

Follow-up  
from last class

The Nucleic  
Acid World

The Structure of  
DNA and RNA  
DNA → mRNA  
→ Protein  
Gene Structure  
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## DNA & RNA Review

### Zvelebil Ch. 1

### Lec'02'slides

# What's going on here???

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## Background:

- 1 Received a prostate tissue sample from a healthy person
- 2 Extracted DNA from the sample
- 3 Used next-generation sequencing on DNA sample
- 4 Looked closely at the androgen receptor (AR) DNA sequence

## Strange results: Found multiple AR DNA sequences!!!

Not just vanilla heterozygosity with two alleles from the parents, but **Many** AR variants in this tissue sample!!!

Think carefully & write on paper:

- How does this contradict Intro-Bio idea of somatic cells?
- What's going on?
- How did it happen?
- If this is common, how would that affect disease treatment?

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## ② The Nucleic Acid World

The Structure of DNA and RNA

DNA  $\rightarrow$  mRNA  $\rightarrow$  Protein

Gene Structure and Control

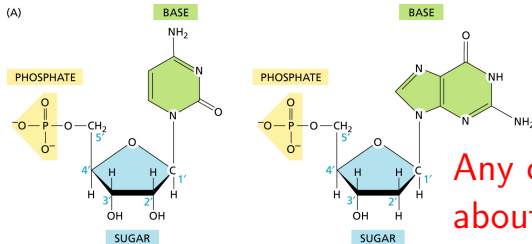
# Building blocks of DNA & RNA

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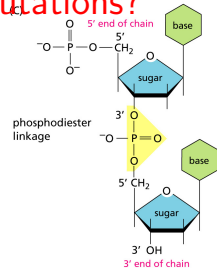
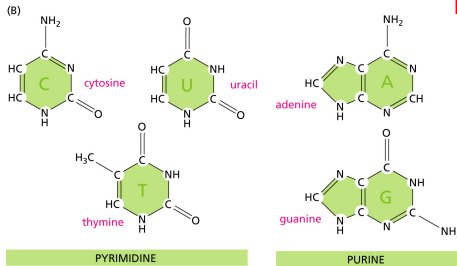
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Any clues  
about  
mutations?



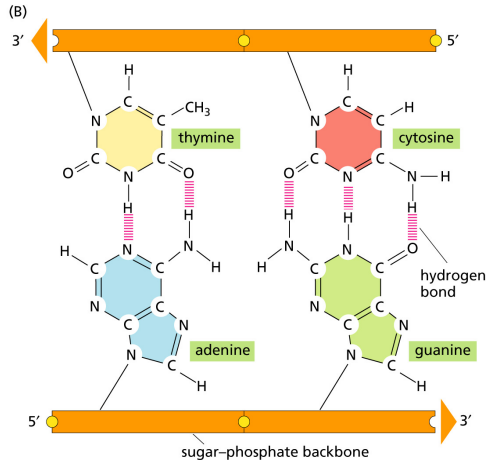
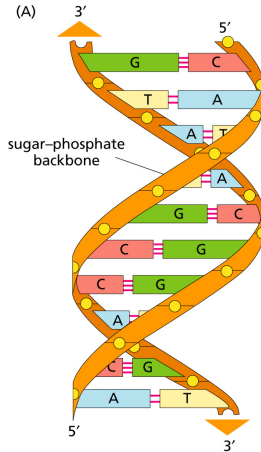
# DNA double helical structure

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# DNA replication needs a template and primer

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## templated polymerization of new strand

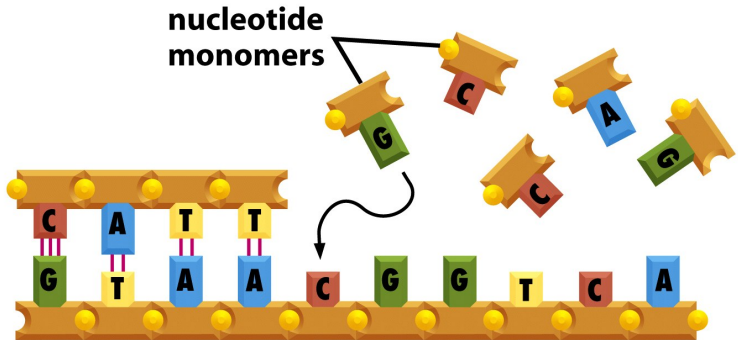


Figure 1-2c Molecular Biology of the Cell 5/e (© Garland Science 2008)

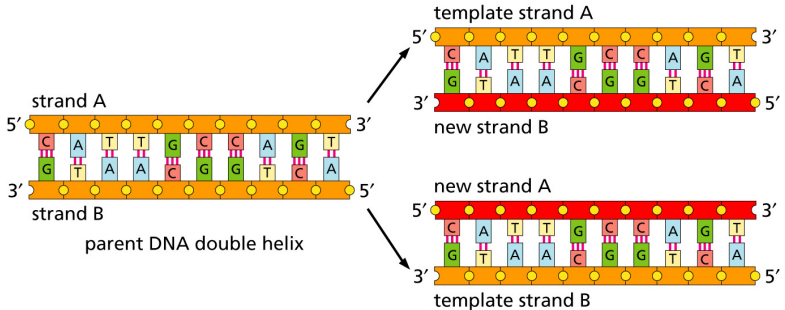
# DNA replication is semi-conservative

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Typical error rate: 1 base in  $10^9$  nucleotides.

So where does genetic diversity come from?

# RNA can fold back on itself

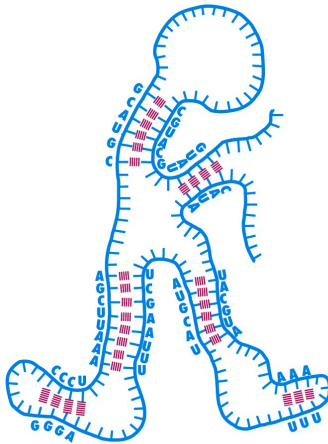
How could we predict RNA folding? Why would we care?

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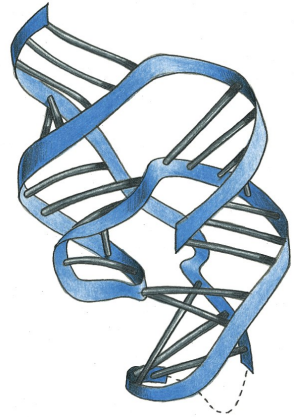
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(A)



(B)

Figure 1-6 Molecular Biology of the Cell 5/e (© Garland Science 2008)



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## ② The Nucleic Acid World

The Structure of DNA and RNA

DNA → mRNA → Protein

Gene Structure and Control

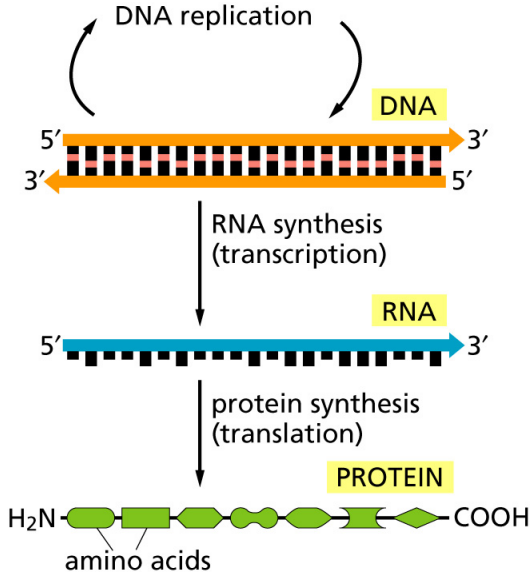
# Central dogma of molecular biology

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# Standard triplet genetic code

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TTT	Phe	TCT	Ser	TAT	Tyr	TGT	Cys
TTC	Phe	TCC	Ser	TAC	Tyr	TGC	Cys
TTA	Leu	TCA	Ser	TAA	stop	TGA	stop
TTG	Leu	TCG	Ser	TAG	stop	TGG	Trp
CTT	Leu	CCT	Pro	CAT	His	CGT	Arg
CTC	Leu	CCC	Pro	CAC	His	CGC	Arg
CTA	Leu	CCA	Pro	CAA	Gln	CGA	Arg
CTG	Leu	CCG	Pro	CAG	Gln	CGG	Arg
ATT	Ile	ACT	Thr	AAT	Asn	AGT	Ser
ATC	Ile	ACC	Thr	AAC	Asn	AGC	Ser
ATA	Ile	ACA	Thr	AAA	Lys	AGA	Arg
ATG	Met	ACG	Thr	AAG	Lys	AGG	Arg
GTT	Val	GCT	Ala	GAT	Asp	GGT	Gly
GTC	Val	GCC	Ala	GAC	Asp	GGC	Gly
GTA	Val	GCA	Ala	GAA	Glu	GGA	Gly
GTG	Val	GCG	Ala	GAG	Glu	GGG	Gly

**Key:**

polar
nonpolar
acid
base

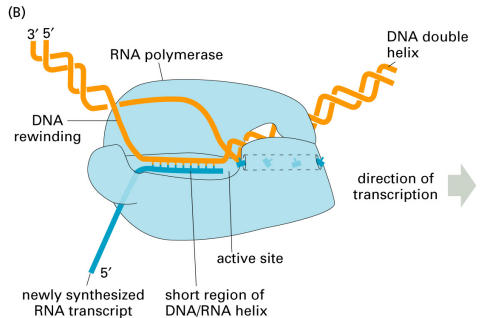
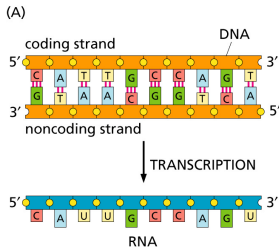
# RNA polymerase transcribes DNA → mRNA

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Which DNA strand  
is the template?

# Transfer RNA (tRNA) adapts codon to amino acid

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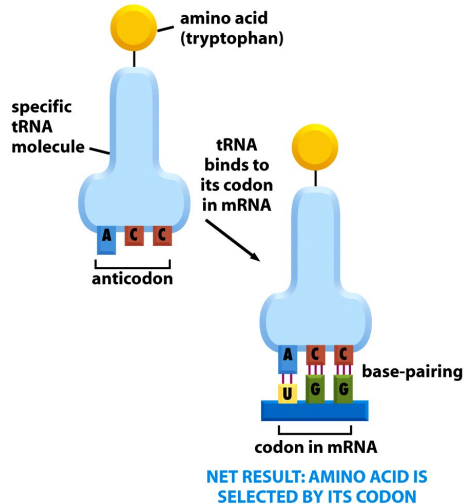
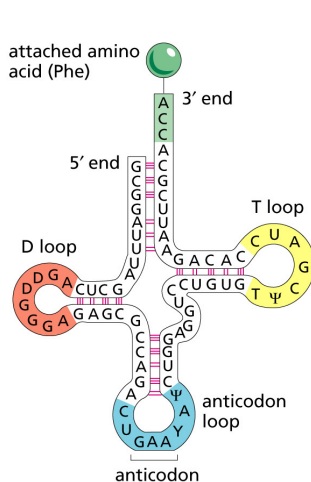


Figure 1-9a Molecular Biology of the Cell 5/e (© Garland Science 2008)

# Ribosome translates mRNA + tRNAs → protein

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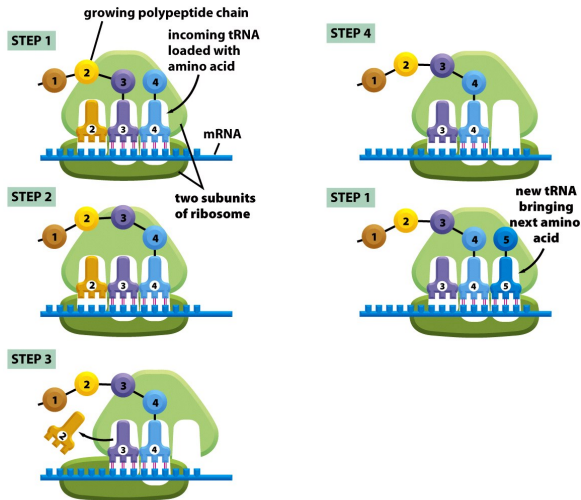


Figure 1-10a Molecular Biology of the Cell 5/e (© Garland Science 2008)

# One sequence with three reading frames

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How does the ribosome get the correct reading frame?

How would a computer get the correct reading frame?

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# Remember this figure? (notice the transcriptional regulation)

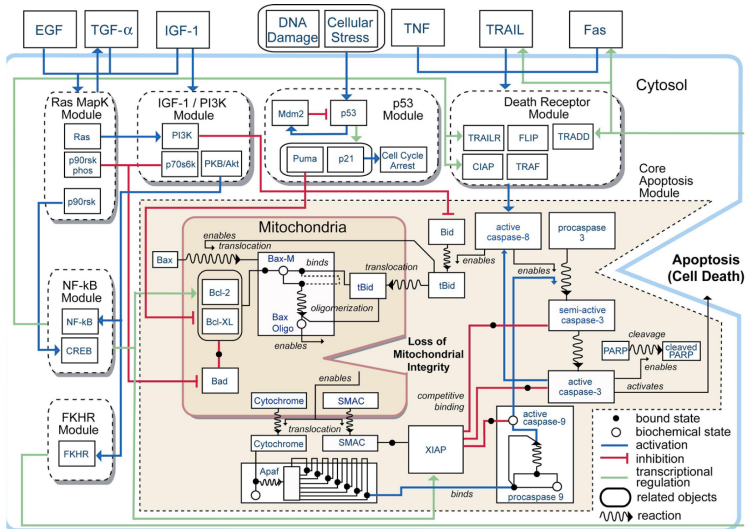
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# Genes are transcriptionally regulated

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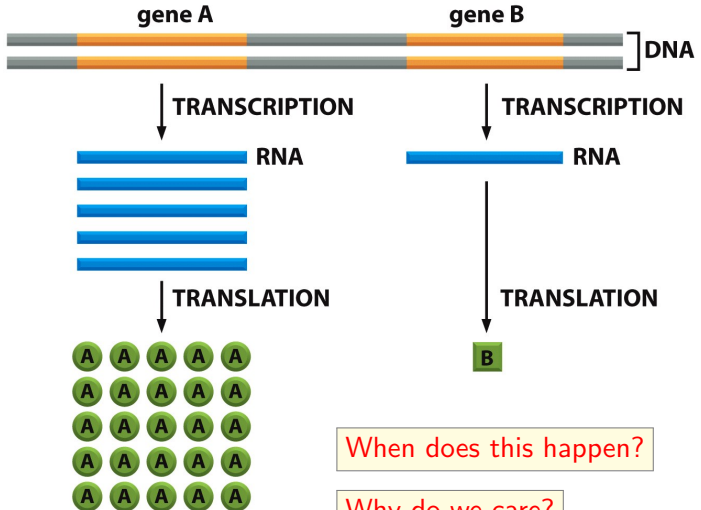


Figure 6-3 Molecular Biology of the Cell 5/e (© Garland Science 2008)

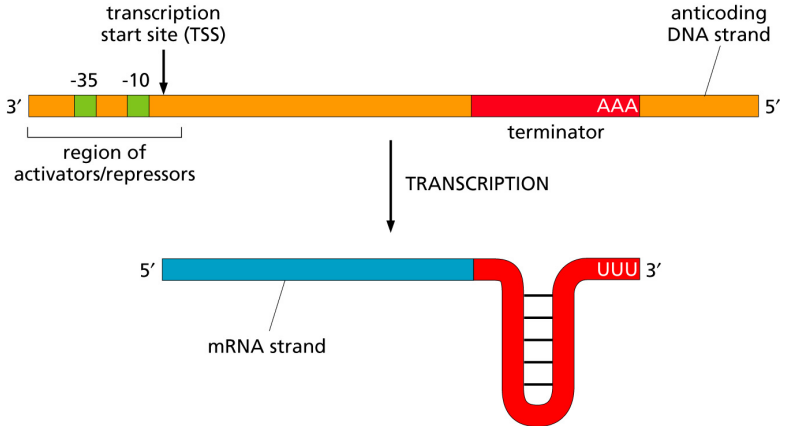
# Prokaryotes regulate transcription

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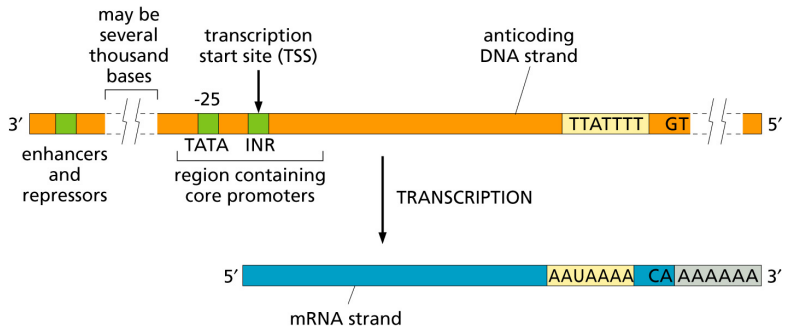
# Eukaryotes have complex transcription control

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# Eukaryotic genes have introns and exons

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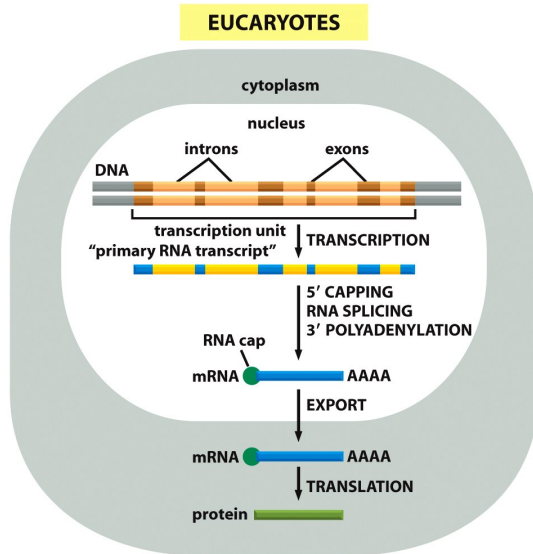


Figure 6-21a Molecular Biology of the Cell 5/e (© Garland Science 2008)

# Introns and exons have splice sites

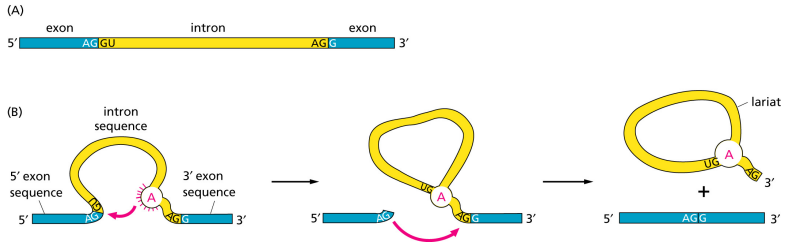
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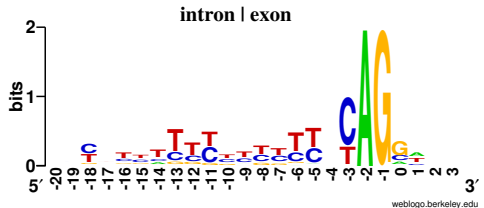
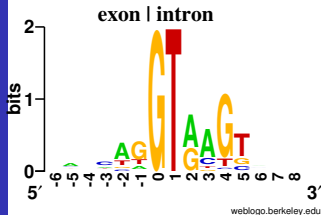
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Can a computer find splice sites?



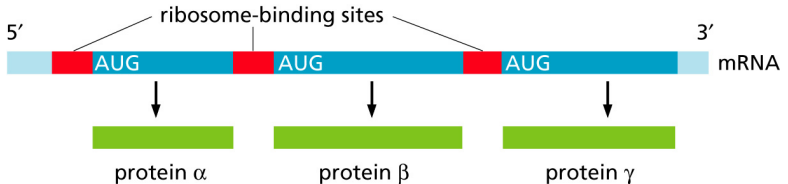
# mRNA has distinct ribosome translation initiation sites

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Above is a prokaryote operon.

How does this differ from eukaryotic translation initiation?

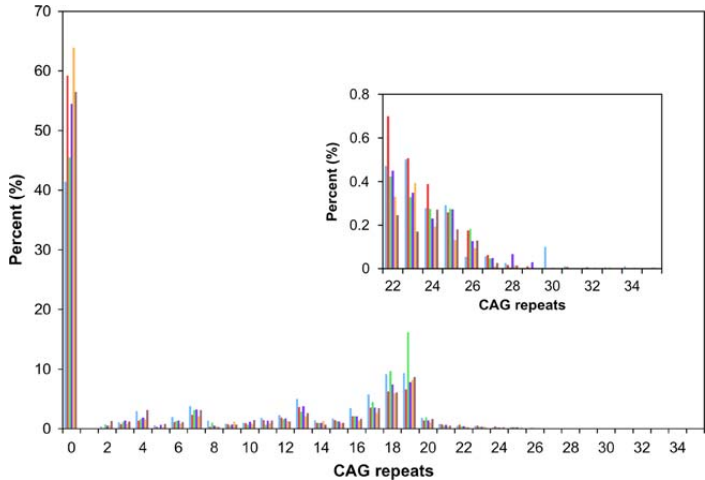
# Sequencing 6 breast cancer samples reveals androgen receptor sequence differences

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# Somatic heterozygosity opens big questions

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- Next-gen sequencing finds **multiple alleles in normal tissue**
- If these alleles were produced during early development, then alleles would be **selected** during growth and adulthood
- Selection would produce *majority and* minority subpopulations
- If selection really is happening within organs, how might somatic heterozygosity benefit the organism?
- If there is genetic heterozygosity, how would medicine adapt?
- For fascinating paper, see Gottlieb2010 on Blackboard.

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Read:

*Bioinformatics and Functional Genomics*, 3rd edition by  
Jonathan Pevsner

Chapter 1

All Sections

Chapter 13

Section “Overview of Protein Structure”

to

Section “Protein Data Bank”

Pages	Notes
3–40	Read
589–601	Read