Nukleinsavak

James Watson

Francis Crick

Maurice Wilkins

Rosalind Franklin

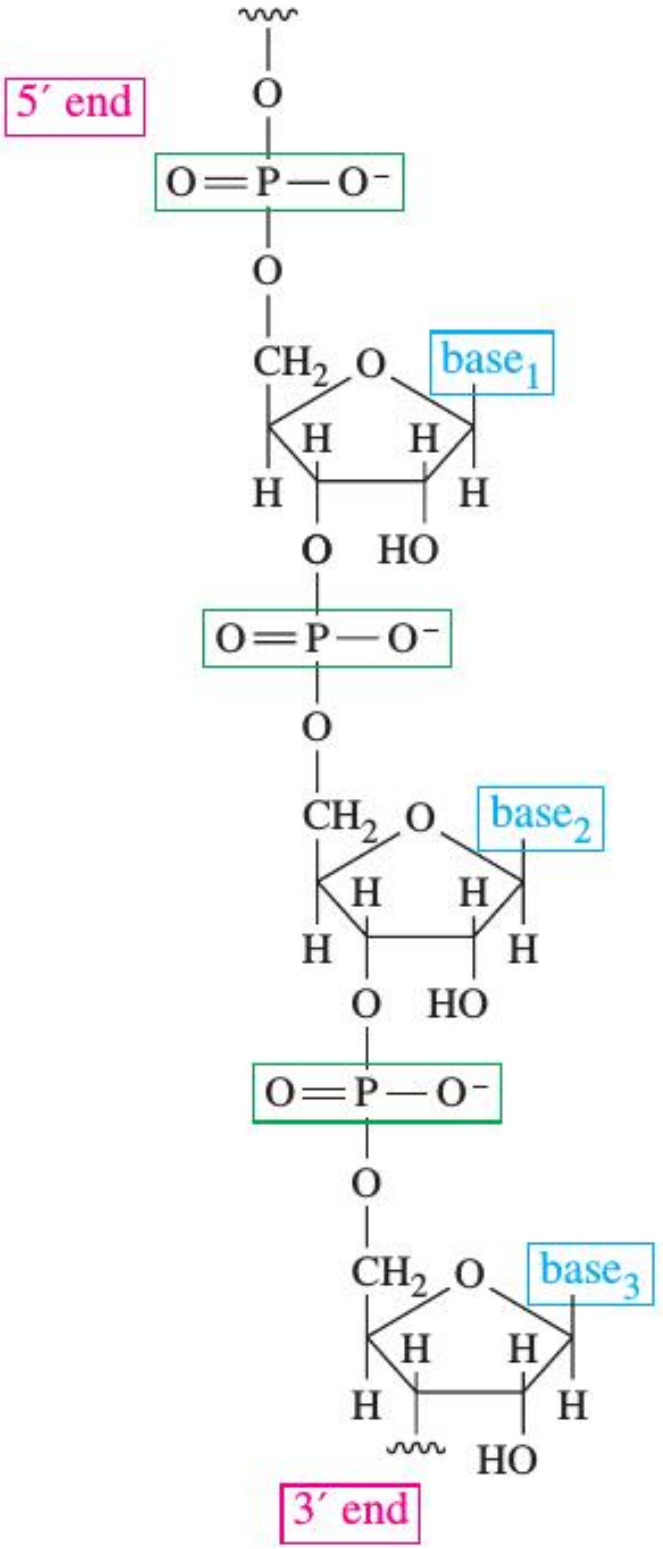
Nukleinsavak

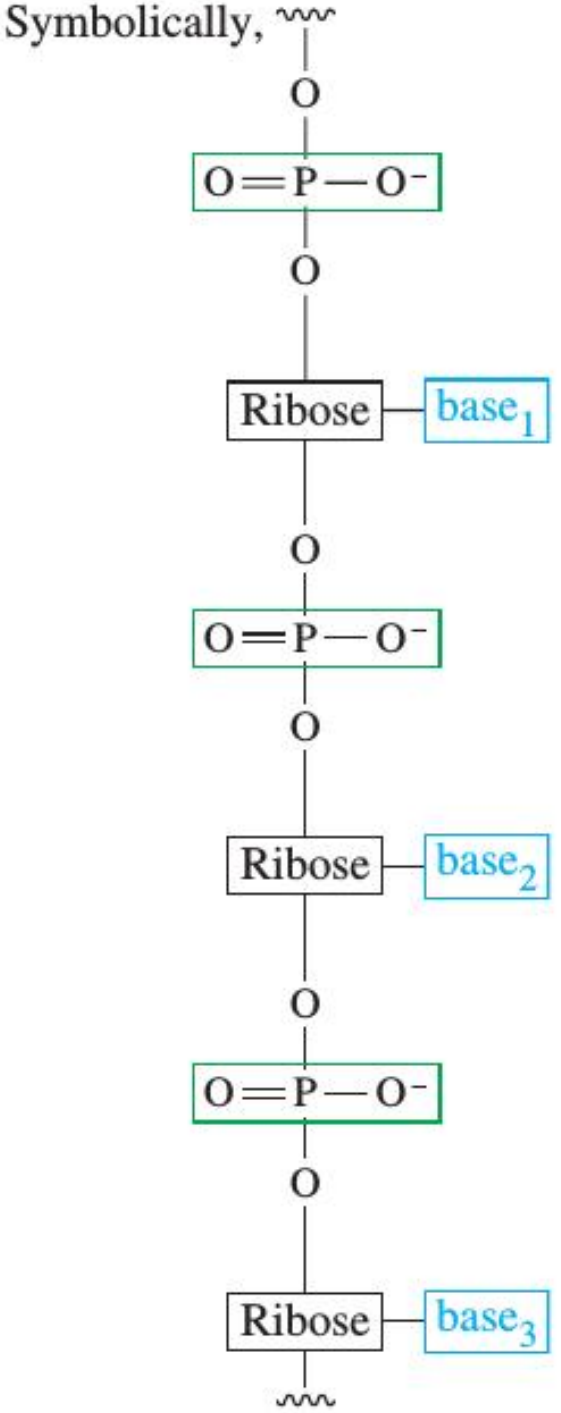
Alkotórészek:

- öt szénatomos cukor:
  ribóz/dezoxiribóz

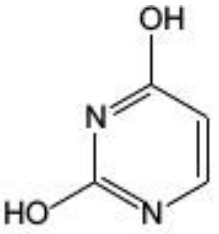
- nitrogéntartalmú heterociklusos vegyületek:
  purin/pirimidinvázas heterociklusok

- foszforsav



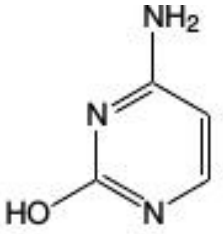


Nukleinsavak építőelemei



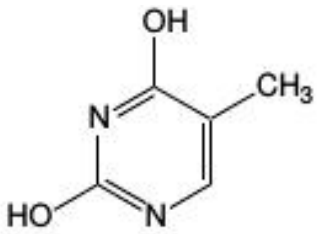
uracil

pirimidin-2,4-diol



citozin

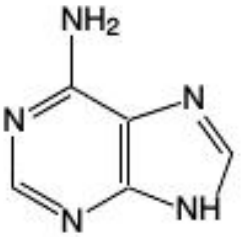
4-amino-pirimidine-2-ol



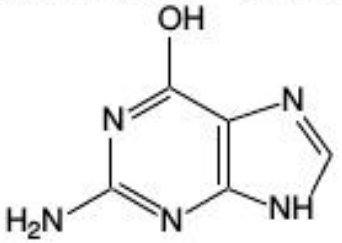
timin

5-methyl-pyrimidine-2,4-diol

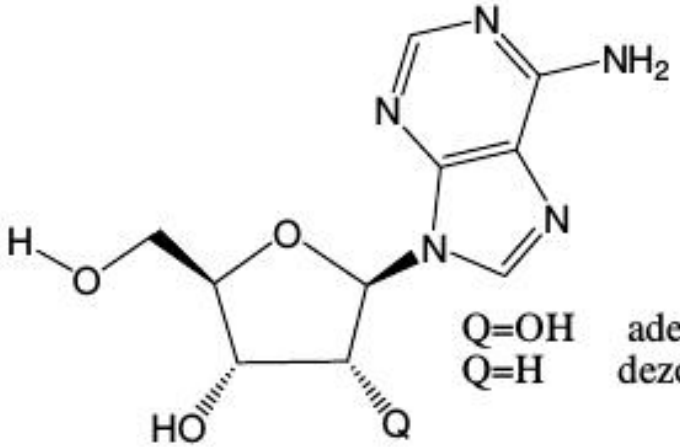
heterociklusok:



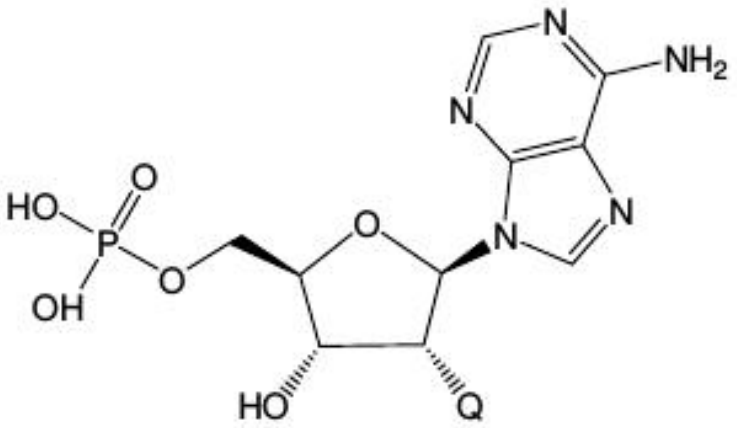
6-amino-purin
adenin



2-amino-6-hidroxi-purin
guanin



Q=OH adenozin
Q=H dezoxiadenozin



Q=OH adenozin-5'-monofoszfát
Q=H dezoxiadenozin-5'-monofoszfát

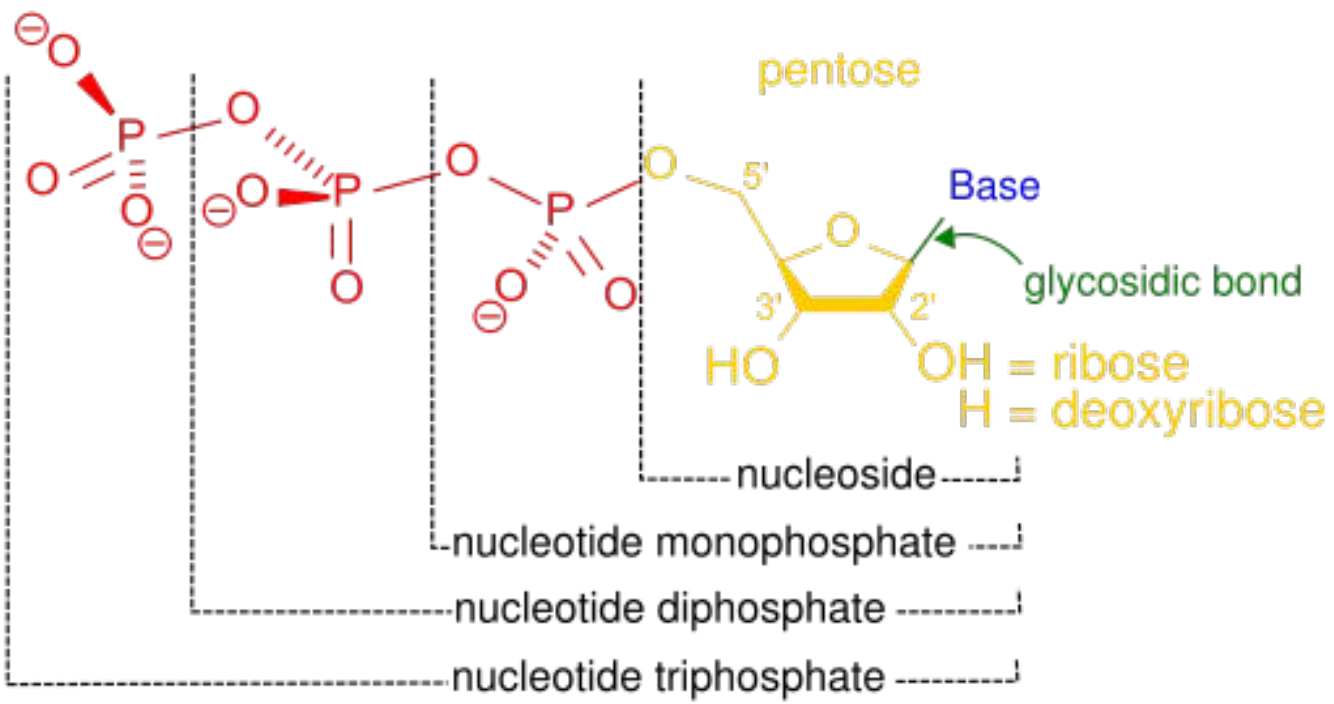
Nukleozidok:

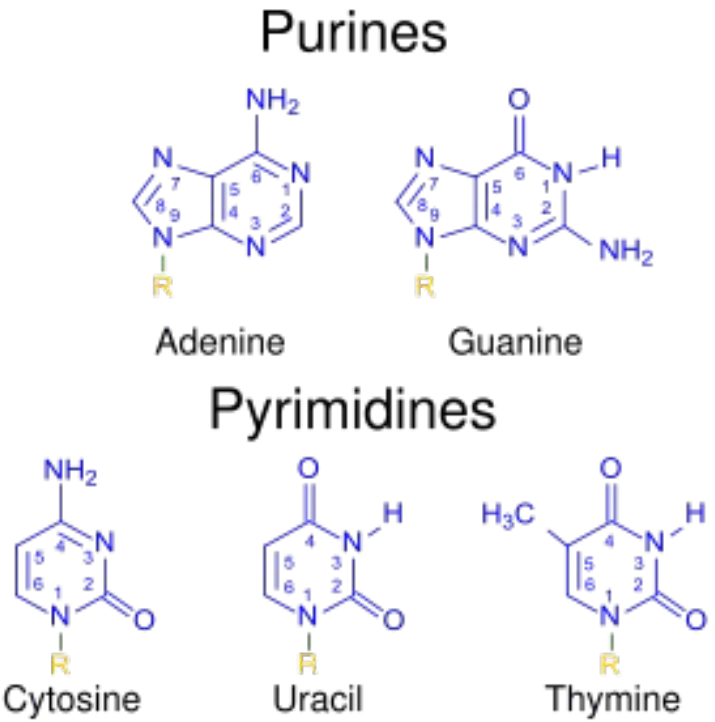
A megfelelő purin- és pirimidinbázisok N-glikozidjai

Nukleotidok:

A nukleozidok foszforsavészterei

Nukleinsavak





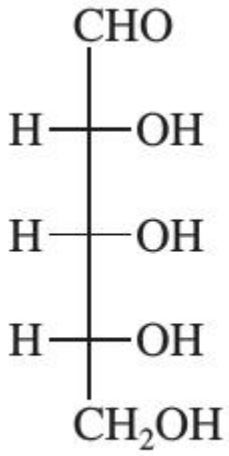
Nukleozid: ribóz/dezooxiribóz bázissal alkotott glikozidja (pl. adenozin)

Nukleotid: nukleozid foszfátésztere (pl. adenozin-monofoszfát, AMP)

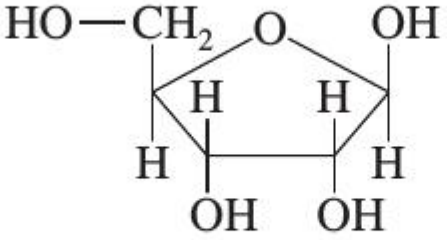
A foszfátcsoportok közötti kapcsolat anhidridnek felel meg!

Mivel a nukleinsavakban a cukorfoszfát gerinc állandó, a szekvenciát a bázisok sorrendjével azonosítjuk.

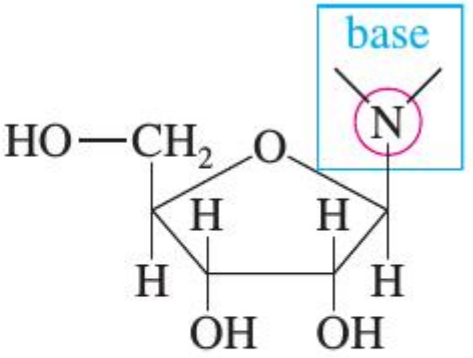
Nukleinsavak: az RNS alkotórészei



D-ribose

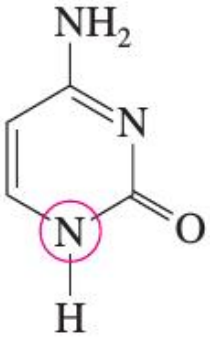


β-D-ribofuranose

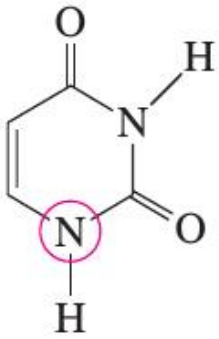


a ribonucleoside

pyrimidine

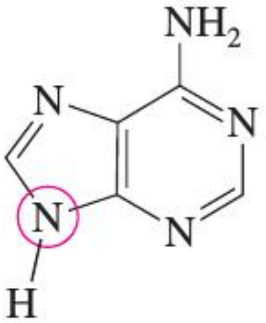


cytosine (C)

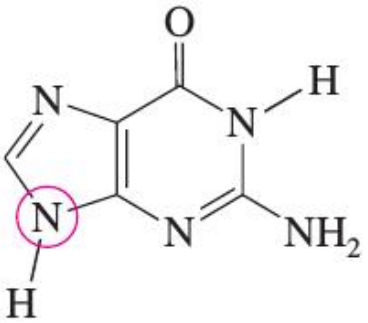


uracil (U)

pyrimidine bases

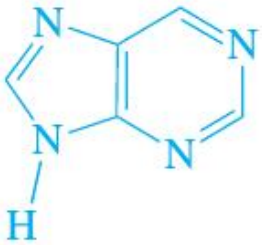


adenine (A)



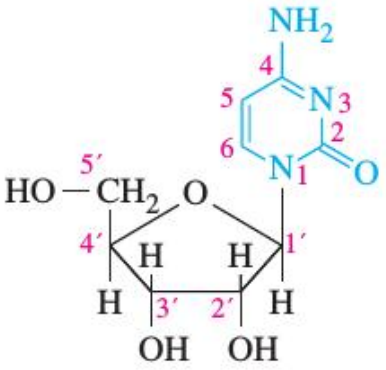
guanine (G)

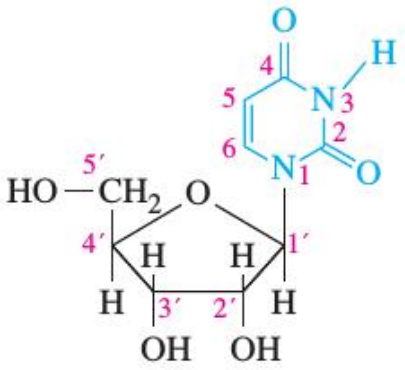
purine bases

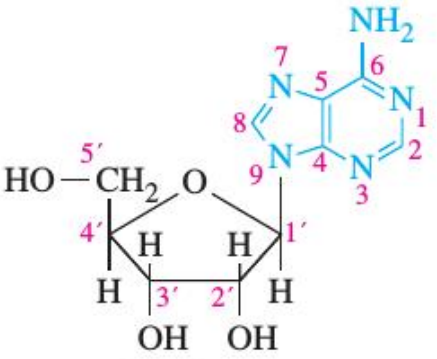


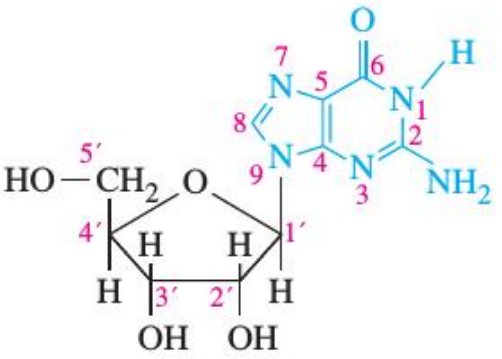
purine

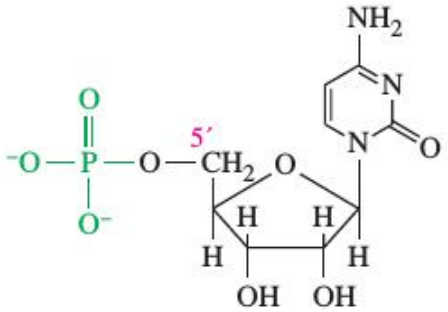
Nukleinsavak: az RNS alkotórészei

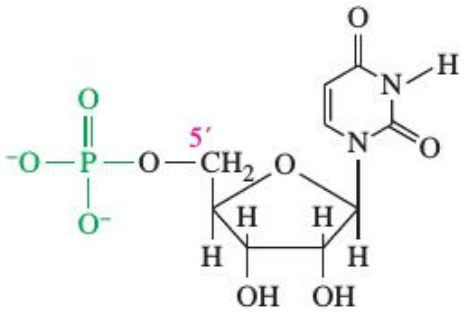

cytidine (C)

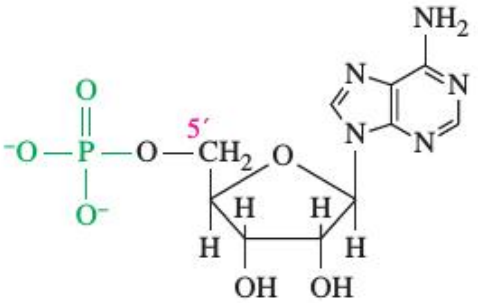

uridine (U)

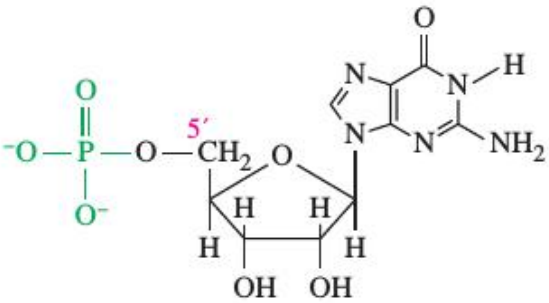

adenosine (A)


guanosine (G)


cytidine monophosphate,
CMP (cytidylic acid)


uridine monophosphate,
UMP (uridylic acid)


adenosine monophosphate,
AMP (adenylic acid)

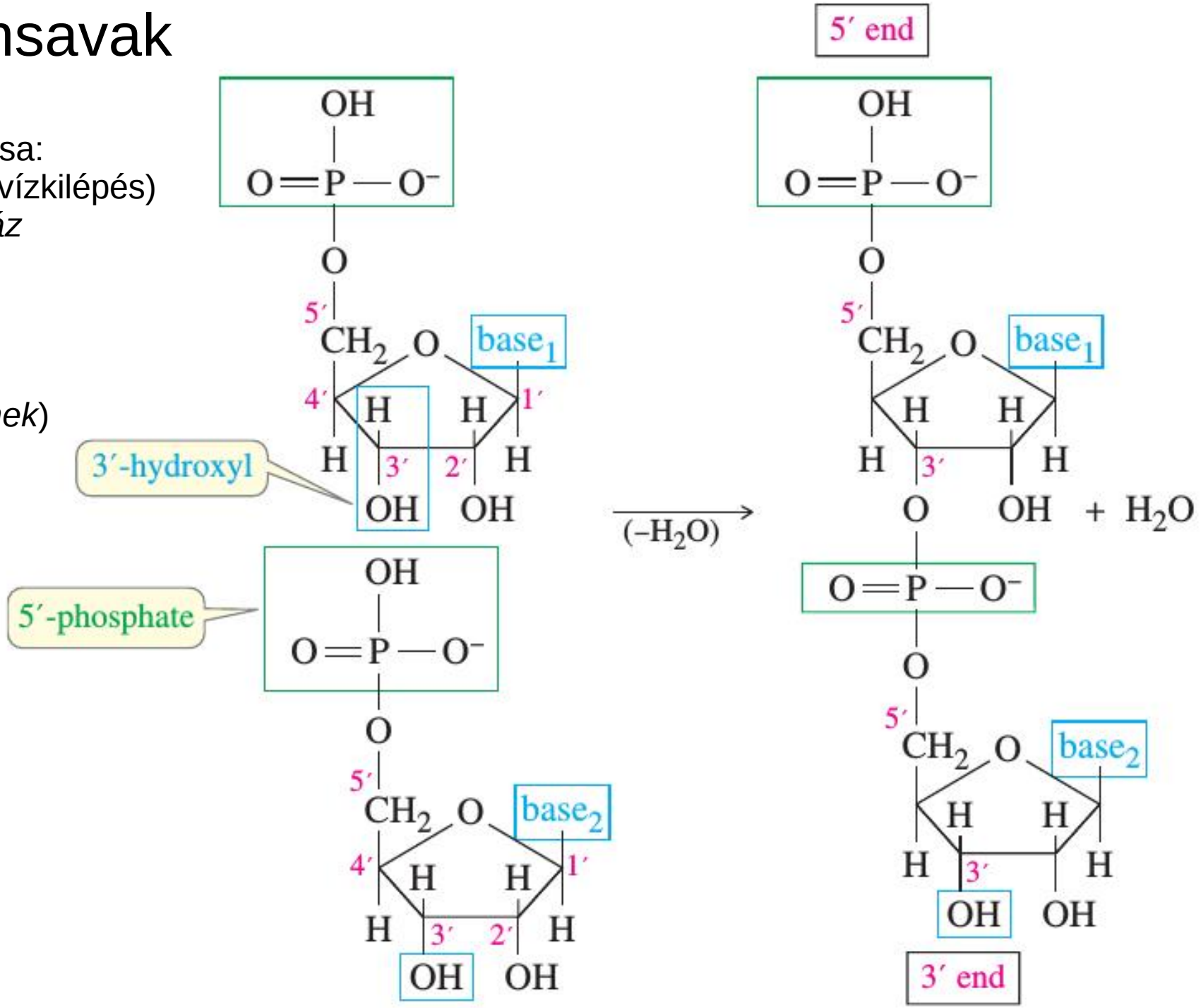

guanosine monophosphate,
GMP (guanidylic acid)

A nukleinsavakban a cukorrész atomainak számozásakor vesszőket használunk, hogy megkülönböztessük a bázis atomjaitól őket.

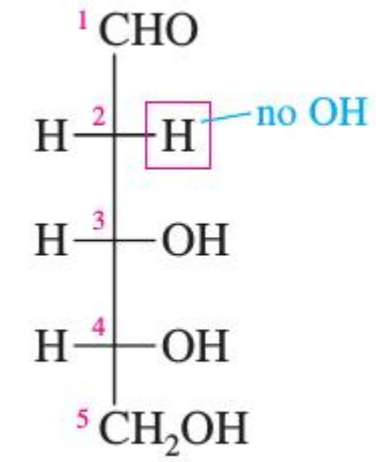
Nukleinsavak

Nukleotidok összekapcsolása: észterképzés (vízkilépés) (*polimeráz, ligáz enzimek*)

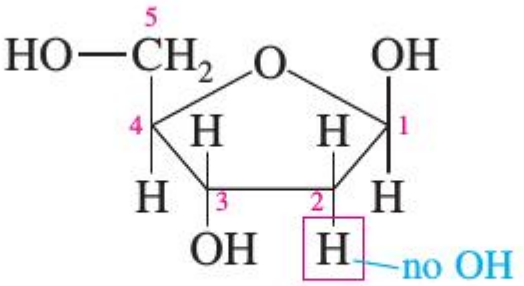
Szétválasztás: hidrolízis (*nukleáz enzimek*)



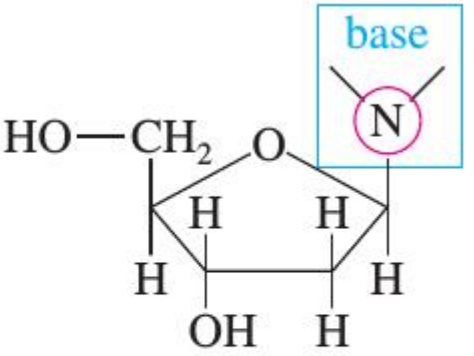
Nukleinsavak: a DNS alkotórészei



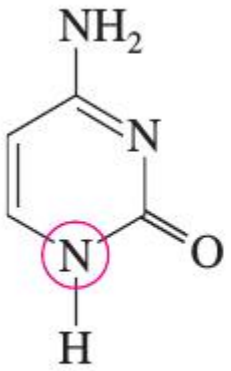
D-2-deoxyribose



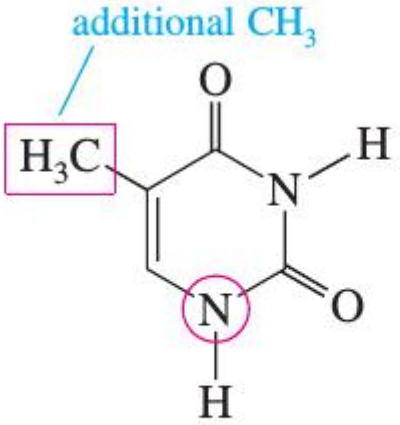
β-D-2-deoxyribofuranose



a deoxyribonucleoside

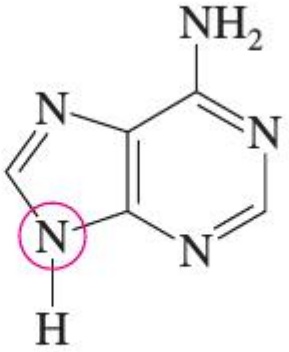


cytosine (C)

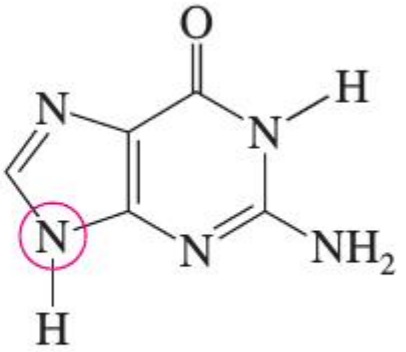


thymine (T)

pyrimidine bases



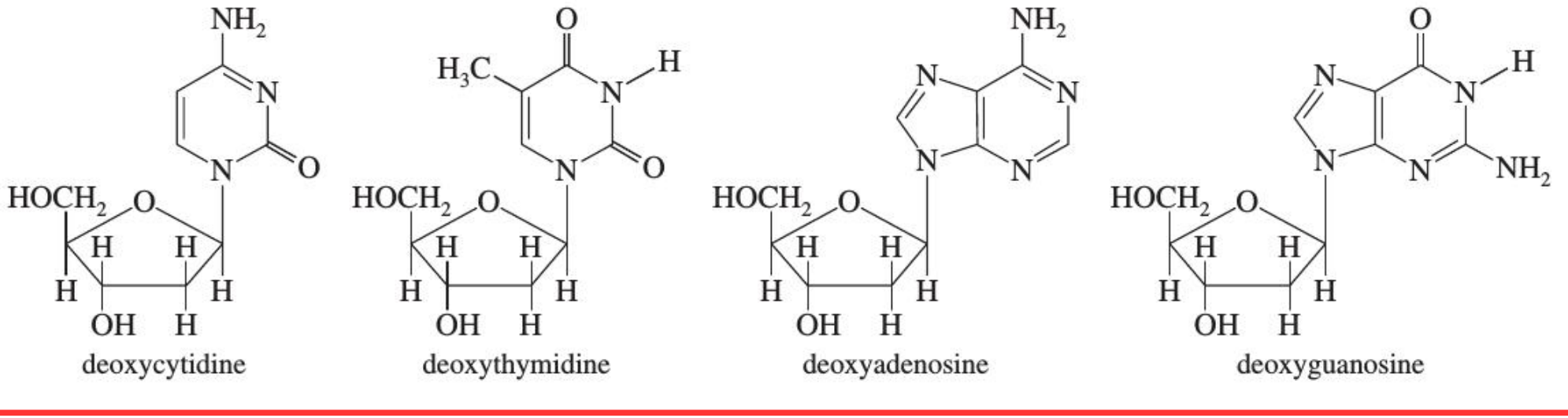
adenine (A)



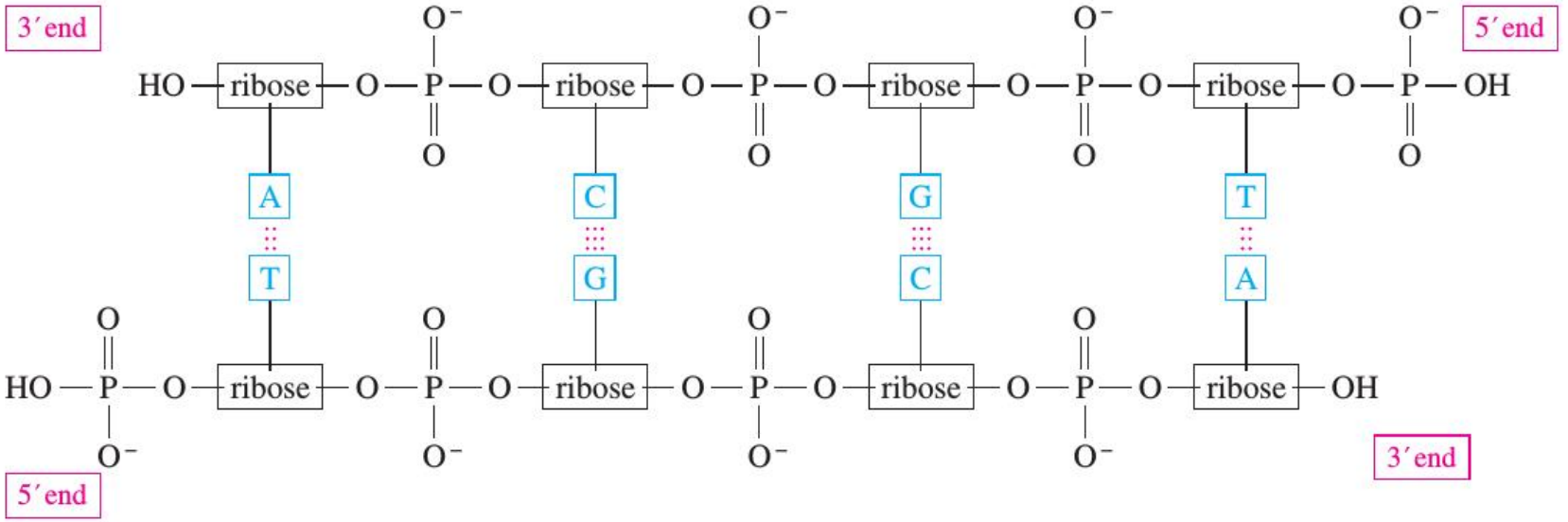
guanine (G)

purine bases

Nukleinsavak: a DNS alkotórészei és a két szál



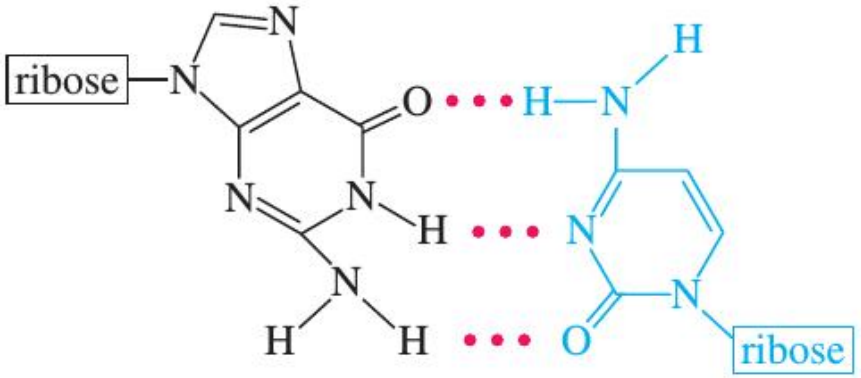
A ribóz itt lehet dezoxiribóz is!



Figyeljük meg, hogy a láncok lefutása ellentétes irányú (antiparalel), és hogy a (dezoxi)ribóz “szabad” (=ahová nem kapcsolódik további nukleotid) hidroxilcsoportjaival azonosítjuk a végeiket. Ha egy szál szekvenciáját írjuk le, azt 5’-3’ irányban tesszük, és ebben az irányban történik a transzkripció és a transzláció is!

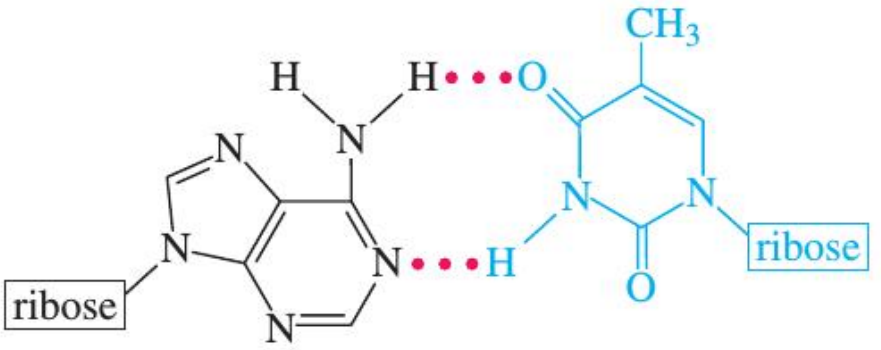
Nukleinsavak: Watson-Crick bázispárok (DNS)

G-C pár: 3 H-kötés

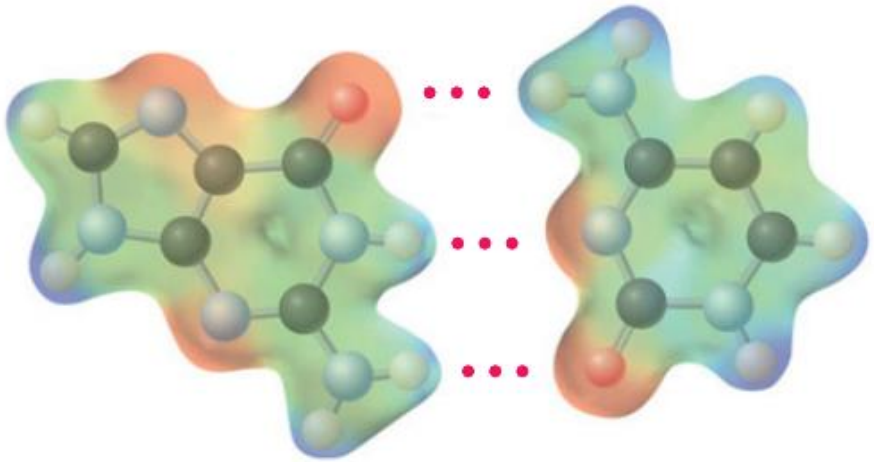


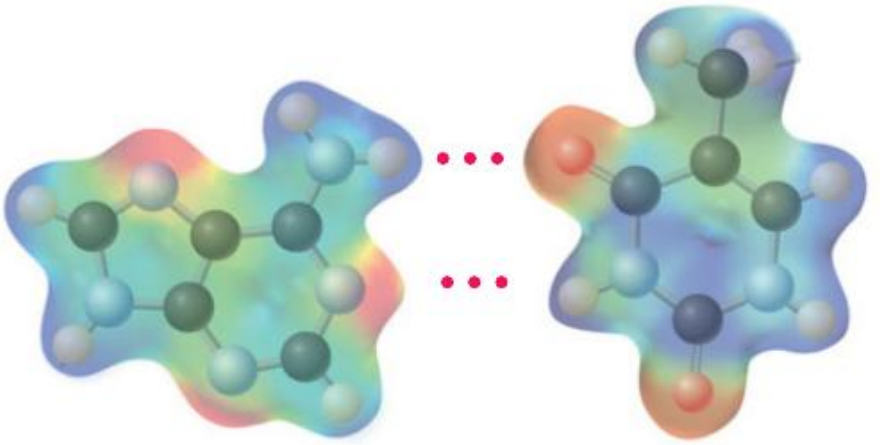
guanine G ⋮⋮⋮ C cytosine

A-T pár: 2 H-kötés



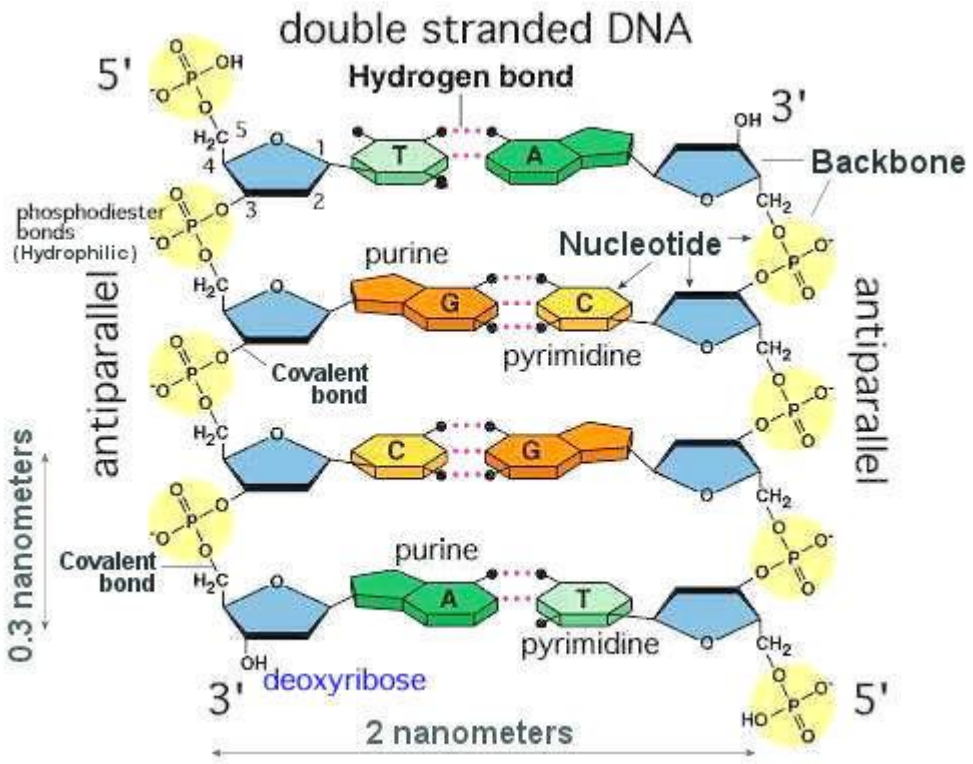
adenine A ⋮⋮⋮ T thymine

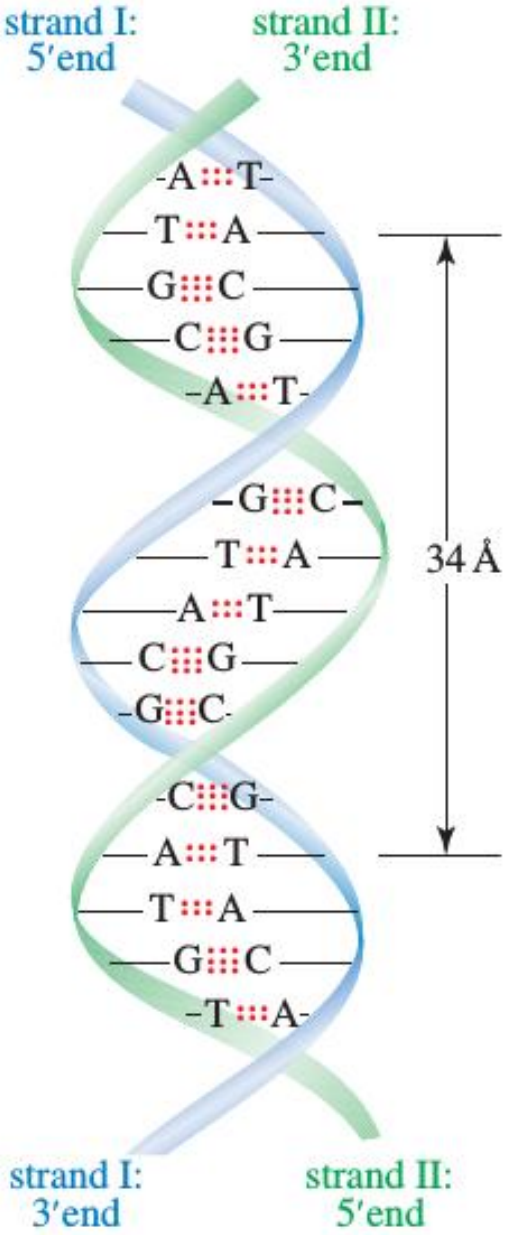


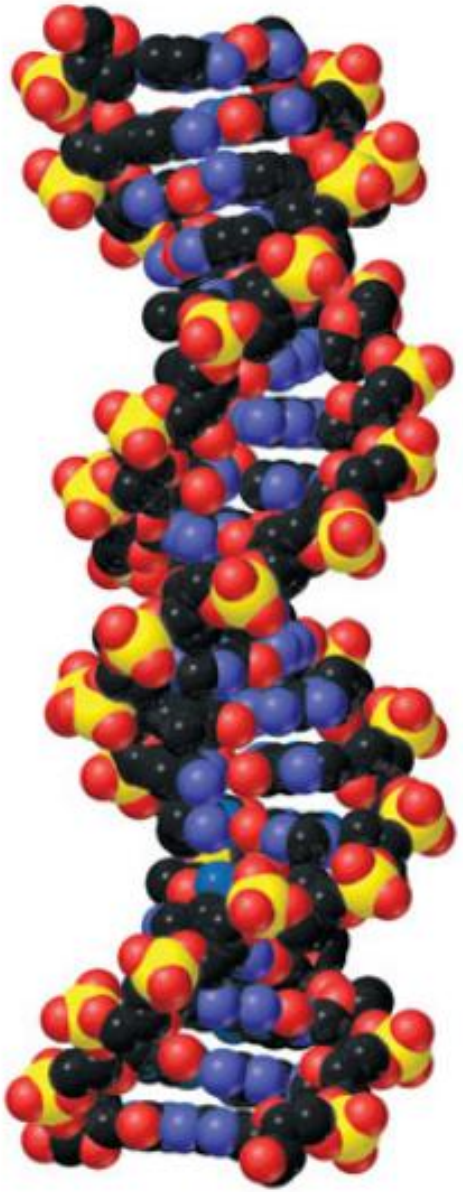


Vegyük észre, hogy nem mindegy, milyen tautomer formákban vannak jelen a bázisok!

Nukleinsavak: a DNS kettős hélix



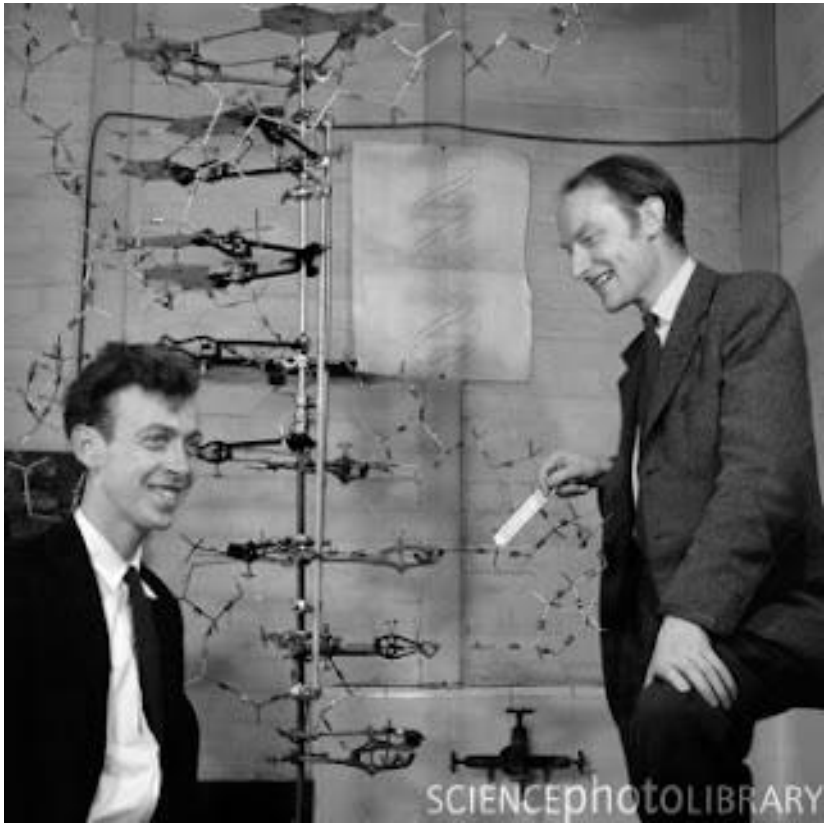




Figyeljük meg, hogy a láncok lefutása ellentétes irányú (antiparalel), és hogy a végeiket a (dezoxi)ribóz “szabad” hidroxilcsoportjaival azonosítjuk.
A nukleinsavakban a cukorrész atomjainak számozásakor vesszőket használunk, hogy megkülönböztessük a bázis atomjaitól őket.

Nukleinsavak: a DNS kettős hélix

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.



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

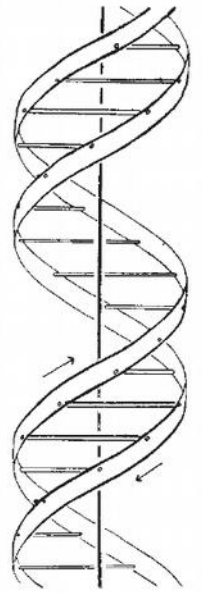
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

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.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There

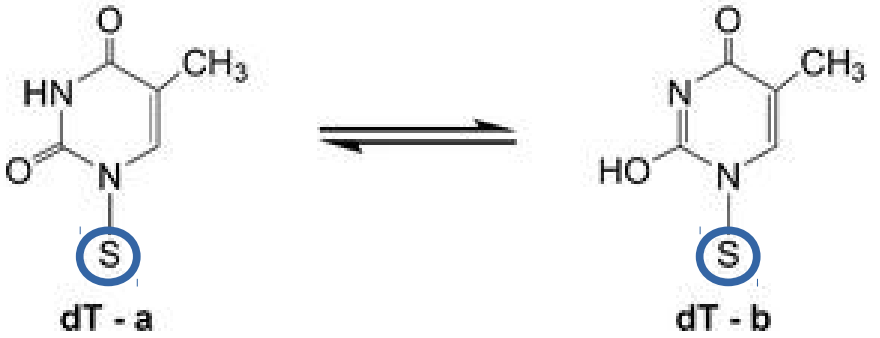
Nukleinsavak: bázisok tautomer formái

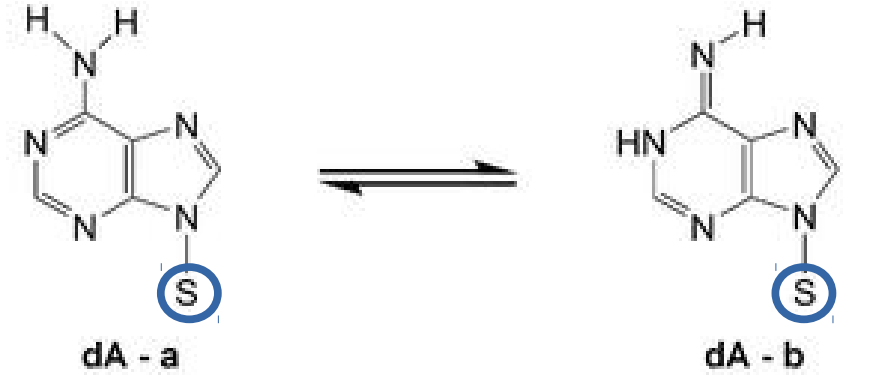
Tautoméria:
egy kettős kötés és egy H helyzete változik meg (“helyet cserélnek”)

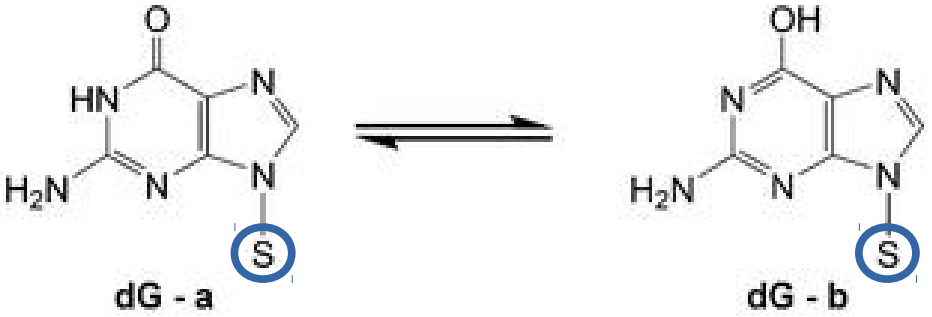
A cukor kapcsolódása miatt az egyik nitrogénen nincs H, az nem vesz részt a tautomerizációban emiatt

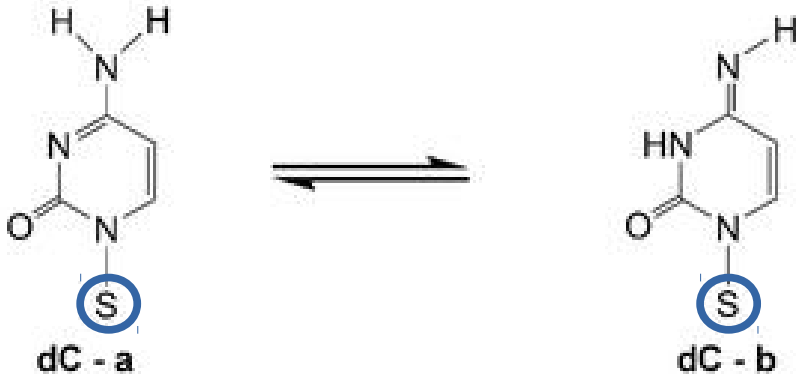
A tautomer formák eltérnek abban, hogy mely atomok viselkedhetnek H-kötés donorként és akceptorként!

S : a cukorrészt jelöli





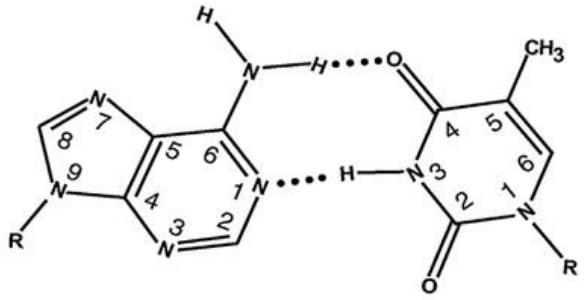




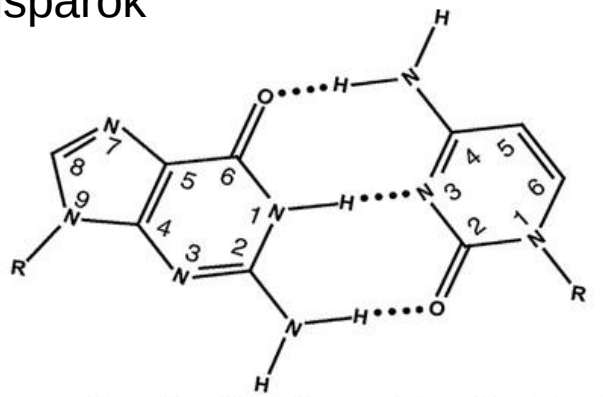
Kitekintés: példák további bázispárokra

Watson-Crick bázispárok

A



Adenine (*anti*) Thymine (*anti*)

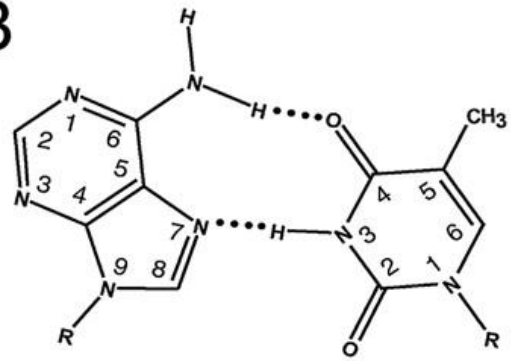


Guanine (*anti*) Cytosine (*anti*)

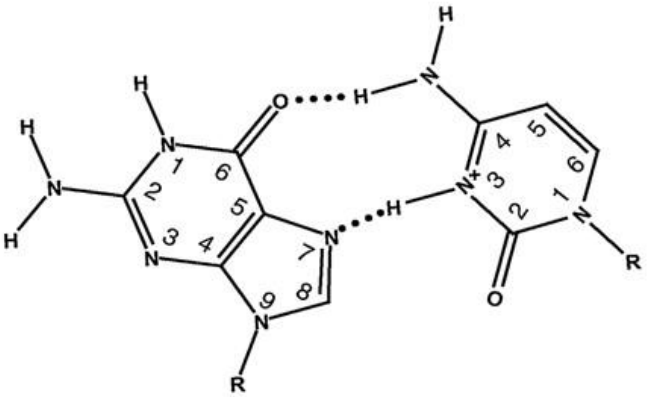
Hoogsteen bázispárok
Egyes DNS-polimerázok aktív helyén ilyenek alakulnak ki!

RNS-szerkezetekben, háromszálú hélixekben pl.

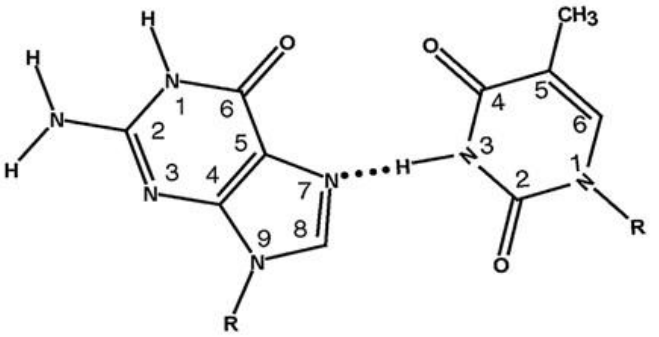
B



Adenine (*syn*) Thymine (*anti*)



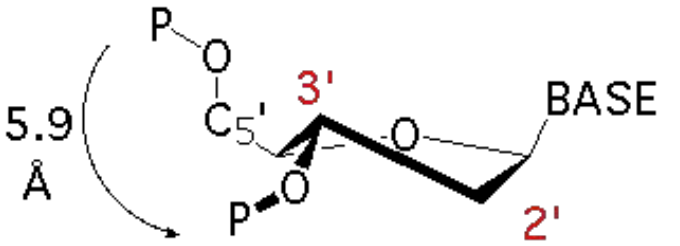
Guanine (*syn*) Cytosine (*anti*)



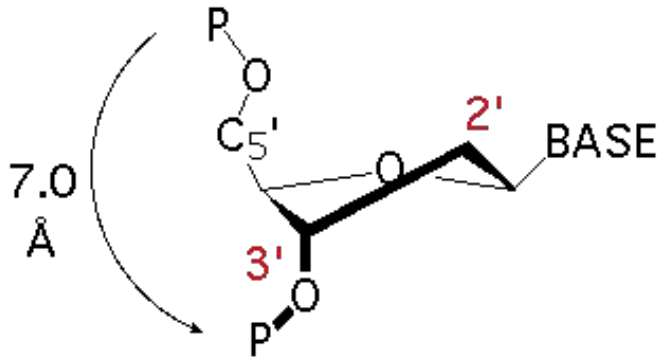
Guanine (*syn*) Thymine (*anti*)

Nukleinsavak: a ribóz/dezoxiribóz gyűrű lehetséges konformációi

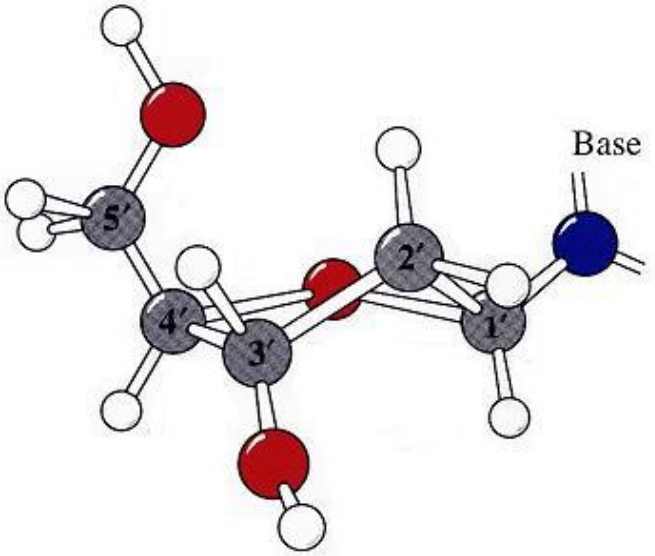
Az öttagú gyűrű minden atomja nem lehet egy síkban, az nagyon kedvezőtlen lenne. Legkedvezőbb, ha vagy a 2., vagy 3. szénatom nincs egy síkban a többi atommal. Ezeket hívjuk C2-endo vagy C3-endo konformációnak.



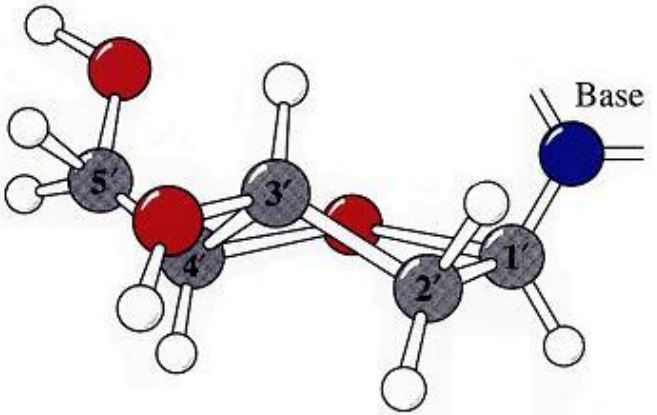
C3'-endo (A-Conformation)



C2'-endo (B-Conformation)



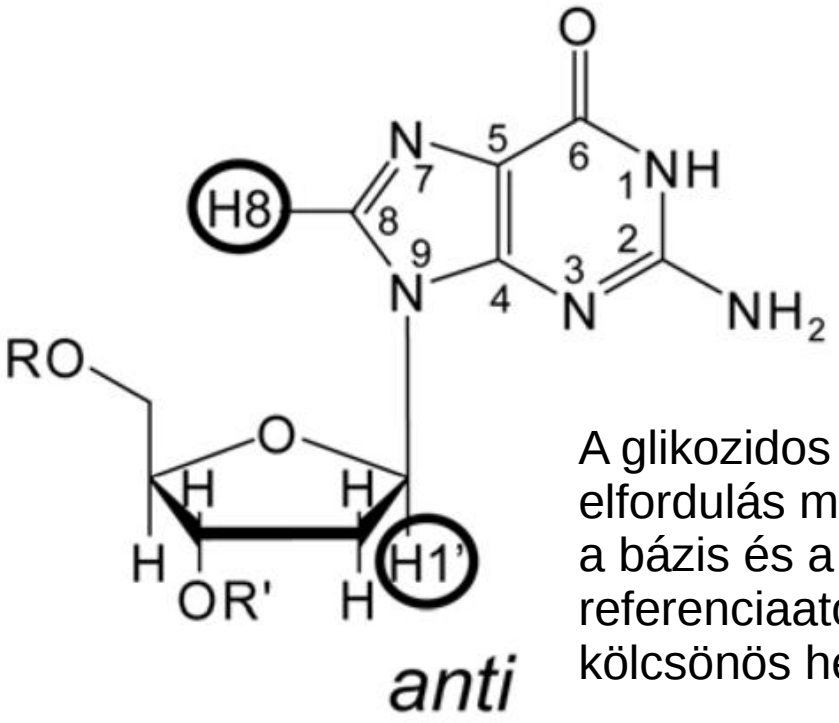
C-2′ *endo*



C-3′ *endo*

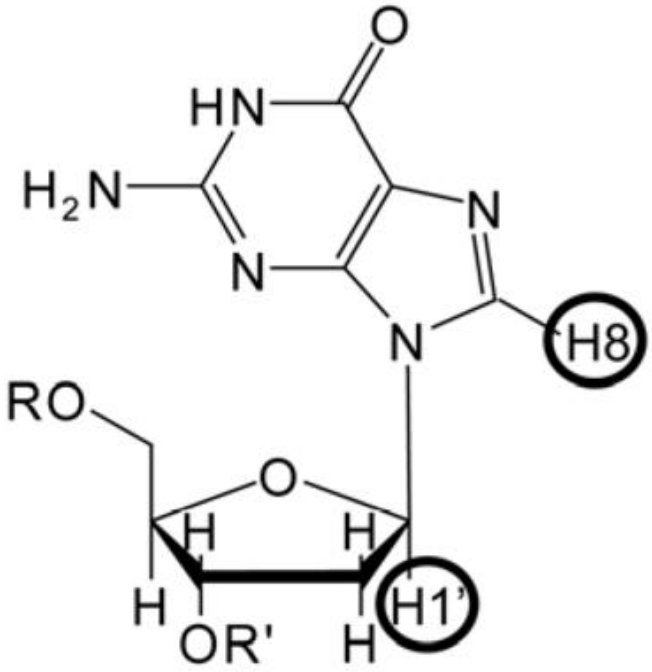
A nukleinsavakban a cukorrész atomjainak számozásakor vesszőket használunk, hogy megkülönböztessük a bázis atomjaitól őket, ezért 2’-endo ill. 3’-endo a konformerek neve.

Nukleinsavak: szin/anti térállású nukleotidok a glikozidos kötés körüli elrendeződés alapján

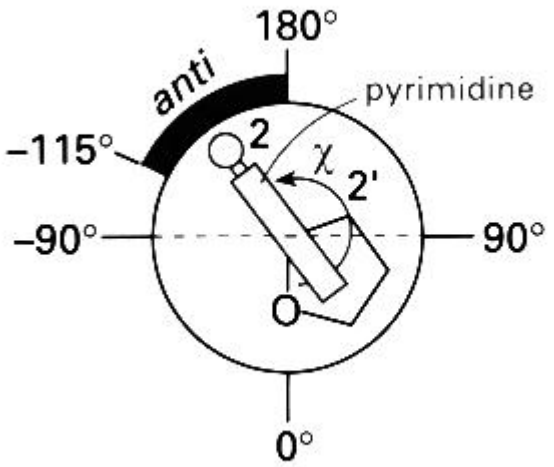


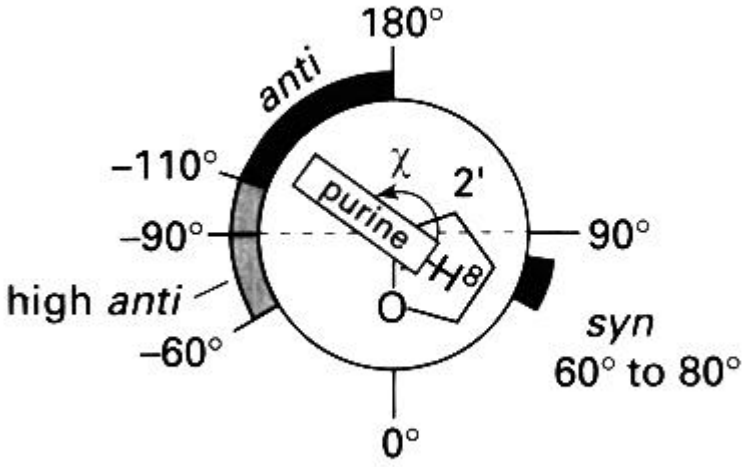
anti

A glikozidos kötés körüli elfordulás meghatározza a bázis és a cukor adott referenciaatomjainak kölcsönös helyzetét.



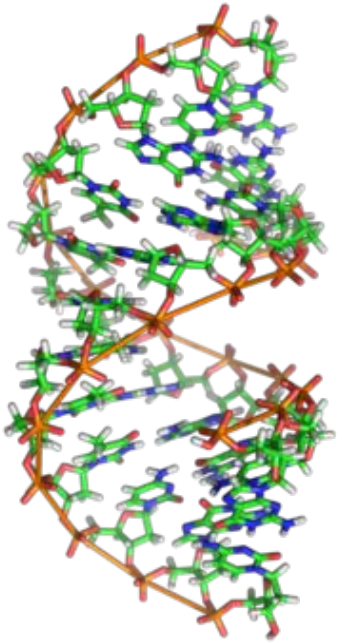
syn

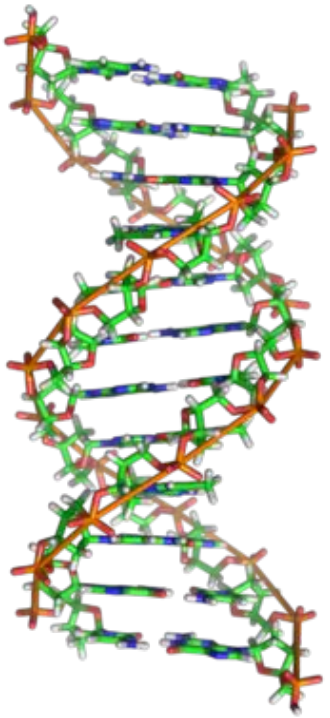


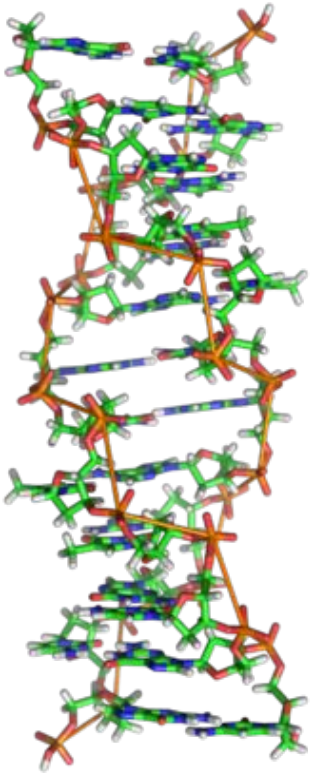


A nukleinsavak 3D szerkezete: variációk egy témára

A 2’ OH csoport térigénye miatt az RNS B-formája nem stabil







Helical forms

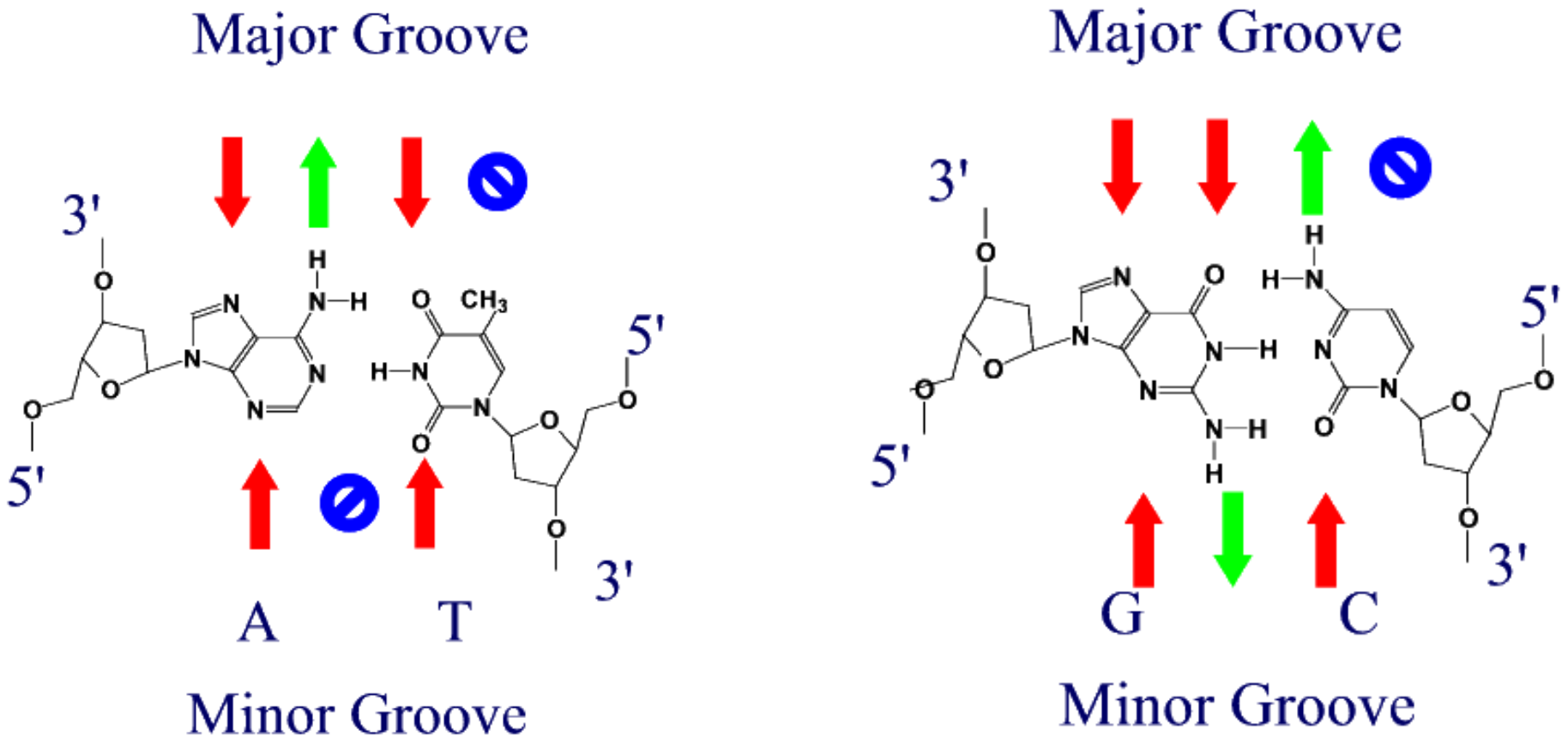
	A - Form DNA	B- Form DNA	Z-Form DNA
Diameter	26 Å	20 Å	18 Å
Pitch (rise/turn)	28 Å	34 Å	45 Å
Residues/turn	11	10	12
Axial rise/residue	2.6 Å	3.4Å	3.7Å
Turn angle/residue	33°	36°	30° (average)
Base tilt rel. to axis	20°	6°	7°
Major groove	narrow / deep	wide / deep	“flat”
Minor groove	wide / shallow	narrow / deep	narrow / deep
Sugar pucker	C_3’ endo	C_2’ endo	C_2’ endo /C_3’ endo
glycosidic bond	*anti*	*anti*	*anti* - C_2’ endo pyr *syn* - C_3’ endo pur

RNS hélixek konformációja

DNS szokásos szerkezete

Biológiai jelentőség=?

Kitekintés: a DNS szekvenciájának kiolvasása a kétszálú hélixből

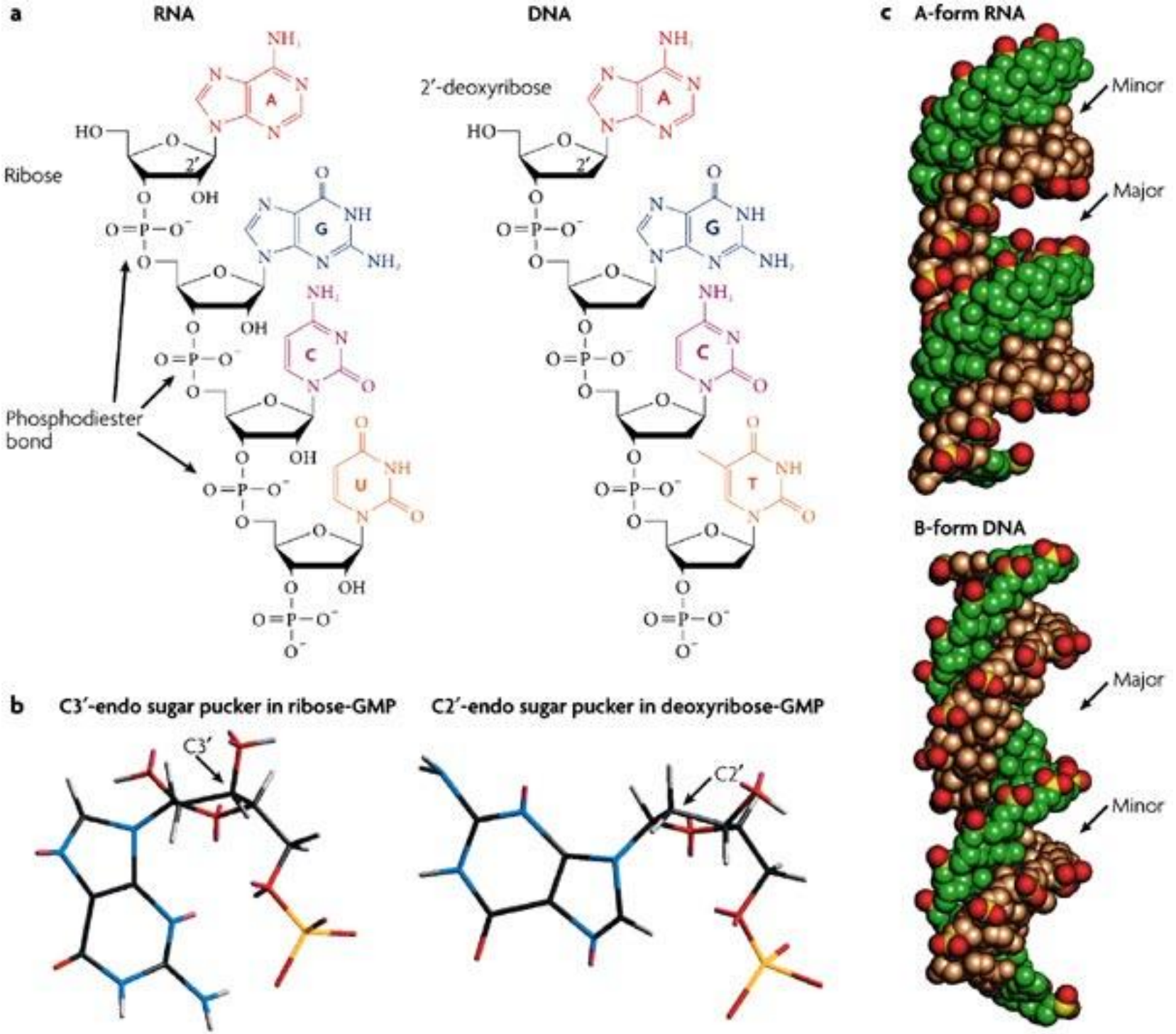


Jelentőség: DNS-kötő fehérjék
A nagy árok felől pontosan kiolvasható a szekvencia, a kis árok felől csak a GC és AT párok különböztethetőek meg egyértelműen.

Hidrogénkötés-akceptor

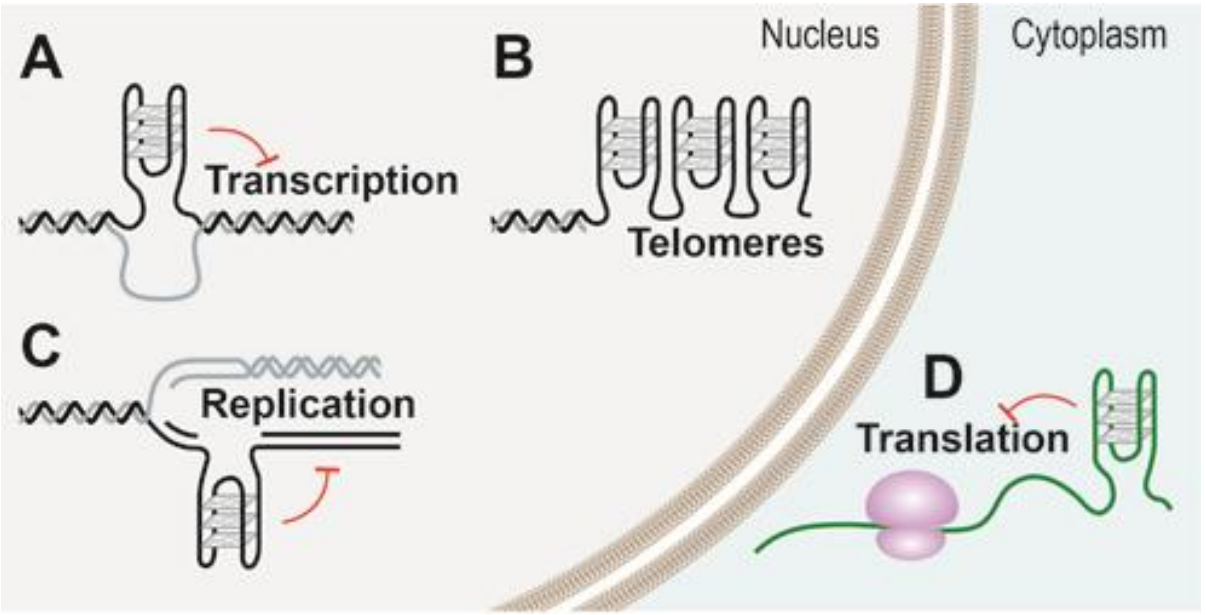
Hidrogénkötés-donor

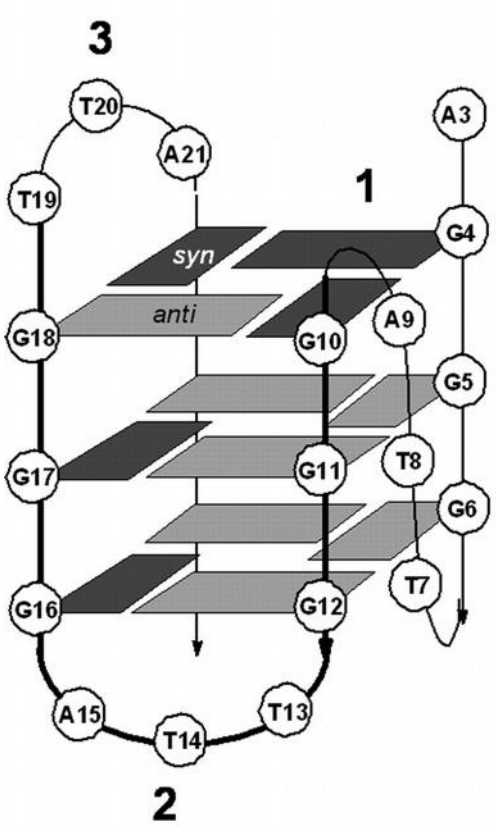
A nukleinsavak 3D szerkezete: variációk egy témára



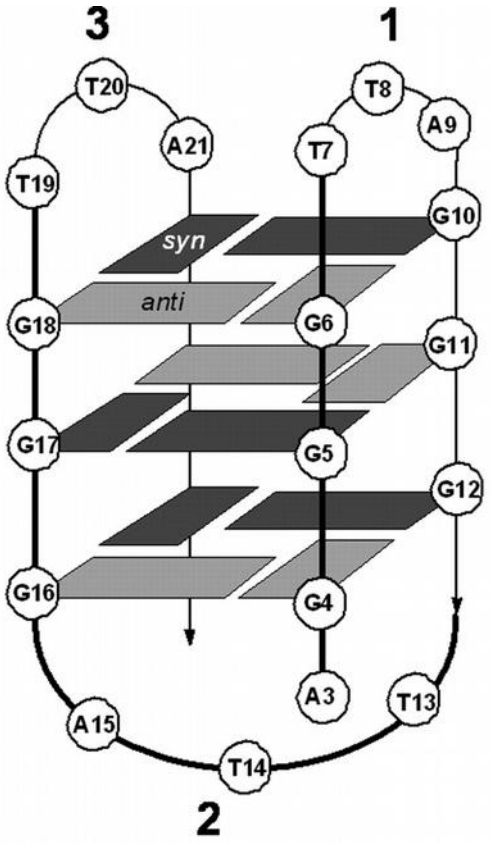
Kitekintés: négyszálú RNS/DNS (G-kvadruplexek)

Jelentőség:
- telomer régiók speciális szerkezete
- transzkripció szabályozás
- transzláció szabályozás

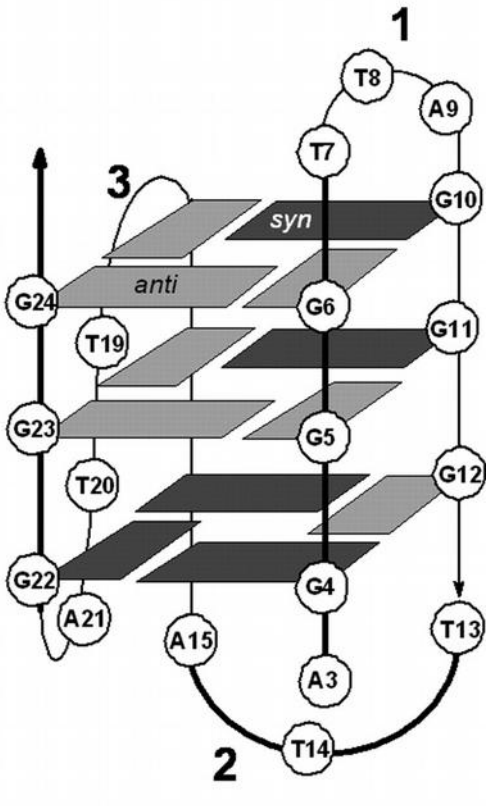




Hybrid-1



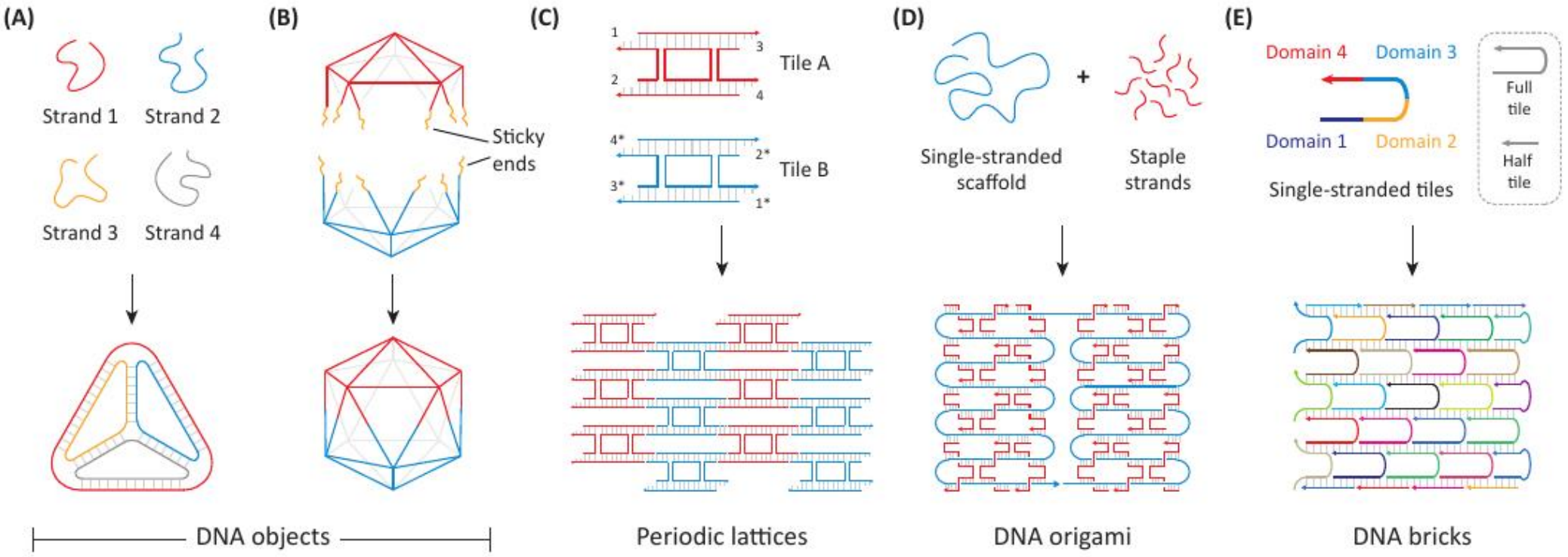
Basket

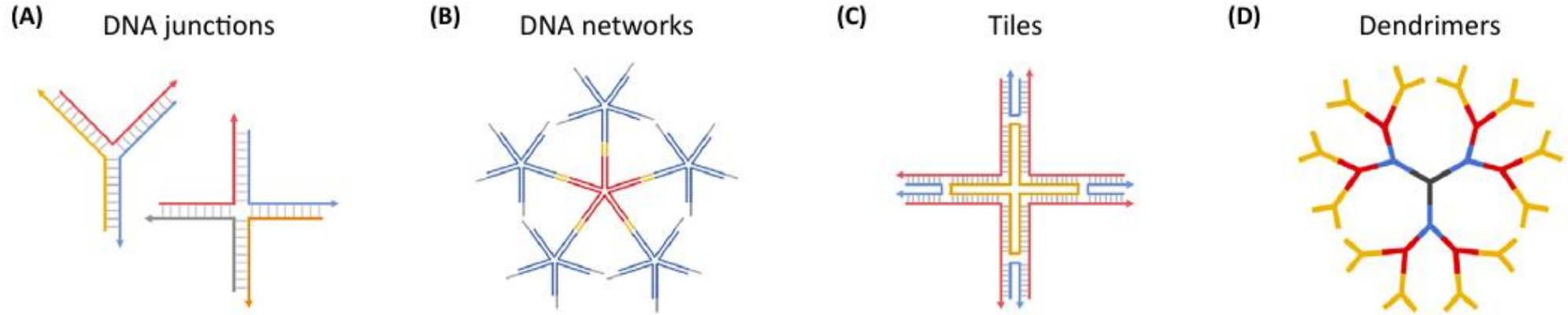


Hybrid-2

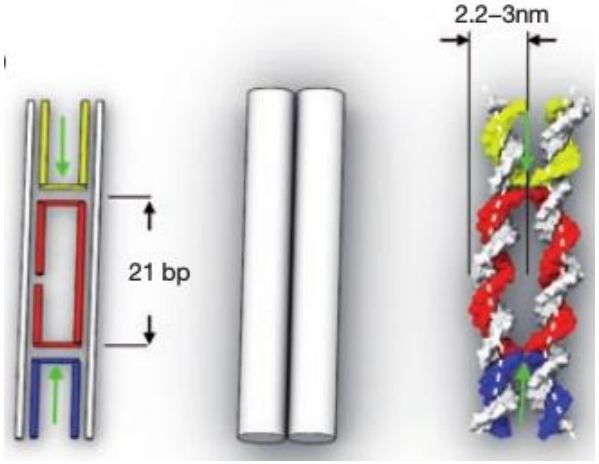
Kitekintés: mesterséges DNS nanoszerkezetek

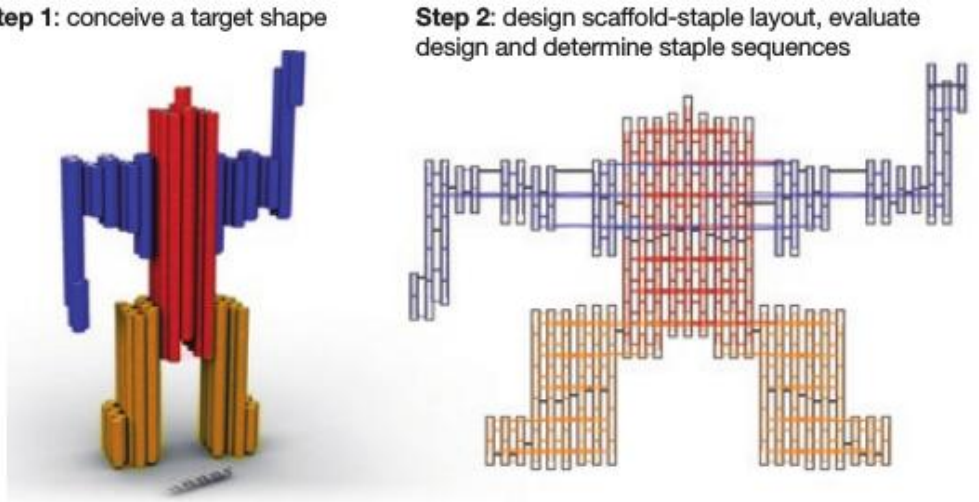
A bázispárosodás elvét kihasználva megfelelően tervezett szekvenciákból szinte tetszőleges struktúra előállítható.

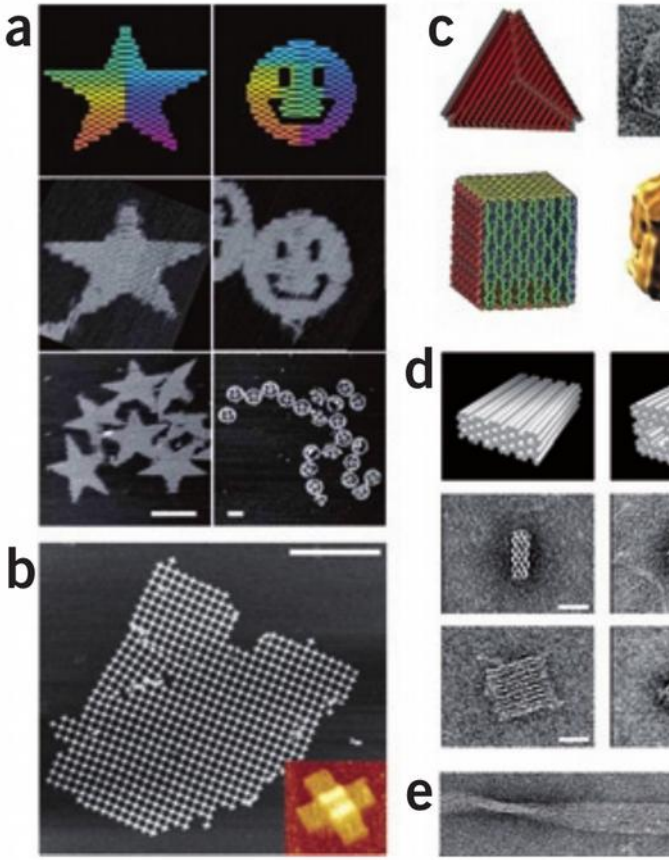




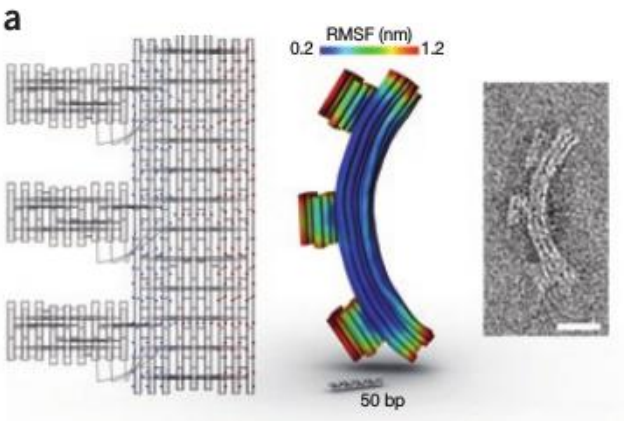
Kitekintés: DNS origami







caDNAno & CanDo: programok tervezéshez és elemzéshez



Kitekintés: RNS térszerkezetek

Nagyfokú szerkezeti változatosság!
Jelentőség:
- tRNS alakja
- szabályozó szekvenciák mRNS-en
  (speciális szekvencia → egyedi szerkezet, amit más molekulák felismernek)
- ribozimek, azaz RNS-enzimek
  (pl. a riboszóma!)

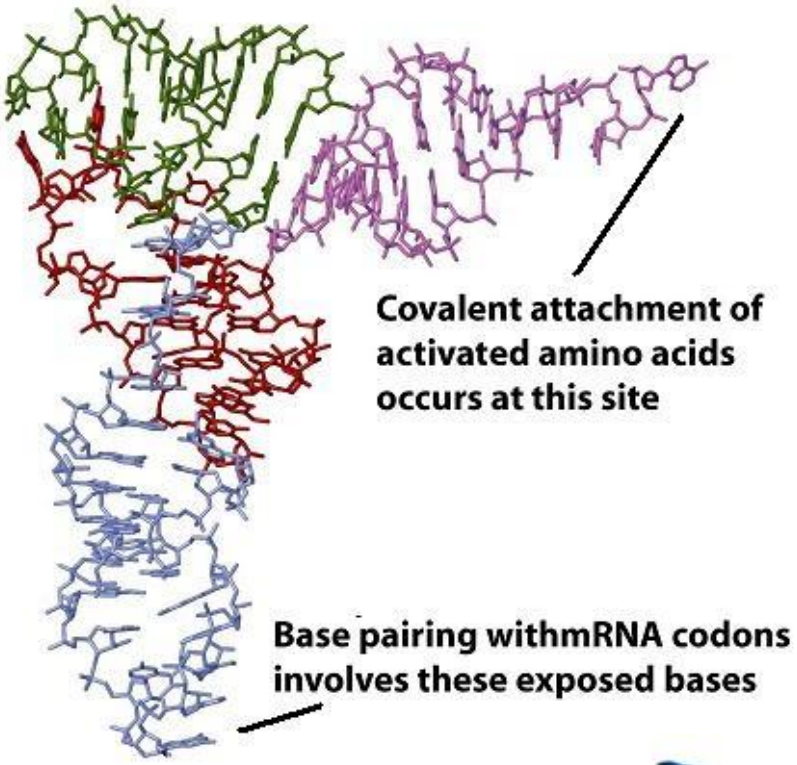
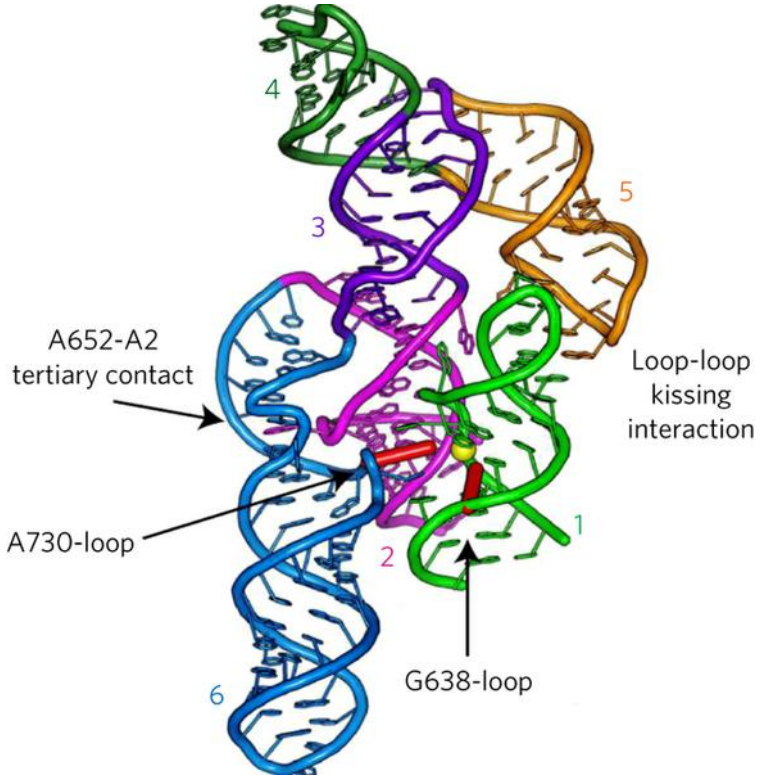
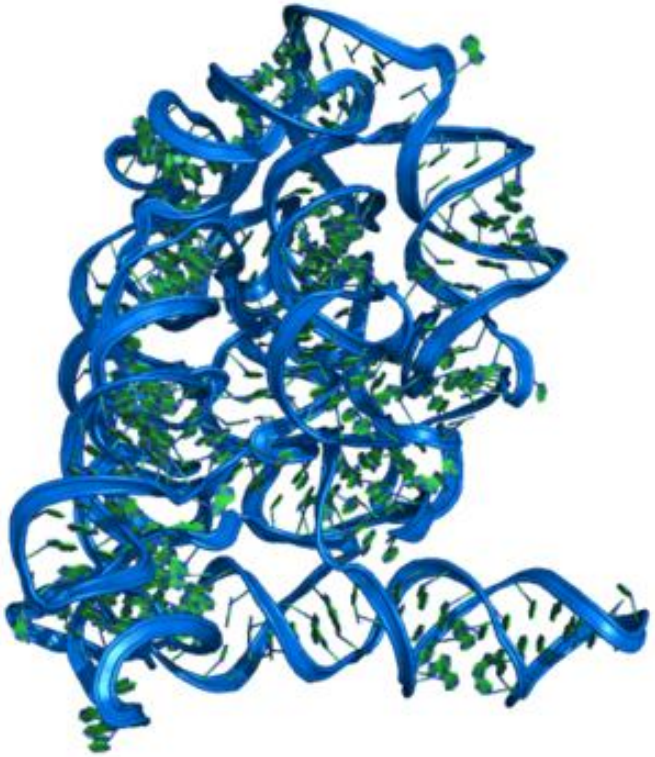
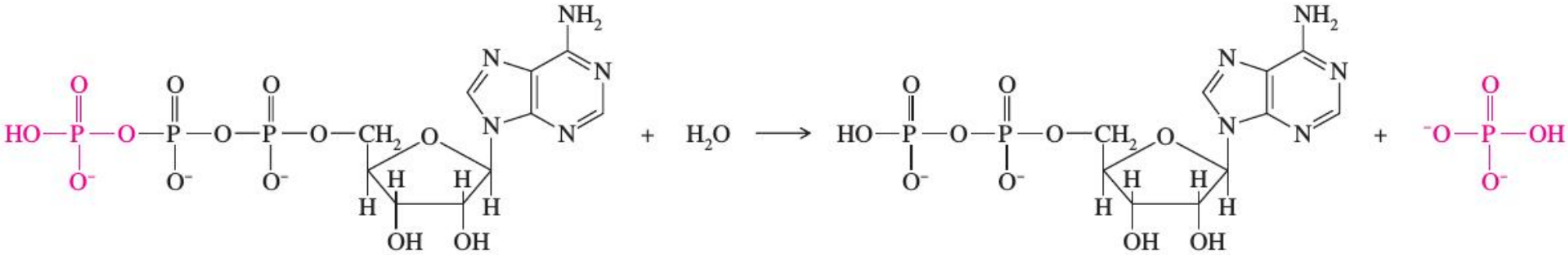


Figure 22-6 Principles of Biochemistry, 4/e
© 2006 Pearson Prentice Hall, Inc.

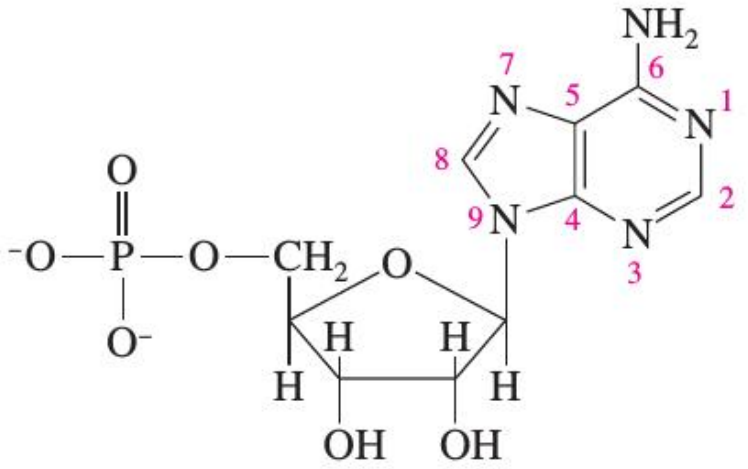


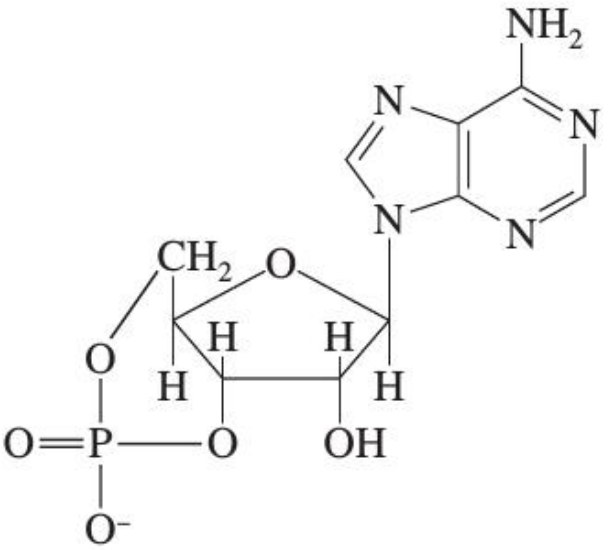


Egyéb nukleotidok

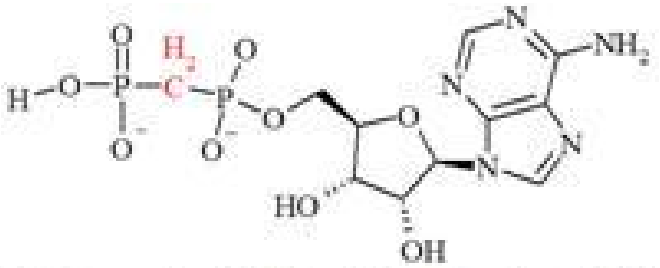


ΔH° = –31 kJ/mol (–7.3 kcal/mol)

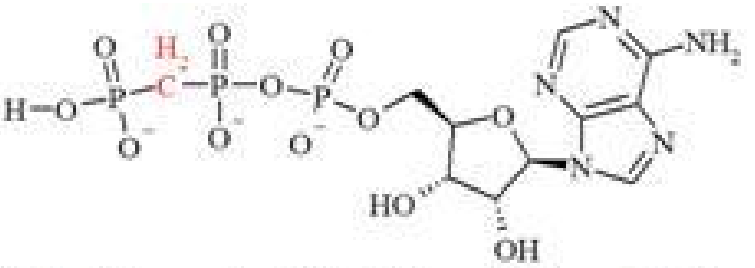




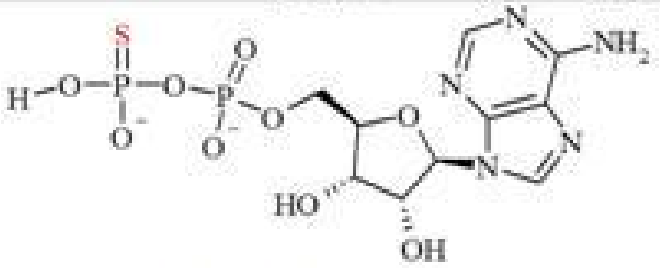
Kitekintés: nem (nehezebben) hidrolizálható nukleotid analógok



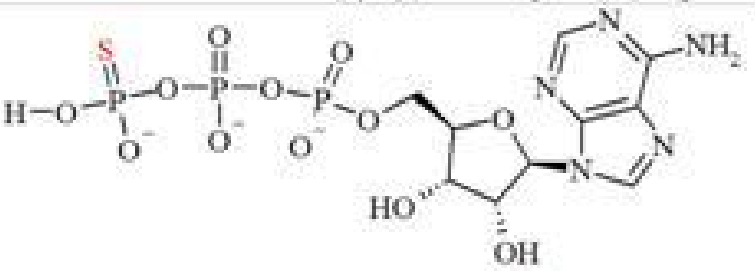
AMPCP: Adenosine 5'-[(α,β)-methyleno]diphosphate



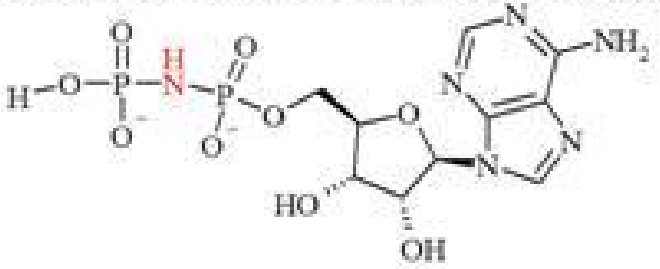
AMPPCP: Adenosine 5'-[(β,γ)-methyleno]triphosphate



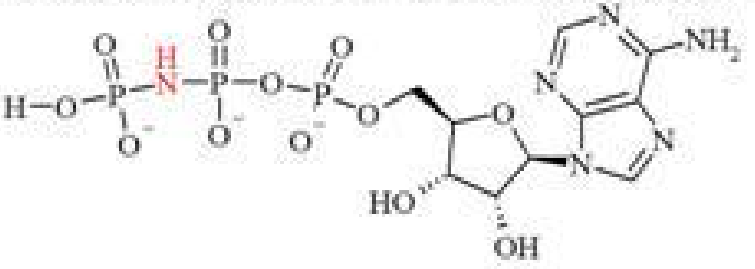
ADPβS: Adenosine 5'-[β-thio]diphosphate



ATPγS: Adenosine 5'-[γ-thio]triphosphate



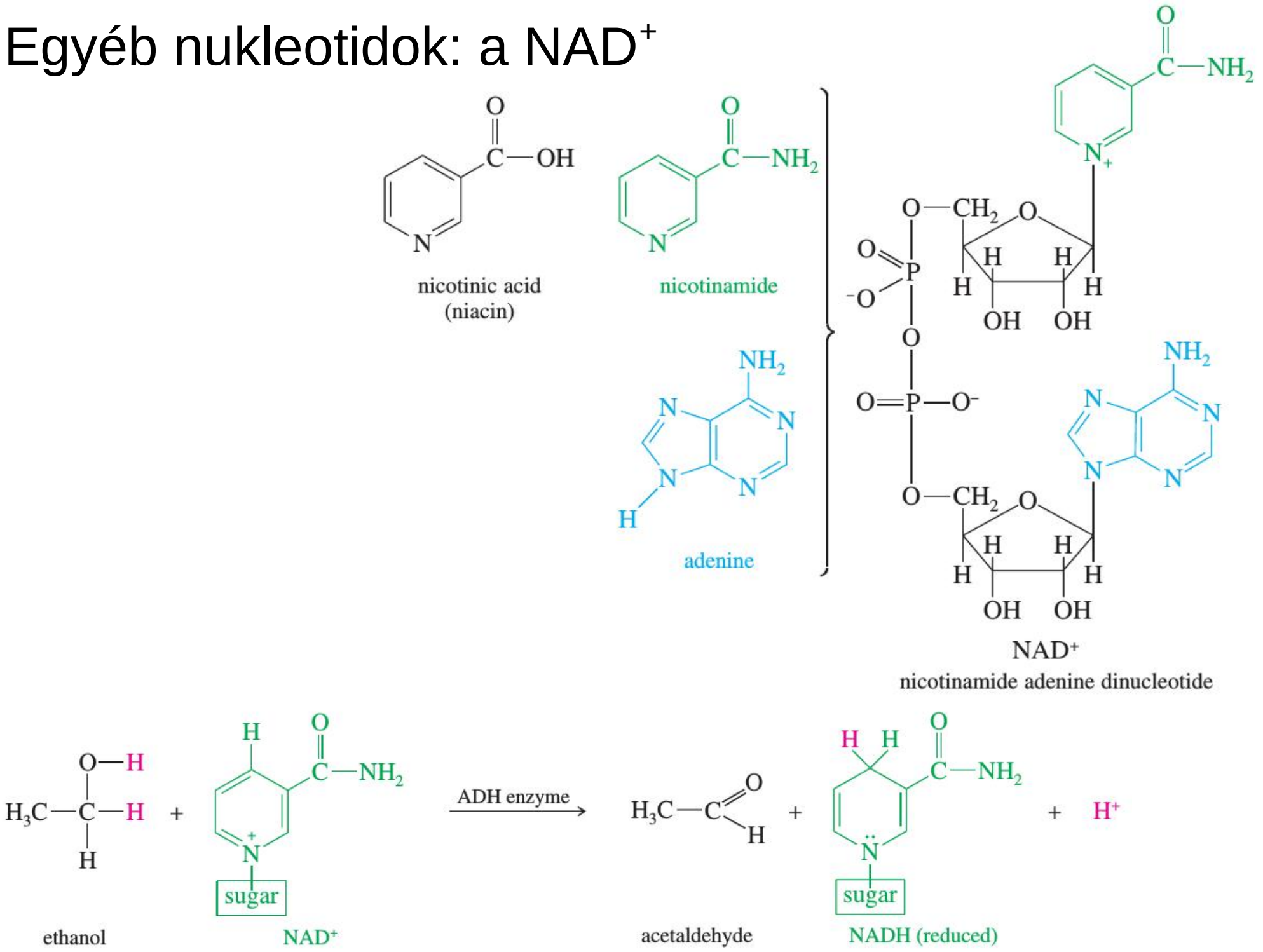
AMPNP: Adenosine 5'-[(α,β)-imido]diphosphate



AMPPNP: Adenosine 5'-[(β,γ)-imido]triphosphate

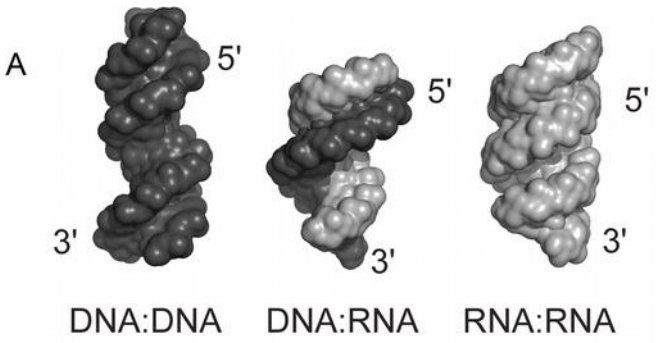
Jelentőség NTPáz enzimek szerkezetének, mechanizmusának vizsgálatában

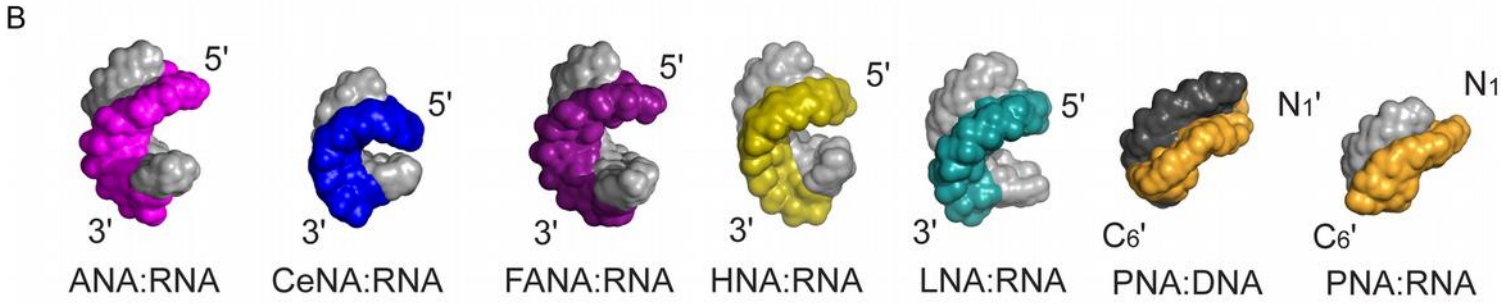
Egyéb nukleotidok: a NAD^+

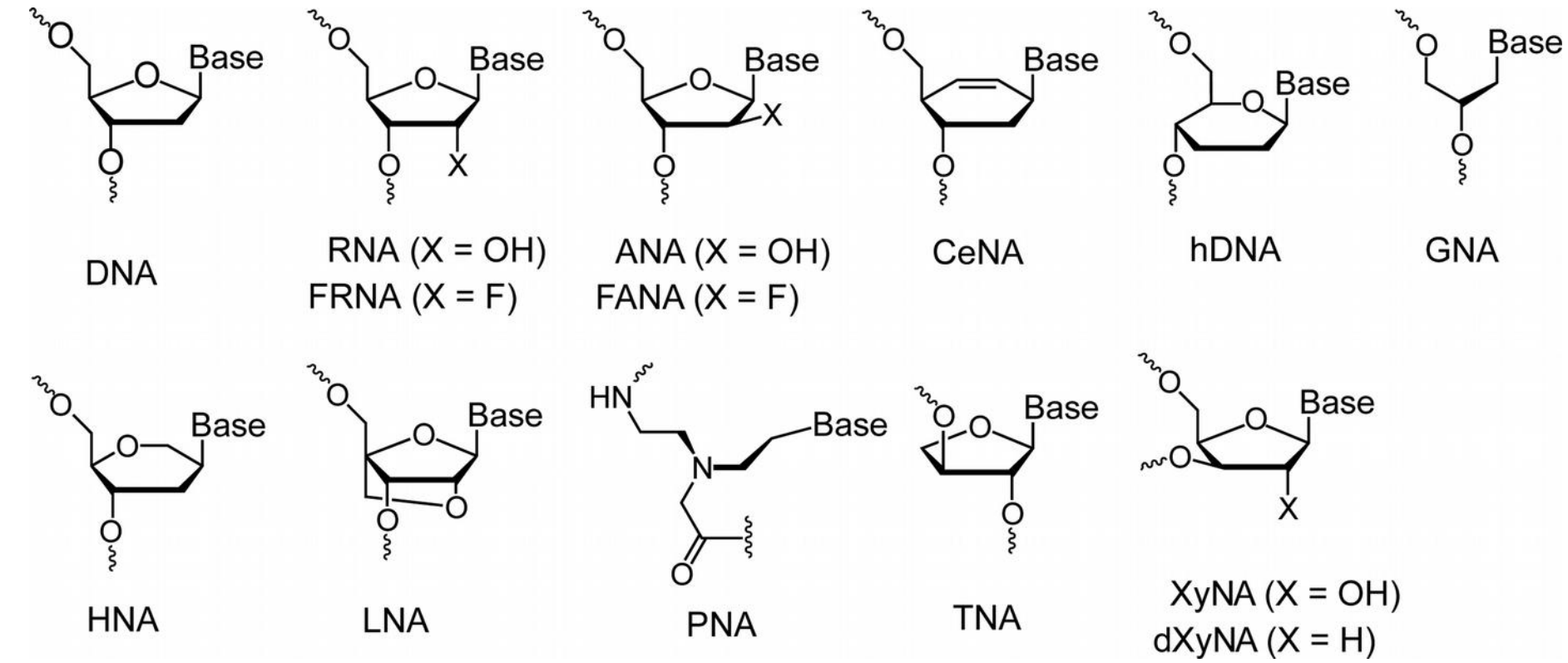


Kitekintés: xenonukleinsavak (XNA)

A szintetikus biológiában fontos, enzimekkel nem lebontható nukleinsav-analógok. Hibrid kettős hélixeik is jellegzetesen eltérnek a DNS/RNS hélixektől.

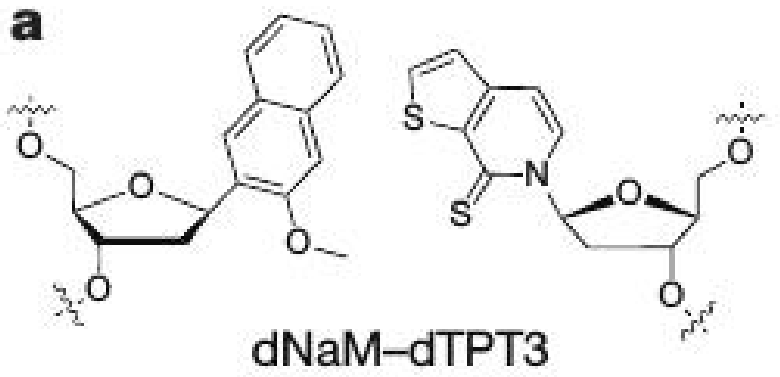


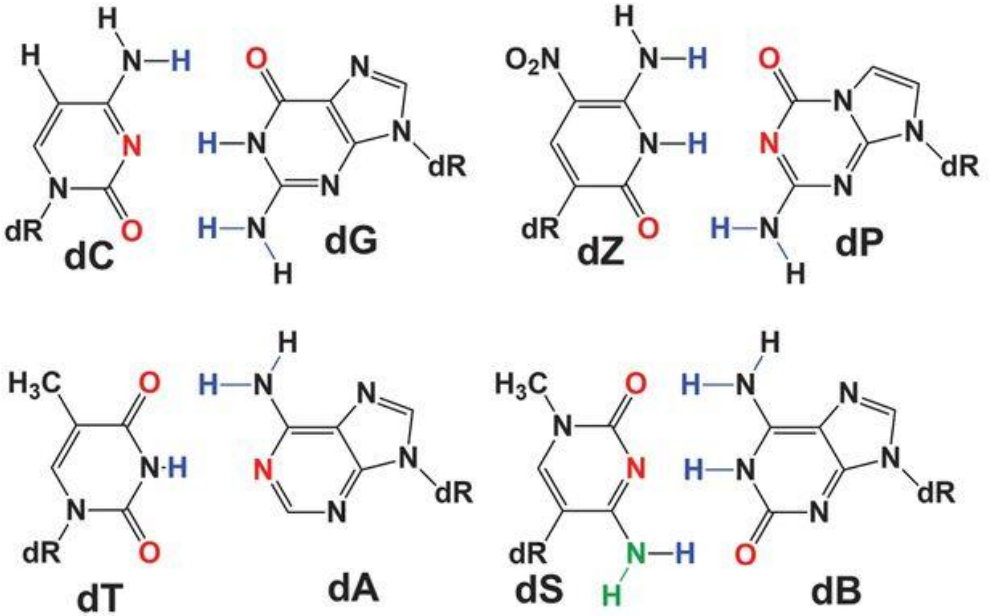




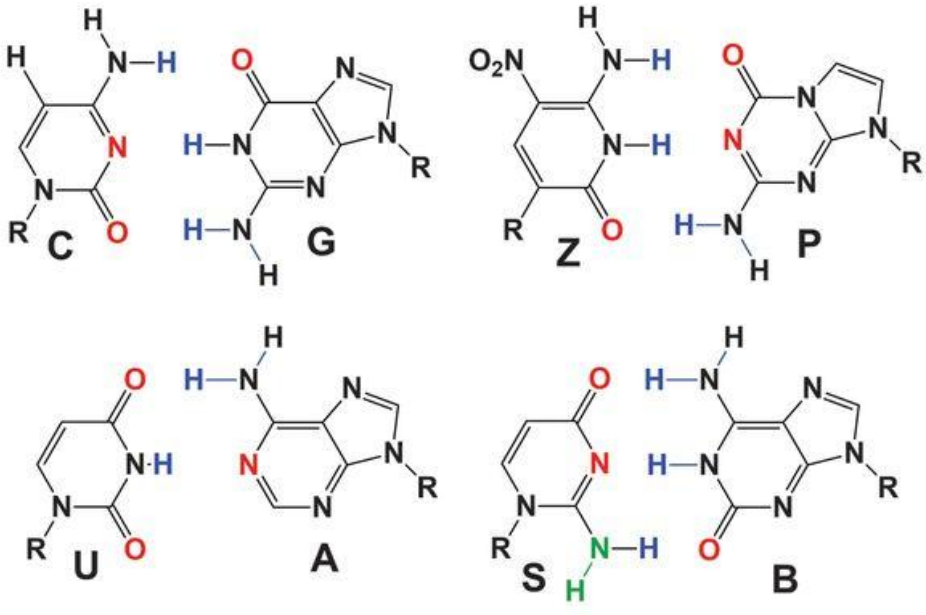
Kitekintés: mesterséges bázispárok

A genetikai ábécé kiterjesztése mesterséges bázisokkal, melyek be tudnak épülni a DNS-be/RNS-be, és akár dekódolhatóak is megfelelő tRNS-sel.
A sejtek nem tudják ezeket a bázisokat előállítani, csak a környezetükből tudják felvenni, ha elérhetőek számukra.
A felső pár azt mutatja, hogy nem csak hidrogénkötéses párok lehetnek működőképesek, az alsó párok a természetesekkel együtt 8 bázist/4 bázispárt tartalmaznak, a természetes bázisokban is meglévő csoportok kombinálásával





hachimoji
=
”nyolc betű”



Mit kell tudni?

- Bázis, nukleozid, nukleotid, nukleotidok kapcsolódása egymáshoz
- Bázisok tautomerizációjának alapjai, jelentősége
- Watson-Crick bázispárok főbb jellemzői
- A kétszálú DNS alapvető jellemzői (számok nélkül)
- A DNS-re és az RNS-re jellemző hélixek különbözősége (számok nélkül), ennek rövid magyarázata