosfato



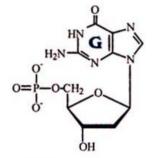
citidilato, CMP, 5'-UMP, C, citidina-5'-fosfato

Nucleósidos-monofosfato componentes del ADN (desoxirribonucleótidos)

Purínicos



desoxiadenilato, dAMP, 5'-dAMP, dA, desoxiadenosina-5'-fosfato



 desoxiguanilato, dGMP, 5'-dGMP, dG, desoxiguanosina-5'-fosfato

Pirimidínicos

desoxitimidilato, dTMP, 5'-dTMP, dT, desoxitimidina-5'-fosfato desoxicitidilato, dCMP, 5'-dCMP, dC, desoxicitidina-5'-fosfato

Funciones de los nucleótidos

Compuestos ricos en energía que participan en intercambios energéticos

Actúan como señales químicas

- Constituyentes de los ácidos nucleicos
 - ADN: ácido desoxirribonucleico
 - ARN: ácido ribonucleico

 Componentes estructurales de cofactores e intermediarios metabólicos

NAD+

O_P
OHOOH
NH2

NH2
NH2
NH2
NH2

TIPOS DE ÁCIDOS NUCLEICOS

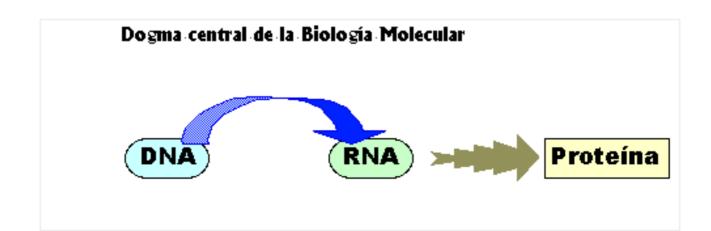
	ARN	ADN		
	Ribonucleótidos	Desoxirribonucleótidos		
Fosfato	enlazando los monómeros (enlace fosfodiéster)			
Azúcar	Ribosa	2'-Desoxirribosa		
Purinas	Adenina, A (6-aminopurina) Guanina , G (2-amino-6-oxopurina)			
Pirimidinas	Citosina, C (2-oxo-4-aminopirimidina)			
	Uracilo, U (2,4-dioxopirimidina)	Timina, T (5-metiluracilo)		

Ácidos Nucleicos

Funciones biológicas

- El ADN es el constituyente primario de los cromosomas de las células y es el portador del mensaje genético.
- La función del RNA es transcribir el mensaje genético presente en el DNA y traducirlo a proteínas.
- Las proteínas son las moléculas que finalmente ejecutarán las "instrucciones" codificadas en los ácidos nucleicos.

Francis Crick introdujo el dogma central de la Biología Molecular para describir el flujo de información biológica y cómo la célula utiliza esa información.



Niveles estructurales de los ácidos nucleicos

Estructura primaria

Polímero lineal formado por la unión de numerosos nucleótidos mediante enlaces fosfodiéster.

Estructura secundaria

Disposición espacial relativa de los nucleótidos que se encuentran próximos en la secuencia.

DNA – Doble cadena polinucleotídicas

 RNA – Protuberancias, bucles y horquillas en determinadas regiones de la molécula

Estructuras de orden superior

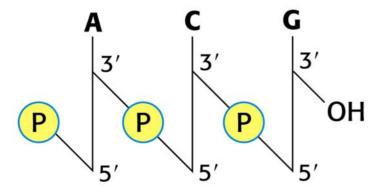
Todas aquellas de orden superior a los niveles primario y secundario.

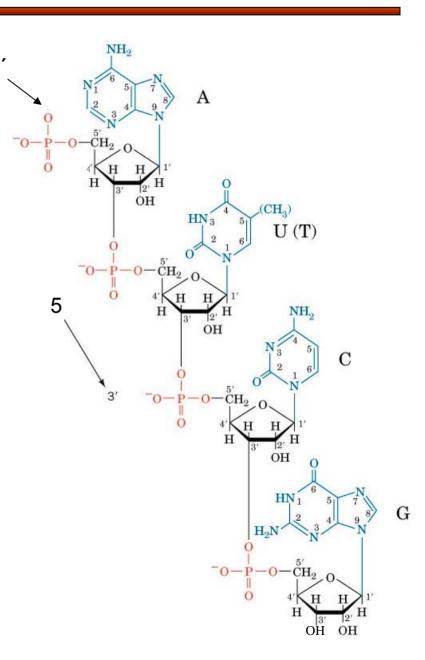
DNA – Resultantes del superenrollamiento y de la asociación con proteínas básicas (cromatina, cromosomas).

RNA - Plegamiento tridimensional definido (tRNA).

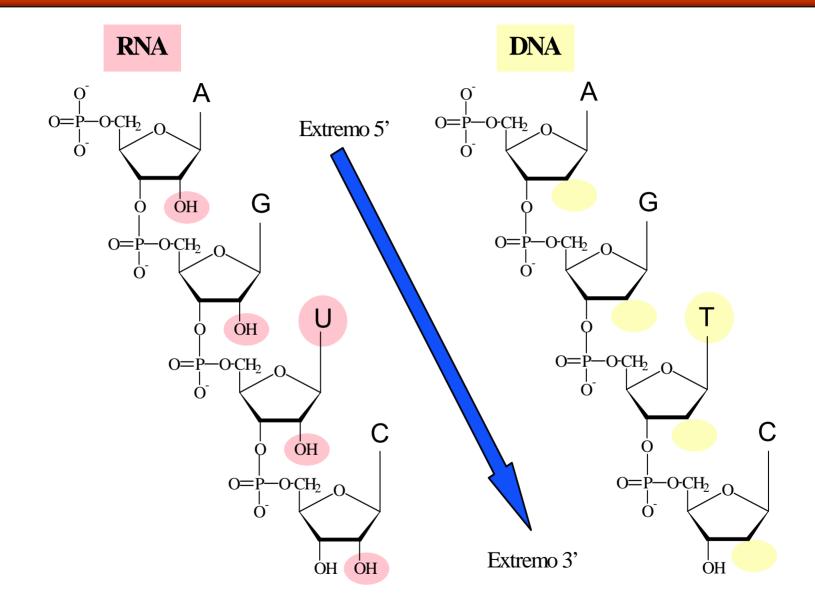
Estructura primaria

- Común para DNA y RNA
- Polímeros de nucleótidos unidos mediante enlaces covalentes 3´- 5´fosfodiéster.
- Secuencia en dirección 5′→ 3′





Estructura primaria



Estructura primaria de los ácidos nucleicos

	L	_ocalización		Función	
	Eucariotas	Procariotas	Virus		
	en núcleo celular	en la zona nucleoide	dentro de la	Depositario y transmisor de la	
DNA	(varios cromosomas),	del citosol	cápsida	información genética,	
	en matriz mitocondrial y	(un cromosoma y	(sólo en	organizada en genes que	
	en estroma de	varios plásmidos)	algunos tipos	codifican productos génicos	
	cloroplastos		de virus)	(proteínas o RNAs)	
RNA	en núcleo celular	en citosol	dentro de la	Interviene en la transmisión de	
	(temporalmente)	en citosoi	cápsida	la información desde el DNA	
	en citosol,		(en otros tipos	hasta los productos génicos	
	en matriz mitocondrial y		de virus)		
	en estroma de				
	cloroplastos				

- Propiedades en disolución
- ADN y ARN son moléculas hidrofílicas debido a se comportan como ácidos polianiónicos a pH fisiológico

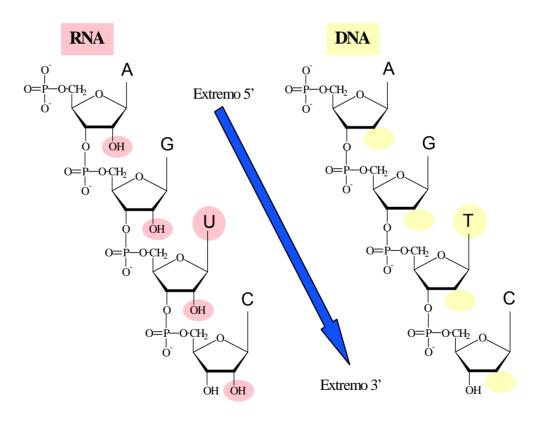
 El ADN genómico se encuentra generalmente estabilizado debido a su interacción con proteínas cargadas positivamente a pH fisiológico (histonas, protaminas, poliaminas)

Las soluciones de ADN son viscosas debido a la relativa rigidez de la molécula

Reactividad

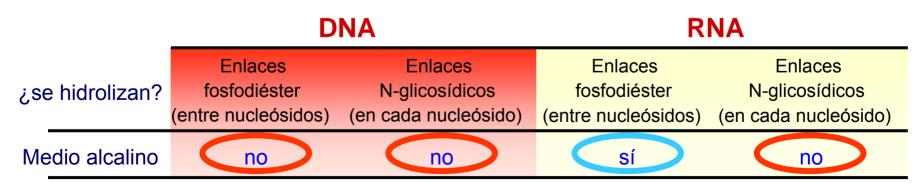
DNA es químicamente muy estable debido a la falta de grupos –OH libres

RNA algo más reactivo debido al grupo 2´-OH libre

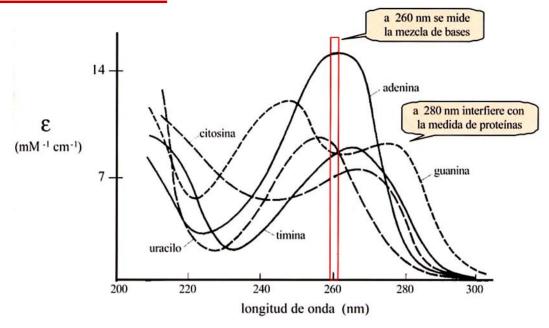


Hidrólisis ácida		DNA		RNA		
¿se hidrolizan?		Enlaces fosfodiéster (entre nucleósidos)	Enlaces N-gicosídicos (en cada nucleósido)	Enlaces fosfodiéster (entre nucleósidos)	Enlaces Nglicosídicos (en cada nucleósido)	
	ácido fuerte	sí	sí	SÍ	sí	
	ácido débil	no	sí (todos o purinas)	no	sí (todos o purinas)	

Hidrólisis alcalina



Absorción en el ultravioleta



Absorción máxima 260 nm Absorción máxima 280 nm

DNA
$$\frac{A_{260}}{A_{280}} = 1.8$$

RNA
$$\frac{A_{260}}{A_{280}} = 2.0$$

Estructura secundaria

- Reglas de Chargaff (1951)
- En todos los DNA estudiados, la proporción molar de A es igual a la de T, y la de G igual a la de C.

$$A \approx T \rightarrow Raz\acute{o}n A/T \approx T/A \approx 1$$
 $G \approx C \rightarrow Raz\acute{o}n G/C \approx C/G \approx 1$

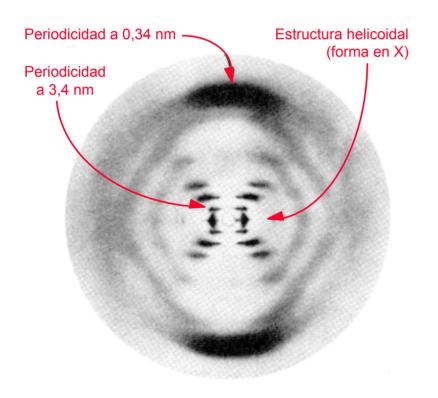
La relación purinas/pirimidinas es igual a 1

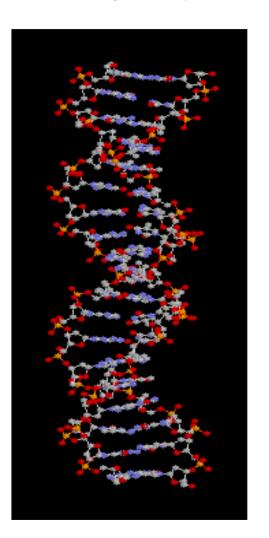
```
A+G ≈ T+C ≈ 50\% → Razón (A+G)/(T+C) ≈ 1
purinas ≈ pirimidinas ≈ 50\% → Razón purinas/pirimidinas ≈ 1
```

Estructura secundaria

Estudiada inicialmente (1951-1953) mediante cristalografía de rayos X por:

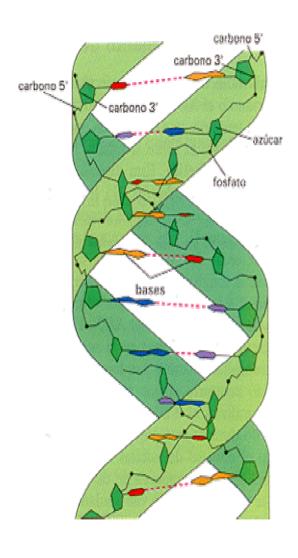
- L. Pauling (Caltech)
- M. Wilkins y R.E.Franklin (Londres)
- J.D. Watson y F.H.C.Crick (Cambridge)

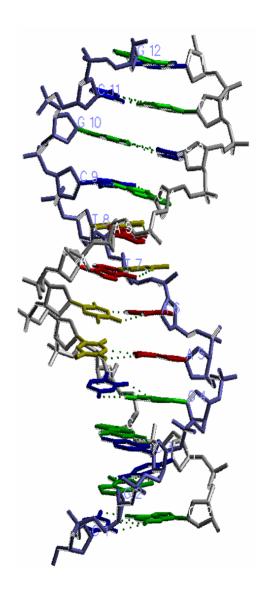




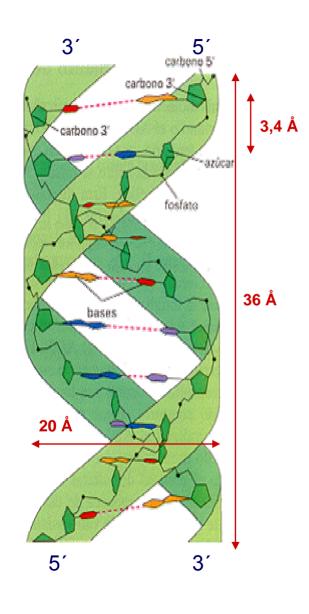
Watson y Crick en 1953 publicaron modelo de doble hélice

ADN-B: Doble hélice

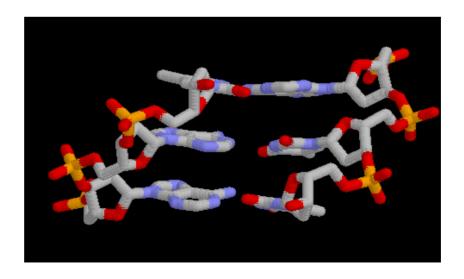


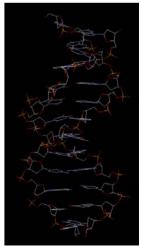


ADN-B: Doble hélice

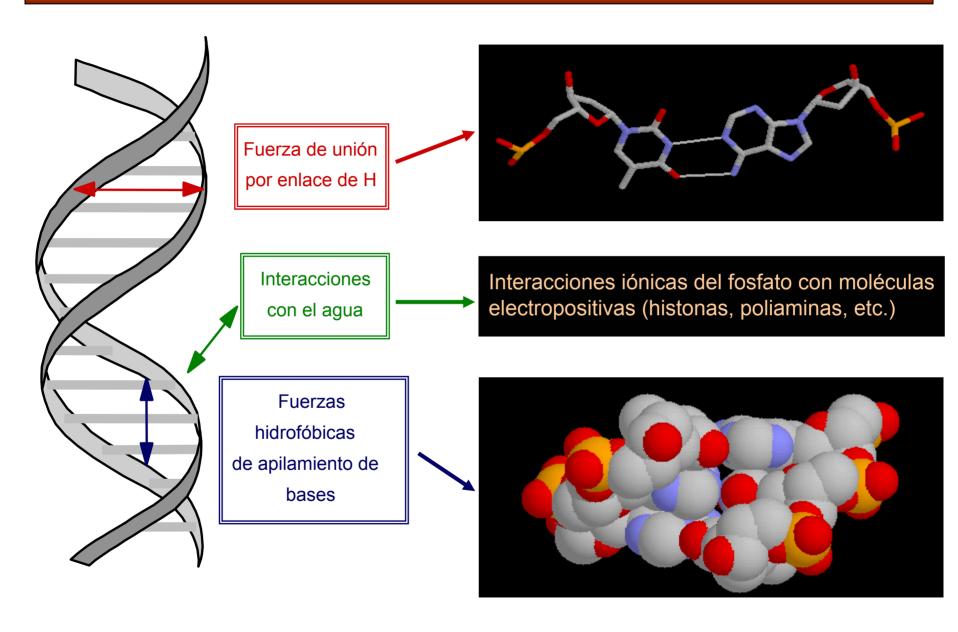


- Cada una de las hebras es un polinucleótido entrelazado con el otro en sentido antiparalelo
- El eje ribosa-fosfato se sitúa hacia el exterior de la doble hélice, en contacto con el solvente
- Las bases nitrogenadas se sitúan, apiladas, en planos aproximadamente perpendiculares al eje de la doble hélice, hacia el interior de la estructura, en un entorno hidrofóbico.





ADN-B: Interacciones que mantienen la estructura del ADN



ADN-B: Helicidad y surcos en la estructura del DNA

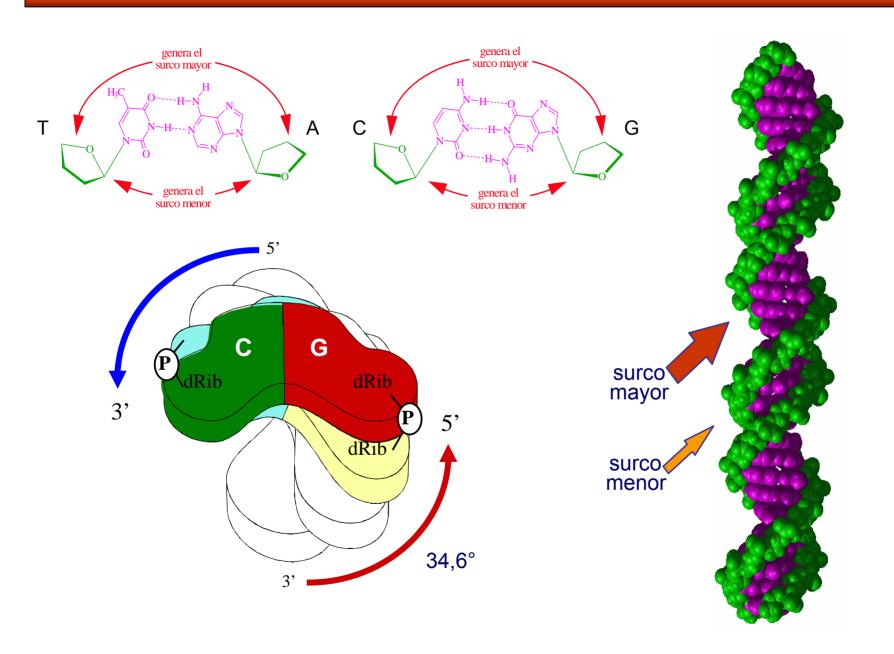


Table 12.1

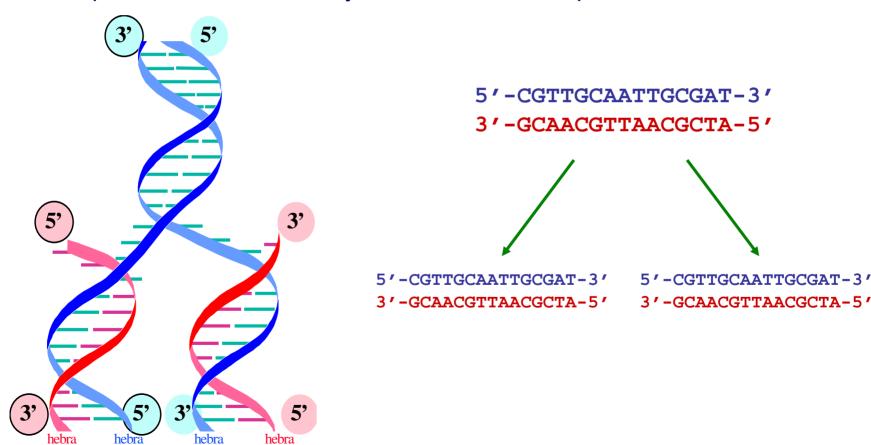
Comparison of the Structural Properties of A-, B-, and Z-DNA

	Double Helix Type		
	A	В	z
Overall proportions	Short and broad	Longer and thinner	Elongated and slim
Rise per base pair	2.3 Å	$3.32 \text{ Å} \pm 0.19 \text{ Å}$	3.8 Å
Helix packing diameter	25.5 Å	23.7 Å	18.4 Å
Helix rotation sense	Right-handed	Right-handed	Left-handed
Base pairs per helix repeat	1	1	2
Base pairs per turn of helix	~11	~10	12
Mean rotation per base pair	33.6°	$35.9^{\circ} \pm 4.2^{\circ}$	$-60^{\circ}/2$
Pitch per turn of helix	24.6 Å	33.2 Å	45.6 Å
Base-pair tilt from the perpendicular	+19°	$-1.2^{\circ} \pm 4.1^{\circ}$	-9°
Base-pair mean propeller twist	+18°	$+16^{\circ} \pm 7^{\circ}$	~0°
Helix axis location	Major groove	Through base pairs	Minor groove
Major groove proportions	Extremely narrow but very deep	Wide and with intermediate depth	Flattened out on helix surface
Minor groove proportions	Very broad but shallow	Narrow and with intermediate depth	Extremely narrow but very deep
Glycosyl bond conformation	anti	anti	anti at C, syn at G

Adapted from Dickerson, R. L., et al., 1982. Cold Spring Harbor Symposium on Quantitative Biology 47:14.

Significado biológico

- El material genético ha de ser lineal y aperiódico; el DNA cumple esa condición.
- El apareamiento de bases sugiere un modelo para la replicación del mismo de forma que las dos moléculas hijas son idénticas a la parental:



paterna

paterna

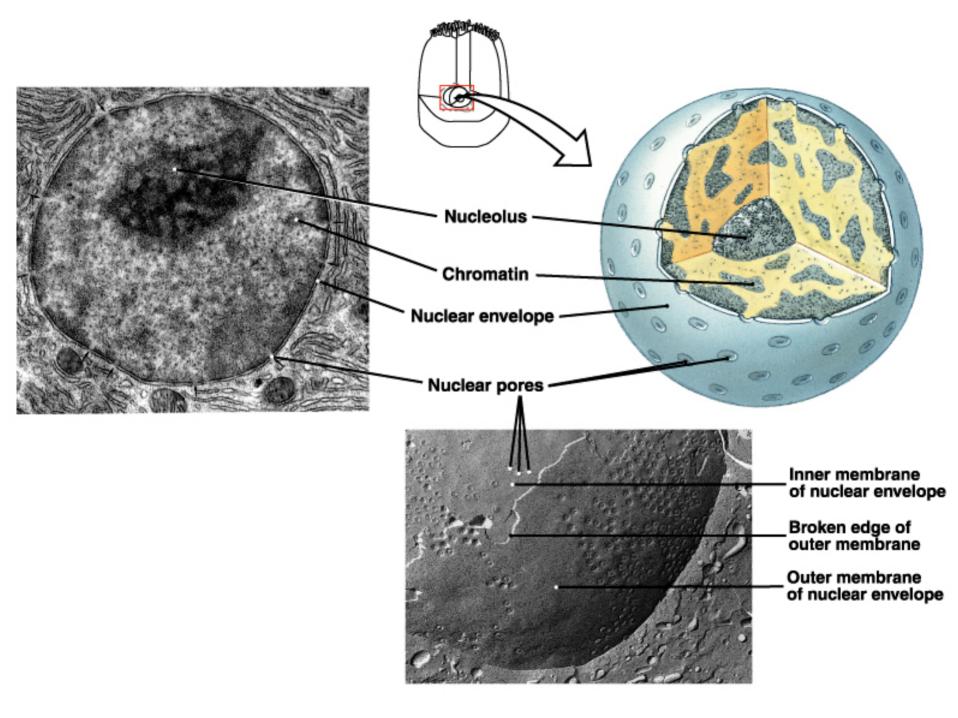
Ácidos Nucleicos

• Aunque sus componentes químicos son muy semejantes, el DNA y el RNA desempeñan papeles biológicos muy diferentes. El DNA es el constituyente primario de los cromosomas de las células y es el portador del mensaje genético.

La función del RNA es transcribir el mensaje genético presente en el DNA y traducirlo a proteínas. El descubrimiento de la estructura y función de estas moléculas es hasta ahora, indudablemente, el mayor triunfo del enfoque molecular en el estudio de la biología.

La información contenida en los ácidos nucleicos (DNA) es transcripta (RNA) y luego traducida a las proteínas. Son las proteínas las moléculas que finalmente ejecutarán las "instrucciones" codificadas en los ácidos nucleicos.

ADN ARN Proteínas



"We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest."

"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

-James Watson and Francis Crick

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MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Decay-bose Nucleic Reid

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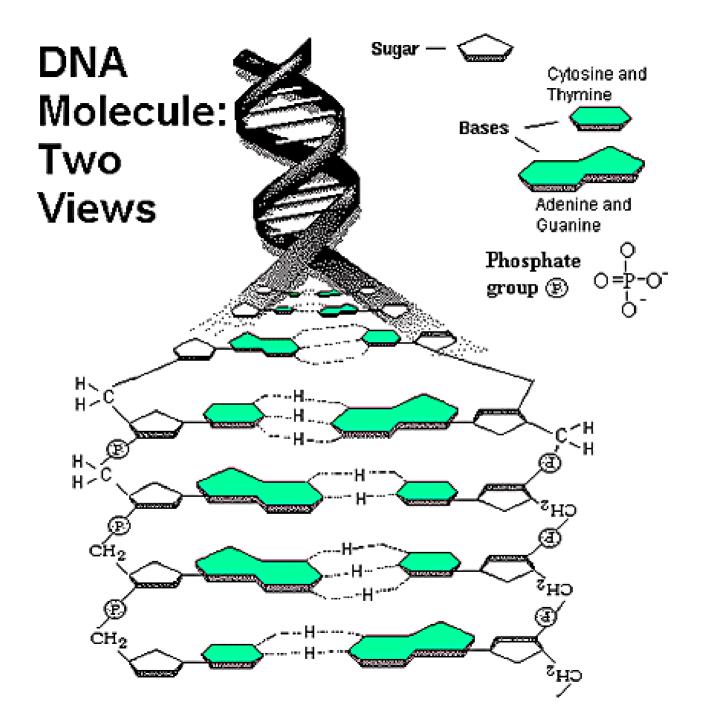
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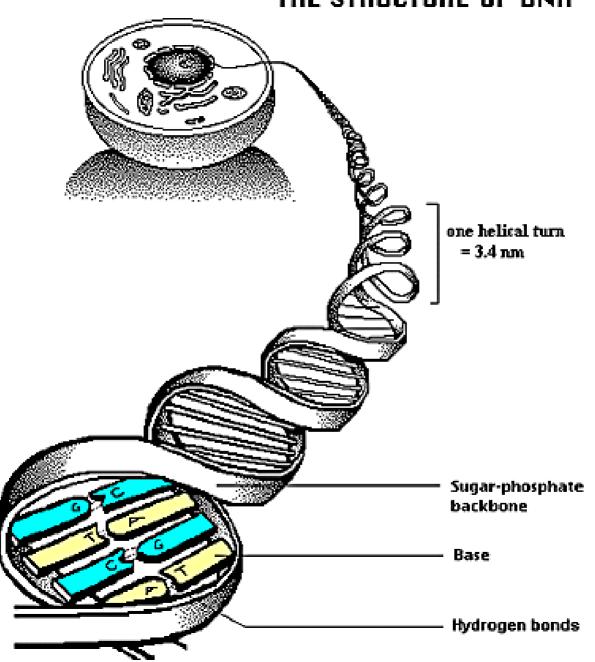
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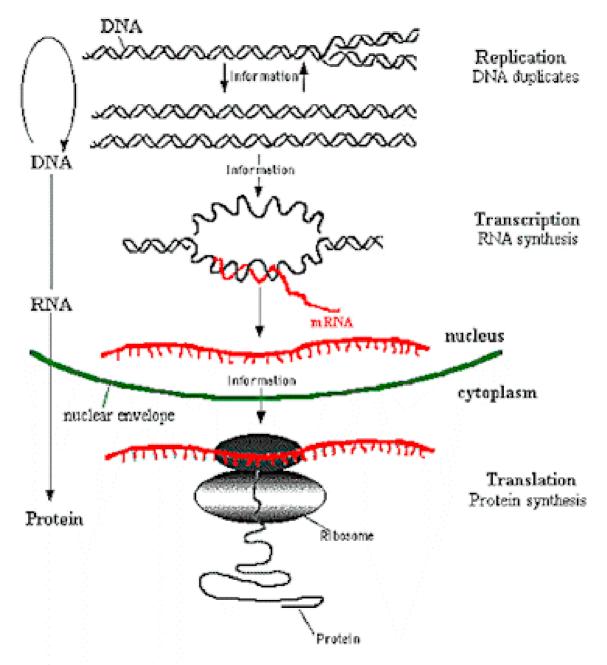
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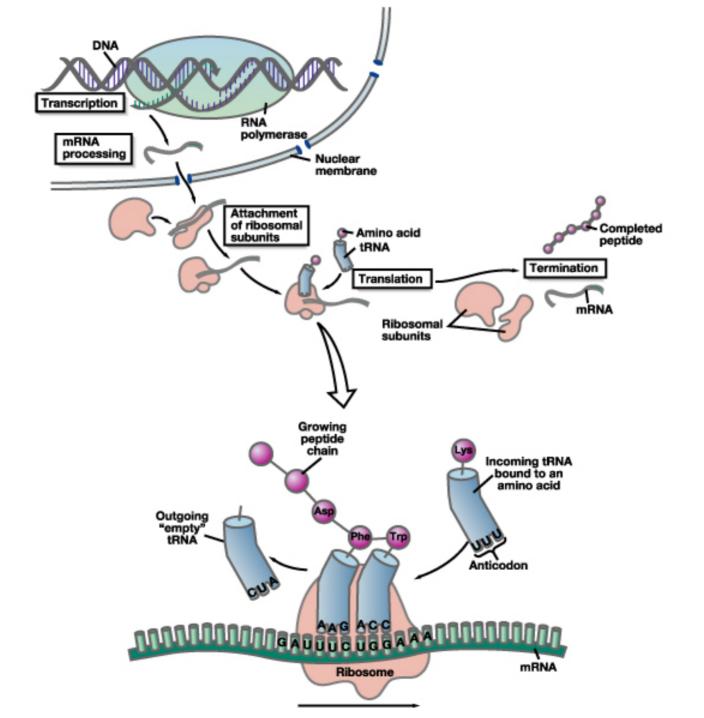


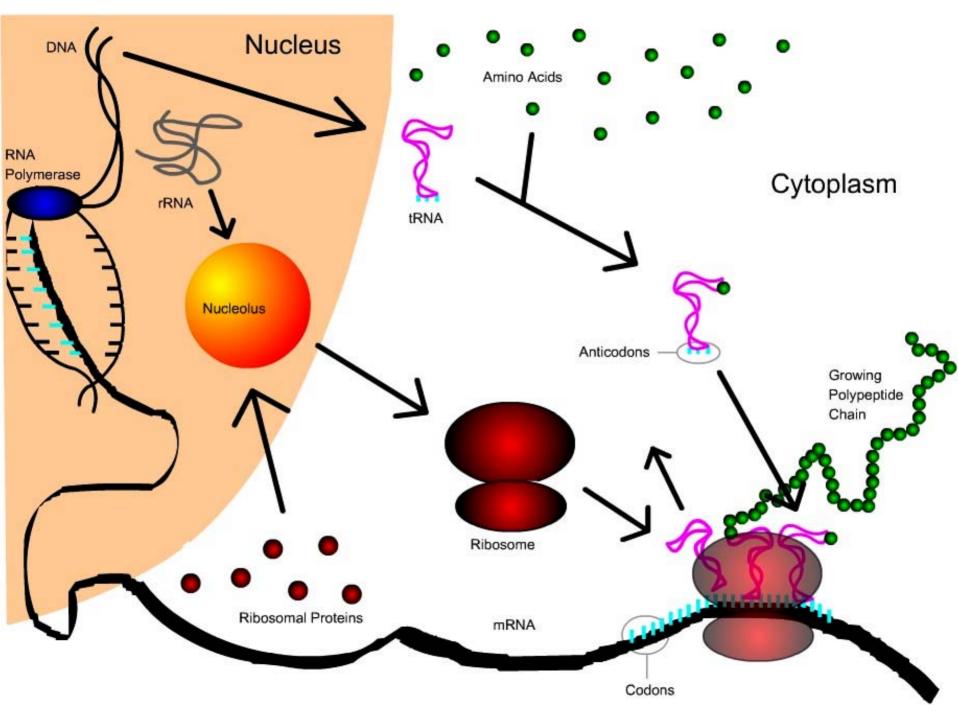
THE STRUCTURE OF DNA



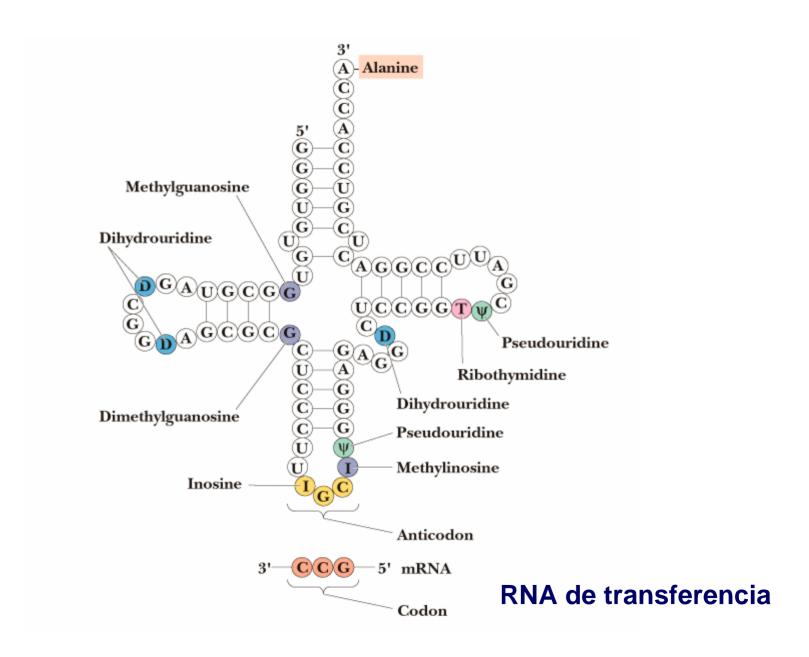


The Central Dogma of Molecular Biology





ESTRUCTURA DEL RNA



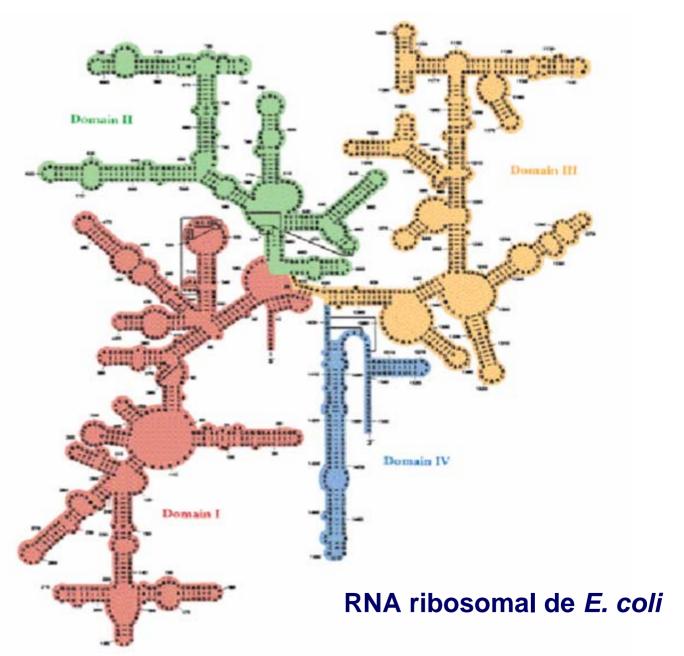


Imagen de Garett & Grisham, 1999, *Biochemistry*, 2^d ed., Harcourt Brace & Co., USA.