第六章　核 外 遗 传
Extranuclear Inheritance

核外遗传的发现:

Leaf Variegation in Four O'clock Plant

Carl Correns, 1909

Mirabilis jalapa （紫茉莉）

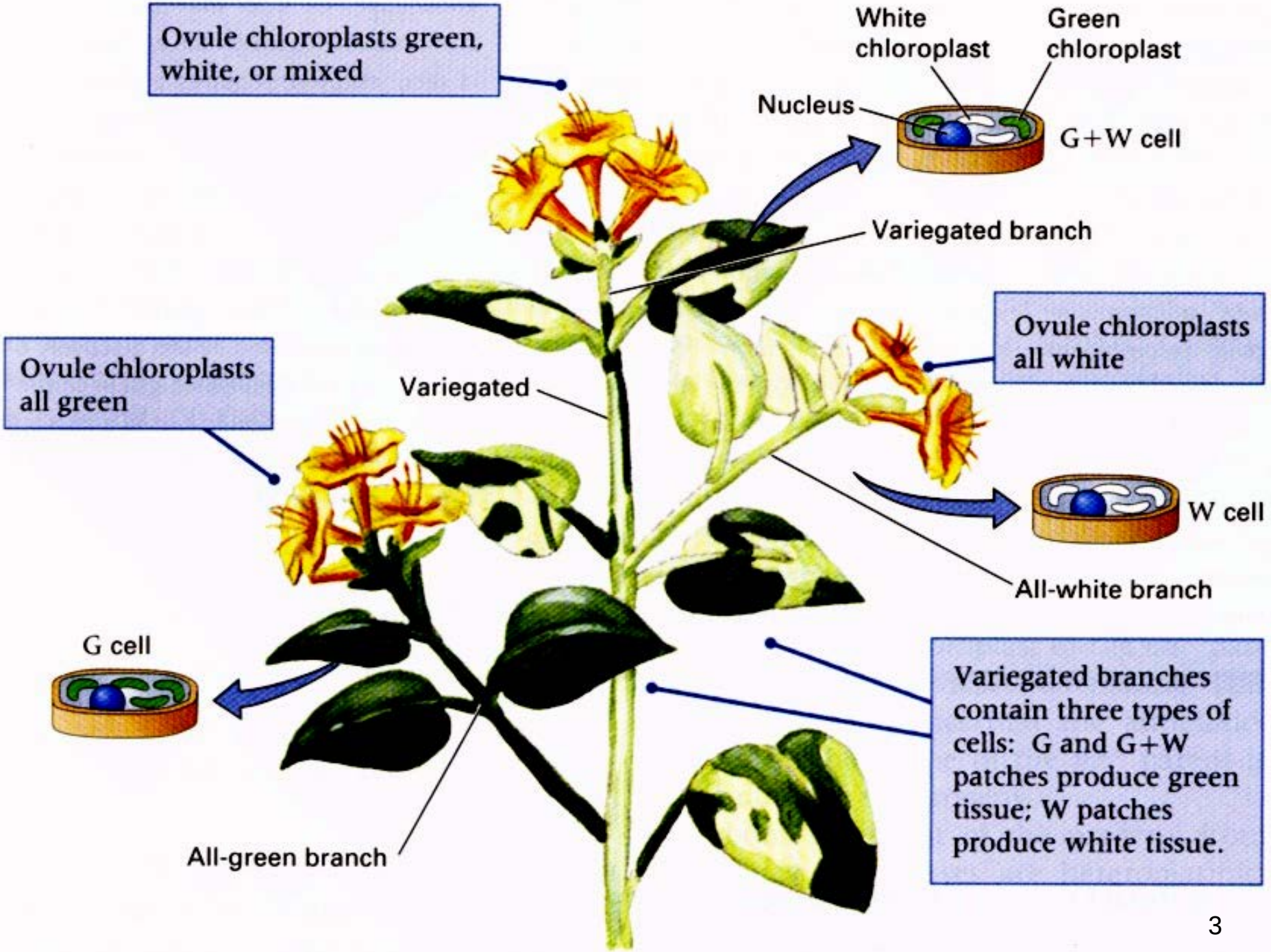
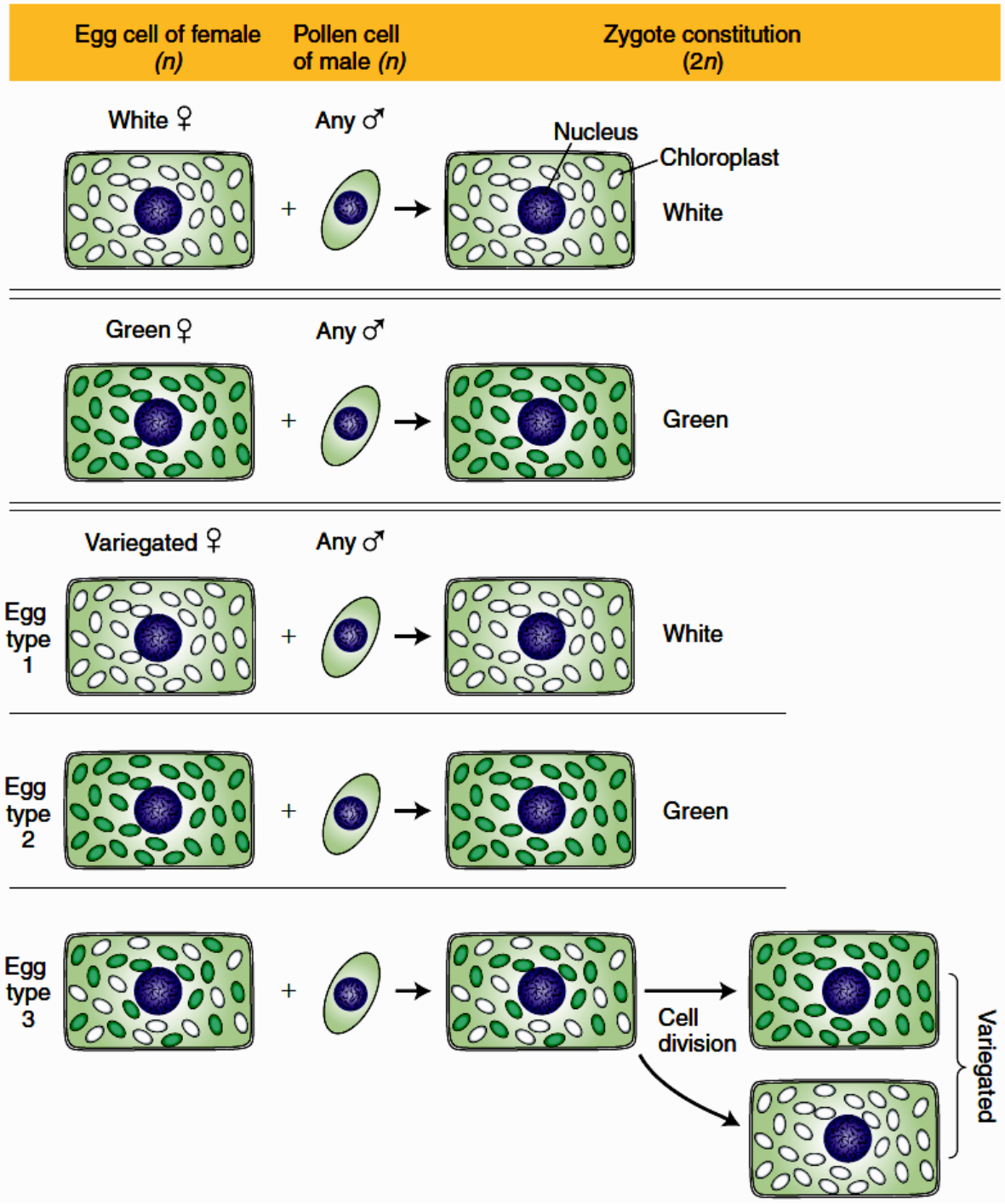

Ovule chloroplasts green, white, or mixed
White chloroplast
Green chloroplast
Nucleus
G+W cell
Variegated branch
Ovule chloroplasts all white
Ovule chloroplasts all green
Variegated
W cell
All-white branch
G cell
Variegated branches contain three types of cells: G and G+W patches produce green tissue; W patches produce white tissue.
All-green branch

Table 16.2 Crosses and progeny phenotypes in variegated four-o'clock plants

Phenotype of branch bearing egg parent	Phenotype of branch bearing pollen parent	Phenotype of progeny
white	white	white
white	green	white
white	variegated	white
green	white	green
green	green	green
green	variegated	green
variegated	white	variegated, green, or white
variegated	green	variegated, green, or white
variegated	variegated	variegated, green, or white


Egg cell of female (n)
Pollen cell of male (n)
Zygote constitution (2n)
White ♀
Any ♂
Nucleus
Chloroplast
White
Green ♀
Any ♂
Green
Variegated ♀
Any ♂
Egg type 1
White
Egg type 2
Green
Egg type 3
Cell division
Variegated

Drug resistance in *Chlamydomonas*
衣藻抗性的遗传

$str^R\ mt^+ \times str^S\ mt^-$

$1/2\ mt^+$	$1/2\ mt^-$
all str^R	

$str^S\ mt^+ \times str^R\ mt^-$

$1/2\ mt^+$	$1/2\ mt^-$
all str^S	

^{15}N mt^+ × ^{14}N mt^-

↓

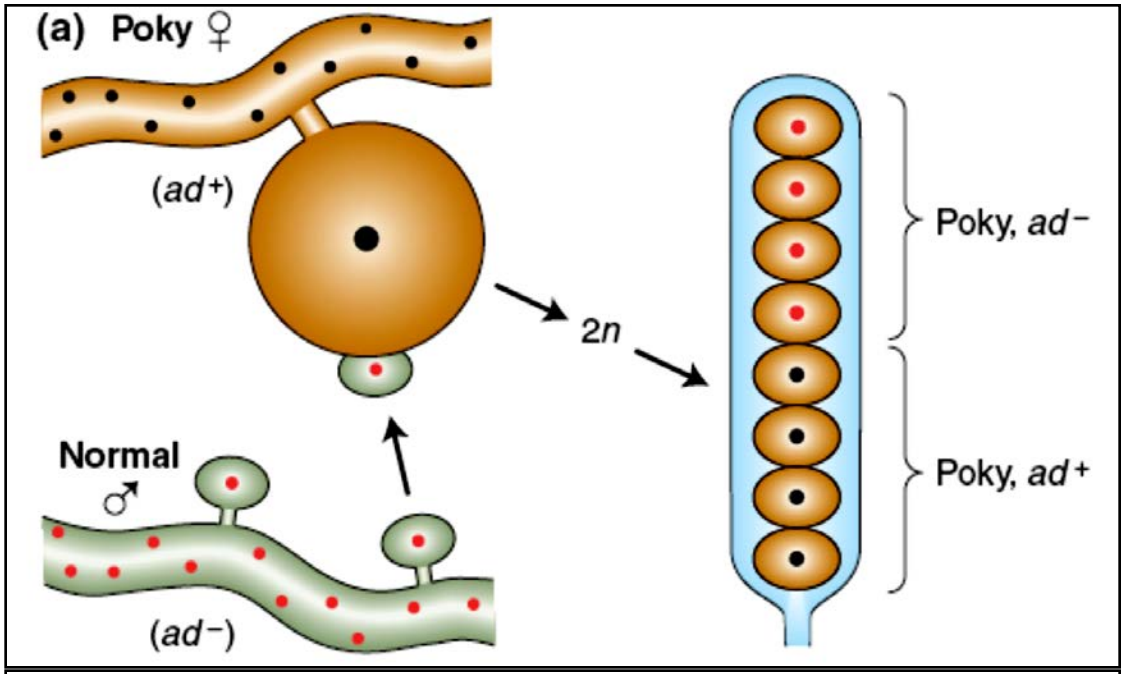
Zygote（chloroplast DNA is ^{15}N）

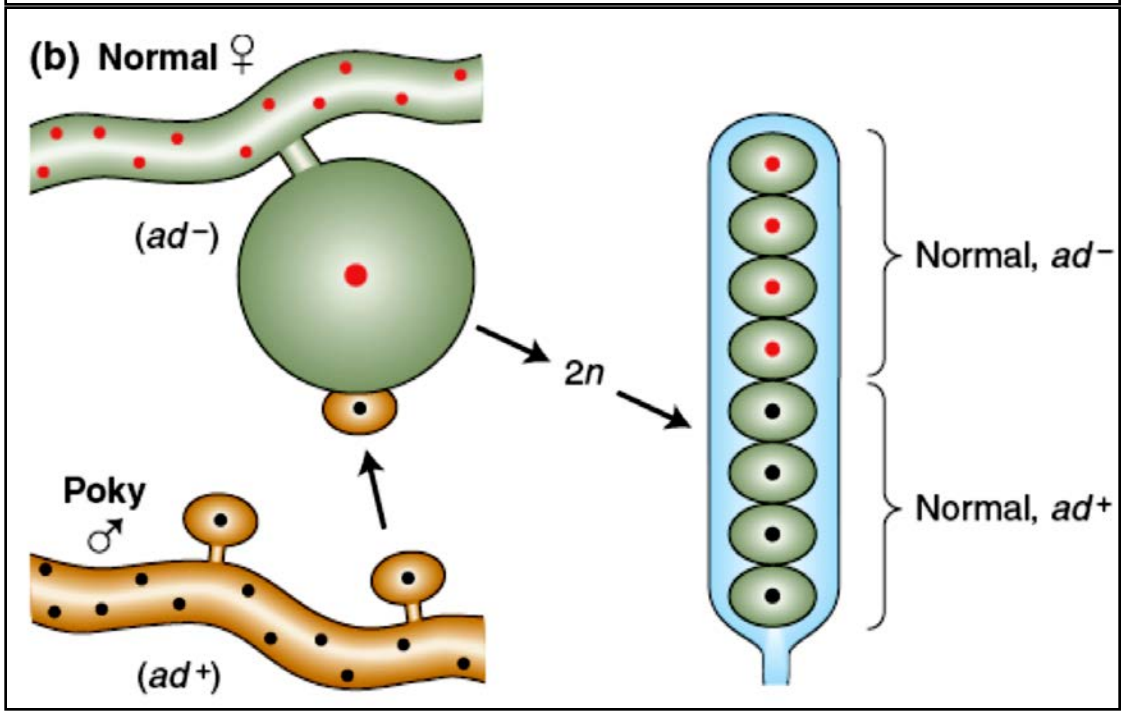
^{14}N mt^+ × ^{15}N mt^-

↓

Zygote（chloroplast DNA is ^{14}N）

The chloroplast DNA of the mt^- parent is lost after mating





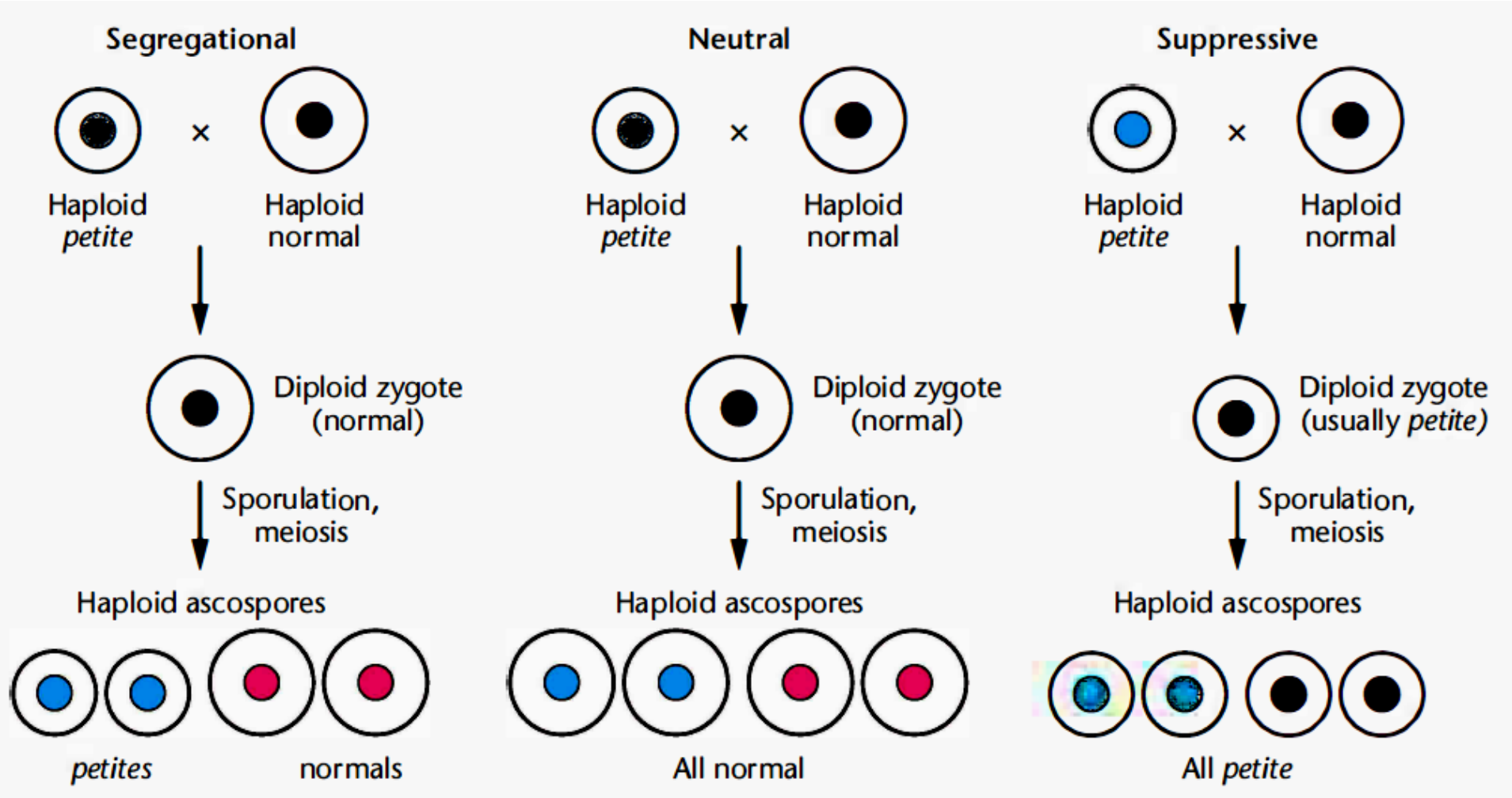
Poky mutation in *Neurospora*

1952

Petite in *Saccharomyces*（酿酒酵母）

Normal colonies

Petite colonies



The outcome of crosses involving the three types of petite mutations affecting mitochondrial function in the yeast *Saccharomyces cerevisiae*

- Segregational petites **分离型小菌落**

  result from nuclear gene mutation

- Neutral petites **中性型小菌落**

  lose nearly complete mtDNA

- Suppressive petites **抑制型小菌落**

Hypotheses for suppressive petite

◇Mutant mtDNA replicates more rapidly, thus dominate by numbers

◇Recombination occurs between the mutant and the wildtype mtDNA, and disrupts the normal mtDNA

Extranuclear Inheritance

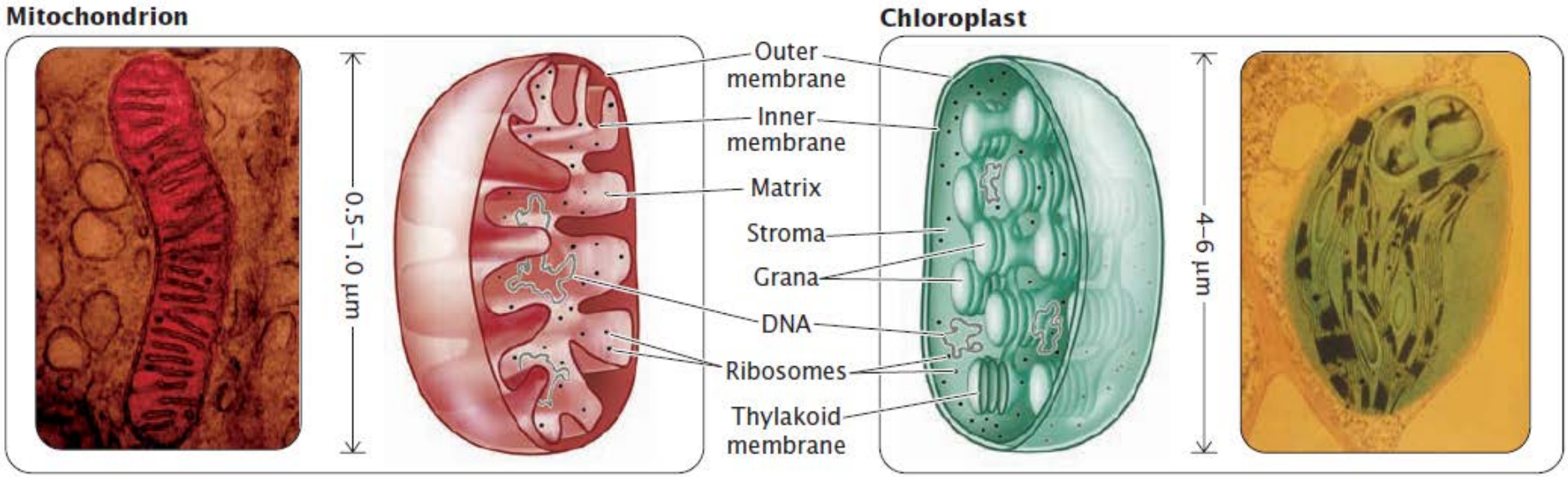
- Organelle heredity（细胞器遗传）
- Infectious heredity（感染型遗传）
  - Kappa in *Paramecium*
  - Virus or protozoan *in Drosophila*
- Maternal effect（母性影响）

Non-Mendelian Inheritance

Non-Mendelian inheritance

- The segregation ratio of parental alleles is 4∶0 rather than 2∶2
- Uniparental inheritance（单亲遗传）, mainly maternal inheritance （母系遗传）
- Mitotic segregation

第一节　细胞器遗传
Organelle Heredity



一、叶绿体**DNA**
(Chloroplast DNA, **cpDNA**)

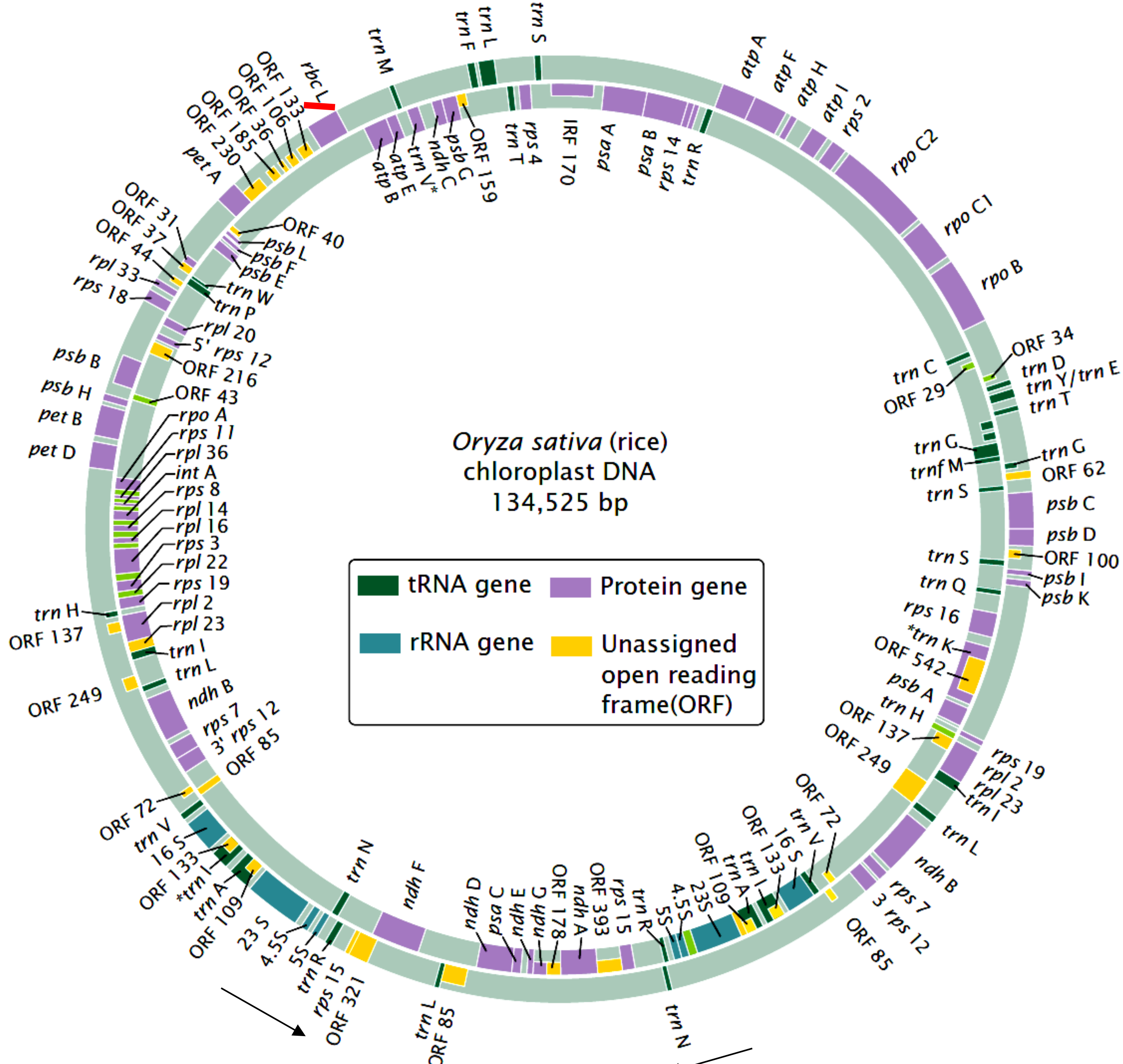
In 1963, chloroplasts were shown to have their own DNA

TABLE **Chloroplast DNA Sizes**

Organism	Size (kb)
Chlamydomonas reinhardtii	196
Marchantia (liverwort)	121
Nicotiana tabacum (tobacco)	156
Oryza sativa (rice)	135

Characteristics of cpDNA

- Most cpDNAs range from 120 to 160 kb
- Most chloroplast genomes consist of single, circular ds-DNA molecule not complexed with histone proteins.
- There are multiple chloroplasts per cell, and multiple copies of cpDNA per chloroplast (usually 15–20 copies)


Oryza sativa (rice)
chloroplast DNA
134,525 bp
tRNA gene
Protein gene
rRNA gene
Unassigned open reading frame(ORF)
rbc L
trn M
trn F
trn L
trn S
atp A
atp F
atp H
atp I
rps 2
rpo C2
rpo C1
rpo B
ORF 34
trn D
trn Y/trn E
trn T
trn C
ORF 29
trn G
trnf M
trn S
trn G
ORF 62
psb C
psb D
ORF 100
trn S
trn Q
psb I
psb K
rps 16
*trn K
ORF 542
psb A
trn H
ORF 137
ORF 249
rps 19
rpl 2
rpl 23
trn I
trn L
ndh B
rps 7
3' rps 12
ORF 85
ORF 72
trn V
16 S
ORF 133
trn I
trn A
ORF 109
23S
4.5S
5S
trn R
trn N
ndh F
ndh D
psa C
ndh E
ndh G
ORF 178
ndh A
ORF 393
rps 15
ORF 321
trn L
ORF 85
ORF 72
trn V
16 S
ORF 133
*trn I
trn A
ORF 109
23 S
4.5S
5S
trn R
rps 15
ORF 321
trn N
ORF 249
ndh B
rps 7
3' rps 12
ORF 85
trn H
ORF 137
trn I
trn L
rpo A
rps 11
rpl 36
int A
rps 8
rpl 14
rpl 16
rps 3
rpl 22
rps 19
rpl 2
rpl 23
psb B
psb H
pet B
pet D
ORF 43
ORF 216
5' rps 12
rpl 20
rps 18
rpl 33
ORF 44
ORF 37
ORF 31
trn W
trn P
psb E
psb F
psb L
ORF 40
pet A
ORF 230
ORF 185
ORF 36
ORF 106
ORF 133
atp B
atp E
trn V*
ndh C
psb G
ORF 159
trn T
rps 4
IRF 170
psa A
psa B
rps 14
trn R

Gene Structure and Organization

- A key protein encoded by cpDNA is large subunit of ribulose-1,5-bisphosphate carboxylase-oxygenase (**RuBisco**)
  - RuBisco makes up about 50% of the protein found in green plants, is the most abundant protein on earth
- The cpDNA has genes on both of its strands.
- Most cpDNAs contain a large **inverted repeat**.
- **Introns** exist in many chloroplast genes
- Many of the sequences in cpDNA are quite similar to those found in equivalent eubacterial genes

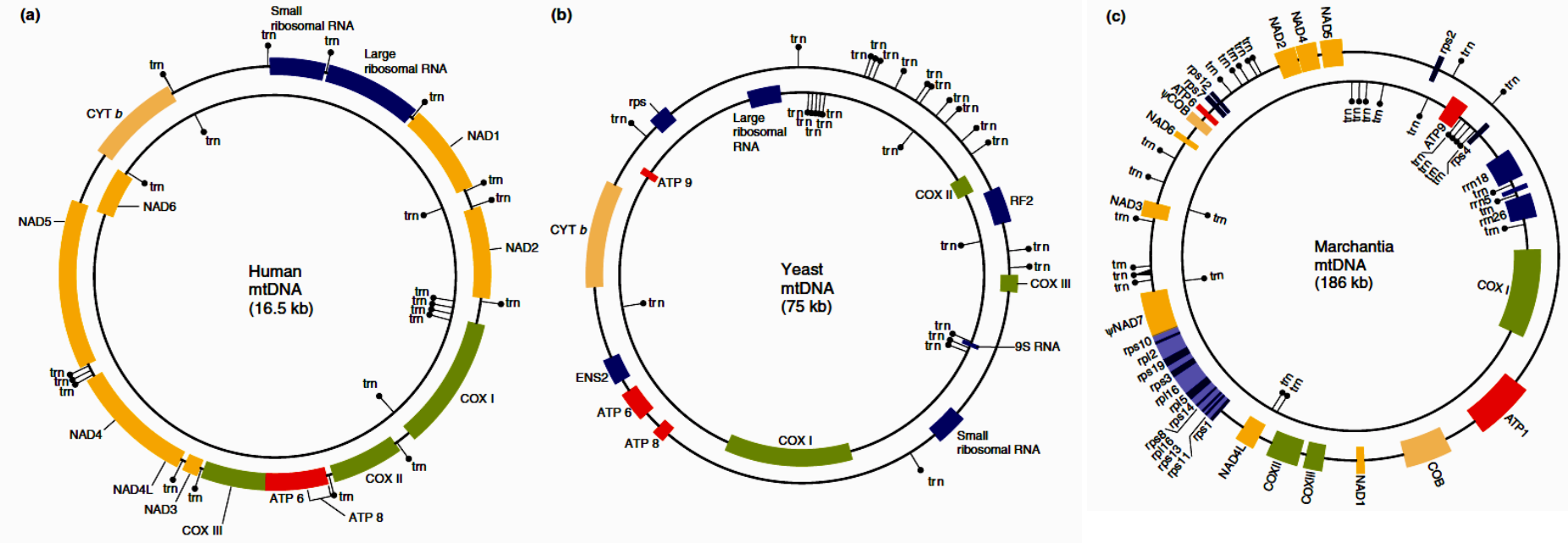
二、线粒体**DNA**
(Mitochondrial DNA, **mtDNA**)

Organism	Size of mtDNA (bp)
Pichia canadensis (fungus)	27,694
Podospora anserina (fungus)	100,314
Saccharomyces cerevisiae (fungus)	85,779*
Drosophila melanogaster (fruit fly)	19,517
Lumbricus terrestris (earthworm)	14,998
Xenopus laevis (frog)	17,553
Mus musculus (house mouse)	16,295
Homo sapiens (human)	16,569
Chlamydomonas reinhardtii (green alga)	15,758
Plasmodium falciparum (protist)	5,966
Paramecium aurelia (protist)	40,469
Arabidopsis thaliana (plant)	166,924
Cucumis melo (plant)	2,400,000

*Size varies among strains.

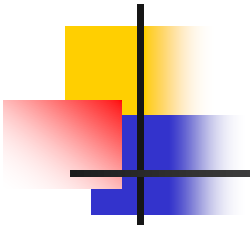
- The mitochondrial genomes of most species are circular DNA with no associated histone proteins.
- The size of mtDNA differs greatly among organisms, most of this size variation is in noncoding sequences such as introns and intergenic regions.
- Each mitochondrion contains multiple copies of the mitochondrial genome, and a cell may contain many mitochondria.
  - Rat liver cell: 5 to 10 mtDNA molecules in each of about 1000 mitochondria
- The GC content of mtDNA is often sufficiently different from that of nuclear DNA

Gene Structure and Organization of mtDNA



green **for cytochrome oxidase proteins;** ***red for*** **ATPase subunit proteins;** ***yellow*** **NADH complex proteins;** ***tan*** **for genes coding for cytochrome complex proteins;** ***purple*** **for ribosomal proteins or ribosomal RNAs;** ***black ball and stick*** **for tRNA gene**

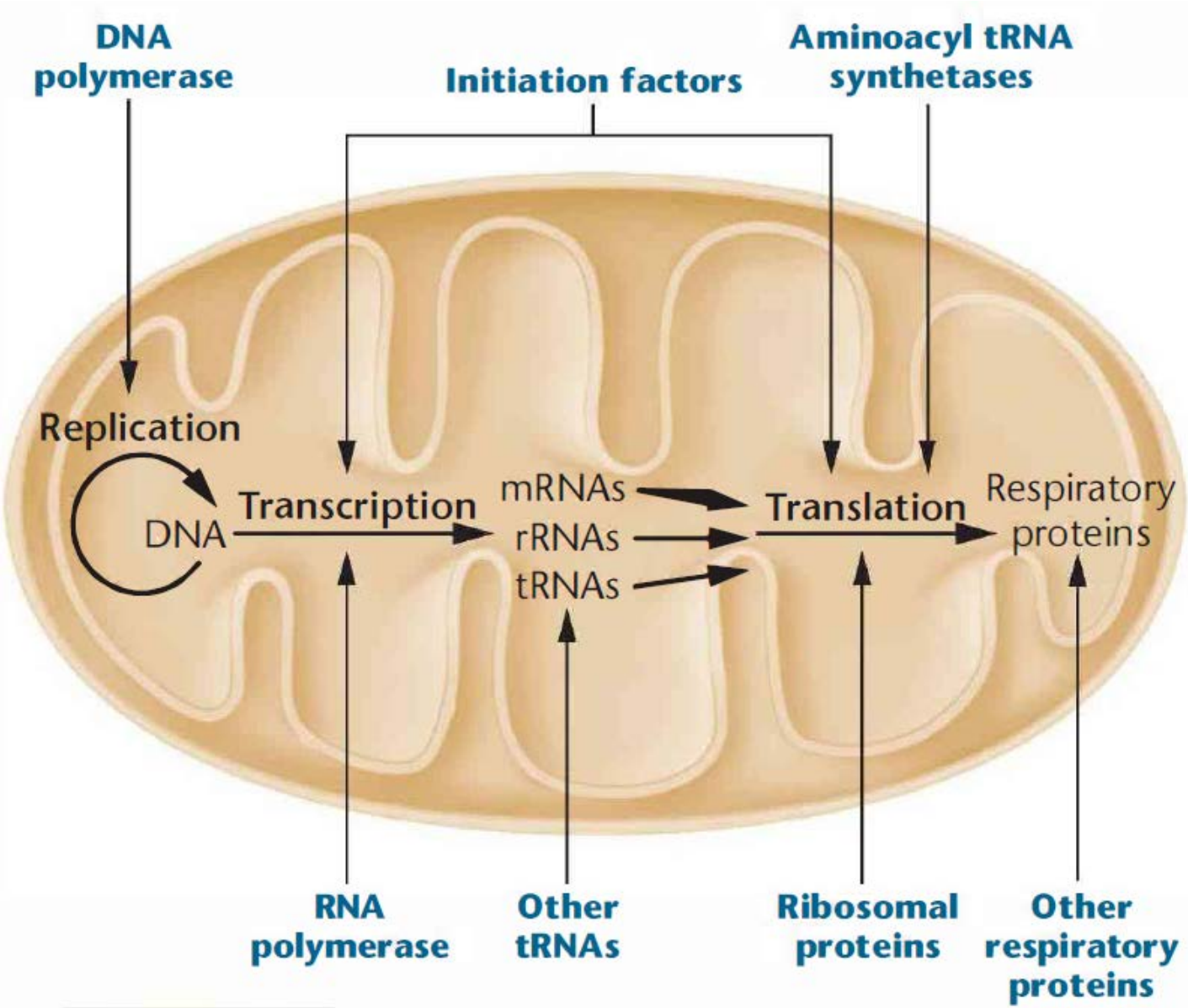
- Human mtDNA packed tightly, most genes are encoded by the H strand
- The larger yeast mtDNA contains spacers and introns
- The liverwort mtDNA contain many more genes



- The mt-genes encode five basic functions
  - respiration and oxidative phosphorylation, translation, transcription, RNA process, and import of proteins
- Some of the mt-genes in yeast and plant contain introns, many of which are **self-splicing**.
- Nonuniversal Codons in mtDNA

TABLE 14.3 Variations in the Genetic Code of Mitochondria

Characteristic	Universal Code	mtDNA Code
Number of tRNAs	32	22
UGG	Trp	Trp
UGA	Stop	Trp
AGG	Arg	Stop
AGA	Arg	Stop
AUG	Met	Met
AUA	Ile	Met

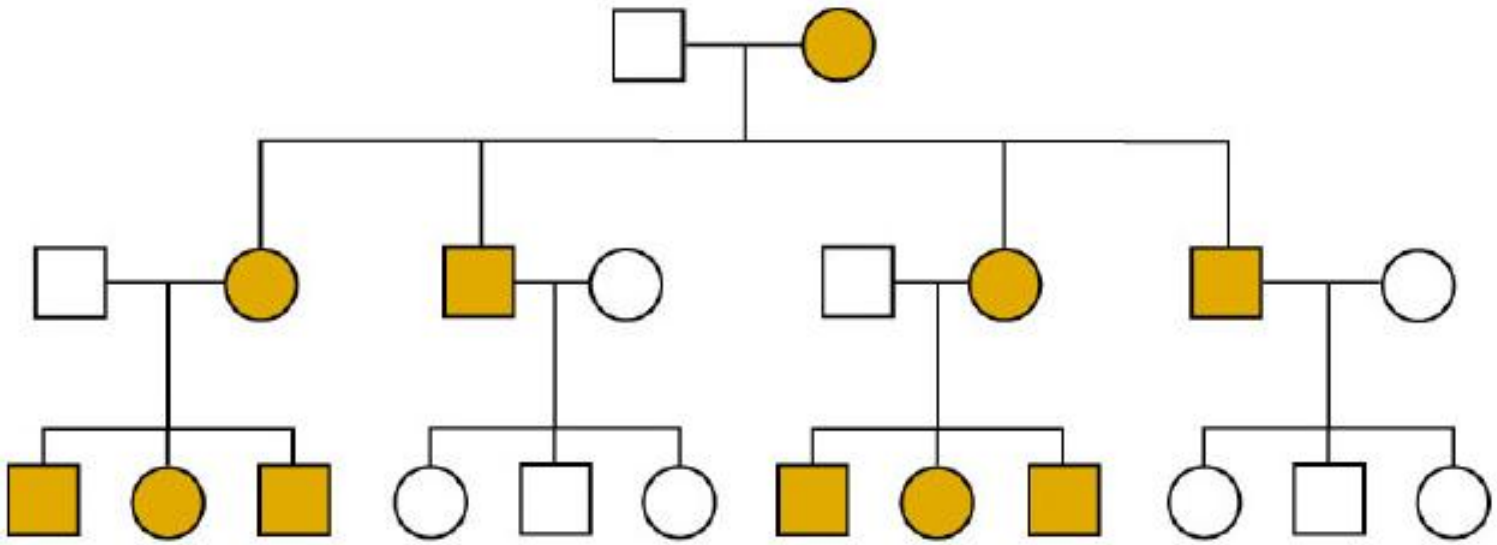

DNA polymerase
Initiation factors
Aminoacyl tRNA synthetases
Replication
DNA
Transcription
mRNAs
rRNAs
tRNAs
Translation
Respiratory proteins
RNA polymerase
Other tRNAs
Ribosomal proteins
Other respiratory proteins

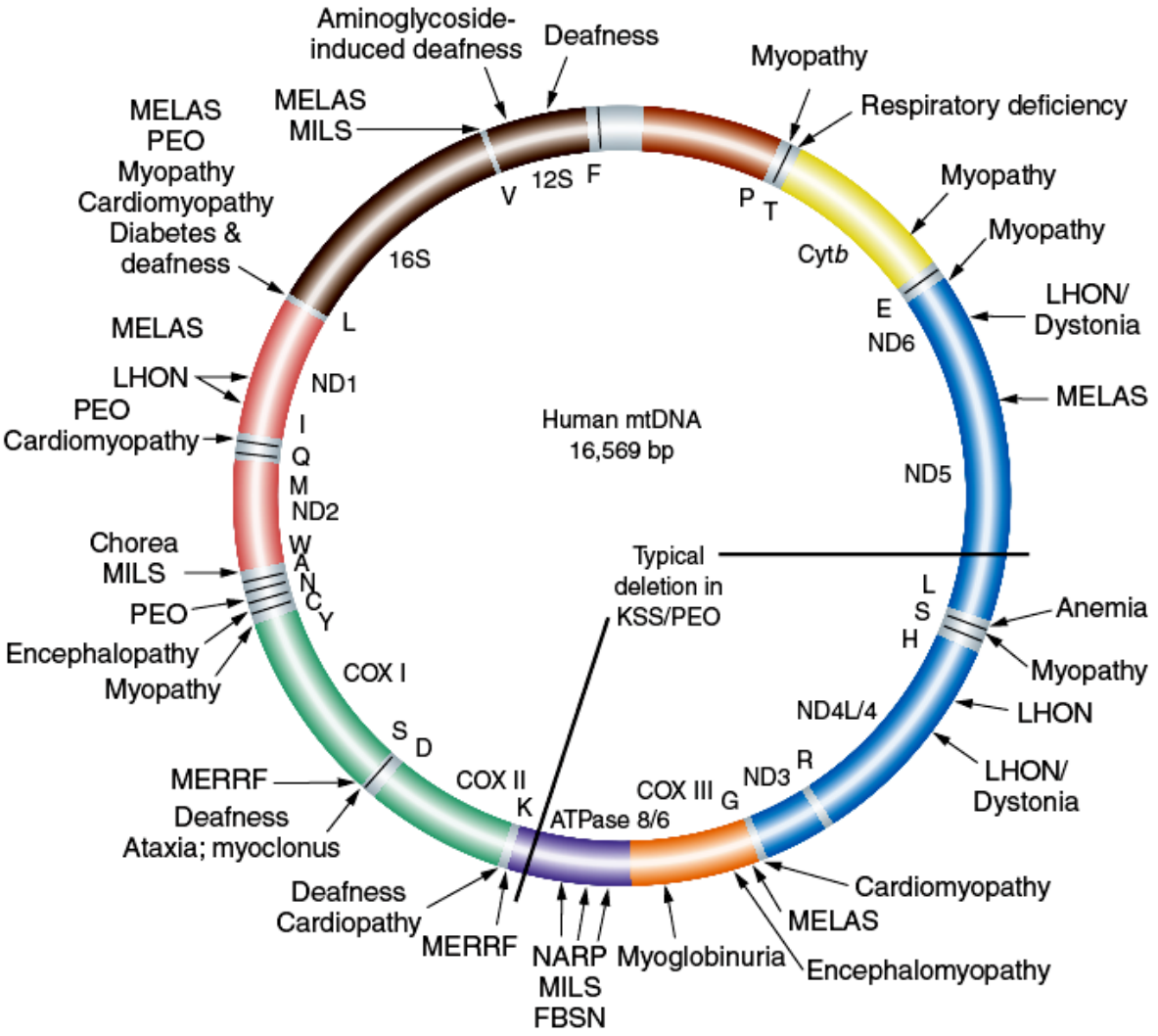
3. **Mutations in mtDNA cause human diseases**

Criteria for mitochondrial disease:

- ◇ Maternal inheritance
- ◇ Deficiency in bioenergetic function
- ◇ Mutation of mitochondrial gene

Characteristic pedigree of mitochondrial disease





Disease

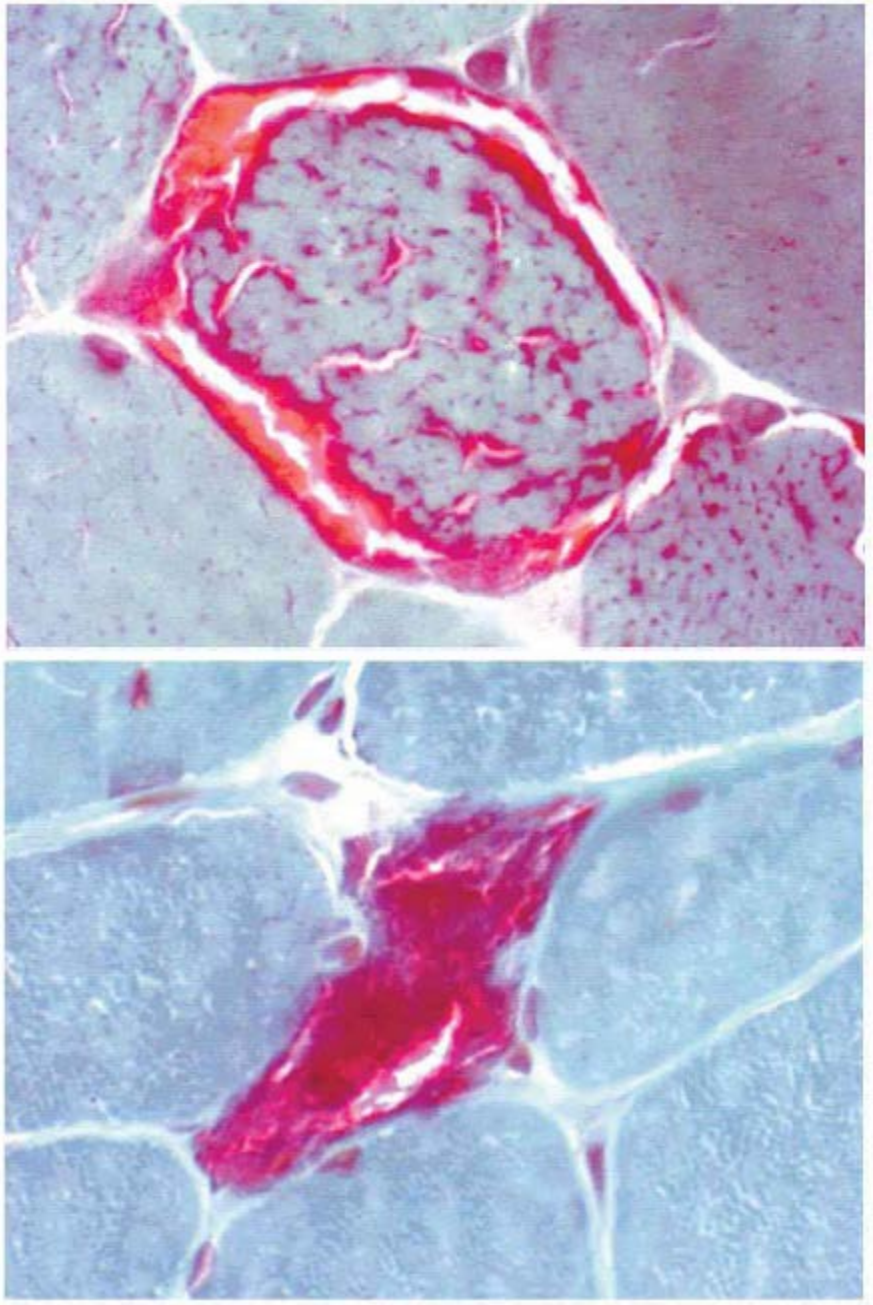
MERRF	Myoclonic epilepsy and ragged red fiber disease
LHON	Leber hereditary optic neuropathy
NARP	Neurogenic muscle weakness, ataxia, and retinitis pigmentosum
MELAS	Mitochondrial encephalomyopathy, lactic acidosis, and strokelike symptoms
MMC	Maternally inherited myopathy and cardiomyopathy
PEO	Progressive external opthalmoplegia
KSS	Kearns-Sayre syndrome
MILS	Maternally inherited Leigh syndrome

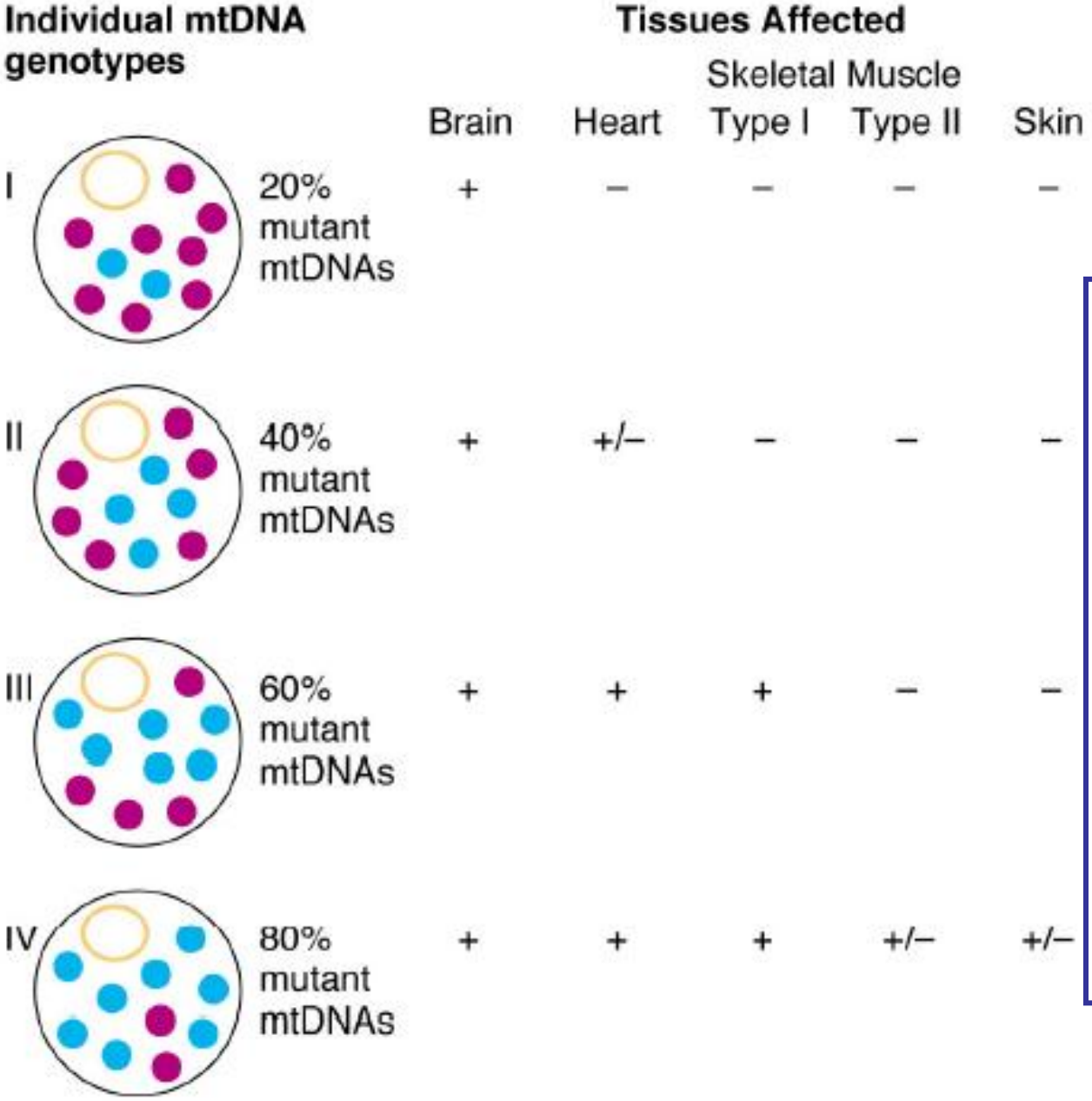
Myoclonic epilepsy and ragged red fiber disease，**MERRF**

肌阵挛性癫痫与破损性红肌纤维病

Uncontrolled jerking, muscle weakness, deafness, heart problems, kidney problems, and progressive dementia

Mutation in $tRNA^{Lys}$





The proportion of mutant mitochondria determines the severity of the MERRF phenotype and the tissue that are affected

Leber´s hereditary optic neuropathy
LHON, leber氏遗传性视神经病

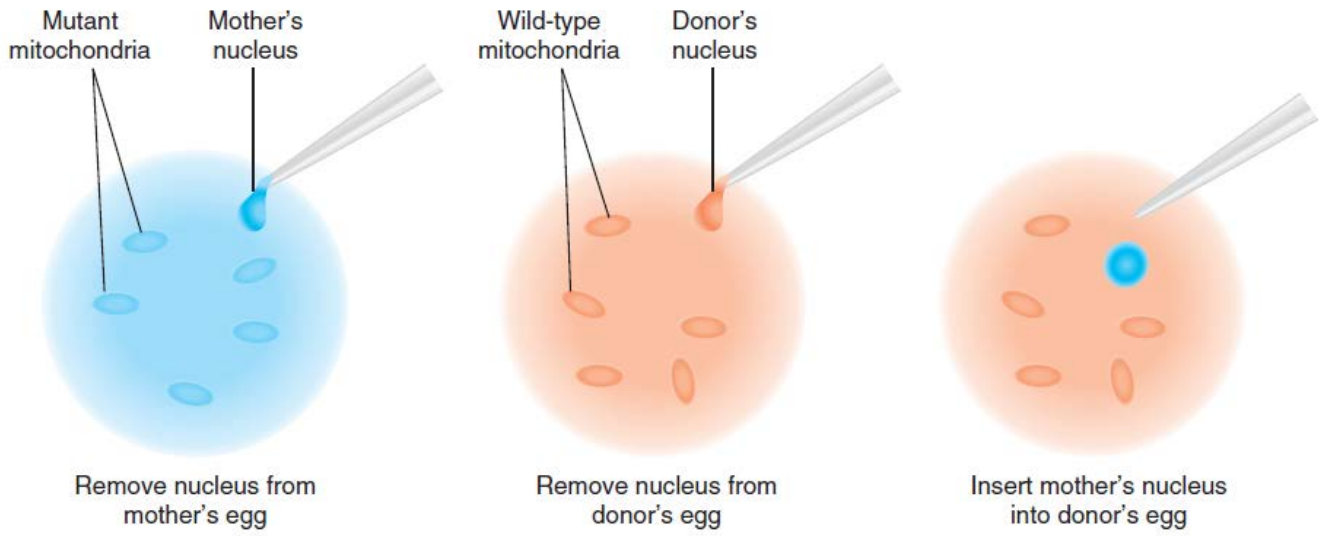
----Mutation in the ND4 gene whose product is one component of the NADH

Keams-Sayre Syndrome

KSS综合征

- In fact, mitochondrial dysfunction seems to be implicated in most all major human disease conditions, including anemia, blindness, Type II (late-onset) diabetes, autism, atherosclerosis, infertility, neurodegenerative diseases such as Parkinson, Alzheimer, and Huntington disease, schizophrenia and bipolar disorders, and a variety of cancers.

Mitochondrial gene therapy



Mitochondrial swapping

Oocyte Nuclear Transplantation Can Sidestep Transmission of Mitochondrial Disease

Mito and Tracker, 2009

First baby born with IVF that uses stem cells to pep up old eggs

Stem cell baby

April 2015 in Canada

Mitochondrial inheritance in identical twins

~2000 mtDNAs in an egg cell

The mutant mitochondria in twins may end up in different cells

Mitochondrial Mutations and Aging

- Mt DNA accumulate much more mutations than nuclear DNA (16 times)
  - ?
- The mutations result in the decline in oxidative phosphorylation, which accounts for some symptomes of aging

Evidence in support of this hypothesis

- The percentage of hearts that had the 7.4 kb deletion increased with age, and the number of 5 kb deletions increased in normal heart tissue after age 40.
- The 5kb deletion is found at a low frequency in normal brain tissue before age 75 but is found in 11% to 12% of mtDNAs in the basal ganglia(基底神经节) by age 80
- Alzheimer's disease (AD) and mutations in two of their three cytochrome c oxidase genes
- ……

4. mtDNA in genetic analysis

Characteristics of mtDNA

- Maternal inheritance
- The small size and a lack of recombination
- A large number of mtDNAs per cell
- High rate of mutation in mtDNA and a high variable non-coding region of 331bp

mtDNA tests are used as evidence in kinship

Reading:

Mitochondrial DNA and mystery of the Romanovs

Russian Tsar, Nicholas II

mtDNA and human emerged and evolved

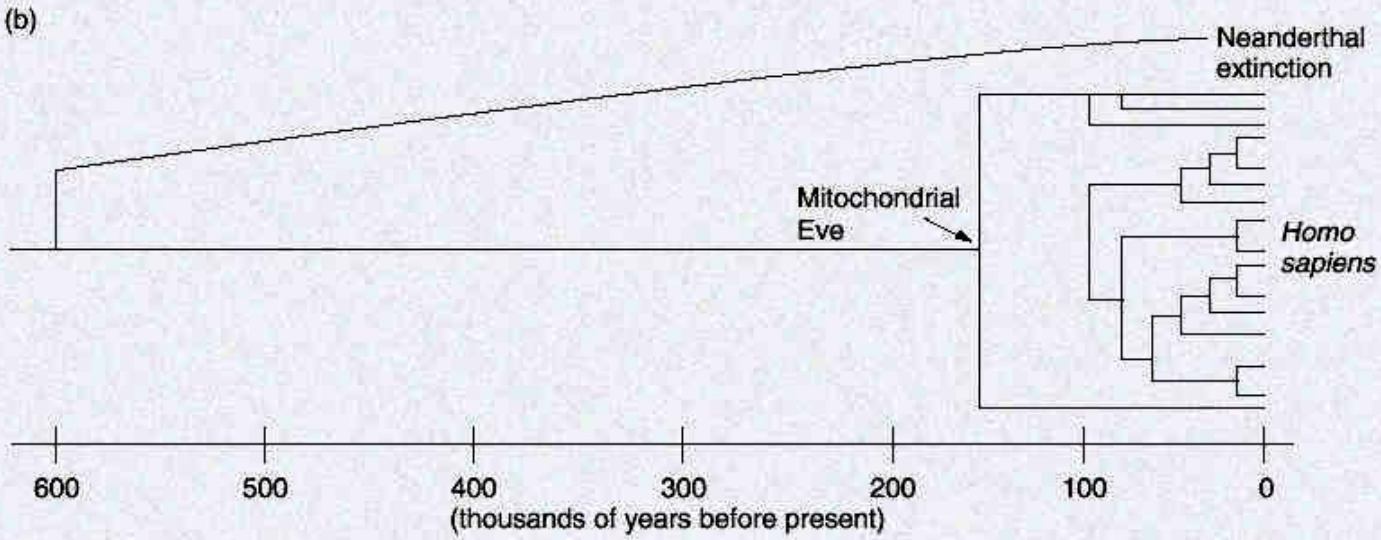


Figure A Analysis of Neanderthal mitochondrial DNA provided proof that our closely related extinct sibling species did not contribute to the gene pool of *H. sapiens*. (a) The first Neanderthal skeleton uncovered in 1856. (b) Evolutionary relationship of Neanderthal to *H. sapiens* as established by mtDNA analysis.

The Endosymbiotic Theory

Further Reading:

细胞质可以父系遗传吗？

细胞质遗传的检测方法

- 经典的遗传学杂交实验
- 电镜技术
- DAPI荧光显微镜技术
- RFLP技术
- 基因组测序技术

第二节　母性影响

Maternal effect

An offspring's phenotype for a particular trait is under the control of nuclear gene products present in the egg

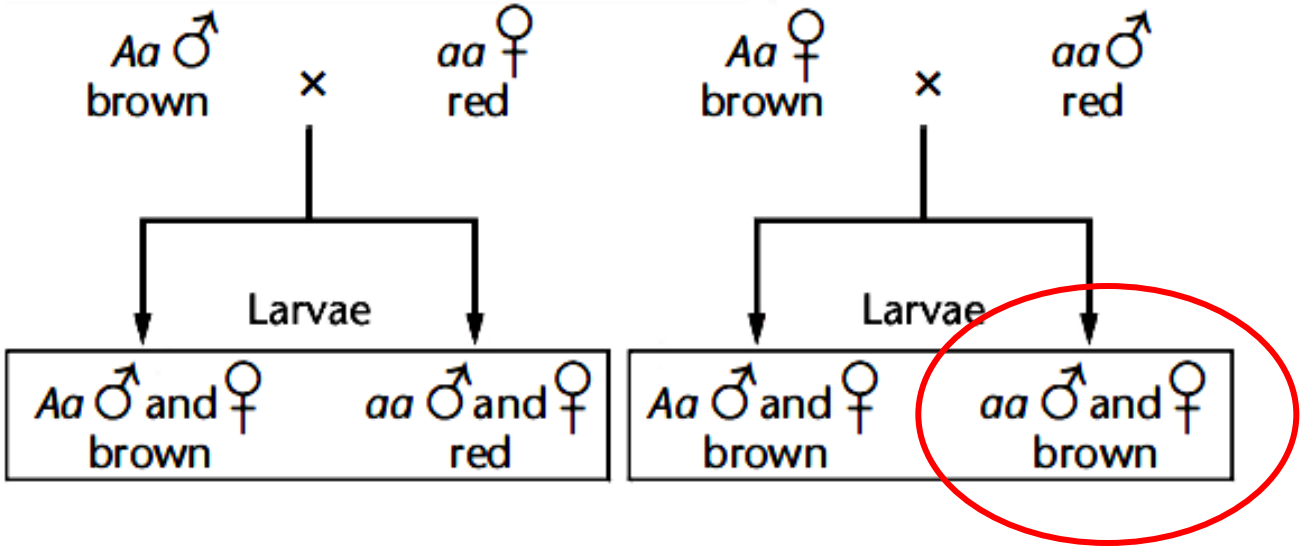
1. *Ephestia* pigmentation
欧洲麦蛾幼虫色素的遗传

wild-type larva (*Aa*)

Pigmented skin
Brown eyes

mutant larva (*aa*)

Little pigmentation
Red eyes

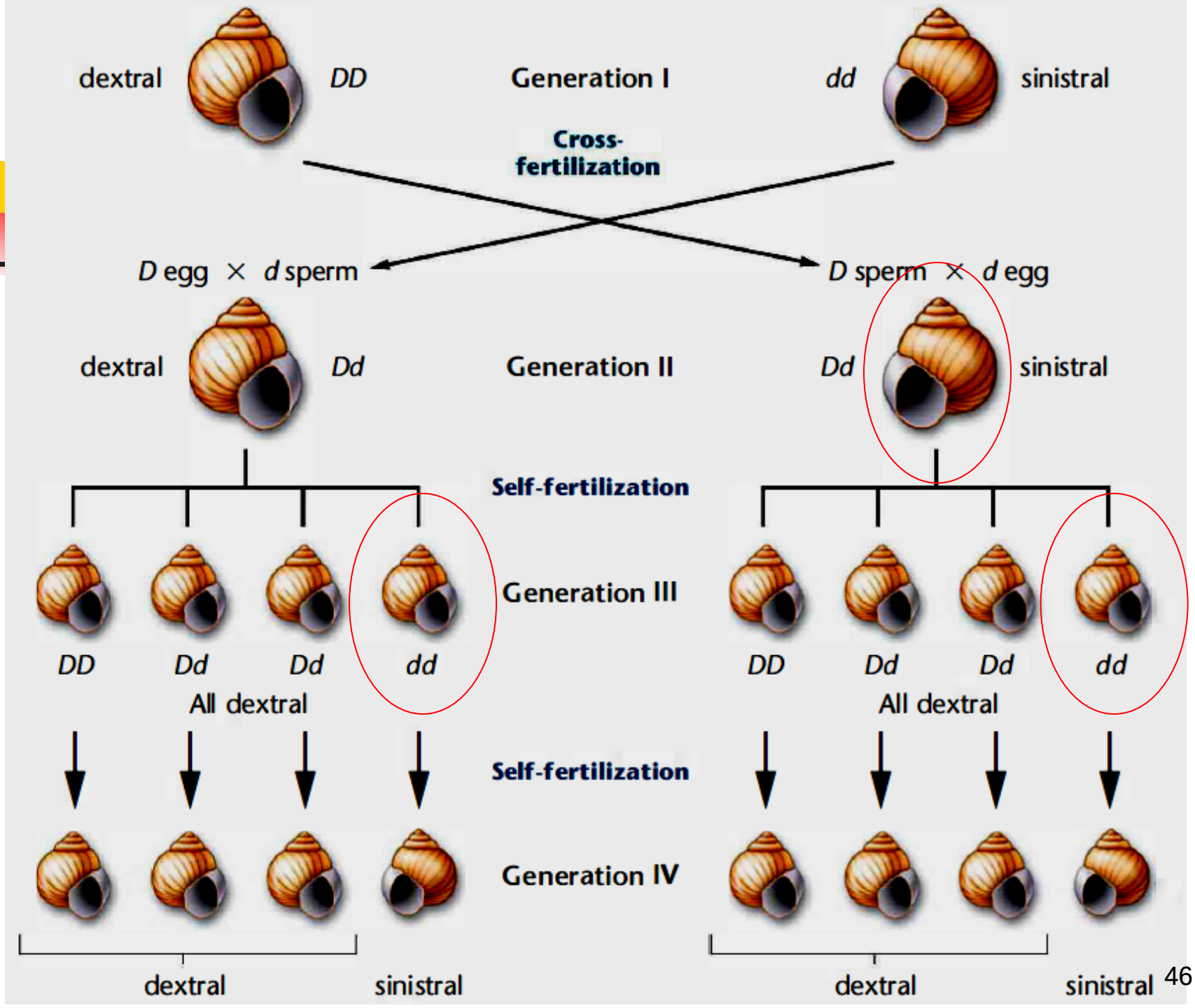


As these larvae develop into adults, they gradually develop red eyes

2. *Limnaea*（椎实螺）coiling

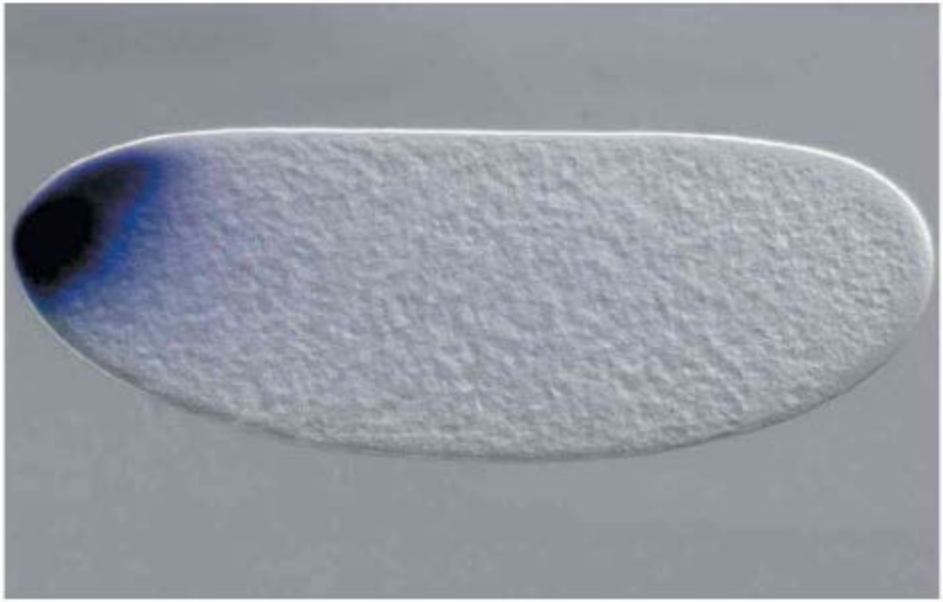
dextral：D
右旋

sinistral：d
左旋


dextral
DD
Generation I
dd
sinistral
Cross-fertilization
D egg × d sperm
D sperm × d egg
dextral
Dd
Generation II
Dd
sinistral
Self-fertilization
Generation III
DD
Dd
Dd
dd
All dextral
DD
Dd
Dd
dd
All dextral
Self-fertilization
Generation IV
dextral
sinistral
dextral
sinistral

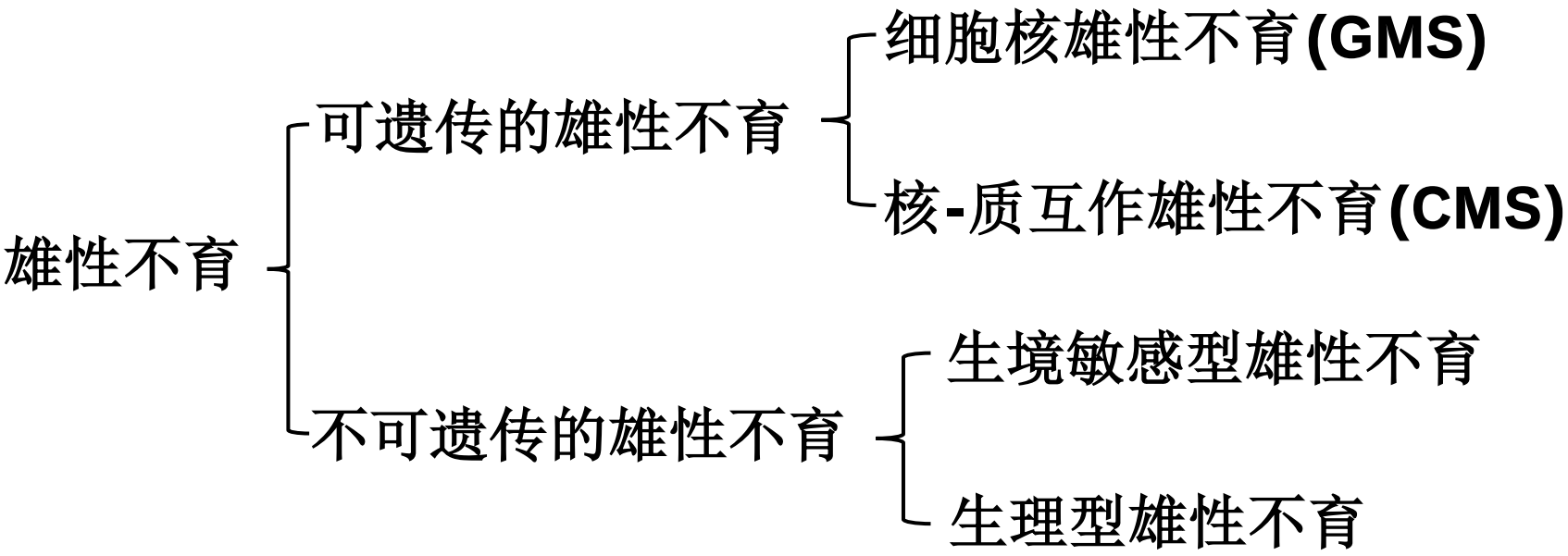
3. Embryonic development in *Drosophila*

果蝇胚胎发育中的母性影响



第三节 植物细胞质雄性不育
Cytoplasmic Male Sterility in Plants

- 植物的雄性不育是指由于生理上或遗传上的原因造成植物花粉败育而雌蕊正常的特性



Genic (Genetic) male sterility (GMS)

- 多数核不育型受简单的一对隐性等位基因控制
- 呈孟德尔分离，育性容易恢复不易保持

Cytoplasmic male sterility (CMS)

- **S**: male sterility cytoplasm（雄性不育细胞质）
- **N**: normal cytoplasm（正常细胞质）
- **Rf**: a nuclear restorer/suppressor gene of S
  （雄性不育的恢复/抑制基因）

Three line hybrid in rice

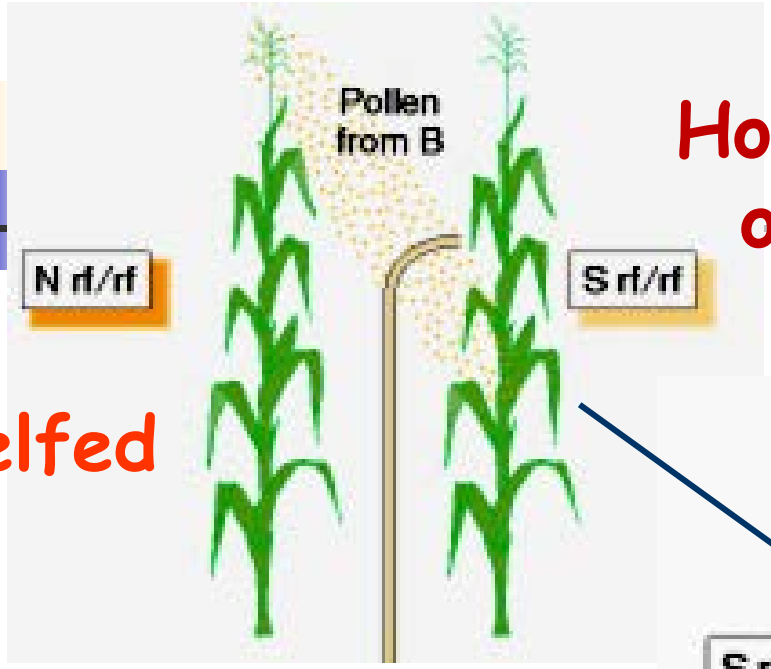
S(rf/rf): male-sterile, **Male sterile line**

N(rf/rf): male-fertile, **Maintainer**

N(Rf/Rf): male-fertile, **Restorer**

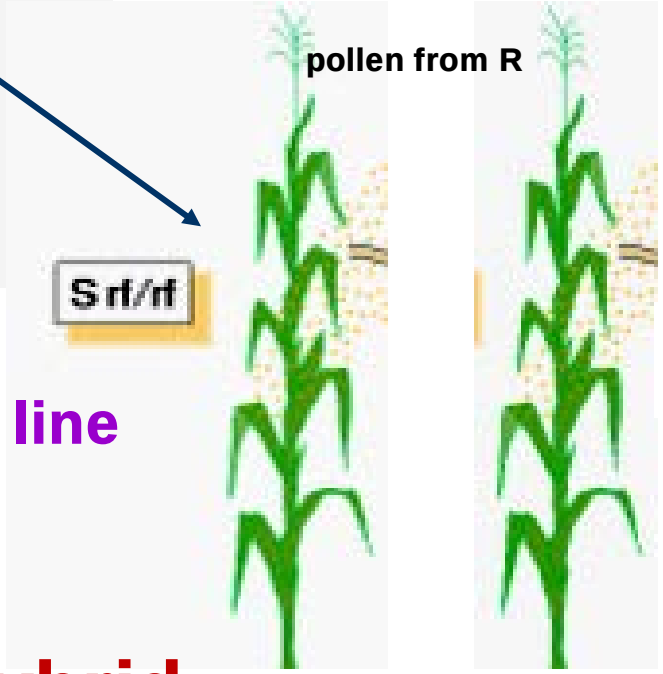
Other male-fertile genotypes?

How is the Male sterile line obtained?



Selfed

Maintainer **B** **A** Male sterile line



Selfed

A **R** Restorer

Where are the F_1 hybrid seeds obtained?