



迷人的DNA双螺旋

教学目标

1

知识目标

- 1、了解DNA双螺旋结构的证据◆
- 2、掌握DNA双螺旋结构要点◆★

2

思政目标

1. 培养勇于探索、追求真理的科学修养
2. 激发奉献社会、报效祖国的赤子情怀
3. 树立团队合作、互帮互助的协作精神
4. 建立顽强拼搏，开拓创新的精神品质

3

能力目标

1. 具备提出、分析、解决与生物化学相关问题的能力
2. 具备批判性、创新性思维习惯及较好的创新能力
3. 具备自主学习、课外阅读、专业知识交流表达等能力

(◆为重点，★为难点)

引入→

1ste Flan'd'n

DNA

“一页纸改变人类的例子不多，但1953年《自然》杂志上的那篇经典论文就是”

no. 4566 April 25, 1953

NATURE

33

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

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

A structure for sodium acid has already been proposed by Fawcett and Gump¹. They kindly made their manuscript available to us in advance of publication. Their model consists of three interwoven chains, with the phosphates near the fibre ends and the hydroxyl groups in the center. In our opinion, this structure is unsatisfactory for two reasons. (1) We believe that the material which gives the X-ray diagram 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 phosphate groups are separated by only one unit. (2) Some of the van der Waals distances appear to be far too small.

Another chain-chain structure has also been suggested by Freese (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.

We wish to present a radically different structure for the unit of cyclohexane metabolism. This structure is based on the idea that each radical in the metabolic reaction has to have inside the enzyme its own active site, its own amino acid, its own cofactor, and its own group just as in the cytochrome reduction with P-450. The two main lines

not too many; the reduced to a
dend perpendicular to the chain
axis. Both chains follow right-
handed helices, but owing to
the rigid the separation of the
units in the two chains runs
in opposite directions. Each
chain is a helix.

[illegible]

is a node on each chain every 2-4 Å, in the z -direction. We have observed no angle of 280° between

adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphate atom from the fibre axis is 19 Å. As the phosphates are on

The structure is an open one, and its water content is rather high. At lower water contents we would

The novel feature of the structure is the manner in which the two chains are held together by the

pyrrole and pyrimidine bases. The planes of the bases are perpendicular to the flow axis. They are joined

together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other strand, so that the two lie side by side with identical π -co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

It is assumed that the bases only occur in the structure in the most plausible tautomeric form; that is, with the base rather than the acid or the conjugate base. In the case of the bases, the only specific points of interest are the bases adenine, guanine, cytosine, thymine, and uracil. The bases adenine, guanine, and cytosine are found in DNA, while thymine and uracil are found in RNA. The bases adenine, guanine, and cytosine are found in both DNA and RNA, while thymine and uracil are found only in RNA. The bases adenine, guanine, and cytosine are found in both DNA and RNA, while thymine and uracil are found only in RNA.

It has been experimentally^{1,2} that the ratio of the rate of polymerization to the rate of the reaction of the monomer with oxygen, are always very close to unity, and this is clearly impossible to build this structure with the regular place of the dicarboxylic acid.

The manuscript published X-ray data¹⁰ on these two complexes are insufficient for a rigorous test of our structure. In fact as we can tell, it is roughly compatible with the experimental data, but it reveals some apparent errors. One of them is given in the following communications. We want also to say that the details of the results presented there when we derived our structure, which were mainly thought to satisfy our published experimental data and stereochemical arguments.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are very indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the triglycidic experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and his co-workers at King's College, London. One of us (J. D. W.) has been aided by a Fellowship from The National Foundation for Infanticide Paralysis.

J. D. Wilson
F. H. C. Choo

Medical Research Council Unit for the
Study of the Molecular Structure of
Biological Systems,
Cambridge Laboratory, Cambridge.
April 5.

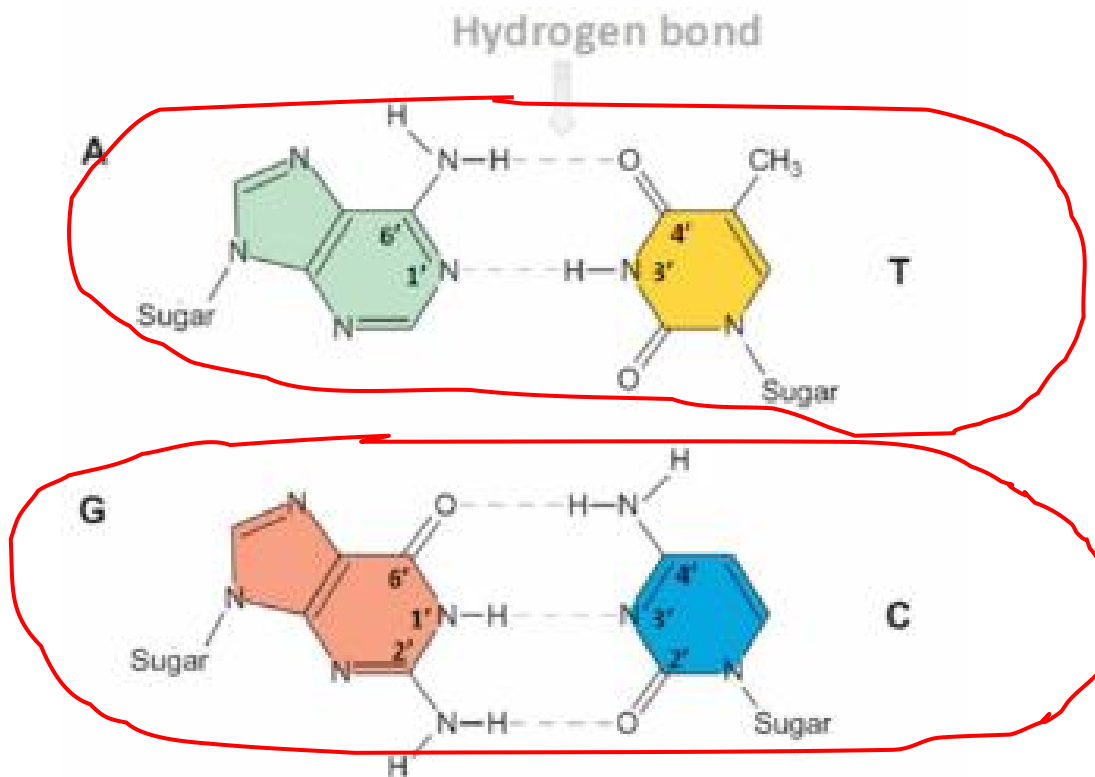
* Buckner, E., and Gentry, R. H., *Science*, 77, 104 (1932); *Proc. U.S. Nat. Acad. Sci.*, 18, 55 (1932).

¹Chapman, E., for letters to see Lippard, G., *Interchange*, 6, and Chapman, E., *Frontier of Science*, Jan. 8, 402 (1975).

² Williams, M. P. F., and Marshall, J. T., *Reactions of Polymers*, Vol. 10, 203 (1976).

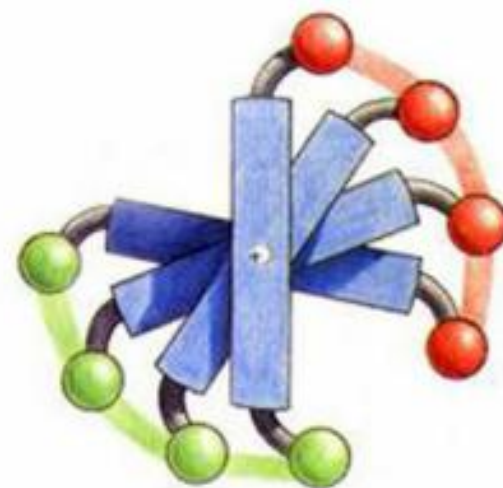
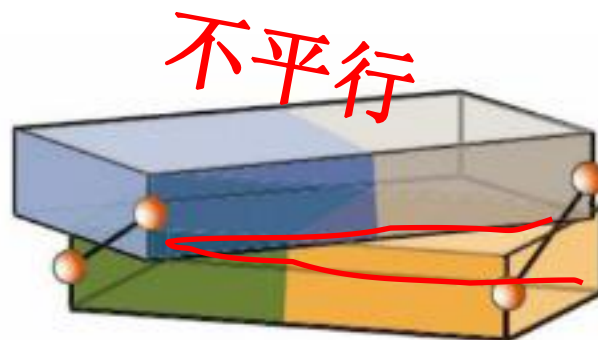
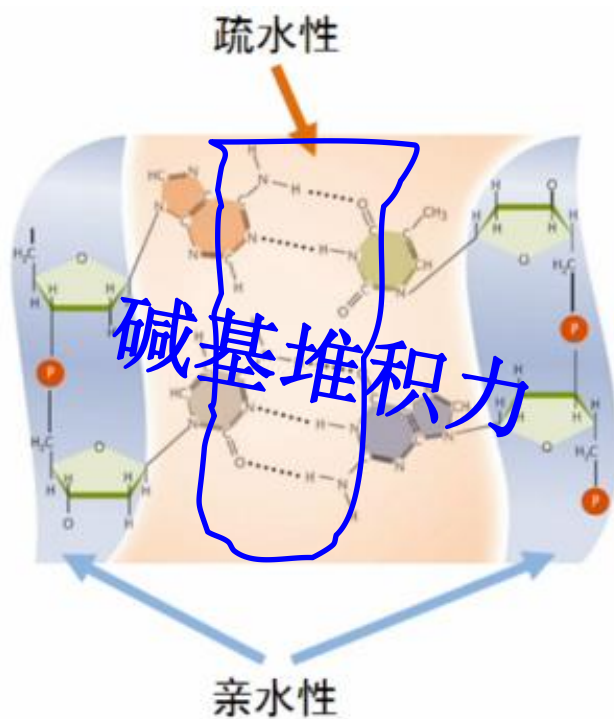
探究问题：DNA是“螺旋状”而非“线性”依据？

证据一： **Chargaff规则**

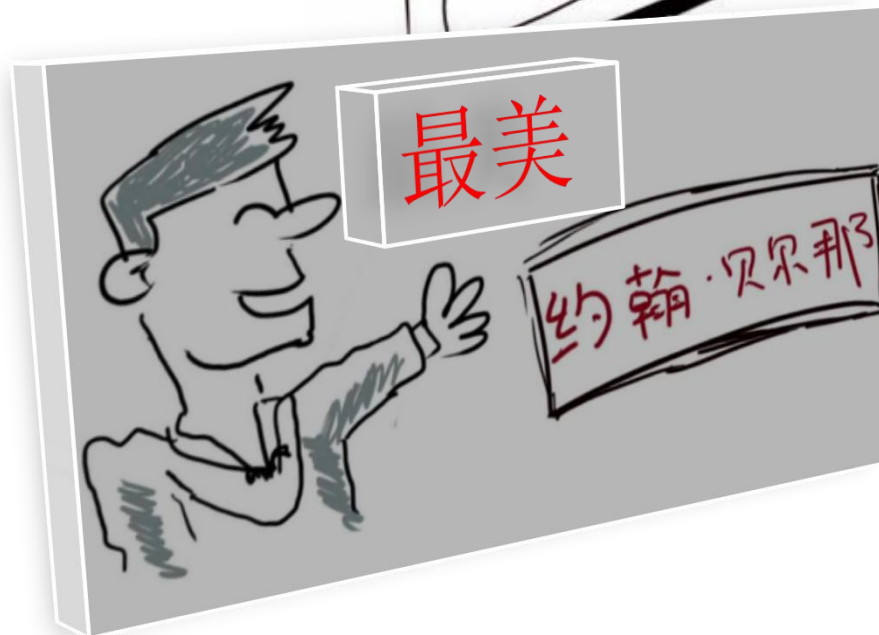


Watson-Crick配对；
互补配对

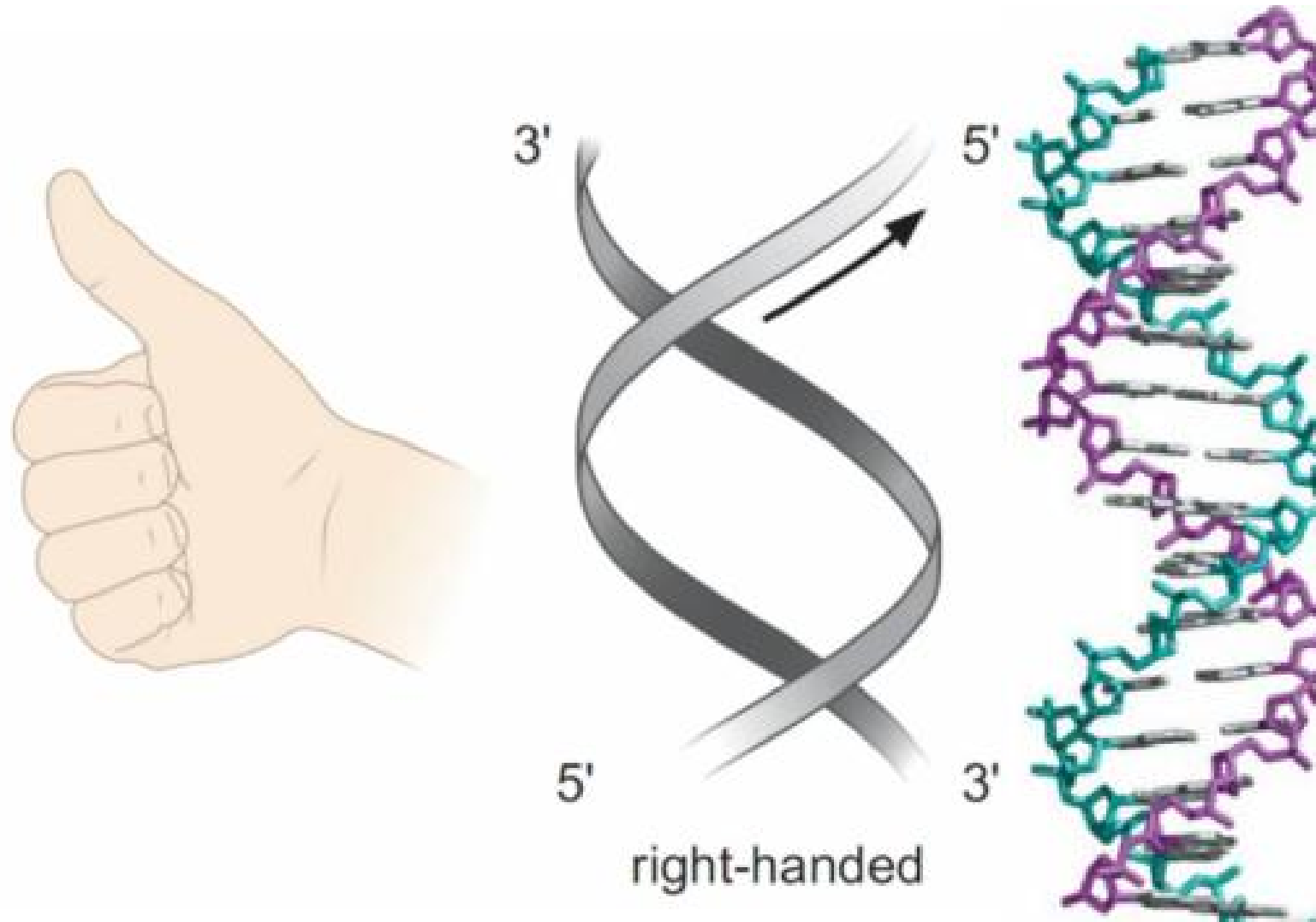
证据二：碱基堆积力



证据三： X-射线衍射照片（Franklin）



1、双螺旋结构的证据



思政教育1

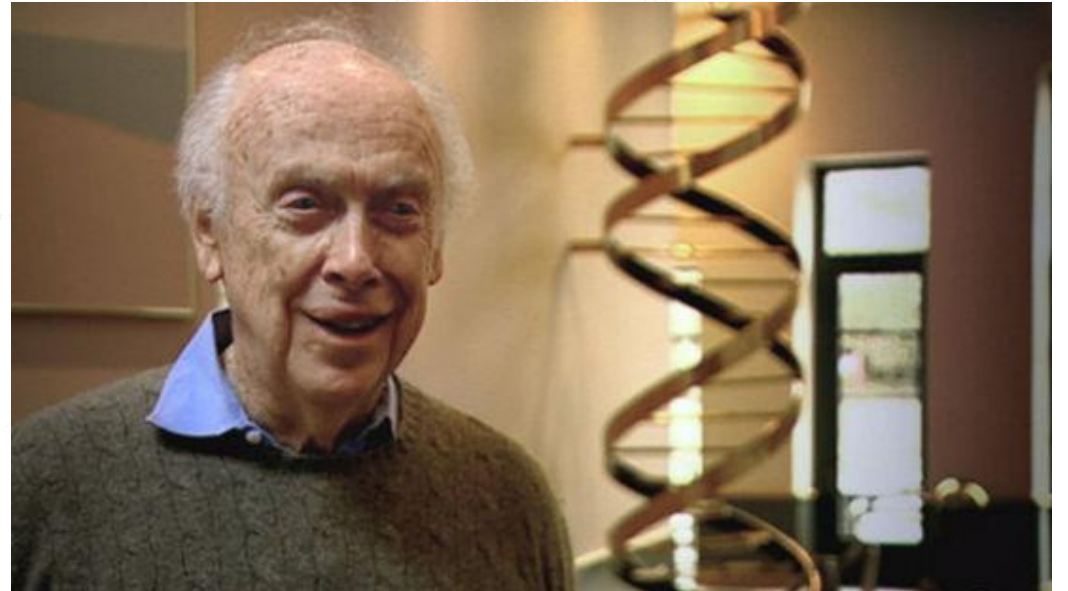
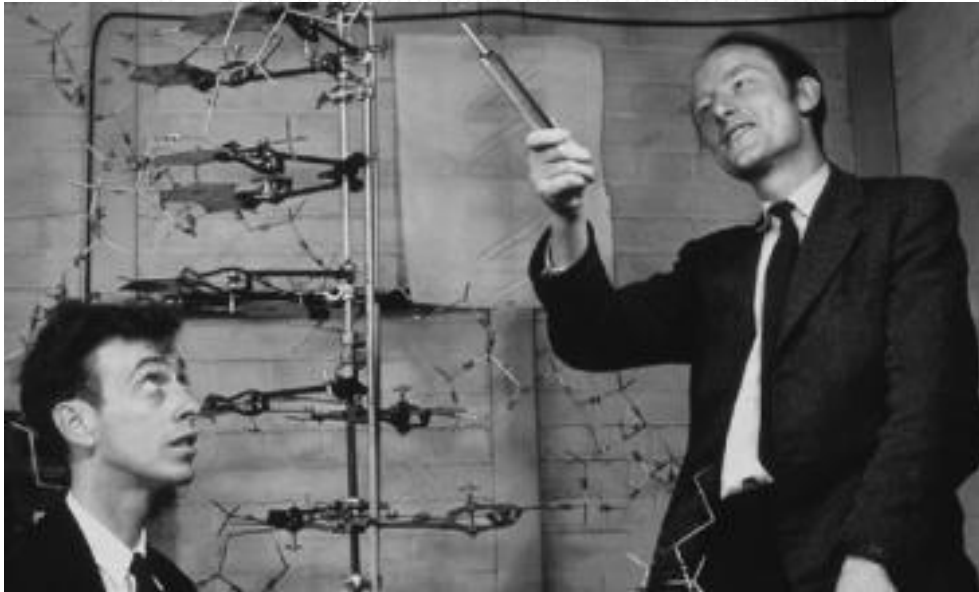
激发学生奉献社会、报效祖国的赤子情怀

20世纪中叶，这一时期西方美欧强国在生命科学等自然科学领域取得了长足发展和突破性成就，DNA双螺旋结构的阐明就是其中的典型代表，此时的祖国处于刚经历完抗日战争、解放战争后的千创万孔、百废待举、积贫积弱的时期，通过这一时期的中外对比，激发奉献社会、报效祖国的赤子情怀。



2、双螺旋结构的提出

1953年，Watson、Crick基于前述研究成果基础上，提出了DNA双螺旋模型。



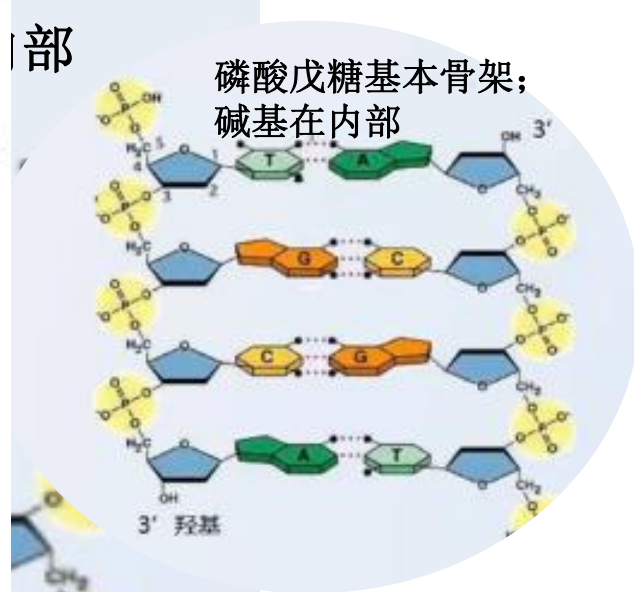
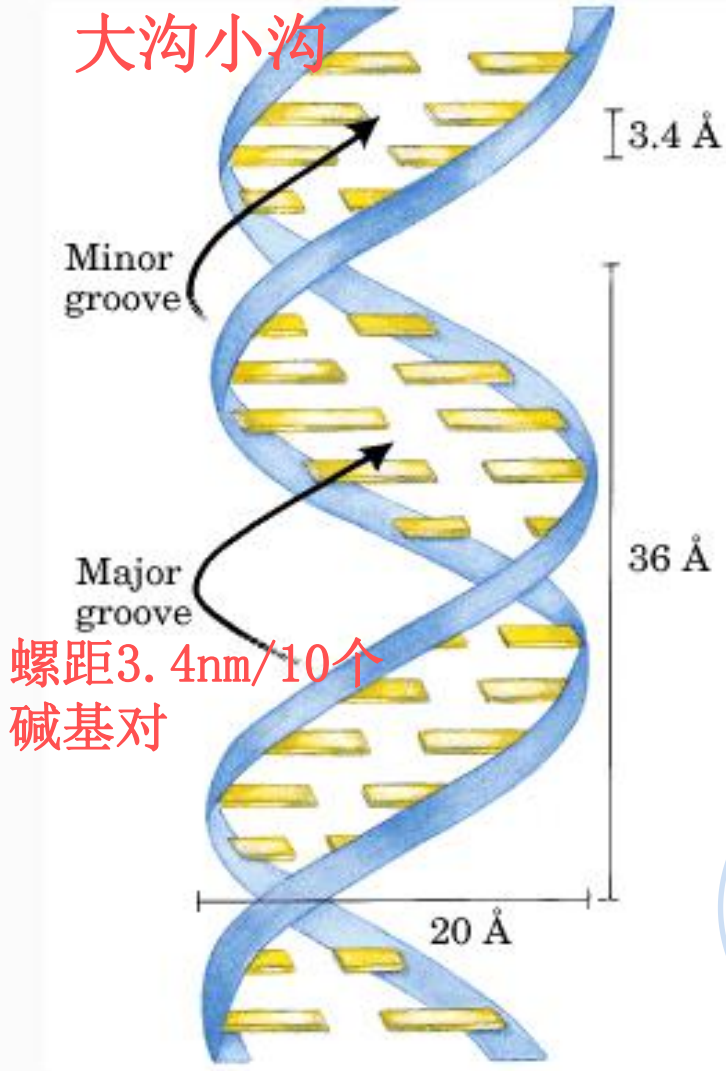
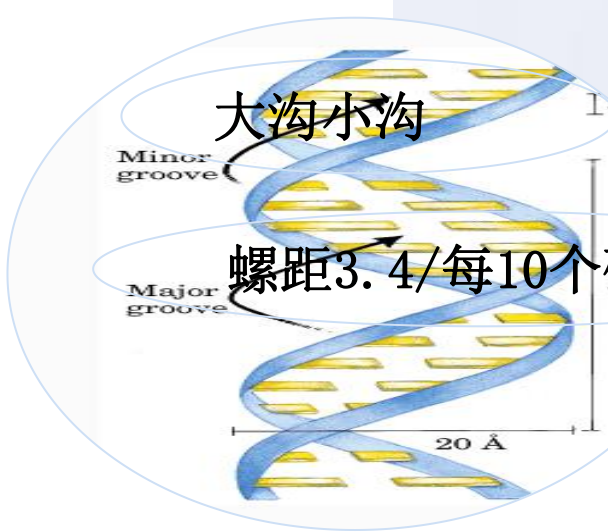
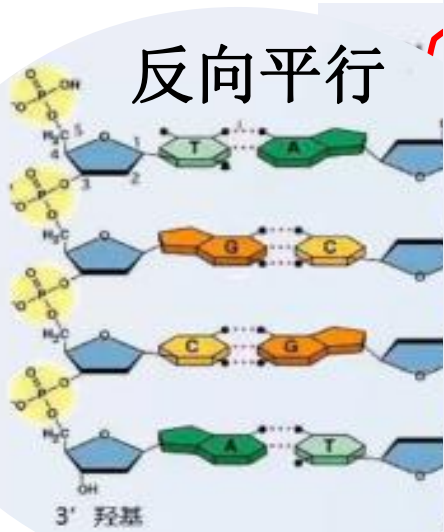
思政教育2

树立团队合作、互帮互助的协作精神

通过介绍Watson与Crick团队基于紧密协作、思想碰撞、讨论分享才令他们得以在世界上最先提出DNA双螺旋，从而取得如此大的突破性成就。引导学生树立团队合作、互帮互助的协作精神。



3、双螺旋结构要点



碱基序列不受限制，
碱基对准确序列携带
遗传信息

思政教育3

培养勇于探索、追求真理的科学修养

DNA双螺旋结构模型的阐明不是某一个科学家一蹴而就，而是多国科学家接力前行和激烈竞争的条件下才得以成功；结合介绍分子空间结构的大牛化学家Pauling提出的“三股螺旋”模型对**DNA**空间结构模型的误导这一背后的故事；培养学生勇于探索、不畏权威、追求真理的科学修养。



前沿进展一

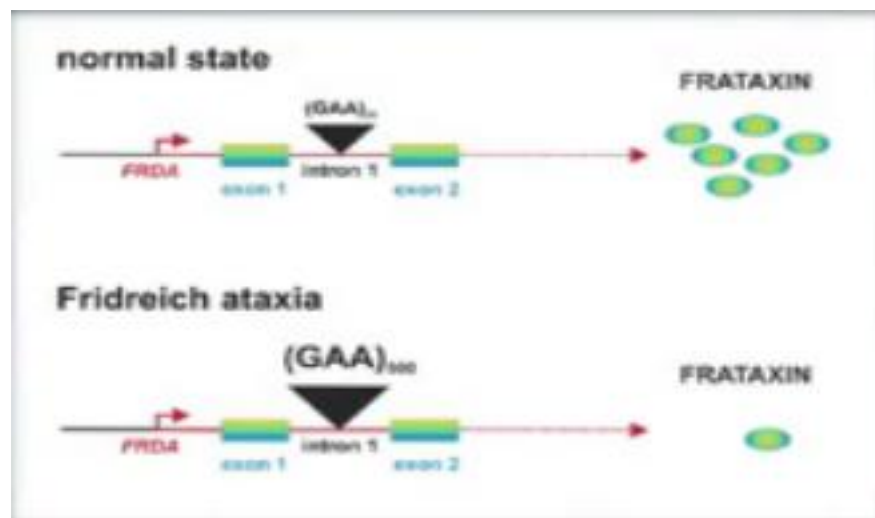
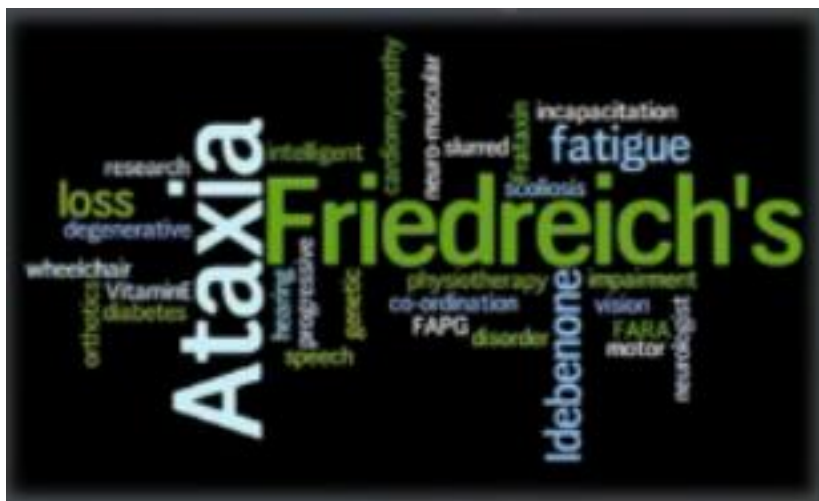
疾病举例：Friedreich's (共济失调症)

发病机制：DNA 双螺旋异常：三股螺旋

9号常染色体隐性遗传，GAA序列重复增加，DNA三股螺旋

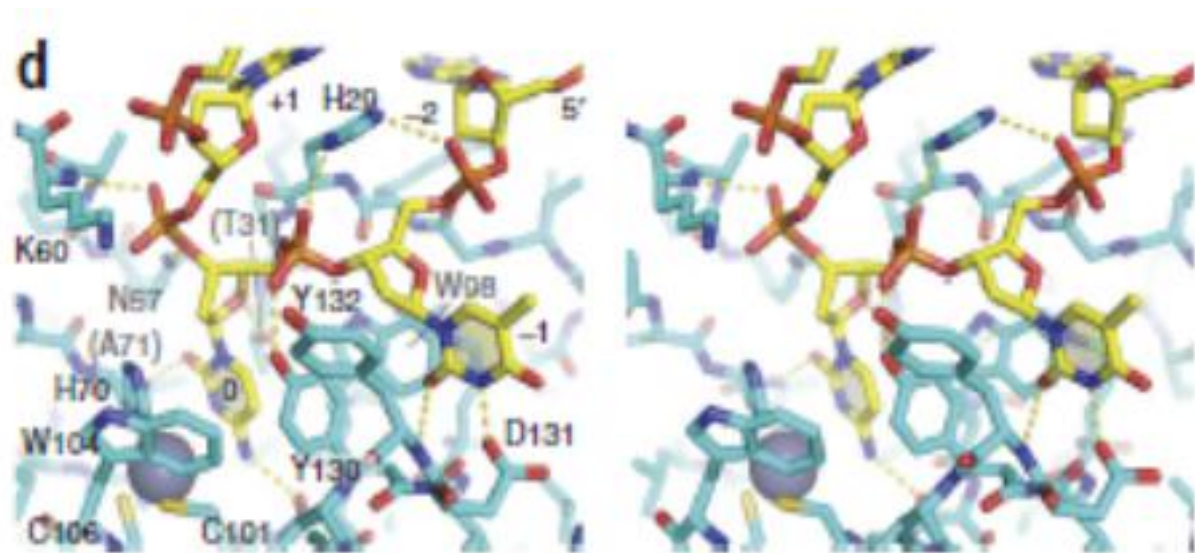
治疗新途径：(2014年)法国生物公司AAVLife公司；1200万美元；

基因敲除疗法。



Nature Structural and Molecular Biology, 2016, Ke Shi

应用：抑制APOBEC活性,使得目前使用的抗癌治疗方法变得更有效。



思政教育4

建立顽强拼搏，开拓创新的精神品质

基于前沿拓展这些令人兴奋的突破性成就、成果蕴藏的创新性思维，以及背后科学家坚韧不拔的坚持，熏陶学生建立顽强拼搏，开拓创新的精神品质。



小结



1

双螺旋证据:

Chargaff规则、碱基堆积力、X衍射照片

2

双螺旋的结构要点: 反向平行、磷酸戊糖基本骨架、螺距3.4nm每个螺旋包括10个碱基对、碱基在内侧通过氢键连接; 有大沟小沟

3

DNA 双螺旋异常: 三股螺旋将导致疾病

THANKS *for your time*

