Lecture 16 Gene Regulation

§1 Gene Regulation

1. The specialization (特化) of cell

1° Cells with the same genetic information can develop into different types of cells through gene regulation, mechanisms that turn on certain genes while other genes remain turned off.

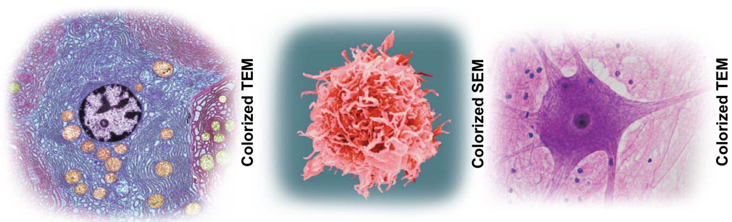
2° Regulation gene activity allows for specialization of cells with the body.

2. Gene expression (基因表达)

1° A gene that is turned on is being transcribed into mRNA, and that message is being translated into specific proteins.

2° The overall process by which genetic information flows from genes to proteins is called gene expression.

3° "On": DNA $\longrightarrow$ RNA $\longrightarrow$ protein



	Pancreas cell（胰腺细胞）	White blood cell	Nerve cell
Gene for a glycolysis enzyme	✓	✓	✓
Antibody gene		✓	
Insulin gene	✓		
Hemoglobin gene			

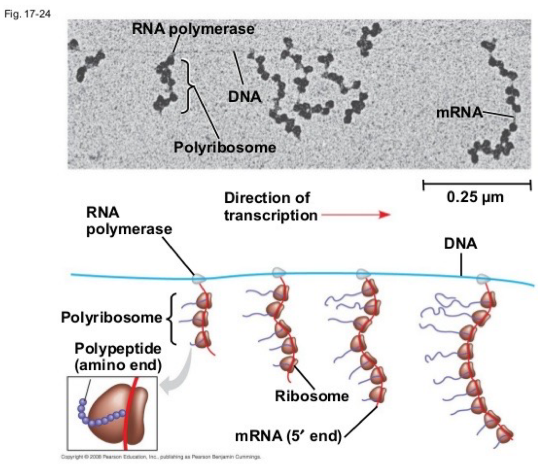
- **Figure 11.1 shows the patterns of gene expression for four genes in three different specialized cells of an adult human.**
  - **Note that the genes for "housekeeping" enzymes, such as those that provide energy via glycolysis（糖酵解）, are "on" in all the cells.**
  - **In contrast, the genes for some proteins, such as insulin and hemoglobin, are expressed only by particular kinds of cells.**
  - **One protein, hemoglobin, is not expressed in any of the cell types shown in the figure.**

3. Differences in the regulation of gene expression of prokaryotic and eukaryotic organisms

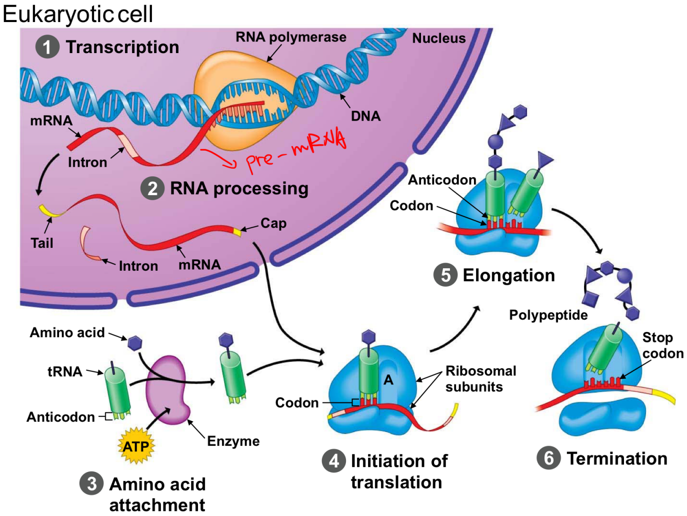
Differences in the Regulation of Gene Expression of Prokaryotic and Eukaryotic Organisms

Prokaryotic organisms	Eukaryotic organisms
Lack nucleus	Contain nucleus
DNA is found in the cytoplasm	DNA is confined to the nuclear compartment
RNA transcription and protein formation occur almost simultaneously	RNA transcription occurs prior to protein formation, and it takes place in the nucleus. Translation of RNA to protein occurs in the cytoplasm.
Gene expression is regulated primarily at the transcriptional level	Gene expression is regulated at many levels (pretranscriptional, transcriptional, post-transcriptional, translational, and post-translational)

Bacterial cell



Eukaryotic cell



§2 Gene Regulation in Bacteria

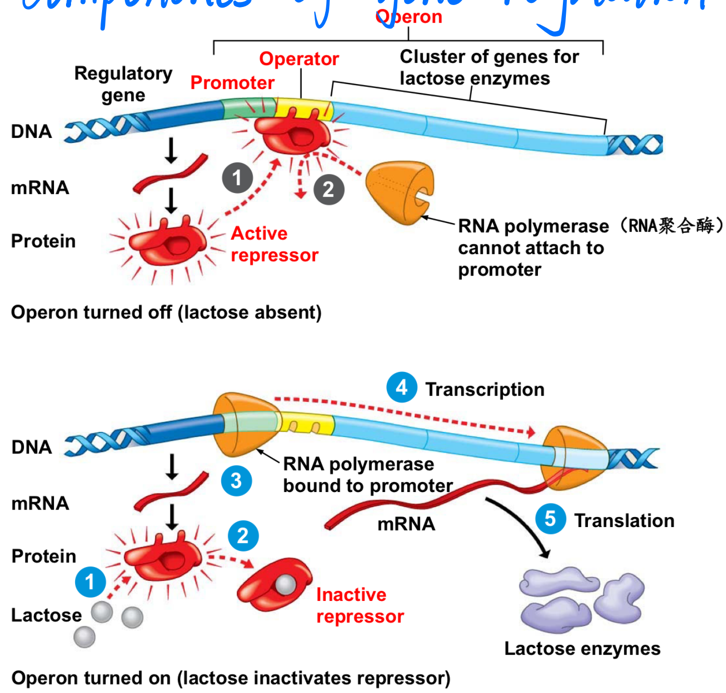
1. An example

- **Imagine an *Escherichia coli* bacterium living in your intestines（肠）.**
  - **If you drink a milk shake, there will be a sudden rush of the sugar lactose.**
  - **In response, *E. coli* will express three genes for enzymes that enable the bacterium to absorb and digest this sugar.**
  - **After the lactose is gone, these genes are turned off.**

1° The key is the way the three lactose-digesting genes are organized: They are adjacent in the DNA and turned on and turned off as a single unit.

2° This regulation is achieved through short stretches of DNA that help turn on and off at once, coordinating their expression.

2. The components of gene regulation in bacteria



1° Operon（操纵子）contains

① a cluster of genes with related functions

② sequences that control them

2° Operator（操纵基因）

Single "on-off" switch, depending on whether a specific protein is bound there.

3° Promotor（启动子）

RNA polymerase can bind and initiates transcription.

4° Repressor（阻遏蛋白）

① can bind to the operator

② physically blocks the attachment of RNA polymease to the promoter

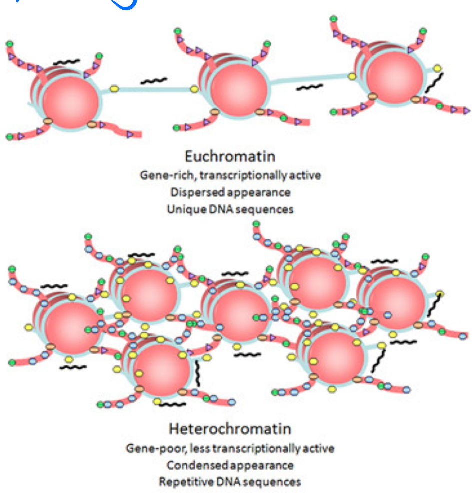
③ Specific substance can bind to the repressor and change its shape. In its new shape, the repressor cannot bind to the operator.

$\begin{cases} \text{no lactose} \rightarrow \text{active} \rightarrow \text{can bind to operator} \rightarrow \text{off} \\ \text{lactose +++} \rightarrow \text{inactive} \rightarrow \text{can't bind to operator} \rightarrow \text{on} \end{cases}$

5° Regulatory gene (调节基因)
codes for repressor (protein)

§3 Gene Regulation in Eukaryotic Cells

1. DNA packing (DNA包装)



1° Cells may use DNA packing for long-term inactivation of genes.

2° Heterochromatin (异染色质): inactive genes located within darkly stained portions of chromatin.
Examples:
① Barr body (X chromosome inactivation) (巴氏小体/X染色体去活化)
② Tortoiseshell cats (玳瑁猫)

3° X chromosome inactivation

① occurs in female animals.

② takes place early in embryonic development

③ is when one of the two X chromosome in each cell is inactived at random.

④ After one X chromosome is inactivated in each embryonic cell, all of that cell's descendants (后代) will have the same X chromosome turned off.

* Red-Green color blindness (红绿色盲)

(1) Affect cone cell (视維细胞)

(2) Recessive disease (隐性遗传疾病)

B → normal b → abnormal

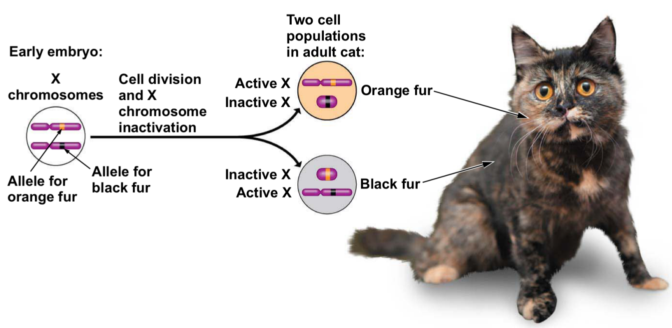
(3)

X^BX^b → X^B → normal cone cells

X^BX^b → X^b → dysfunctional cone cells

⟹ mild symptom

* Tortoiseshell cats

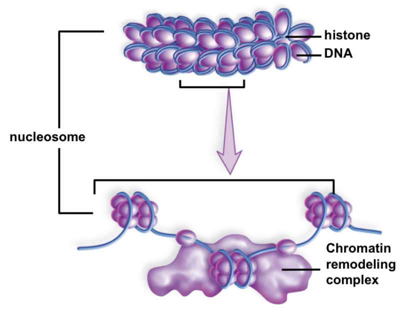


4° Euchromatin (常染色质): loosely packed areas of active genes

① Still needs to be "unpacked" before it can be transcribed.

② Chromatin remodeling complex (染色质重塑复合体)

pushes aside nucleosomes.



2. The initiation of transcription

1° Relevant DNA sequences

① Enhancer (增强子)

(1) Specific proteins can bind to

(2) Can be upstream or downstream to promotor.

(3) Can be away from operator because DNA can bend

(4) Enhance transcription.

② Silencer

(1) Repressor binding region.

(2) Turn off gene expression.

2° Relevant proteins (transcription factor (转录因子))

① Activator (激活蛋白)

(1) Bind to enhancer

(2) Make RNA polymerase easier to bind.

② Repressor (阻遏蛋白)

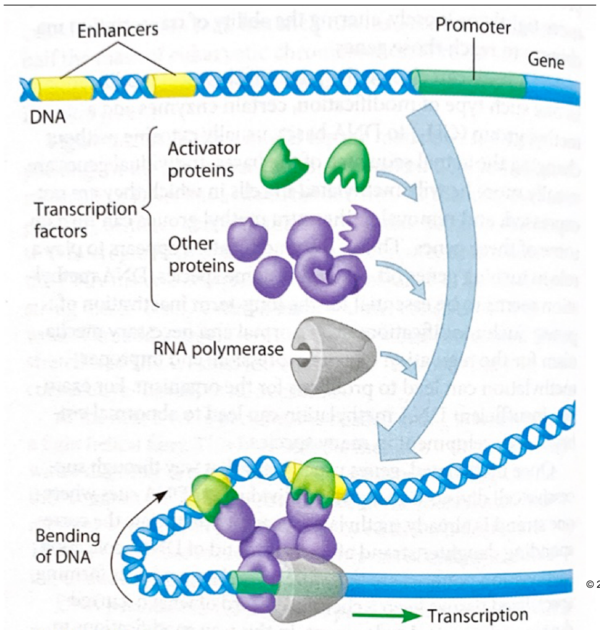
(1) Bind to operator and silencer

(2) Turn off gene.

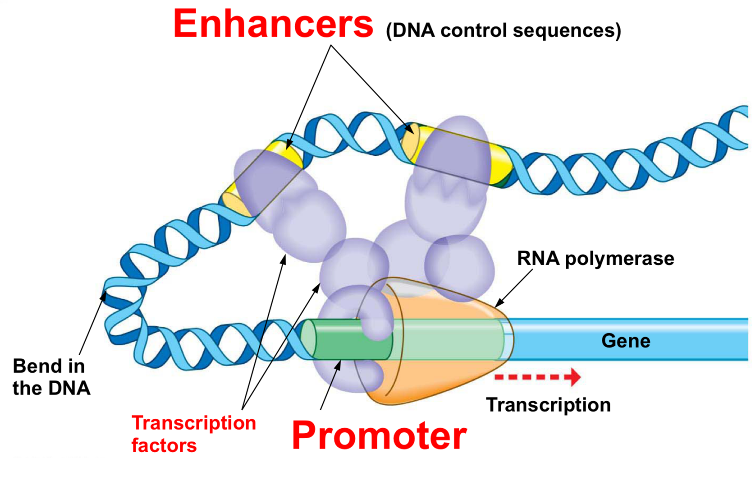
3° Default state:

Most genes in multicellular eukaryotes seems to be off.

With the exception of "housekeeping" gene (管家基因) for routine activities.



▲ Figure 11.3 A model for the turning on of a eukaryotic gene



A very important figure!

3. RNA processing and breakdown

1° Addition of a cap and tail.

It will extend the life span of mRNA.

Exonuclease will chew down nucleic acid from the two ends

2° removal of introns and splicing together of the remaining exons

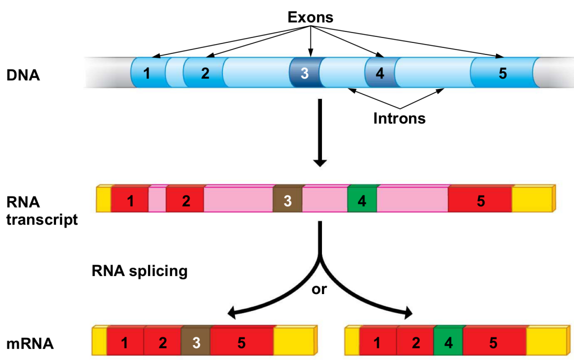
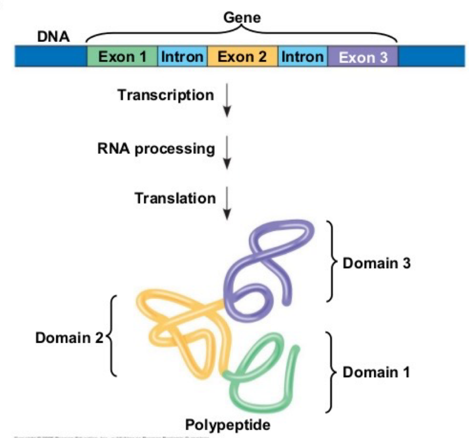


Fig. 17-12



4. MicroRNAs (微核糖核酸)

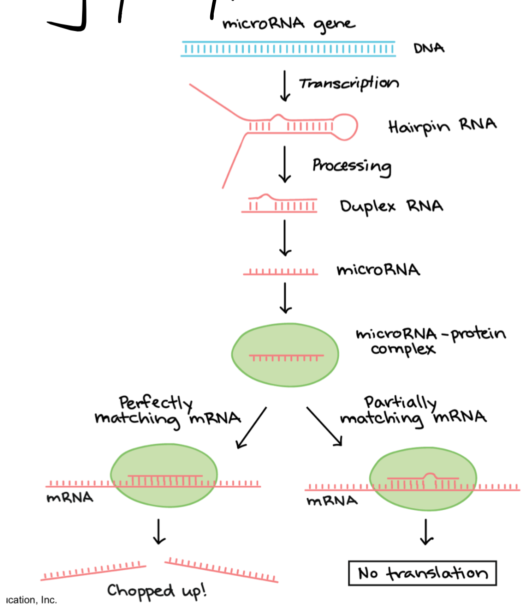
1° about 20 nucleotides long

2° regulate half of human genes

* RNA interference (RNA干扰)

Inject miRNA into a cell ⟶ turn off gene expression.

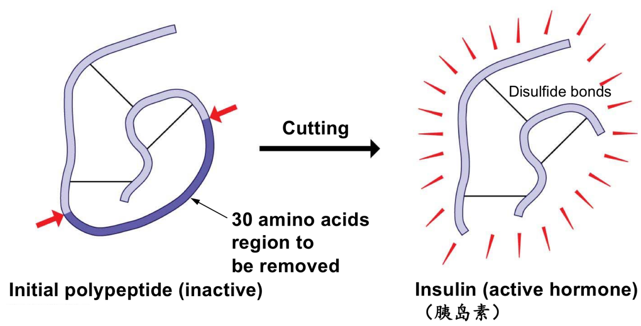
3° Working principle



5. Protein activation and breakdown

1° Protein activation

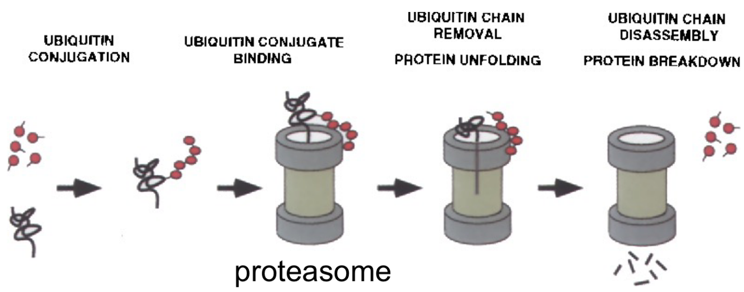
- The final opportunities for regulating gene expression occur after translation.
  - For example, the hormone insulin is synthesized as one long, inactive polypeptide（多肽） that must be chopped into pieces before it comes active.
  - Other proteins require chemical modification before they become active.



2° The selective breakdown of proteins

- Some proteins that trigger metabolic changes in cells are broken down within a few minutes or hours.
- This regulation allows a cell to adjust the kinds and amounts of its proteins in response to changes in its environment.

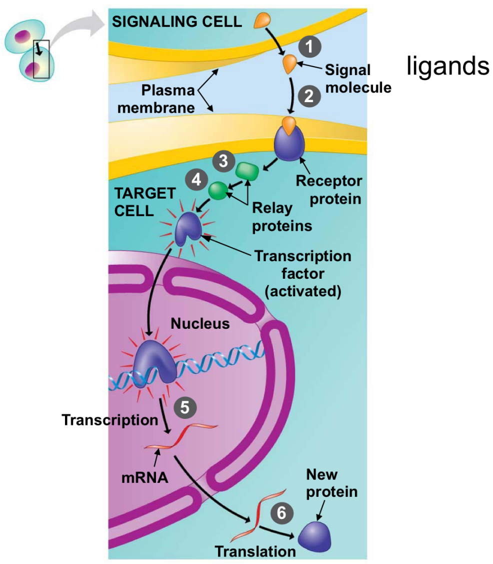
Selective protein degradation



6. Information flow: cell signaling

1° In a multicellular organism, gene regulation can cross cell boundaries using chemicals like hormones (激素)

2° Within a cell, a signal molecule can act by binding to a receptor and initiating a signal tranduction pathway.



§4 Homeotic Genes

1. What is homeotic gene (同源基因)

1° Master control gene

2° Regulate groups of other genes that determine what body parts will develop in which locations (anatomical structures (解剖结构))

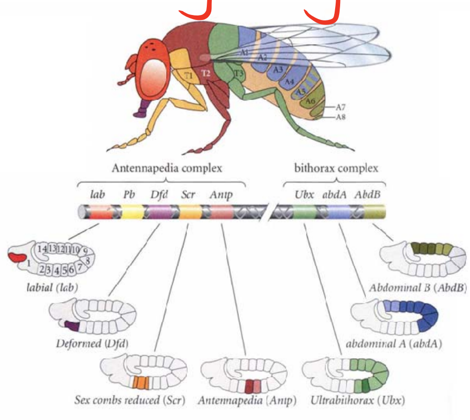
3° Is also called Hox gene.

2. Function

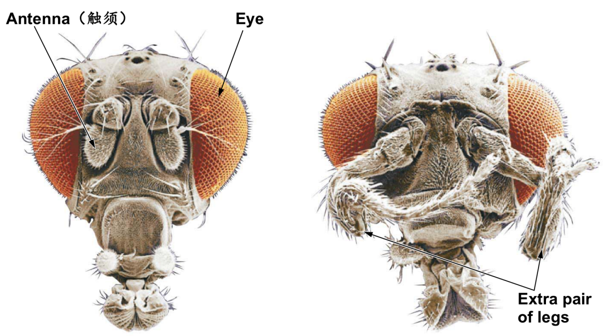
1° Most animal homeotic genes transcription factor proteins

2° Those proteins are called homeodomain (同源域)

3° Similar homeotic genes help direct embryonic development in nearly every eukaryotic organism.



- **Mutations in homeotic genes can produce bizarre effects. For example, fruit flies with mutations（突变） in homeotic genes may have extra sets of legs growing from their head (Figure 11.9).**



Normal head due to presence of normal homeotic gene

Head with extra legs growing due to presence of mutant homeotic gene

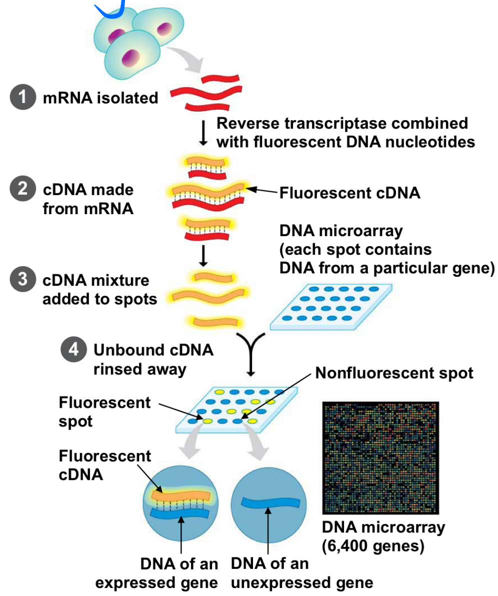
§5 DNA Microarrays: Visualizing Gene Expression

1. DNA microarray (DNA 微阵列)

1° A glass slide with thousands of different kinds of single-stranded DNA fragments attached in a tightly spaced array (grid)

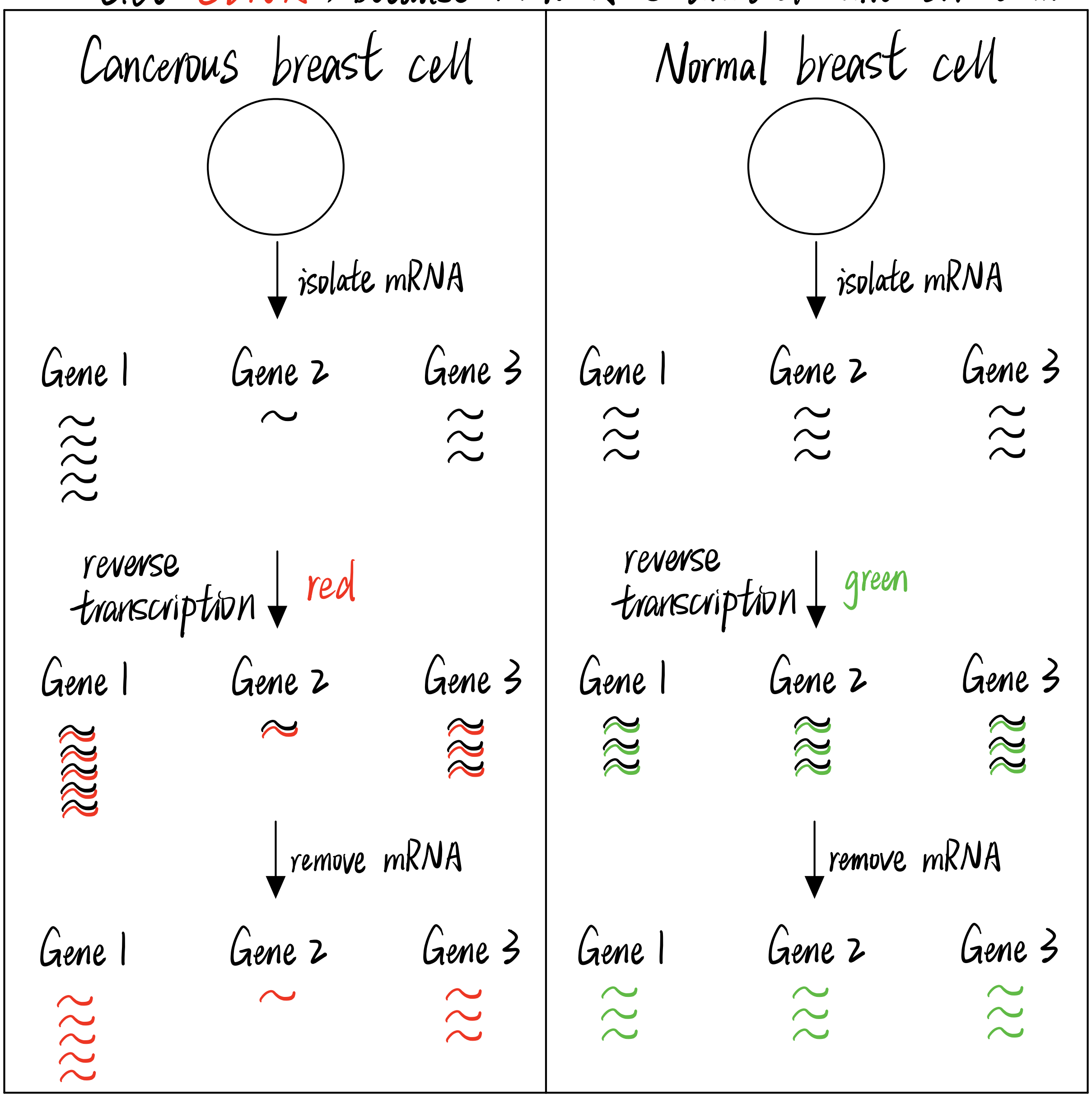
2° Each DNA fragment is obtained from a particular gene

2. How microarrays are used



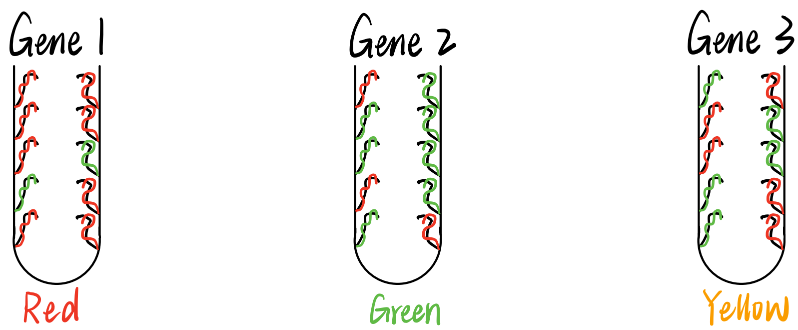
Step 1:

Get cDNA, because m-RNA is unstable and short-lived.



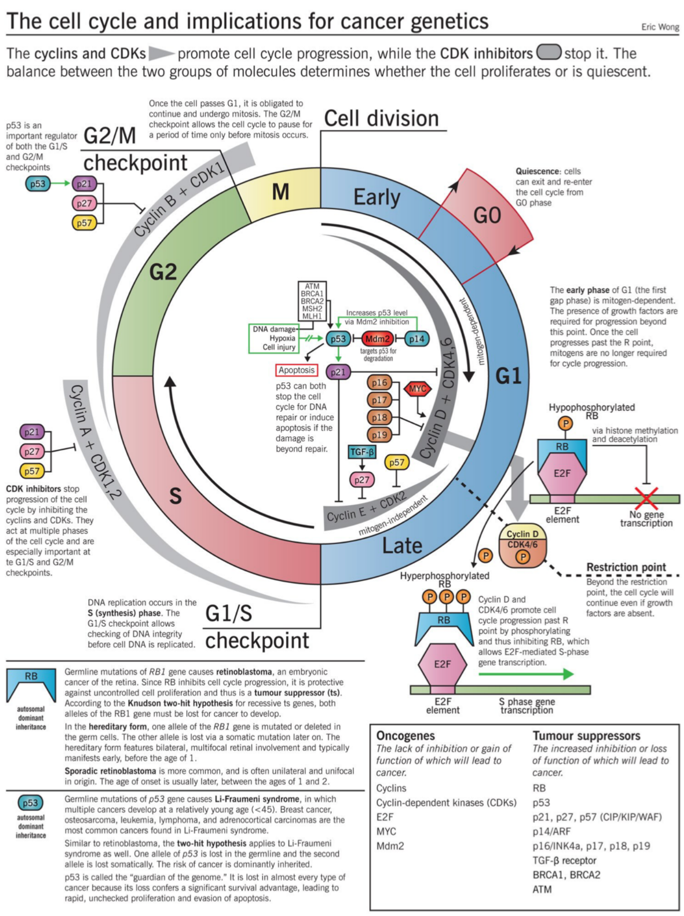
Step 2 :

Mix red and green cDNA. Added them to spots. The color of spots will show the transcription condition of genes in two cells.



§6 Genetic Basis of Cancer

1. The cell cycle and implications for cancer genetics



2. Oncogenes (致癌基因), proto-oncogene (原癌基因) and tumor suppressor genes (抑癌基因)

1° Oncogene

A gene that causes cancer is called an oncogene.

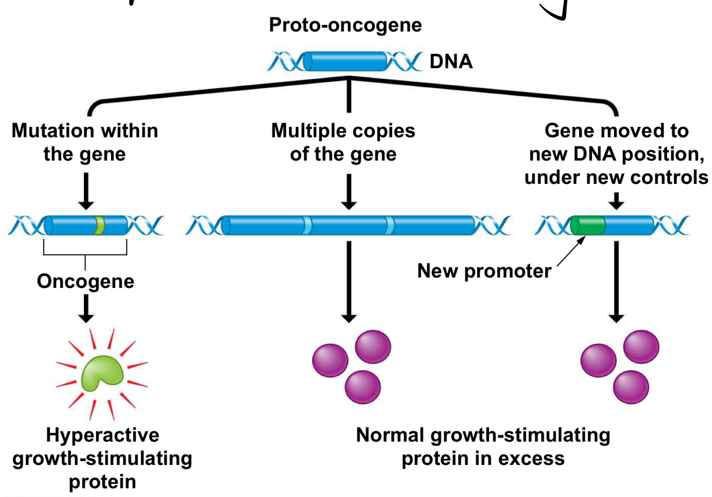
2° Proto-oncogene

① A normal gene

② Has the potential to become an oncogene

③ Encodes for growth factors (生长因子), proteins that stimulate cell cycle.

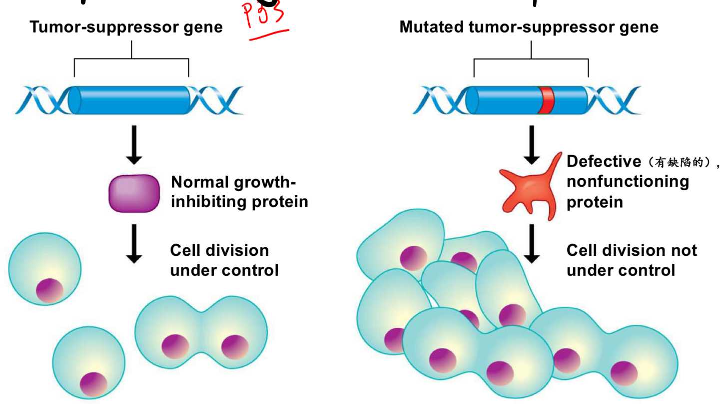
④ Three kinds of changes about proto-oncogene that can produce active oncogenes.



3° Tumor-suppressor gene

① Inhibit cell division to prevent uncontrolled cell growth

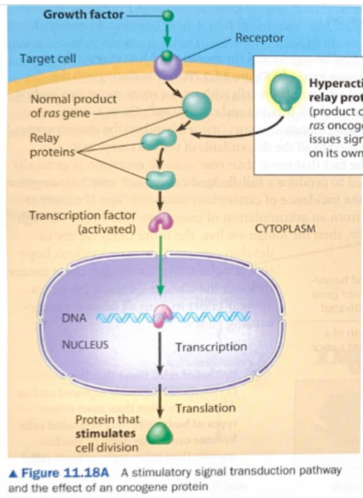
② Stop cell cycle and promote apoptosis (凋亡)



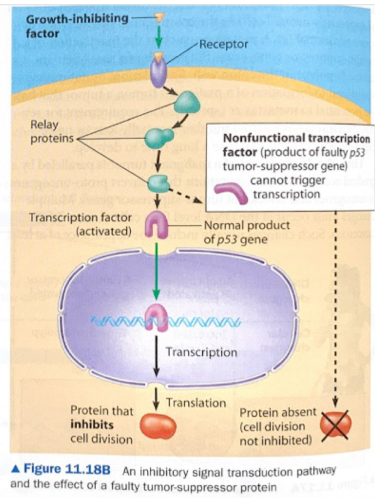
(a) Normal cell growth

(b) Uncontrolled cell growth (cancer)

4° Two kinds of mutations



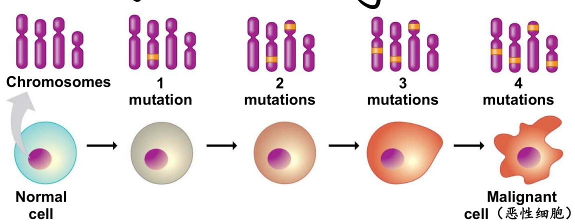
RAS oncogene



Mutated p53 suppressor gene

3. The progression of a cancer

1° Multiple genetic changes are required to produce a cancer cell.

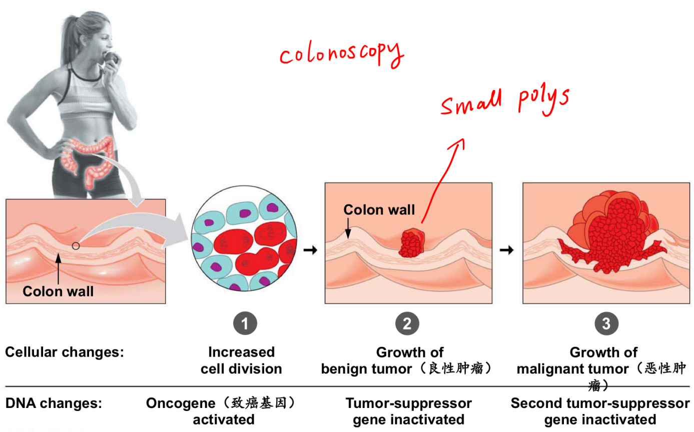


2° The mutations involve

① convert proto-oncogenes to oncogenes

② knock out tumor-suppressor genes

Stepwise development of colon cancer



4. Cancer risk and prevention

1° Most cancers arise from mutations that are caused by

Carcinogene (致癌物), including

① ultraviolet (UV) radiation

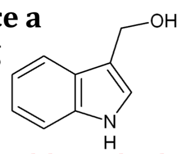
② tobacco products

Table 11.1	Cancer in the United States (Ranked by Number of Cases)		
Cancer	**Known or Likely Carcinogens or Factors**	**Estimated Cases (2014)**	**Estimated Deaths (2014)**
Breast	Estrogen; possibly dietary fat	235,000	40,400
Prostate	Testosterone; possibly dietary fat	233,000	29,500
Lung	Cigarette smoke	224,000	159,000
Colon and rectum	High dietary fat; low dietary fiber	136,800	50,310
Skin	Ultraviolet light	81,200	13,000
Lymphomas	Viruses (for some types)	80,000	20,100
Bladder	Cigarette smoke	74,700	15,600
Uterus	Estrogen	65,000	12,600
Kidney	Cigarette smoke	63,900	13,900
Leukemias	X-rays; benzene; viruses (for some types)	52,400	24,100
Pancreas	Cigarette smoke	46,400	39,600
Liver	Alcohol; hepatitis viruses	33,200	23,000
Brain and nerve	Trauma; X-rays	23,400	14,300
Stomach	Table salt; cigarette smoke	22,200	11,000
Ovary	Large number of ovulation cycles	22,000	14,300
Cervix	Viruses; cigarette smoke	12,400	4,000
All other types		259,940	101,010
Total		1,665,540	585,720

Data from: Cancer Facts and Figures 2014 (American Cancer Society Inc.).

2° Some food choices

- **Some food choices significantly reduce a person's cancer risk, including eating**
  - **20–30 g of plant fiber daily,**
  - **less animal fat, and**
  - **Cabbage（卷心菜） and its relatives, such as broccoli（西兰花） and cauliflower（菜花）.**



Indole-3-carbinol

- **Determining how diet influences cancer has become an important focus of nutrition research.**