分子生物学
Molecular Biology

魏晨曦 博士 讲师

2号楼2楼
基因功能与调控实验室
1号楼2楼
生态安全监测与评价实验室

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Introduction

1. Definition of molecular biology

Molecular biology seeks to explain the relationships between the structure and function of biological molecules and how these relationships contribute to the operation and control of biochemical processes.

分子生物学是解释生物分子的结构和功能的关系，以及这种关系是如何操纵和调控各种生化过程的。

---Turner et al.

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Of principal interest are the macromolecules and macromolecular complexes of DNA, RNA and protein and the processes of replication, transcription and translation.

分子生物学是在分子水平上研究生物大分子的结构与功能，以及分子之间信息传递和调控的一门生物学分支学科。

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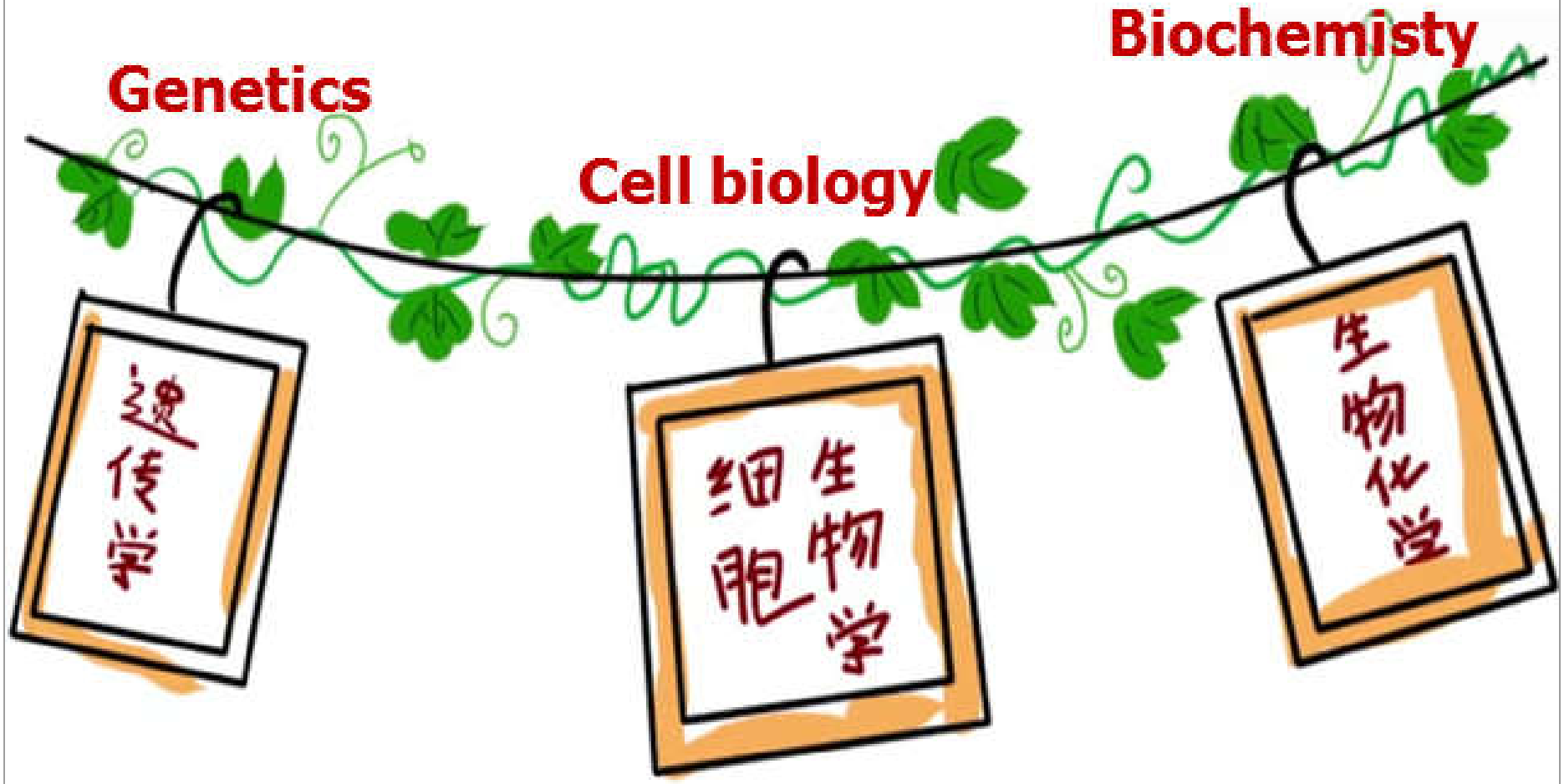
2. A brief history of molecular biology



1865年，Mendel提出奠定遗传学基础的性状遗传法则。

1909年，丹麦生物学家W. L. Johannsen赋予了“gene”的名称。

某一性状是由一对遗传因子(genetic factor)决定的。

genotype——基因型
phenotype——表型

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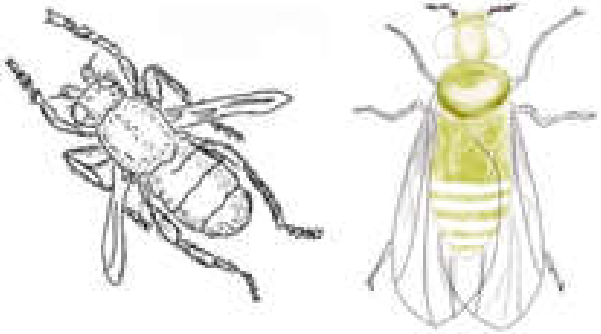
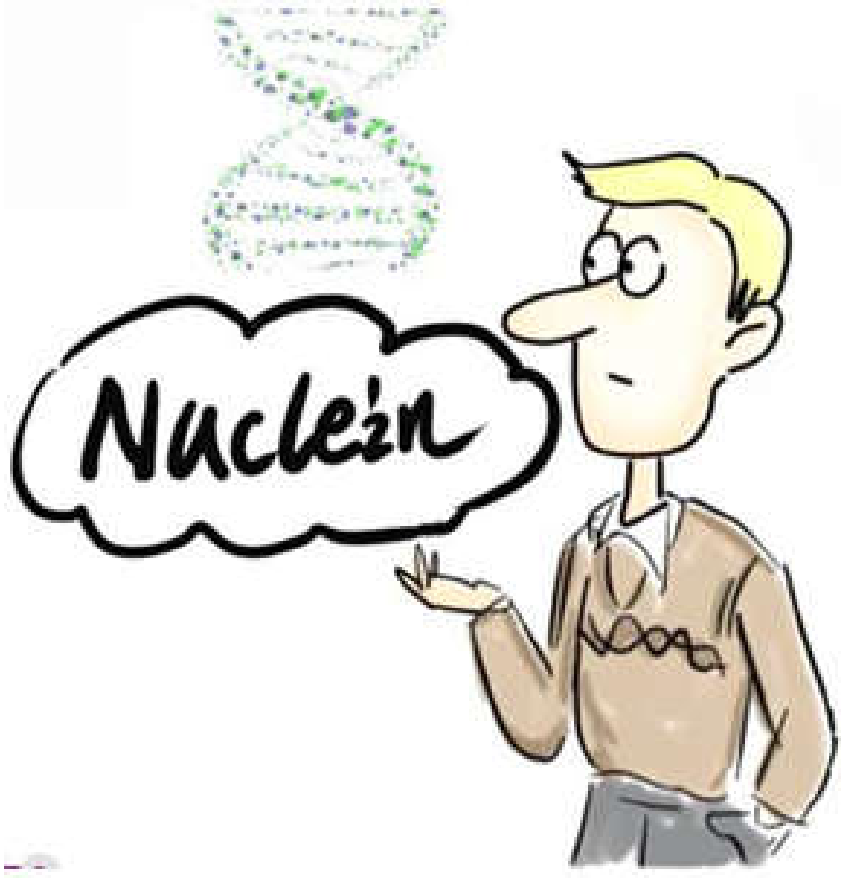
1902年，T. Boveri和W. Sutton观察到染色体在减数分裂(meiosis)过程的分配规律，并提出染色体是遗传因子的载体——染色体理论。

1910年被遗传学家T. H. Morgan用果蝇证实。

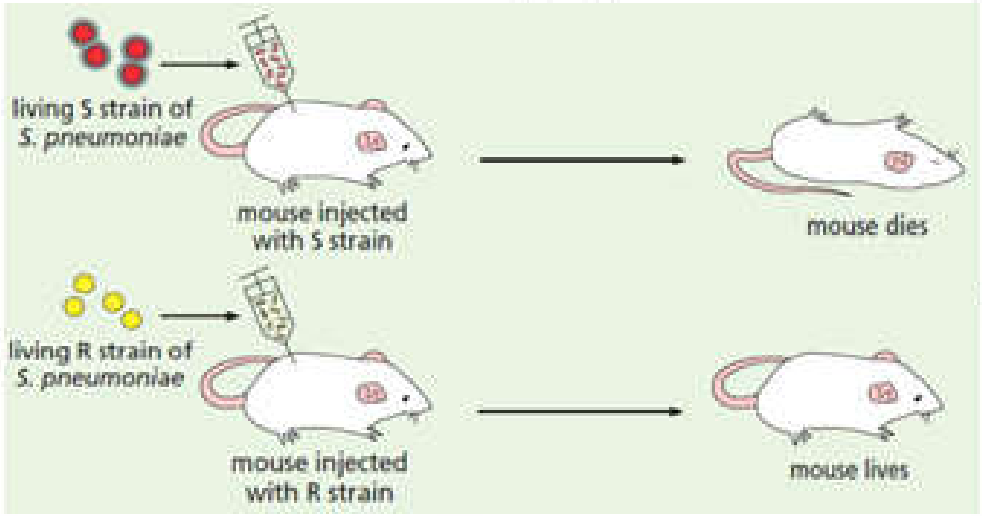


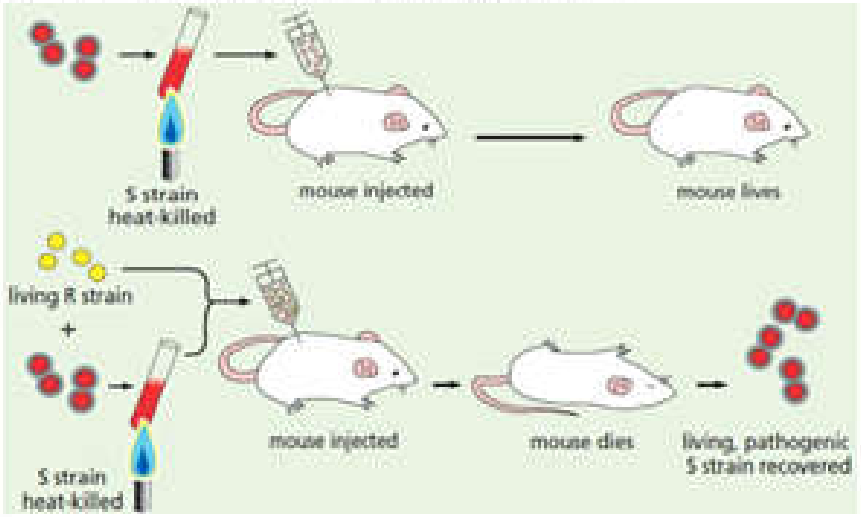
遗传学研究的模式生物

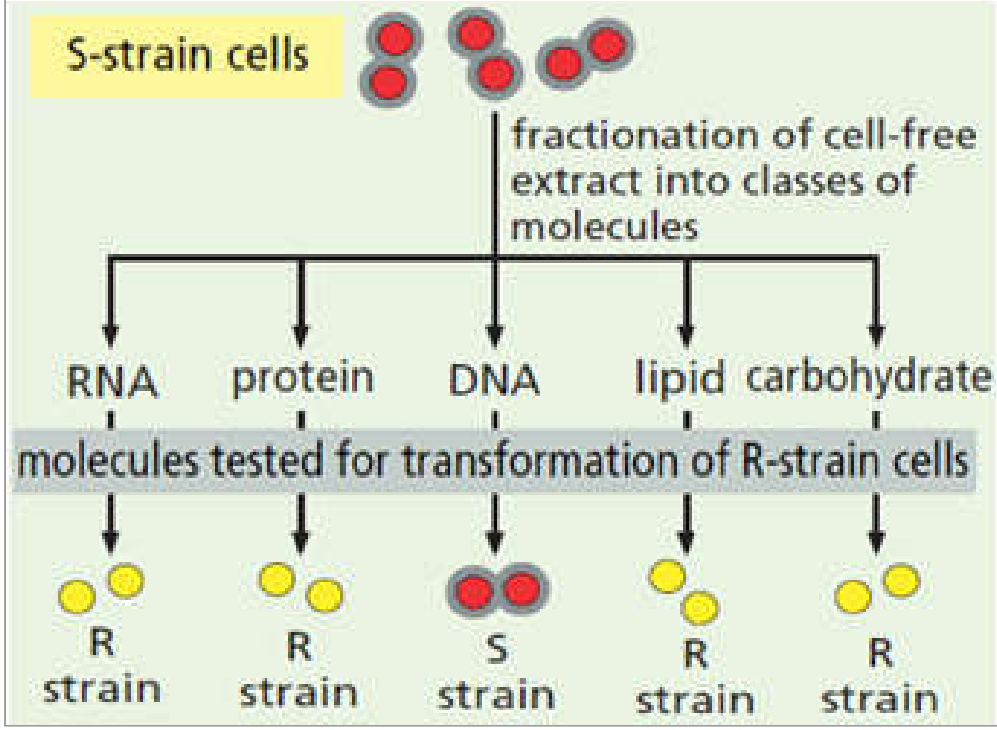
1869年，F.Miescher在白细胞中首次分离到“nuclein（核素）”，其实就是我们所说的DNA。



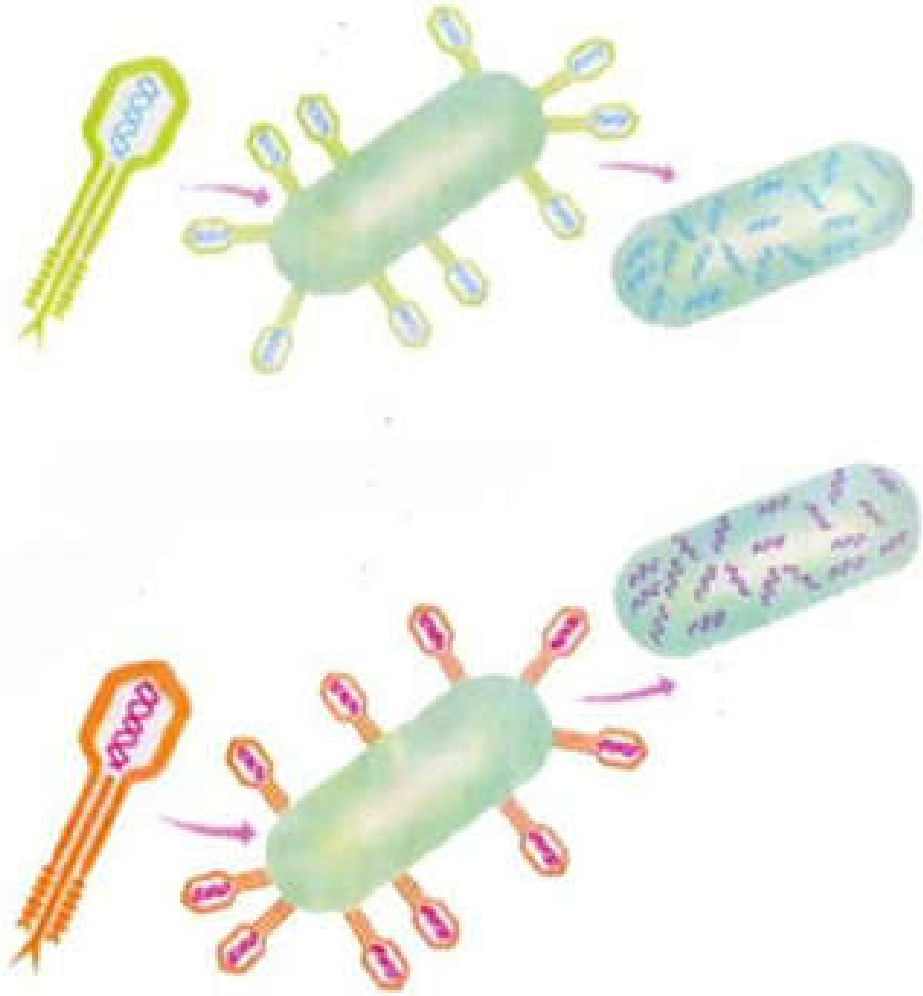
1928年，F.Griffith细菌毒力转化实验







1944 年，O. Avery, C. MacLeod 和 M. McCarty 三位科学家证明纯化的S型菌株的 DNA 可以使无毒的 R 型菌株发生转化。

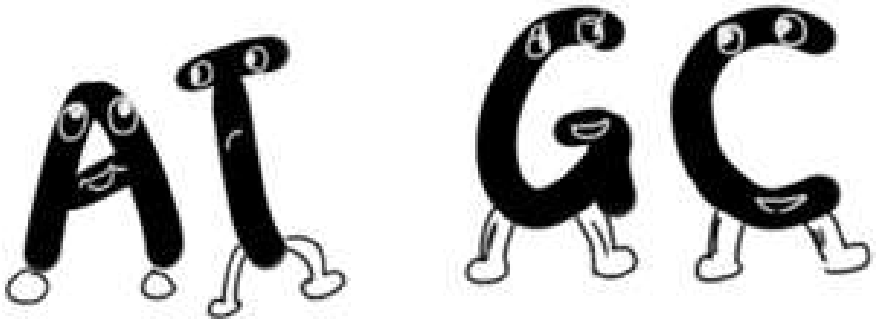


1952年，A. D. Heershey和M. Chase的T2噬菌体侵染细菌实验。

DNA is the genetic material.

1950年，E. Chaargaff碱基组成规律

不同生物来源的4种DNA碱基数不同。



[A]=[T]
[G]=[C]

为DNA 双螺旋结构的建立奠定了基础。

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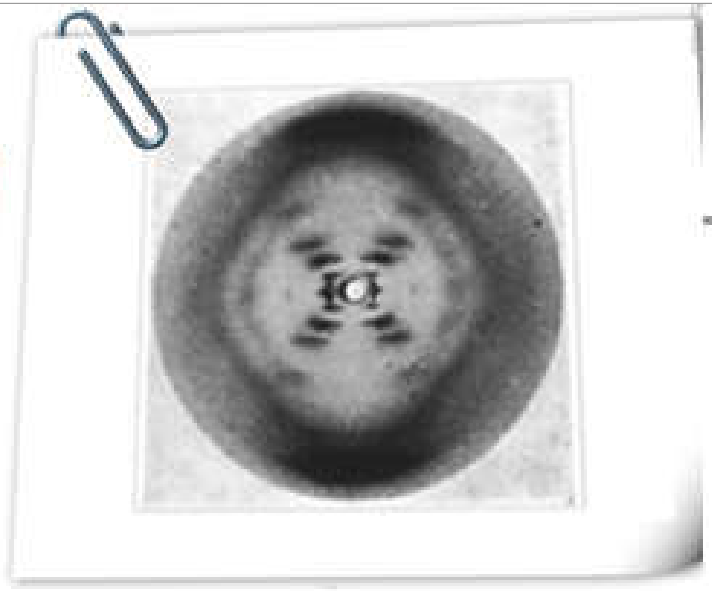
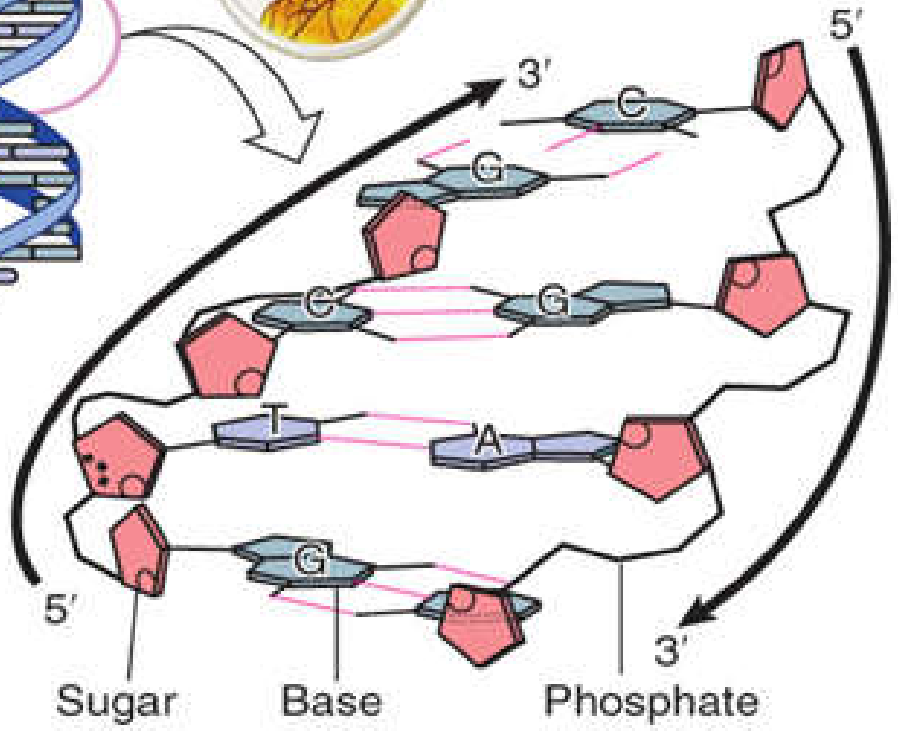


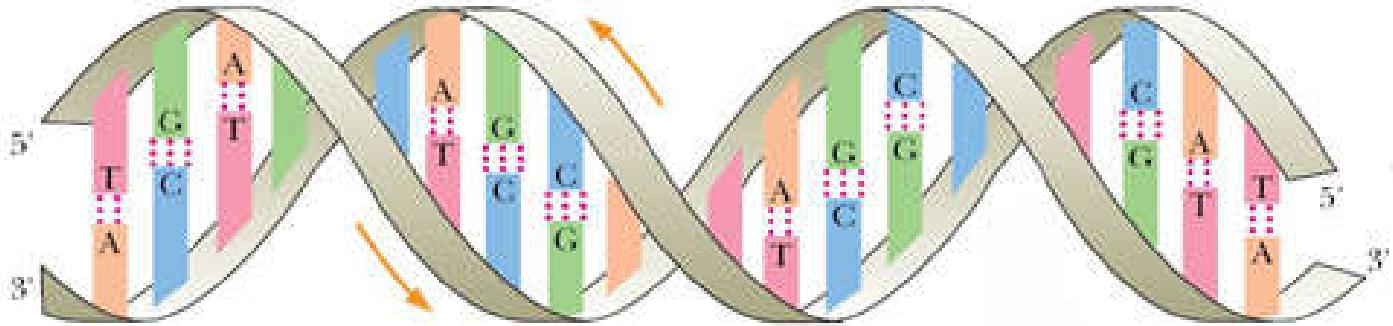
伦敦大学R. E. Franklin和M. Wilkinss采用 X 射线衍射技术得到了著名的 B 型双螺旋衍射图。

1953年，J. Watson和F. Crick在这张照片的启发下很快构建了 DNA双螺旋模型(double helix)。

DNA双螺旋模型的建立标志着分子生物学成为了生命科学领域的一门独立的学科。

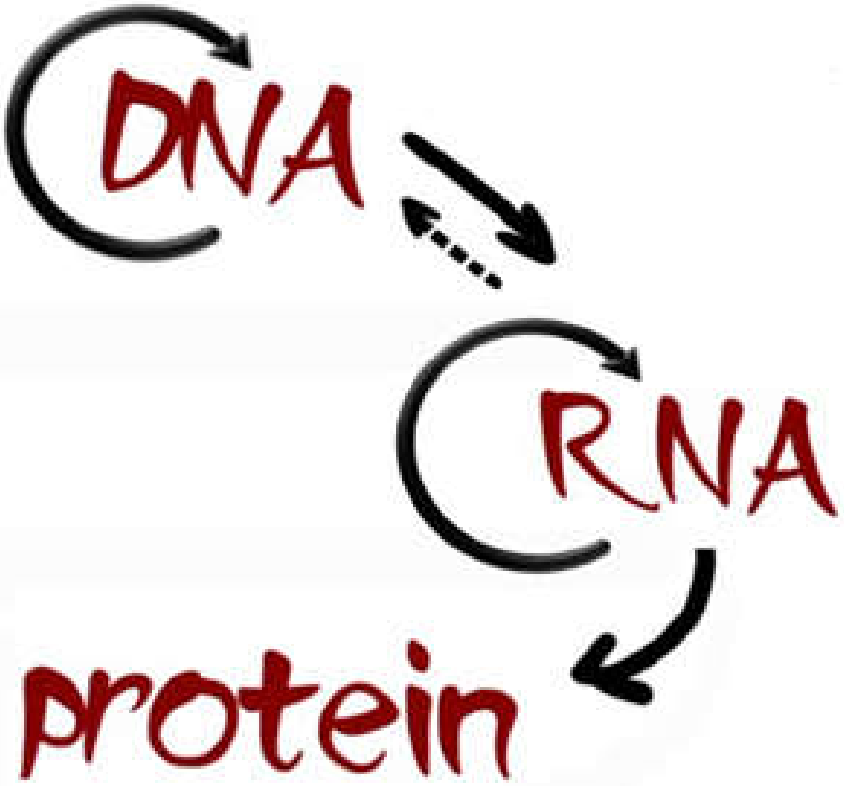
1962 Nobel Prize in Physiology or Medicine



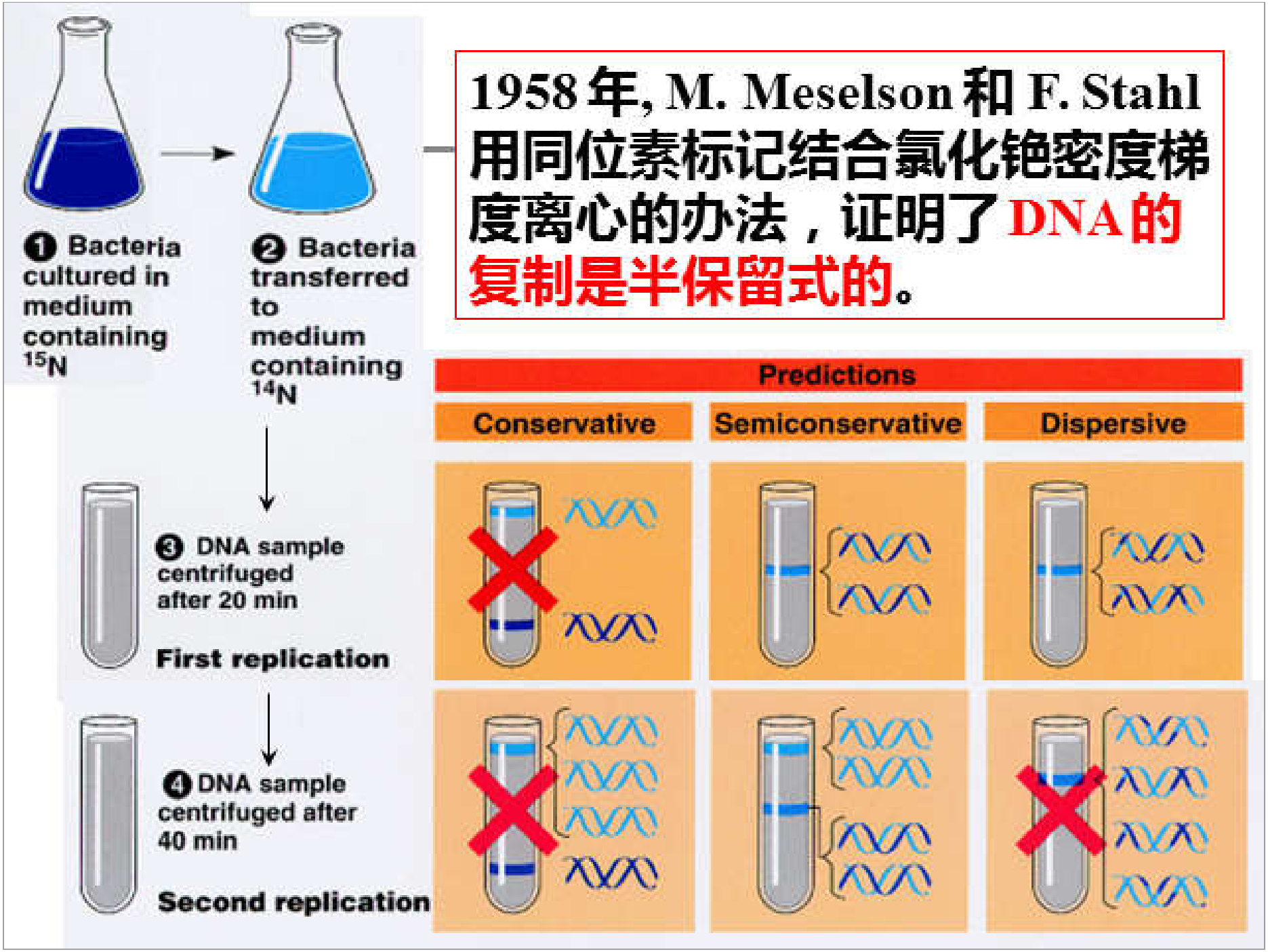


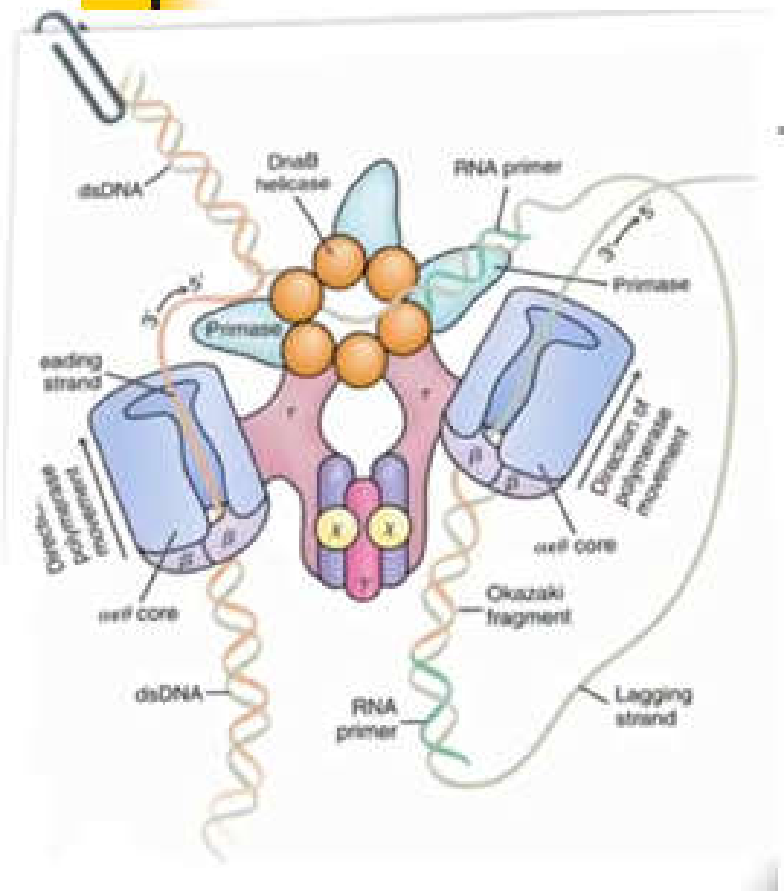
F. Crick从DNA互补配对的双链结构推测其和遗传信息的复制密切相关。

1957年，F. Crick又提出了**中心法则**（Central dogma）。搭建了狭义分子生物学的研究框架。



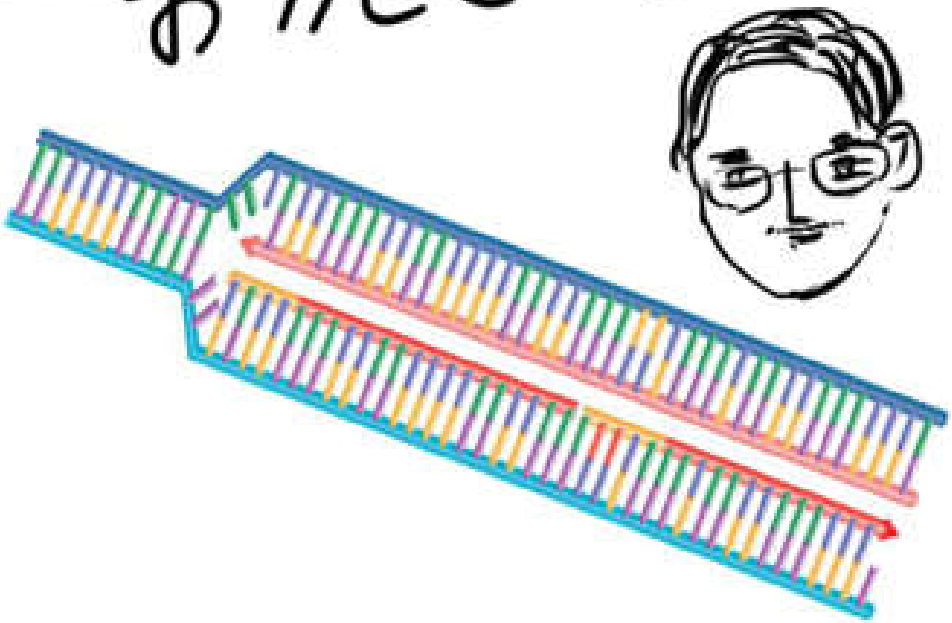
1958年, M. Meselson和F. Stahl用同位素标记结合氯化铯密度梯度离心的办法，证明了DNA的复制是半保留式的。





1956年，A. Kornbberg发现了DNA聚合酶。

おかざきれいじ



1968年，冈崎证明了DNA 复制的半不连续方式。1972年，冈崎夫人发现DNA新链合成的起始需要 RNA引物。

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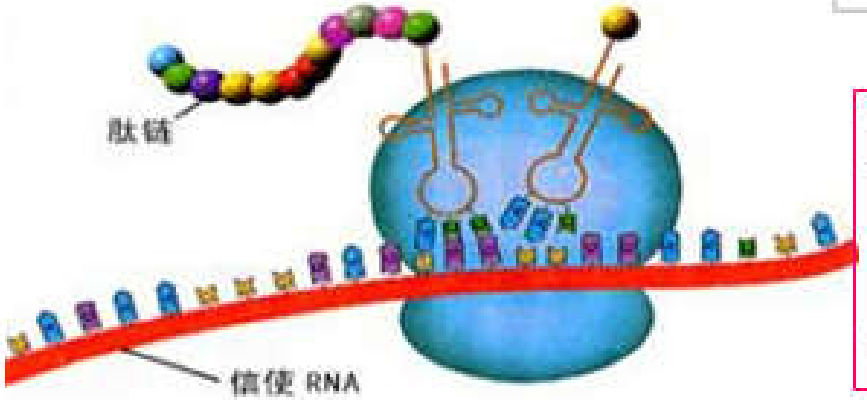
1959年，J. Hurwitz等人发现了RNA聚合酶。

20世纪60年代初，M. Nirenbergg等解密了遗传密码。

密码子的第一位（5′端）	密码子的第二位 U		C		A		G		密码子的第三位（3′端）
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



F. Jacob和S. Brenner证明了核糖体通过阅读mRNA将遗传信息翻译成为蛋白质。

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20世纪70年代，H. M. Temin和D. Baltimorre发现了反转录酶，补充了F. Crick提出的中心法则。

Viral RNA-dependent DNA Polymerase

Two independent groups of investigators have found evidence of an enzyme in virions of RNA tumour viruses which synthesizes DNA from an RNA template. This discovery, if upheld, will have important implications not only for carcinogenesis by RNA viruses but also for the general understanding of genetic transcription: apparently the classical process of information transfer from DNA to RNA can be inverted.

RNA-dependent DNA Polymerase in Virions of RNA Tumour Viruses

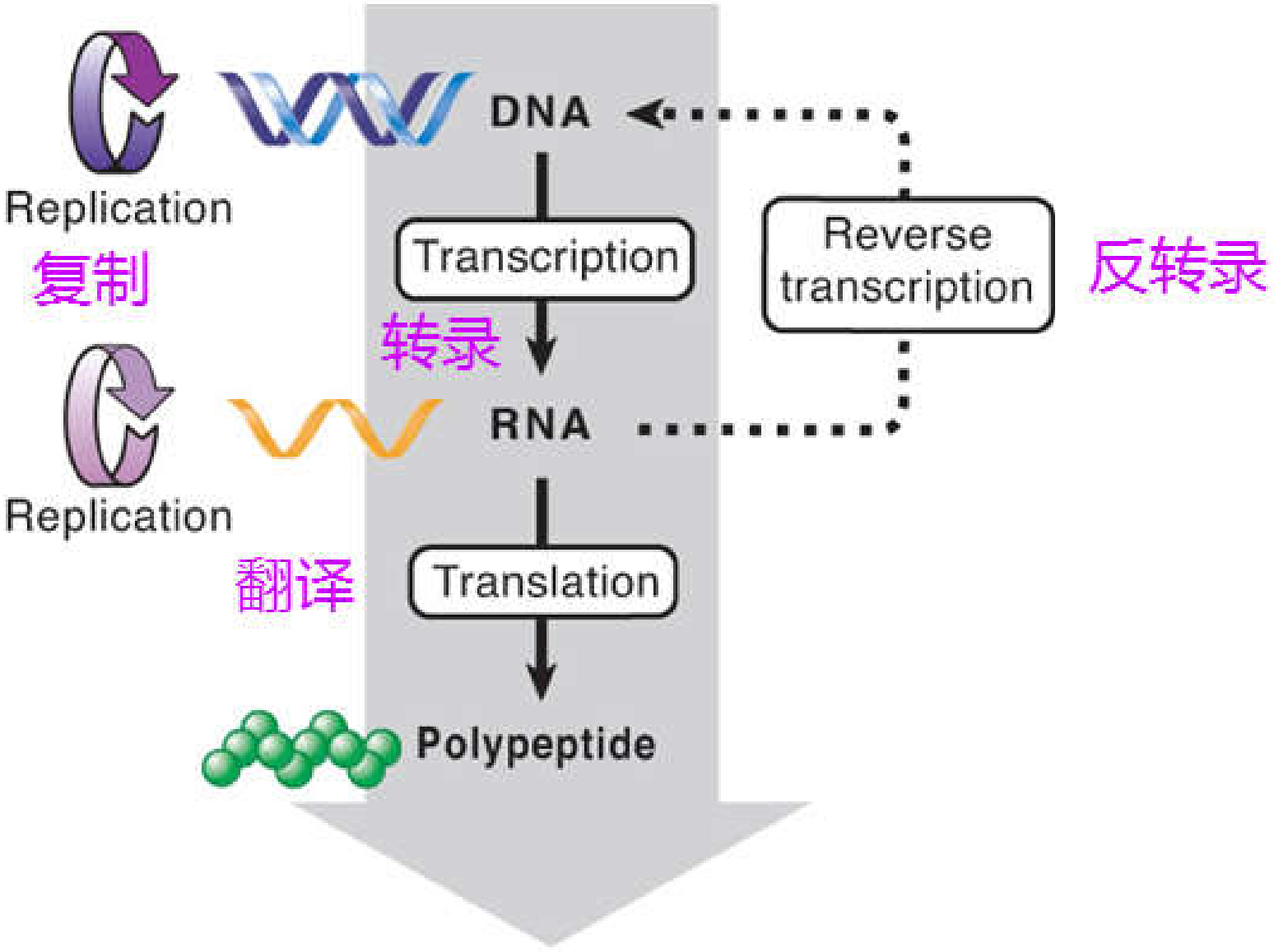
DNA seems to have a critical role in the multiplication and transforming ability of RNA tumour viruses[1]. Infection and transformation by these viruses can be prevented by inhibitors of DNA synthesis added during the first 8–12 h after exposure of cells to the virus[1–4]. The necessary DNA synthesis seems to involve the production of DNA which is genetically specific for the infecting virus[1,4], although hybridization studies intended to demonstrate virus-specific DNA have been inconclusive[1]. Also, the formation of virions by the RNA tumour viruses is sensitive to actinomycin D and therefore seems to involve DNA-dependent RNA synthesis[1–6,7]. One model which explains these data postulates the transfer of the information of the infecting RNA to a DNA copy which then serves as

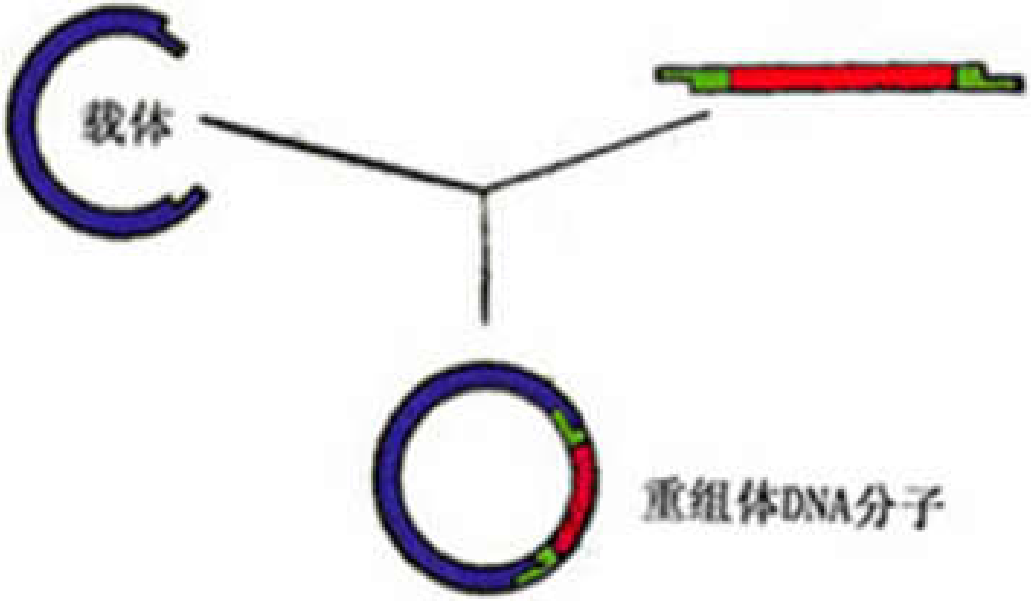
course may indicate the occurrence of a slow activation of the polymerase in the reaction mixture. The activity is approximately proportional to the amount of added virus.

For other viruses which have nucleotide polymerases in their virions, there is little or no activity demonstrable unless the virions are activated by heat, proteolytic enzymes or detergents[8–12]. None of these treatments increased the activity of the R-MLV DNA polymerase. In fact, incubation at 50° C for 10 min totally inactivated the R-MLV enzyme as did inclusion of trypsin (50 μg/ml.) in the reaction mixture. Addition of as little as 0·01 per cent 'Triton N-101' (a non-ionic detergent) also markedly depressed activity.

Table 1. PROPERTIES OF THE RAUSCHER MOUSE LEUKAEMIA VIRUS DNA POLYMERASE

Central dogma 中心法则



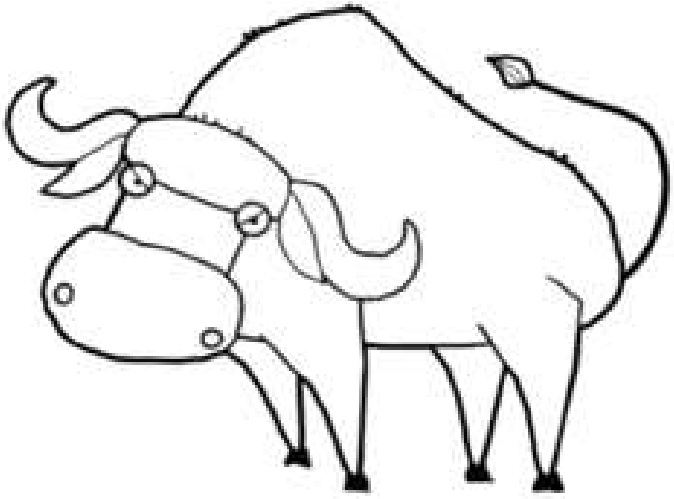


1980 Nobel Prize in Chemistry

1972年，P.Berg建立了重组DNA技术，堪称现代基因工程之父。

1975年，F. Sanger建立了一种称为双脱氧终止法的技术来测定DNA序列，也称做Sanger法。

Phage Φ-X174



1980 Nobel Prize in Chemistry

1958 Nobel Prize in Chemistry

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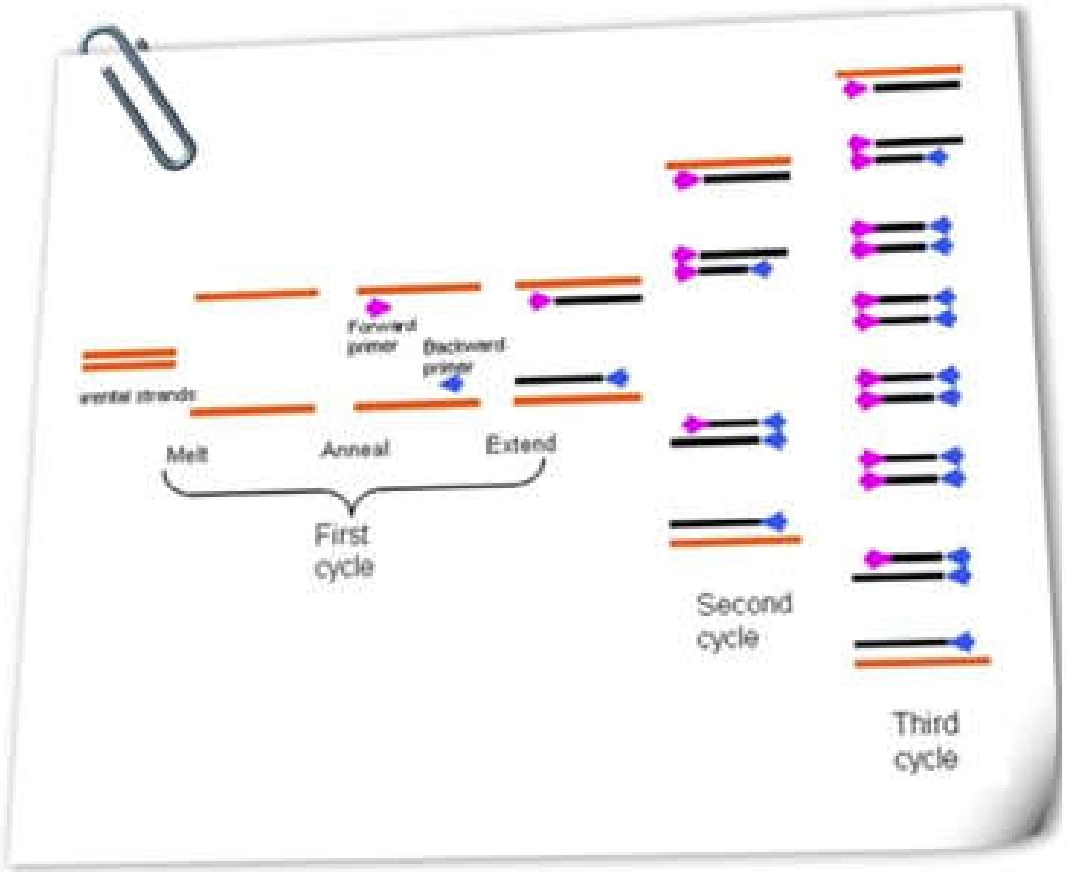
1982年，M. Smith 建立了基于核酸的定点突变技术。从此人们得以通过对基因特定位点的突变来进行基因功能的研究或对基因进行定向改造。

1993 Nobel Prize in Chemistry

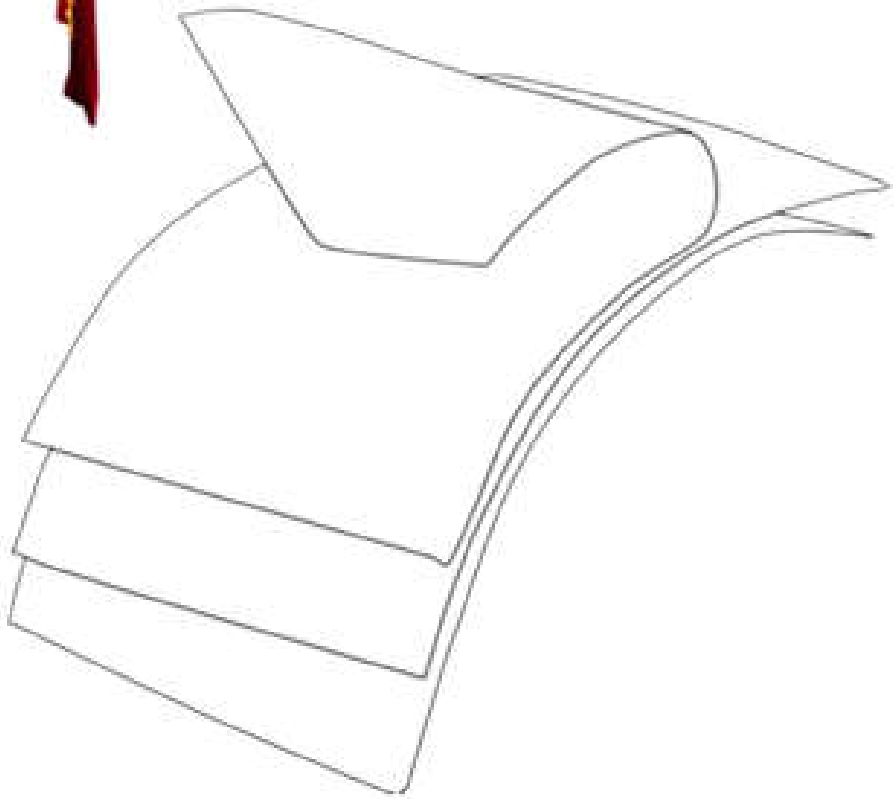
1983年，K.B. Mullis发明了PCR技术。



1993 Nobel Prize in Chemistry

1990 年起，人类基因组计划拉开序幕。

2001年，人类基因组草图发表。



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2003年，更为精细的基因组图谱公布。

2006年5月18日，英美科学家宣布人类最大和最后一个染色体——1号染色体的基因测序工作已经完成。

后基因组时代　　Functional genomics

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3. Relationship between molecular biology and other discipline of biology

- Genetics
- Cell biology
- Biochemistry
- Microbiology
- …

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分子生物学

分子结构生物学	分子细胞生物学	分子毒理学
分子发育生物学	分子免疫学	分子遗传学
分子神经生物学	分子病毒学	分子生态学
植物分子生物学	分子生理学	分子进化学
动物分子生物学	分子肿瘤学	……

分子生物学渗透到生物学几乎所有学科!

分子生物学成为现代生命科学的共同语言!

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4. Application of molecular biology

4.1 Medical Science

- PCR、ELISA等广泛用于临床医学疾病的诊断
- 通过基因工程生产药品、疫苗和抗体。如胰岛素、乙肝疫苗和单抗药物等。

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4.2 Fermentation (发酵) industry

基因工程菌的发酵，生产柠檬酸、氨基酸等。

4.3 Agriculture and animal husbandry

畜牧业

- 抗病虫害的作物有烟草、蕃茄、土豆、小麦、水稻等
- 抗病、快速生长的转基因动物品系

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5. Course content

Part Ⅰ Gene structure and function

Chapter 1	Prokaryotic and eukaryotic chromosome structure	Sec. D

Part Ⅱ DNA biosynthesis and recombination

Chapter 2	DNA replication	Sec. E
Chapter 3	DNA damage, repair and recombination	Sec. F
Chapter 4	DNA cloning	Sec. G

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Part Ⅲ Gene expression

Chapter 5 Transcription in prokaryotes	Sec. K
Chapter 6 Transcription in eukaryotes	Sec. M
Chapter 7 RNA processing	Sec. O
Chapter 8 Protein synthesis	Sec. P Q

Part Ⅳ Regulation of gene expression

Chapter 9 Regulation of transcription in prokaryotes	Sec. L
Chapter 10 Regulation of transcription in eukaryotes	Sec. N
Chapter 11 Translational control	Sec. Q4…

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Part Ⅴ Molecular biology of tumors

Chapter 12 Tumor viruses and oncogenes Sec. S

Part Ⅵ New molecular technologies

Chapter 13 Functional genomics and new technologies Sec. T

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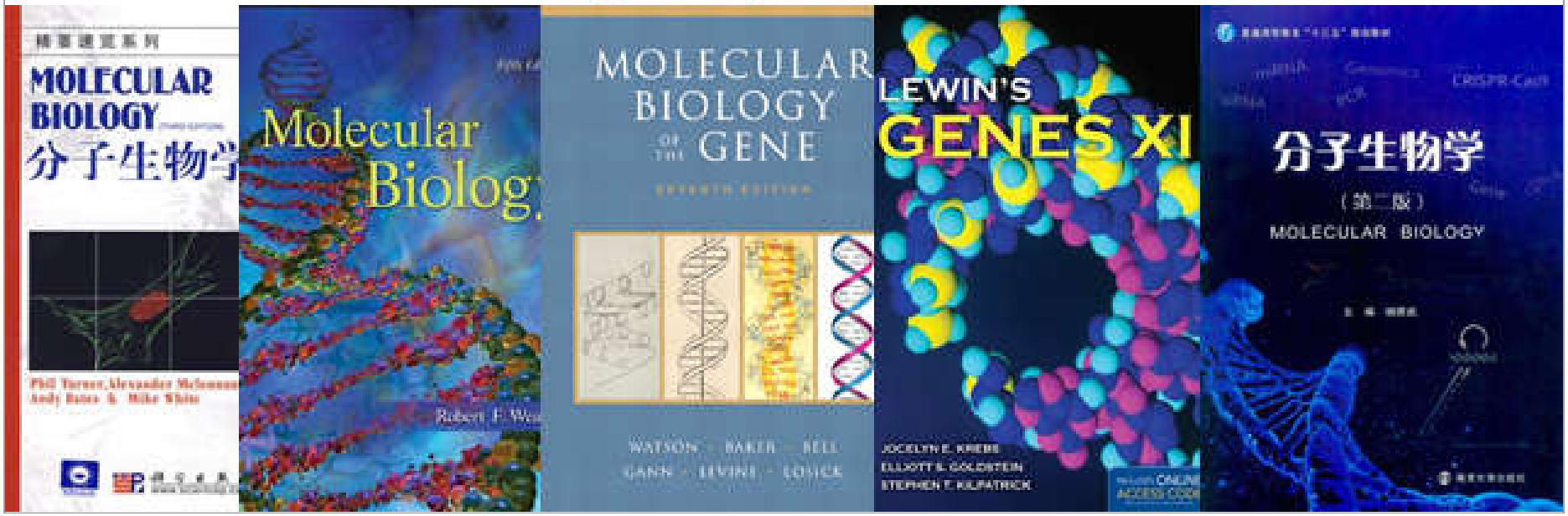
6. Main reference books

- P. Turner et al. Instant Notes in Molecular Biology (导读版) 第三版, 科学出版社, 2009
- R. F. Weaver. Molecular Biology, Fifth Edition, The McGraw-Hill Companies. 2012
- J. D. Watson et al. Molecular Biology of the Gene, Seventh Edition, Pearson Education. 2014
- J. E. Krebs et al. Lewin's GENES XI, Jones & Bartlett Learning, 2014
- 杨荣武 主编. 分子生物学(第二版), 南京大学出版社, 2017.



7. Suggestions for studying molecular biology

- Listen carefully and take notes moderately in the class. (打印课件https://www.yuketang.cn/web)
- Learn by understanding, not by rote.
- Review timely. Don't wait until the day before the exam to cram.
- Ask questions (雨课堂-讨论区/成员-发送私信).
- Complete homework.
- Do experiments and read references.

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Course scores

期末考试：60%

平时成绩：40%

（作业30%，考勤10%）

注：1. 作业将发布在雨课堂。可在手机（“雨课堂”微信公众号）或电脑（雨课堂网页版 https://www.yuketang.cn/web）完成。

2. 作业有时间限制，请在规定时间内完成。

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