

Unit 3.

13. Sexual Life cycles and Meiosis

heredity (inheritance) : transmission of traits from one generation to the next.

gene : hereditary units , gametes : reproductive cells.

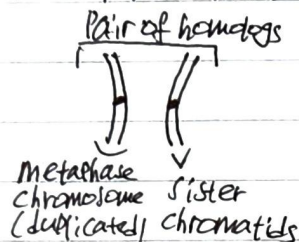
locus : gene's specific location along the length of chromosome.

asexual reproduction : sole parent. , no fusion. , exact genetic copy (clone) , mutation.

Sexual reproduction : Two parents , family resemblance (X exact replicas) , Genetic variation + mutation

Karyotype : Image of chromosomes arranged in pairs , starting with longest chromosomes.

Homologous chromosomes (homologs) : two chromosomes of pair of same characteristic



Two chromosomes referred to X, Y = important exception of general pattern of homologous chromosomes in human somatic cells

Female: XX. Male: XY

X do not have counterparts on tiny Y , Y has genes lacking on X.

X, Y chromosomes = sex chromosomes (성염색체)

Others = autosomes (자염색체)

46 chromosomes [23 : Maternal set (from mother)
23 : Paternal set (from father)

single set = n

two chromosome sets = diploid cell (2n)

(human : 2n = 46)

2n = 46

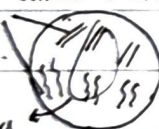
(X X) = 2n

(XX XY) = 2n

has only two sets of information regardless of number of chromatids.

which merely copies of information in one set.

consists of two chromatids.



Maternal set : n = 3

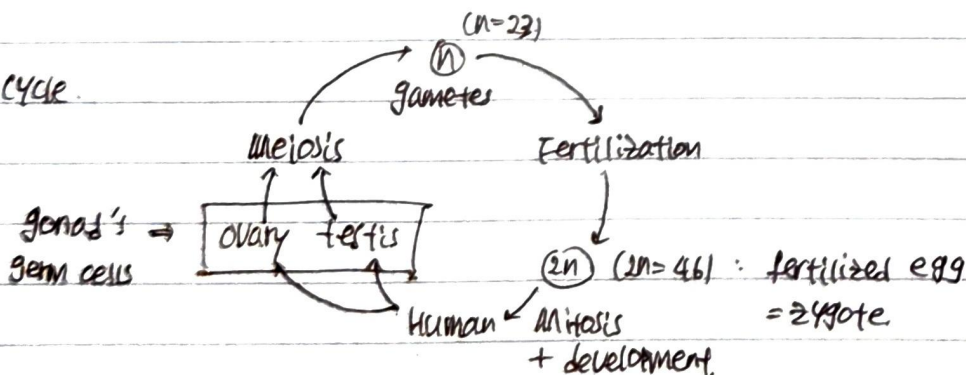
Paternal set : n = 3

2n = 6 → chromosome set

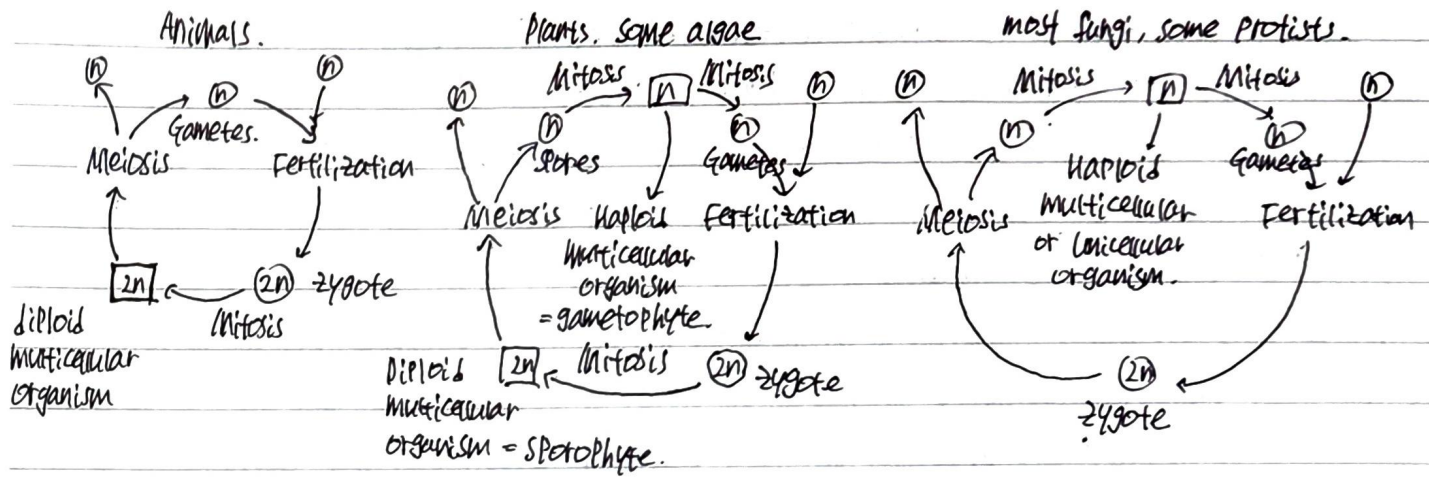
set

2n / n = 2 sets of information

Human life cycle



Variety of sexual life cycle (3 main types)



Meiosis reduce chromosome sets from diploid to haploid.

two consecutive cell division: meiosis I, meiosis II $\Rightarrow$ four daughter cells.

Sister chromatids are two copies of one chromosome - associated all along their length

= sister chromatid cohesion $\rightarrow$ sister chromatids make one duplicated chromosome.

two chromosomes of homologous pair are individual chromosomes - inherit from each parent.

$\therefore$ they have different version of genes at corresponding "loci"

each version is called "allele"

MEIOSIS I: Separate homologous chromosomes.

Prophase I - Centrosome movement / Spindle formation / Nuclear envelope fragment / Chromosome condense.
Chromosome pairs with its homolog. Crossing over occur $\rightarrow$ DNA molecules of nonsister chromatids are broken and rejoined each other.

$\Rightarrow$ homologous pair's X-shaped region: chiasmata (singular, chiasma), crossover occurred place.

microtubules from one pole attach to kinetochores at centromere of each homologs.

$\Rightarrow$ two kinetochores on sister chromatids of homolog - linked together by proteins

$\Rightarrow$ act as single kinetochore.

Metaphase I - Pairs of homologous chromosomes arranged at metaphase plate.

Independent assortment: each pair lined up independently of other pairs.

Anaphase I - Breakdown sister chromatid cohesion responsible proteins along chromatid arms.

$\Rightarrow$ it allows homologs separate, move toward opposite pole.

Sister chromatid cohesion persist at centromere $\rightarrow$ two chromatids of each chromosome move as unit.

Telophase I + cytokinesis - Each chromosome composed of two sister chromatids

→ one or both chromatids include regions of non-sister chromatid DNA



cytokinesis → form 2 haploid daughter cells.

At some species, chromosome decondense, Nuclear envelope form.

MEIOSIS II : Separates sister chromatids

Prophase II - Spindle apparatus forms, still chromosome composed of two chromatids associated at centromere

Metaphase II - Chromosomes positioned at metaphase plate.

two sister chromatids are not genetically identical by crossing over in meiosis I

Kinetochore of sister chromatids attached to microtubules.

Anaphase II - chromatids separate by breakdown proteins holding sister chromatids

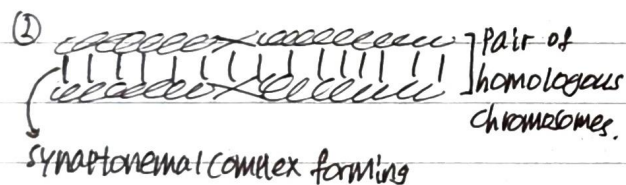
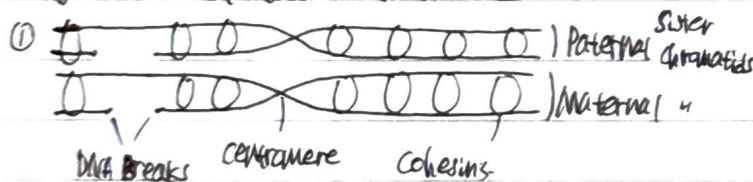
Moving toward opposite side. Each chromatid = individual chromosome.

Telophase II + cytokinesis - nuclei form / chromosome decondensing / cytokinesis occur.

Produce 4 daughter cells (haploid set)

↳ genetically distinct from one another and parent cell.

Crossing over + synapsis in Prophase I



Chromosomes start condense

③ Synaptonemal complex fully formed.

two homologs are in synapsis.

During synapsis, DNA breaks are closed up when broken end joined to corresponding segment of non-sister chromatid, producing crossovers.

④ After synaptonemal complex disassembles,

homologs move slightly apart from each other

but remain attached because of

sister chromatid cohesion the point of attachment when crossovers occurred, show up as "chiasmata"

Chromosomes continue to condense.

Mitosis vs Meiosis

Unique to meiosis occur during Meiosis I. : Synapsis and crossing over.

Alignment of "homologous pairs" at metaphase plate.

Separation of homologs.

Sister chromatid cohesion released in 2 steps

Cohesion of arms at start of anaphase I

Cohesion of centromeres at anaphase II

Chiasma : formation by result of crossing over + sister chromatid cohesion along arms.

↳ it hold homologs together for the first meiotic division.

Genetic Variation.

- Independent Assortment of chromosomes (Meiosis I - metaphase I)

daughter cell → maternal / paternal chromosome $\frac{1}{2}$ → 4 cells : $2^{23} \times 21$ gametes.

- Crossing over : Produce recombinant chromosomes. $\frac{1}{2}$ per chromosome pair.

- Random Fertilization : Independent assortment $2^{23} \times 2^{23}$ (partner) → $2^{46} \times 21$.

bdelloid rotifer - sexual reproduction is not only way of diversity.

When their cell membrane crack, it allow entry of DNA from others or more distantly related species.

• foreign DNA incorporated into genome of bdelloid.

14. Mendelian Genetics

Mendel's experimental - Quantitative approach.

character → 특성 trait → 특성 (?)

F₁, F₂ ... → filial generation 잡종세대

true-breeding (순종) : 순종끼리 아무리 교배해도 Produce only same as parent plant.

hybridization (교배, 혼성)

deduce 추론하다.

elusive 파악하기 어렵

교묘히 잘 짜여져 있다

1. Law of segregation (분리)

과거에는 blending hypothesis 가 있었

Dominant trait 우성 형질 Recessive trait 열성형질

① Alternative version of genes (allele, 대립유전자) account for variation in inherited character

each genes is sequence of nucleotides at specific place (locus)

it can vary slightly in its nucleotide sequence.

→ can affect the function of encoded protein.

② for each character, organism inherits two versions (two alleles) of genes, one from each parent.

③ if two alleles at locus different, dominant allele determines the organism's appearance, the other, recessive allele, has no noticeable effect on organism's appearance.

④ Law of Segregation. - two alleles for heritable character segregate during

gametes formation and end up in different gametes.

→ egg/sperm only get one of alleles

(Allele for Purple flower
Locus for flower-color gene
Allele for white flower)

Punnett Square

	P	p
P	PP	Pp
p	Pp	pp

PP, pp : homozygote (동형접합)

Pp : heterozygote (이형접합) ≠ true-breeding.

Phenotype : 표현형 Purple, white = 3 : 1

genotype : 유전자형 PP, Pp, pp = 1 : 2 : 1

Testcross : Phenotype of purple flower, Genotype of PP인지 Pp인지 알아내는 법.

= recessive homozygote (pp) 와 교배 → Purple 안 나오면 PP

White 도 나오면 Pp (1:1)

2. Law of Independent Assortment

separate 유전자

law of segregation $\rightarrow$ only single character에 대한 것.

Monohybrid (단위잡종) - heterozygous for one particular character being followed in cross.

dihybrid - individuals heterozygous for the two characters being followed in cross ($YyRr$)

dihybrid cross = $YyRr - YyRr$

만약 hybrids transmit their alleles in the same combinations in which the alleles were inherited from P generation, will produce only 2 gametes : YR, yr .

하지만, 실제로는 Independent 해서 YR, Yr, yR, yr 4개.

$\Rightarrow$ law applies only to genes (allele pairs) located on different chromosomes or far distance in same chromosome. (not homologous)

Probability laws govern mendelian inheritance. (probability) 2개 law의 기원

Multiplication rule: And. / Addition rule: Or. $\rightarrow YyRr: \frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$

Extending Mendelian Genetics for single gene.

when alleles are not completely dominant / recessive

Degrees of dominance.

- complete dominance

- Incomplete dominance (불완전 우성): F_1 hybrids have phenotype somewhere between two parental varieties.

ex) red snapdragon + white snapdragon $\Rightarrow$ pink snapdragon : intermediate phenotype.

heterozygote에서 두 형질이 충분히 발현되든지, 안되든지 차이! (by enzyme)

Pink가 blending hypothesis를 강박하는 예가 아님.

F_2 에서 다시 R, w 나타내기 때문.

$C^R C^R + C^W C^W \rightarrow C^R C^W \rightarrow C^R C^R, C^R C^W, C^R C^W, C^W C^W$ (1:2:1)

$\Rightarrow$ segregation law 역시 (discrete rather than blendable)

- codominance (공존 우성) - two alleles each affect phenotype in separate, distinguishable ways.

ex) human MN blood group

$I^M I^M$: have blood cells with only M molecules.

$I^M I^N$: both M, N molecules are present on red blood cells.

$\neq$ intermediate phenotype.

Relationship between dominance and phenotype

- Tay-sachs disease : brain cells cannot metabolize certain lipids because crucial enzyme does not work well.

organismal level : complete dominant

activity level of lipid metabolizing enzyme = intermediate level.

biochemical level : codominant - 정상 enzyme, dysfunctional enzyme 둘 다 생성

but. 그 정도만 있기도 병에 안 걸릴 만큼 충분함.

- frequency of dominant alleles : dominant 하다고 more common 한 것은 아님.

ex) Pk/dactivity (파킨슨) - 유병

Multiple alleles - ABO blood groups : three alleles (I^A , I^B , i)

$I^A I^A$, $I^A i$ / $I^B I^B$, $I^B i$ / $I^A I^B$ / $i i$
(A) (B) (AB) (O)

Pleiotropy 4면 발현 : 하나의 유전자가 2개 이상의 형질 발현에 기여

ex) Pea flower - seed color

Extending Mendelian Genetics for Two or More Genes

→ Two or more genes are involved in determining particular phenotype

- Epistasis : phenotype expression of gene at one locus alter that of gene at second locus.

ex) 리터러 털 : $BbEe \rightarrow B$: black, b : brown, E : pigment deposit in the hair

$BbEe \times BbEe \rightarrow$ black 9, brown 3, yellow 4
(3+1)

e : pigment not deposit in the hair.

$\therefore BBee, bbee$ All yellow.

- Polygenic Inheritance (quantitative characters) $\Rightarrow$ additive effect of two or more genes

: gradation along a continuum.

on a single phenotypic character.

(converse of pleiotropy)

Nature and Nurture : Environmental impact on phenotype

→ Multifactorial : many factors both genetic and environmental collectively influence phenotype

Many human traits follow Mendelian patterns of inheritance. (Pedigree chart analysis)

Recessively Inherited disorders

behavior of recessive alleles - heterozygotes may transmit recessive allele to offspring

⇒ Carriers (보인자) : ~~만약~~ disorder is lethal before reproductive age.

No heterozygote individuals will reproduce

consanguineous (same blood) mating is dangerous (disorder probability ↑)

Cystic Fibrosis (낭포성 섬유증) : Normal gene - codes for membrane protein that transport of chloride ions (transport channel)

문제 생길 수 high concentration of intracellular chloride ion

- cause ~~thick~~ mucus (점액) that coats cells to become thicker, stickier.

Sickle-cell disease (낫모양(경상) 적혈구) - molecular levels : Codominant

⇒ 혈관막이 강함.

organismal levels : Incomplete dominant

Dominantly inherited disorder

achondroplasia (dwarfism) 연골형성(골절) 부전증 (대인종) : 유성 형질. recessive allele is much more prevalent.

lethal dominant allele : almost cannot pass it.

Genetic Testing and Counseling.

- Counseling based on Mendelian Genetics and Probability rules : 아게르 및 Punnett square.

- Test for identifying carriers → dominant homozygotes or heterozygotes carriers

- Fetal testing (태아 검사)

⇒ screening test (noninvasive)

imaging test

ex) ultrasound.

⇒ anatomical abnormalities 판독

blood test.

⇒ look for fetal proteins that might signal genetic disorder.

ex) analyze fetal DNA that escape into mother's blood. (cell-free fetal DNA)

diagnostic test (수검)

- Amniocentesis (양수 검사) : 양수 채취

- Chorionic Villus Sampling (CVS) 태반 조직 채취

태반의 Villus 채취

↳ derived from fetus

= have same ~~the~~ genotype and DNA.

- Newborn screening - blood from baby's heel.

ex) Phenylketonuria (PKU) : Phenylpyruvate accumulate toxic level.

= Phenylalanine을 3mg 미만으로 유지

15. Linkage and chromosomes

Chromosome theory of inheritance - Mendelian genes have specific loci/sites along chromosomes.

Morgan's Experiment. → fruit fly have 4 chromosomes : 3 Autosomes / 1 sex chromosome.

w^+ (red eyes: wild type (most common)) , w (white eyes: mutant phenotype.)

Correlating Behavior of Gene's Alleles with behavior of chromosome pair.

$w^+w^+ + ww \rightarrow F_1$ All Red (w^+ (red) dominant) $\rightarrow F_2$ 3:1 (red, white) 성비.

$\Rightarrow$ White eye only show in Males of F_2 : fly's eye color linked to sex

$\Rightarrow$ on X chromosome. (Y X)

$w^+w^+ (F) \times wY (M)$

$w^+w (F) \times w^+Y (M)$

Female of white eye 되려면 ww .

$w^+w^+ \cdot w^+w, w^+Y, wY$ 하지만 그걸 실험하면 F male of red eye 2개 불가능.

Sex-linked genes exhibit unique patterns of inheritance.

human : X, Y - short segments at either end of Y chromosome are only region that homologous with region on X. $\Rightarrow$ 이것만으로도 make behave like homologs.

Egg : always have X. Sperm : X or Y

Mammalian X-Y system isn't the only chromosomal system for determining sex.

X-O system: XX-female, X-male.

Z-W system: ZW-female, ZZ-male

haplo-diploid system : no sex chromosomes (bee, ant, ...)

{ develop from fertilized egg (Diploid) : Female

develop from not fertilized egg (Haploid) : Male (no father)

SRY : "sex-determining region of Y" $\Rightarrow$ require for development of testes.

$\Rightarrow$ 이걸 없으면 XY라도 Ovaries가 생김.

Sex-linked gene : gene located on either sex chromosome.
 X-linked genes
 Y-linked genes : few disorders. (father to son)

Development of female gonads

$\rightarrow$ require gene called WNT4 (chromosome 1 that's autosome)

XY가 되고 있으면 WNT4 gene의 extra copy 가지고 있으면 develop "rudimentary female gonads."

$\Rightarrow$ sex결정에 수많은 요소들이 network. $\rightarrow$ sex에 수많은 variations exist.

Vary in number of sex chromosomes, intermediate sexual (intersex),

transgender individuals : anatomical features not match on their own gender

Inheritance of X-Linked Genes.

Vestige 자크. 존

Male, female inherit different number of X. → leads to different from that produced by genes located on autosomes.

Y의 차이 X have numerous genes for characters unrelated to sex.

Father's X-linked alleles : all to daughters (no son)

Mother's X-linked alleles : both.

ex) color-blindness, Duchenne (근이영양증) muscular dystrophy (근 위축증), Hemophilia (bleeding prolong)

X chromosome inactivation in female mammals : almost all of one X chromosome in each cell in female mammals become inactivated.

Inactive X condenses into compact object → Barr body (not expressed)

어떤 X가 될지는 random.

Ovaries and Barr body reactivated → that makes every female gametes (egg) have active X after meiosis.

by Inactive X, female consist mosaic of two types of cells { active X from father
active X from mother

X가 inactivate 되면, All mitotic descendants of that cell have same inactive X

⇒ heterozygous female of heterozygous for a sex-linked trait,

half of her cell express one allele, others alternative allele.

ex. cat의 색깔 유전 (patch)

Human의 경우, recessive X-linked mutation that prevent development of sweat glands

Mosaic of patches of normal skin and patches of lacking sweat glands

Inactivating - by Histon protein, DNA bound.

Particular region of each X contains several genes involved in inactivation process

- Gene call XIST (X inactive specific transcript) become active only on

Chromosome that will become Barr body. Multiple RNA product of this gene attach to X on which they are made, almost covering it. ⇒ X inactivation initiated.

→ 100% X : Not always genetically linked ⇒ by Genetic Recombination.

Linked genes find to be inherited together (they located near each other on same chromosomes)

Morgan's Drosophila experiment - body color and wing size (not on sex chromosome)

✓ Linked Gene : 2 or more gene nearby. Sex-linked Gene : single gene on sex chromosome

Genetic Recombination and Linkage.

Recombination of Unlinked Genes - Independent Assortment of chromosome.

Parental type : 부모의 Phenotype 그대로.

Recombinant type (recombinants) : 부모의 Phenotype X

- 만약 50% of all offspring are recombinants $\Rightarrow$ There's 50% frequency of recombination.
= Not linked.

Recombination of Linked Genes : Crossing over.

two genes (ex. body color, wing size) were on same chromosome, 50% ~~is~~ high

(83% of parental type) 40% 17% : recombinants.

$\downarrow$
break physical connection
= crossing over.

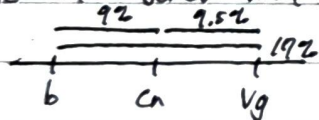
Mapping the Distance between Genes using Recombination Data.

Constructing Genetic MAP - ordered list of genetic loci along particular chromosome.

Recombination Frequency (Percentage of recombinant offspring) $\rightarrow$ depends on distance between genes on chromosome.

- $\Rightarrow$ Can predict that the farther apart two genes are, the higher probability cross over will occur between them and therefore higher recombination frequency.

Linkage map : Genetic map based on recombination frequency.



"Sturtevant" excess distance between genes in Map Units.

defining one map unit = 1% recombination frequency.

recombination frequency maximum : 50% = same result indistinguishable from that for genes are genetically unlinked.

$\neq$ actual physical distance.

Q. 156P. 이렇게 50를 넘어서 104.5가 가능한 것이지.

Genetic disorders cause by Alterations of chromosome number or structure

- Abnormal chromosome number.

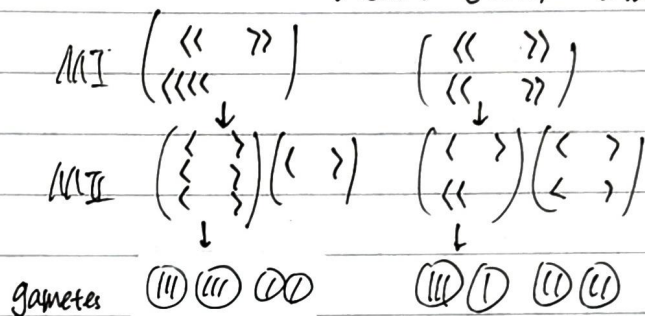
"Nondisjunction": pair of homologous chromosomes do not move apart properly during separation.

- aneuploidy: zygote that have abnormal number of chromosome condition.

aneuploid cell

monosomic ($2n-1$): no copy of particular chromosome.

trisomic ($2n+1$): triplicate copy of particular chromosome.



Polyploidy: some organisms have more than two complete chromosome sets in all somatic cells.

(Triploidy ($3n$): by abnormal diploid egg produced by nondisjunction of all its chromosomes

(Tetraploidy ($4n$): failure of $2n$ zygote to divide after replicating its chromosomes.

Alterations of chromosome structure.

Deletion: chromosomal fragment lost $\rightarrow$ missing certain genes.

Duplication: broken fragment may reattached as an extra segment to sister or nonsister chromatid.

Inversion: chromosomal fragment may reattach to original chromosome but in reverse orientation.

Translocation: fragment to join nonhomologous chromosome.

Deletion / Duplication - likely to occur in meiosis, by crossing over (unequal crossing over)

Reciprocal translocation (상호 전위): segments exchanged between nonhomologous chromosomes.

Human conditions due to chromosomal Alteration.

Syndrome: Down Syndrome (Trisomy 21) 3염색체증, by extra chromosome 21 (total 47 chromosomes)

Aneuploidy of sex chromosomes (Y 염색체 결핍, X5 inactive 되는 것 때문에 생음색채빛다 영향↓)

XXY (Klinefelter syndrome) - male sex organ, testes ↓, sperm ↓, height ↑, muscle, breast ↑

XYY: slightly height ↑, not exhibit any well-defined syndrome.

XXX: trisomy X. slightly height ↑, learning disability, not exhibit any well-defined syndrome

X (monosomy X): Turner syndrome, phenotypically female, but sterile because their sex organs do not mature.

Disorder caused by structurally altered chromosomes

cri du chat (cry of the cat) syndrome - specific deletion in chromosome 5

: small head, unusual facial features, severe intellectual disability, cry sounds like meowing.

Chronic myelogenous leukemia (CML): reciprocal translocation happens during mitosis of cells that are precursors (stem) of white blood cells. (chrom 2) $\leftrightarrow$ (chrom 9), cause cancer.

Philadelphia chromosome

Some inheritance patterns are exceptions to standard Mendelian inheritance.

- Genomic imprinting (유전자 발현): variation in phenotype depending on whether an allele is inherited from the male or female parent (most in autosomes)

: occur during gamete formation, result in silencing of particular allele of certain genes.

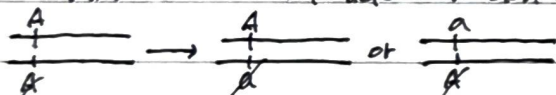
→ offspring expresses only one allele of an imprinted gene.

imprints transmitted to all body cells during early development.

In each generation, old imprints erased in gamete-producing cells.

Chromosomes of developing gametes are newly imprinted according to the sex of individual ~~for~~ forming gametes

Q (* Gene imprinted for maternal allele expression always imprinted this way, generation to generation.



imprinting can involve either silencing, activating an allele.

imprinting seems to consist of methyl (CH₃) groups added to cytosine nucleotides of one allele. (methylation silencing / activating)

- Inheritance of organelle genes : extranuclear genes or cytoplasmic genes.

Mitochondria, Chloroplast, +x - have circular DNA.

most plants get organelle genes from egg (sperm x)

사람 미토콘드리아도 마찬가지.

Mitochondrial disease → Mitochondrial myopathy : weakness, muscle deterioration.

Leber's hereditary optic neuropathy : sudden blindness 20-30s.

two mother egg : 핵이랑 미토콘드리아 둘다 다름 → three parent babies

16. Nucleic Acids and Inheritance.

Search for genetic materials $\rightarrow$ DNA / Protein.

Pneumonia 예방.

- Evidence of DNA transform bacteria.

$\rightarrow$ protein modified.

Pneumonia [Pathogenic (bacteria) : S cell. Living S $\rightarrow$ dead. Heat killed S $\rightarrow$ healthy.
nonpathogenic : R cell. Living R $\rightarrow$ healthy. Heat killed S + Living R $\rightarrow$ dead.
 $\Rightarrow$ Living S founded.

$\Rightarrow$ transformation : change in genotype and phenotype due to assimilation of external DNA (종이)

- Evidence of Viral DNA can program cells.

bacteriophages (Hershey and Chase 실험) : use T2 Phage - turn E. coli into T2-producing factory.
 $\Rightarrow$ T2 reprogram host cell.

liquid
Batch 1 - Phage grown in radioactive sulfur (^{35}S), incorporated into phage protein.
Centrifuge mixture of phage with bacteria $\rightarrow$ radioactivity in liquid (phage-protein)
Batch 2 - Phage grown in radioactive phosphorus (^{32}P), incorporated into phage DNA
Pellet
Centrifuge Mixture of phage with bacteria $\rightarrow$ radioactivity in pellet (phage-DNA)

- Additional evidence of DNA (by Erwin Chargaff)

Chargaff's rule. - DNA base composition varies between species (DNA는 특이성이 있다) (생각할 것)
- Percentage of A, T base are roughly equal. / G, C base either.

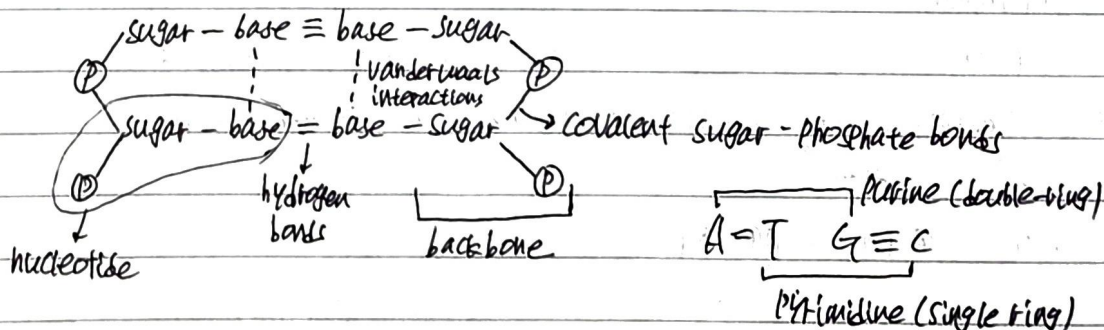
Building Structural Model of DNA.

James Watson and Francis Crick - X-ray crystallography (X-ray diffraction image by Rosalind Franklin)

Sugar-Phosphate backbone + Nitrogenous bases $\Rightarrow$ Diameter : 2nm

$\hookrightarrow$ double helix (right handed) $\hookrightarrow$ inside.
outside. / antiparallel.

one full turn : every 10 base pairs = 3.4nm
 $= 0.34\text{nm}$.

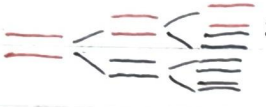


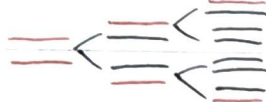
DNA replication and repair

Base pairing to template strands.

- Separate two chains act as template for new companion chain. (each is complementary)

- three alternative models of DNA replication.

Conservative Model  : two parental strands reassociate after acting as templates for new strands - restore parental double helix

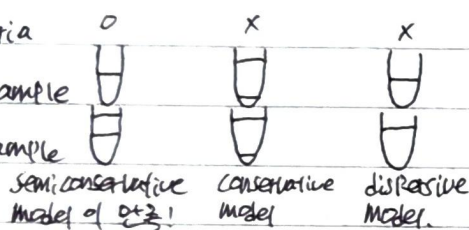
Semiconservative Model  : two strands of parental molecule separate, each function as template for synthesis of new complementary strands

Dispersive Model  : Each strand of both daughter molecules contains mixture of old and newly synthesized DNA.

- 실험 : ¹⁵N으로 배양한 bacteria

- 첫 번째 replication sample

- 두 번째 replication sample



DNA replication

Replication start at specific sites : Origins of replication (복제원)

Circular DNA - one origin, one replication bubble

Eukaryotic chromosome - 100~500개 origins, 100~500개 replication bubbles

Several kinds of proteins.

- Helicases : Enzyme that untwist double helix at replication fork + separate two parental strands.

- Single-strand binding proteins : keeping DNA strands re-pairing

- Topoisomerase : Untwisting double helix causes tighter twisting and strain ahead of replication fork.

This enzyme helps relieve this strains by breaking, swivels, rejoining DNA strands

- Primase : Synthesize RNA primers.

- DNA polymerase : 3' end에서 DNA synthesis 시작, cannot initiate synthesis polynucleotide.

↓
이때 필요한 3' end에서 부위만 만들 수 있음 + Primase의 RNA Primer. (5~10 nucleotide long)
2D. 배양한 결과 5' ← → 3' 5'

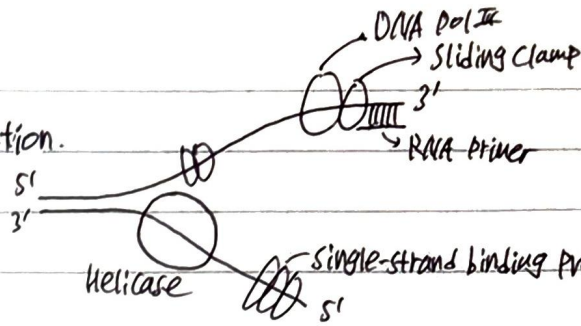
종류 다양함. ex) E. coli : DNA Pol I, DNA Pol III

↓ add DNA nucleotides to RNA primer { 500/s in bacteria
80/s in human.

ATP : sugar component : ribose, dATP : sugar component : deoxyribose

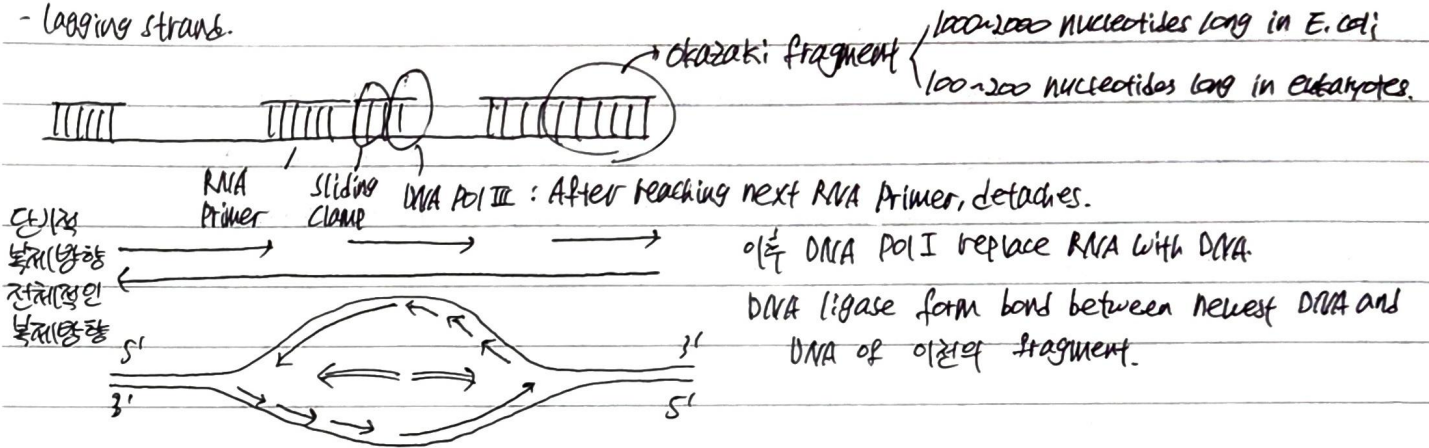
Anti-Parallel elongation.

- leading strand



⇒ leading strand elongated continuously 5' → 3'

- lagging strand.



Summary.

1. Helicase unwind parental double helix. - 2. molecules of single-strand binding protein stabilize two unwound template strands - 3. leading strand is synthesized continuously 5' → 3' by DNA Pol III - 4. Primase begin synthesis RNA primer for Okazaki fragment 5. - 5. DNA Pol III complete synthesis of fragment 4. When it reach to RNA primer on fragment 3, detach and begin adding DNA nucleotides to the 3' end of fragment 5 primer. - 6. DNA Pol I removes primer from 5' end of fragment 2, replacing with DNA nucleotides. - 7. DNA Ligase joins 3' end of fragment 2 to 5' end of fragment 1.

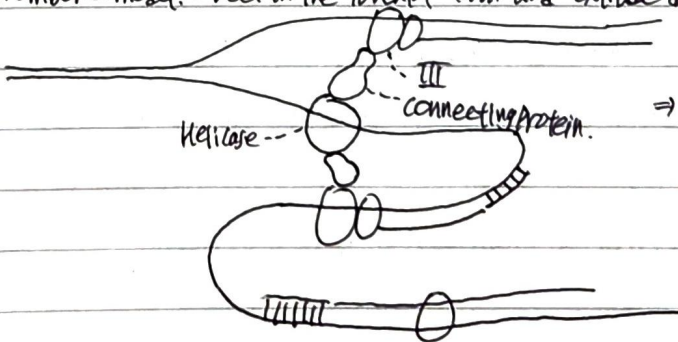
DNA replication complex.

actually, various proteins participate in DNA replication form single large complex (DNA replication machine)

DNA replication complex of DNA 따라 trailing 해리도 있음. - DNA가 move through complex.

- trombone model: reel in the parental DNA and extrude daughter DNA.

anchors to nuclear matrix.



⇒ lagging strand template DNA loops through complex. resembling the slide of trombone.

Proofreading (교정) and Repairing DNA. - Polymerase remove nucleotides and resume synthesis
segment of strand containing damage cut out by "Nuclease" (DNA cutting enzyme)
and filling the gap (DNA polymerase, DNA ligase)

- 많은 DNA repair system 중 하나 : Nucleotide excision repair (핵산 절제 복구)

enzymes detect and repair DNA

- Nuclear enzyme cut damaged DNA strand at 2 points (removed) → repair synthesis by DNA
polymerase fills in missing nucleotides, using undamaged strand as template. →
DNA ligase seals free end of new DNA to the old DNA, making strand complete.

Xeroderma pigmentosum (색소성 건피증) : DNA 복구 기능 결함.

Evolutionary significance of permanently altered DNA nucleotides ⇒ Mutation.

Replicating the Ends of DNA molecules. (ON Linear DNA!)

Usual replication machinery cannot complete 5' ends of daughter DNA strands.

End of  ⇒ 5' _____
(lagging strand).

프라이머가 리가된 5' 끝은 3' 끝이 계속 nucleotide addition 불가.

⇒ shorter and shorter daughter molecules. (리가된 primer 단편의 DNA 서열은 excision)

- Telomere : not contain genes, consist of multiple repetitions of one short nucleotide sequence

Human - TTAGGG가 100 ~ 1000번 반복

2가지 protective function 1. prevent staggered ends of daughter molecules.

남아있는 장단(교정)의 단편 있으면 leads to cell death. DNA 대문자 있으면 안됨.

2. acts as buffer zone, protection against organism's gene shortening
but just postpone

Shortening of telomeres = aging process

Germ cells : telomerase & telomere repeat (catalyze lengthening telomeres)

↳ contains its own RNA molecule, uses as template to artificially extend
leading strand, allowing lagging strand to maintain given length.

Thus, normal shortening of telomeres may protect from cancer by limiting the number of division.

DNA molecule packed with proteins.

One human DNA molecule : 4cm. long.

Chromatin = complex of DNA and protein.

Interphase chromatin

euchromatin (loosely packed) : less compacted.

- make DNA accessible to proteins and available for transcription.

heterochromatin (tightly packed) : more compacted

- 10nm fiber folded and bent back on itself to much greater degree than euchromatin.

- inaccessible to proteins for transcribing genetic information

basic unit = 10nm fiber
= nucleosomes joined by linker DNA.



Chromatin of each chromosomes occupies specific restricted area.



DNA - double helix.

Histones (protein) : main level of DNA packing in interphase chromatin.

↳ Positively charged : bind with DNA (negatively charged)

Nucleosomes in 10-nm fiber - nucleosome consist of DNA wound twice around protein core of 8 histones, 2 each of four main histone types.

Amino end of each histone (histone tail) extends outwards, involved in regulation of gene expression.

Prophase - When Mitosis begin, each sister chromatid begins to condense.

Condensin II : bind to 10nm fiber and form DNA loops that get larger and larger. (central scaffold)

Condensin I : At Prometaphase, it bind to outside of central scaffold, make smaller loops out of larger loops generated by Condensin II

More and more loops, scaffold itself twist into helix.

Metaphase : fully condensed.

17. Expression of Gene.

Gene expression - Process by which DNA directs the synthesis of proteins or just RNAs.

Evidence from studying Metabolic Defects. (one gene - one enzyme hypothesis)

Artificial mutants in Neurospora (Haploid) - cause mutation by bombarding Neurospora with X-rays.

Precursor $\xrightarrow{\text{enzyme A}}$ Ornithine $\xrightarrow{\text{enzyme B}}$ Citrulline $\xrightarrow{\text{enzyme C}}$ Arginine.

Wild type: can grow on minimal medium.

mut⁻ mutation in gene B, [Precursor, Ornithine]: dead. [Citrulline, Arginine]: alive

- not all proteins are enzyme: one gene - one polypeptide hypothesis (RNA만 만들고 끝나는 genes도 있음)

Eukaryotic gene can code a set of closely related polypeptides; process called "Alternative Splicing"

→ deoxyribose and ribose, T and U

DNA → RNA → Protein synthesis

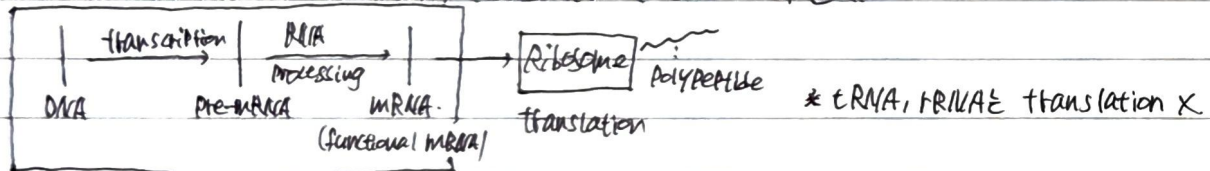
Transcription: Synthesis of RNA using information in DNA.

Protein-coding gene or RNA? Protein synthesizing machinery? Genetic message? (mRNA)

Translation: Synthesis of polypeptide using mRNA. (on ribosome)

Bacterial cell: coupled transcription, translation 동시에 발생 가능.

Eukaryotic cell: coupled not transcription, translation 이 끝난 후 시작 가능.



Central Dogma: DNA → RNA → Protein. (but RNA is template of DNA synthesis in prokaryotes)

Codons: Triplets of Nucleotides - flow of information from gene to protein based on triplet code

only one of two DNA strand transcribed → template strand

for any given gene, same strand is used as template every time that gene is transcribed.

- opposite strands may function as template for different gene.

mRNA: Complementary with DNA (5' → 3'), leading by translation machinery in 5' → 3'

Coding strand: nontemplate DNA (template strand의 반대)

ACG: start signal or Met (∴ 항상 Met을 시작하는 43종 enzyme의 시작 신호)

Particular amino acids differ only in third nucleotide base of triplet (redundancy but no ambiguity)

reading frame of 3' ex) The red dog ate the bug → her edd oga tet heb ug

Genetic code is nearly universal, shared genetic vocabulary is reminder of kinship of all life

codon table for mRNA (3A1P)

	U	C	A	G	
U	UUU } Phe UUC } F UUA } UUG } Leu	UCU } Ser UCC } S UCA } UCG }	UAU } Tyr UAC } Y UAA } stop UAG } stop	UGU } Cys UGC } C UGA } stop UGG } Trp	U C A G
C	CUU } CUC } L CUA } CUG }	CCU } Pro CCC } CCA } P CCG }	CAU } His CAC } H CAA } Gln CAG } Q	CGU } Arg CGC } R CGA } CGG }	U C A G
A	AUU } Ile AUC } I AUA } AUG } Met (start)	ACU } ACC } Thr ACA } T ACG }	AAU } Asn AAC } N AAA } Lys AAG } K	A GU } Ser A GC } S A GA } Arg A GG } R	U C A G
G	GUU } GUC } Val GUA } V GUG }	GCU } Ala GCC } A GCA } GCG }	GAU } Asp GAC } D GAA } Glu GAG } E	GGU } Gly GGC } G GGA } GGG }	U C A G

Transcription - DNA directed synthesis of RNA.

RNA Polymerase: Pries two strands of DNA apart, join together RNA nucleotides complementary to DNA (5'→3')

- Unlike DNA polymerase, able to start a chain from scratch. (don't need pre-existing primer)

Promoter: DNA sequence where RNA polymerase attaches and initiate transcription

Terminator (on bacteria): sequence that signal end of transcription.

Upstream, downstream: Promoter is said to be upstream from terminator.

transcription unit: stretch of DNA downstream from promoter that is transcribe into RNA.

Synthesis of RNA Transcript: stages - initiation → elongation → termination.

Initiation: After RNA polymerase binds to promoter, polymerase unwinds DNA strands and initiate RNA synthesis at the start point on template strand.

Elongation: Polymerase move downstream, unwinding DNA, elongate RNA transcript 5'→3'

After transcription, DNA strands re-form double helix.

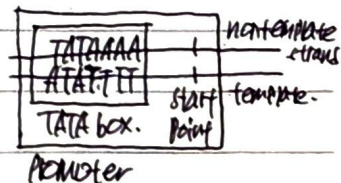
Termination: RNA released, polymerase detaches from DNA.



→ Initiation at eukaryotic promoter (include TATA box - sequence containing TATA)

several "transcription factors", one recognizing TATA box

Must bind to DNA before RNA pol II can bind in correct position.



Additional transcription factors, bind to DNA along with RNA pol II, forming "transcription initiation complex"

RNA pol II unwinds DNA double helix, and RNA synthesis begin at start point.

Transcription initiation complex - whole complex of transcription factors + RNA pol II

⇒ Elongation of RNA strand.

Unwisted double helix expose about 10-20 DNA nucleotides at a time.

Enzyme adds nucleotides to 3' end of growing RNA. - As transcription proceed, newly synthesized RNA behind RNA polymerase peels away from DNA template, DNA double helix reform. (40 nucleos/sec)
여러개의 RNA 폴리머라아제가 있다.

⇒ Termination of Transcription.

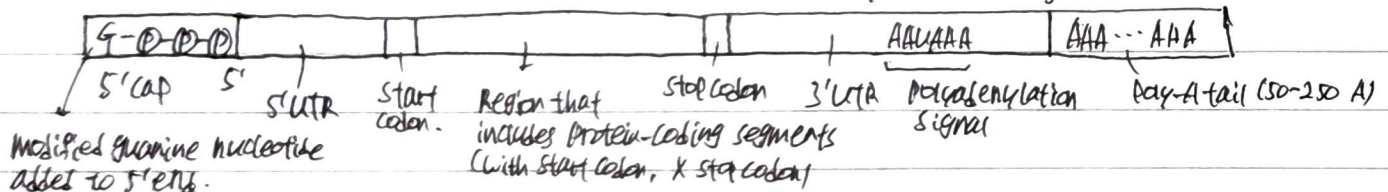
bacteria : transcription proceed through terminator sequence in DNA, transcribed terminator function as termination signal, causing polymerase to detach from DNA, release transcript (no further modification)

Eukaryotes : RNA pol II transcribe polyadenylation signal sequence → AAUAAA (polyadenylation signal) in pre-mRNA. → signal because it immediately bound by certain proteins, cut the RNA transcript free from polymerase. (cleave)

- Although cleavage (cut) marks the end of mRNA, RNA pol II continues to transcribe
Enzyme begin to degrade RNA made after cleavage. → Enzyme = Polymerase activity
이후 RNA 폴리머라아제가 분해된다.

RNA Processing : Eukaryotic cells modify RNA after transcription (modify pre-mRNA)

- Alteration of mRNA Ends. ⇒ Addition of 5' cap and poly-A tail. 3'

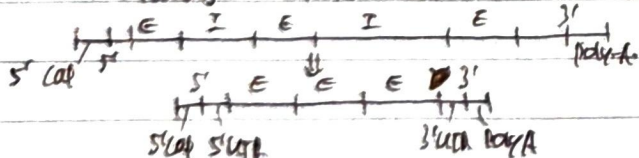


5' cap, poly-A tail 의 역할

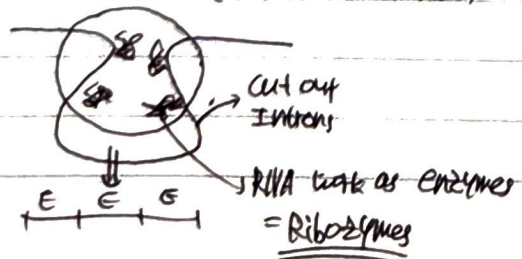
- facilitate export of mature mRNA from nucleus.
- protect mRNA from degradation by hydrolytic enzymes.
- help ribosomes attach to 5' end of mRNA once it reach cytoplasm.

UTRs (untranslated regions) : protein or translation을 시작할 ribosome binding site의 function 수행

- RNA splicing : Introns removed and remain exons are reconnected.



Spliceosome (proteins + small RNA)



Introns : noncoding segment (intervening sequence)
Exons : coding segment (expressed (exit the nucleus))

Ribozymes - catalytic role for RNAs (RNA work as enzymes)

Ciliate Protist *Tetrahymena* (클레프 디브렐) : self-splicing occur in production tRNA
: pre-tRNA removes its own introns.

3 Properties of RNA, enable RNA to function as enzymes.

- RNA is single strand. : by base-pairing, gives molecule particular 3D structure.
- Some base in RNA contain functional groups, that can participate in catalysis.
- Ability of RNA to hydrogen-bond with other nucleic acid molecules add specificity to catalytic activity.

Alternative RNA splicing : Single gene can encode more than one polypeptide, depending on which segments are treated as exons during RNA processing.

Domains : proteins have modular architecture consisting of discrete structural, functional region.

- might include active site, or allow enzyme to bind cellular membrane.

Different exon codes for different domains of protein.

Intron 재조합 이론 : Exon shuffling. - Intron increase probability of crossing over between exons of alleles of gene (simply by providing more terrain for crossover)

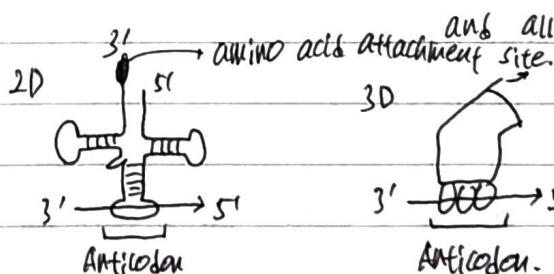
- new combinations of exons and proteins occasionally beneficial variant might arise

Translation - RNA directed synthesis of polypeptide (mRNA to protein)

mRNA move through ribosome, codons translated into amino acids.

translator (interpreter) : tRNA - each type with specific anticodon at one end.) transfer amino acid to and corresponding amino acid at other end.) growing polypeptide in ribosome

tRNA : single RNA strand, about 80 nucleotides long. - some complementary stretches can bond each other



ribosome add amino acids onto growing polypeptide.

tRNA transcribed from DNA template, reusable.

Accurate translation require 2 instances.

① tRNA must carry that amino acid, no other to ribosome.

- **Aminoacyl-tRNA synthetases** : 20 different synthetases, one for each amino acid

: it joins given amino acids to appropriate tRNA.

if synthetase catalyzes covalent attachment of amino acid to tRNA by hydrolysis of ATP

=> make aminoacyl tRNA (charged tRNA)

② Pairing of tRNA anticodon with appropriate mRNA codon.

↳ mRNA codon 3개 중 2개만 61개의 tRNA가 있을 수 있음. but bacteria only 45개 있음.

→ possible because rule of base pairing between third nucleotide base of codon and corresponding base of tRNA anticodons are relaxed compare to other codon positions.

It's "wobble": flexible base pairing at this codon position.

Structure and function of Ribosome.

bacterial ribosome & eukaryotes ribosome은 비슷하지만 다르다. → tetracycline, streptomycin are used to combat bacterial infection (affect only on bacterial ribosome)

Ribosome facilitate coupling tRNA anticodons with mRNA codons.

Ribosome = Proteins + rRNAs (ribosomal RNA)

→ in eukaryotes, subunits are made in nucleolus, completed ribosomal subunits exported via nuclear pores to the cytoplasm.

both in bacteria and eukaryotes, large and small subunit join only when attach to mRNA molecule

Structure of ribosome. (mRNA itself has binding site for ribosome)

Ribosome: binding site for mRNA + 3 binding sites for tRNA.

P site (peptidyl-tRNA binding site): hold tRNA carrying growing polypeptide chain.

A site (aminoacyl-tRNA binding site): hold tRNA carrying next amino acid to be added to chain.

E site (Exit site): discharge tRNA, leaves the ribosome from E site.

CARBOXYL END (C-terminus) of growing polypeptide or new amino acid add.

polypeptide exit tunnel 통해서 나가면서 3'에서 다 만들어지면 거기서 나옴.



Ribosome only tRNA가 들어있음. Protein은 tRNA의 shape change를 assist 해줌.

↳ catalyst of peptide bond formation, main constituent of A, P site and interface between two subunits.

Building polypeptide → 3 stages: initiation, elongation, termination. anti of AUG (mRNA)

Initiation: small subunit binds to both mRNA and initiator tRNA, carry methionine.

[bacteria - small subunit can bind two in either order

eukaryotes - small subunit + tRNA bind to 5' cap of mRNA and move (scan) downstream

along mRNA until it reach AUG (start codon) - initiator tRNA then hydrogen bond.

↳ AUG signal start of translation - important because it establish

codon "reading frame"

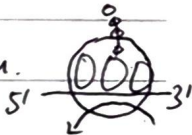
Union of mRNA, initiator tRNA, small ribosomal subunit $\Rightarrow$ followed by attachment of large subunit.
 $\downarrow$
 $\Rightarrow$ completing "translation initiation complex" GTP (energy) req.

initiation factor: Proteins bring all these component together.

이때, initiator tRNA는 P site에 들어간다 (A site)

Polypeptide always synthesized in one direction, from initial methionine at amino end (N-terminus) toward final amino acid at carboxyl end (C-terminus)

Elongation: Amino acids added to previous amino acid at C-terminus of growing chain.



elongation factor: several proteins involve in addition.

① Codon recognition - A site $\geq$ aminoacyl-tRNA가 들어옴. 이때, hydrolysis of GTP increase accuracy and efficiency.

② Peptide bond formation - large subunit의 rRNA가 catalyze formation of peptide bond. Polypeptide가 A site에 옮겨 붙음.

③ translocation - $A \rightarrow P$, $P \rightarrow E$ (방출) 이때 GTP hydrolysis 필요.

Termination.

mRNA.

① Ribosome의 stop codon (UAG, UAA, UGA) 만났을 A site accept "release factor" - Protein shape like tRNA.

② "release factor" promote hydrolysis of bond between tRNA in P site and last amino acid of polypeptide, freeing polypeptide from ribosome through Exit Tunnel in P site.

③ Two ribosomal subunits and other components dissociate by (GTP hydrolysis $\times 2$)

Completing and targeting Functional proteins.

Protein Folding and Post-translational Modification.

- Coil and fold as consequence of its amino acid sequence. (Primary structure $\rightarrow$ Secondary $\rightarrow$ tertiary)

$\approx$, Gene determine primary structure, which in turn determines shape.

- Post-translational modification. - Chemically modified by attachment of additions.

- Enzyme may remove amino acids from leading (amino) end.

- May enzymatically cleaved into pieces.

- Two or more polypeptides may come together (ex. Hemoglobin)

targeting polypeptides to specific locations.

→ Ribosome of ER is free / bound org!

Polypeptide synthesis always begin in cytosol (free ribosome)

"Signal peptide" (sequence of about 20 amino acids at or near N-terminus) recognized as it emerges from ribosome by Protein-RNA complex "Signal-recognition particle" (SRP)

→ it escort Ribosome to receptor protein built into ER membrane. → signal peptide가 붙어있는 것임

→ SRP leaves, polypeptide synthesis resume (ribosome of ER membrane on bound 된 채로)

Simultaneous translocation across membrane and enter ER lumen.

→ Ribosome 부터 ER membrane protein of further in the chain's amino acid sequence cause to remain embedded in ER membrane.

target of ER membrane system of ER mito, chloro, nucleus, others of translation completed in cytosol. and imported into organelle. (only signal peptides &)

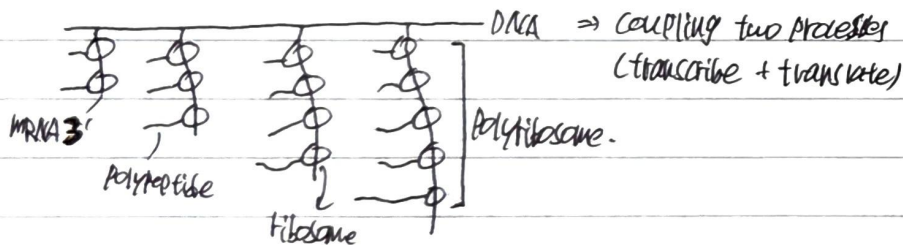
Making Multiple polypeptides in bacteria and Eukaryotes.

Multiple ribosomes translate mRNA at the same time. (single mRNA is used to make many copies of

⇒ polyribosomes (polysomes)

polypeptide simultaneously)

bacterial cell ⇒



Mutation of one or few nucleotides can affect protein structure and function.

Point mutation: change in single nucleotide pair of gene. ex. sickle-cell disease

Small-scale mutation - single nucleotide-pair substitution.

familial cardiomyopathy. 아픈 심장병

- nucleotide pair insertion, deletion.

- substitution (replacement of one nucleotide pair)

영양 결핍 : 3' CCA 5' → 3' CCA 5' stops glycine 184 → "silent mutation"

Missense mutation: substitutions that change one amino acid to another one.

little effect to protein or major change to protein

↓
changes in crucial area of protein.

Nonsense mutation: change codon of amino acid into stop codon.

make translation terminates prematurely (mostly nonfunctional protein)

- Insertion / deletion $\Rightarrow$ disastrous effect

Frameshift Mutation : alter reading frame when inserted / deleted nucleotides is not multiple of three. (mostly nonfunctional)

- causing immediate nonsense (stop)

- causing extensive missense (ending much later)

3-nucleotide-pair deletion : no frameshift but one amino acid missing (insertion) (added)

coding region ~~변화~~ ~~변경~~ affect how a gene express 등 과정의 영향을 받을 수 있다.

New Mutations and Mutagens.

Spontaneous Mutation : ~~외부~~ Physical, chemical 자극 없이, 세포 분열, DNA 복제시 자연적으로 발생하는 유전자 변화. (Per 10^{10} nucleotides change is passed to next generation.

Mutagens : Physical, Chemical agents that cause mutations. ex) Xrays, UV light, ...

CRISPR to edit genes and correct Disease - causing Mutations.

CRISPR-Cas9 System.

[↓]
bacterial protein that help defend bacteria against viruses

Cas9 : Nuclease. cut any sequence to which it is directed to target by Guide RNA that binds. Cutting DNA sequence that is "complementary" to Guide RNA.

Cas9-Guide RNA complex 통하여 Cas9 효소 (cut both strands of target DNA)

$\Rightarrow$ broken ends of DNA trigger DNA repair system. = =

broken strands of DNA repaired by cell in one of 2 ways

① With no Normal gene for template

- Scientist can disable (knock out) target gene to study its normal function.

No template provided, and repair enzymes insert or delete "random" nucleotides

Making gene nonfunctional

② With Normal gene for template

- If target gene has mutation, can be repaired by providing normal copy of gene.

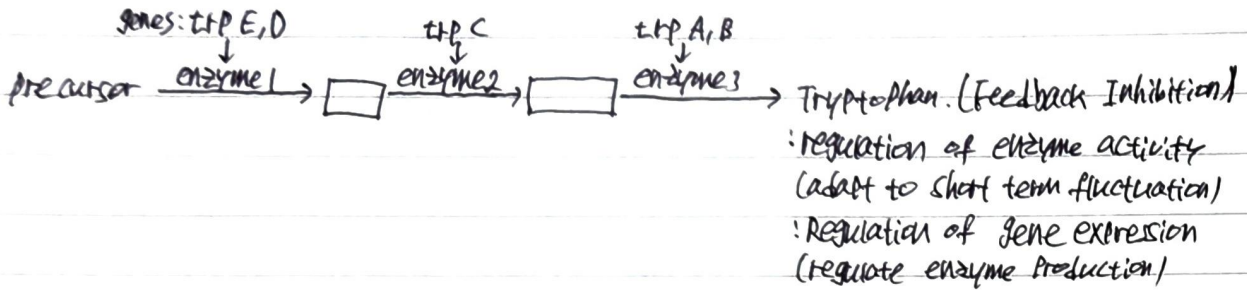
Repair enzyme use normal gene as template and synthesize correct gene sequence

A gene is a region of DNA that can be expressed to produce a final functional product that is either a polypeptide or an RNA molecule.

18. Control of Gene Expression.

Bacterial cells

Regulation of metabolic pathway. (E. coli's pathway for tryptophan synthesis)

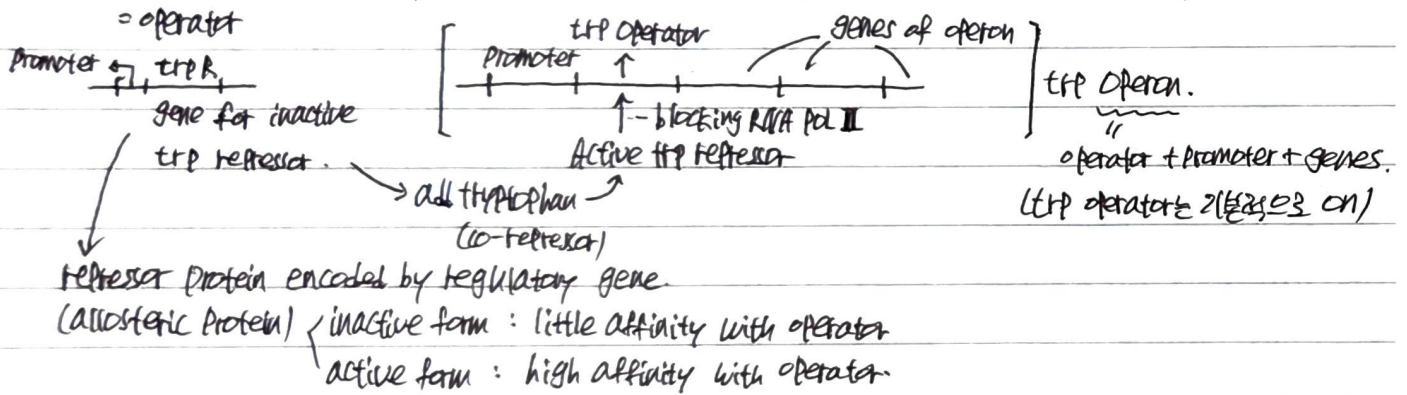


operons.

예) E. coli tryptophan synthesis operon single promoter of 5' genes all serve.

예) long mRNA code for 5 polypeptides $\Rightarrow$ advantage to grouping genes of related function. into one transcription unit.

Single on-off switch control whole cluster of functionally related genes. (coordinately controlled)



two types of negative gene regulation.

repressible operon: transcription usually on, can be inhibited (repressed)

inducible operon: transcription usually off, can be stimulated (induced)

ex) lac operon: disaccharide lactose by β -galactosidase. $\text{lactose} \xrightarrow{\beta\text{-galactosidase}} \text{glucose} + \text{fructose}$

regulatory gene lacI make active lac repressor.

With inducer (Allolactose), became inactivated $\rightarrow$ lac operon genes transcription $\uparrow$ (ex. β -galactosidase ...)

isomer of lactose.

enzymes of lactose pathways are referred to "inducible enzyme" because their synthesis is induced by chemical signal. $\leftrightarrow$ Repressible enzyme

usually for catabolic pathway (분해작용)

$\neq$ + negative control of gene.

- raw materials 을 보존하기 위함

$\Rightarrow$ operons switched off by active form of respective repressor protein.

Positive gene regulation : regulatory protein interacts directly with genome to increase transcription.

E. coli : $\left\{ \begin{array}{l} \text{glucose + lactose - only use glucose} \\ \text{X glucose, only lactose - use lactose} \end{array} \right.$ by cyclic AMP (cAMP)
 $\Rightarrow$ accumulated when glucose scarce

CRP (cAMP receptor protein) : regulation protein that is activator (bind to DNA and stimulate transcription of gene)

cAMP + inactive CRP $\rightarrow$ Active CRP (bind to CRP-binding site upstream end of lac promoter)

: This attachment increase affinity of RNA polymerase for lac promoter.

Glucose ~~glucose~~ cAMP $\downarrow$ - CRP inactivate - lac operon proceed low level even lactose present.

$\therefore$ lac operon is under dual control : $\left\{ \begin{array}{l} \text{negative control by lac repressor} \\ \text{positive control by CRP} \end{array} \right.$

$\Rightarrow$ transcription on/off : by allolactose $\left\{ \begin{array}{l} 0 : \text{inactive lac repressor, operon on} \\ X : \text{active lac repressor, operon off} \end{array} \right.$

transcription rate : by whether cAMP binds to CRP $\left\{ \begin{array}{l} \text{binds : rate } \uparrow \\ X : \text{rate } \downarrow \end{array} \right.$

Eukaryotic gene expression.

Differential Gene expression.

Almost all cells in multicellular organism contain identical genome

$\rightarrow$ Subset of genes expressed in each cell type / housekeeping genes : expressed by many cell types

others : uniquely expressed genes carry out their specific function.

$\rightarrow$ Difference between cell type = different gene expression

Control points of Eukaryotic gene expression.

Regulation of chromatin structure.

Histone Modifications and DNA Methylations.

Histone tails - N-terminus of histone protein in nucleosome protrude outward.

Accessible to various modifying enzymes : catalyze addition or removal of specific chemical groups

Histone acetylation : addition of acetyl group to histone tail - promote transcription by opening up chromatin structure.

Histone methylation : addition of methyl group to histone tail - reduce transcription by condensing chromatin.

DNA methylation : methylate DNA on certain bases.

ex. Inactivated mammalian X chromosomes are more methylated than active one.

⇒ once methylated, methylate patterns passed on to daughter cells.

Genomic imprinting in mammals: methylation permanently regulate expression of either maternal or paternal allele.

Epigenetic Inheritance: Inheritance of traits transmitted by mechanisms not involving nucleotide sequence itself (유전자 다른 것들처럼)

- mutation in DNA or modification to chromatin은 영구적 X.

responding more rapidly to environmental conditions

ex) mouse mutant (agouti mutant): mother have different diets { with methyl group: brown fur (normal)
without methyl group: yellow fur (abnormal)
ex) Dutch hunger winter. ∴ 환경에 반응하는 유전자 발현 다른 수 있다.

Regulation of Transcription initiation.

Eukaryotic gene transcription. - "transcription initiation complex" assemble on promoter.

이후 RNA POL II Proceed, transcribe gene. → pre-mRNA → RNA processing (5' cap, poly-A tail 추가, intron 제거)
→ matured mRNA.

Control elements: segment of noncoding DNA that is binding sites for proteins called transcription factors (bind to control elements and regulate transcription)

Role of General and specific transcription Factors.

General transcription Factors: act at promoter of all genes.

Specific transcription factors: act at control elements that may close to, farther away from ~~transcription~~ Promoter.

TATA Box 같은 다른 Proteins, 다른 transcription factor like RNA pol II 이 함께 한

Protein-Protein interaction 중요! - complete initiation complex assemble after polymerase move.

결과로, Interaction of General transcription factors and RNA pol II with promoter leads to "low rate" initiation and production of few RNA transcriptions.

→ high level transcription of these particular genes depend on interaction of control elements with another set of proteins: specific transcription factors.

Enhancers and specific transcription factors - proximal control elements (close to promoter)

- Distal control elements (enhancers)

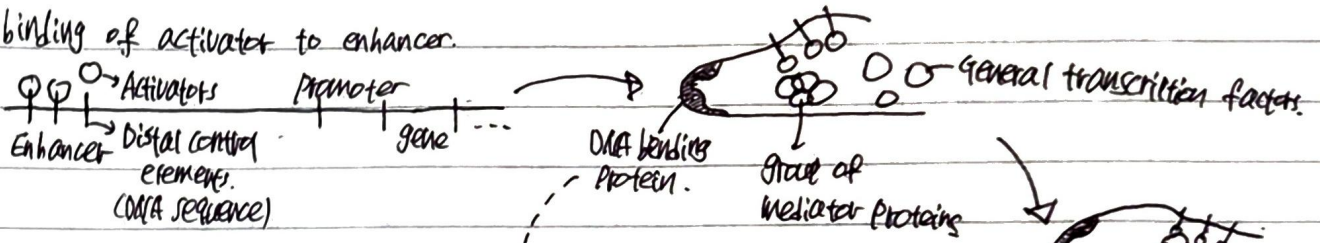
→ upstream 또는 downstream에 위치, or intron에.

each enhancers associated with only that gene.

rate of gene expression (increase by activator, decrease by repressor) (다른 specific transcription factor)

Domain { DNA binding domain - commonly found in large num of transcription activators
part of protein's 3 dimensional structure that binds to DNA.
one or more activation domains - It binds other regulatory proteins or component of transcription machinery
facilitating protein-protein interactions.

binding of activator to enhancer.



DNA bending protein bring the bound activators closer to promoter.

Activators bind to Mediator proteins and general transcription factors.

= active transcription initiation complex.

function of repressors - repressors bind directly to control elements : blocking activator binding.

- interfere with activator itself : X bind DNA.

- affect chromatin structure. ex) remove acetyl groups from histone.

→ reduce transcription (silencing)

each cell type contains different group of transcription activators.

- control elements 전체 종류 개수 ↓ but 조합의 의해 다양한 gene 의 transcription control.

Coordinately controlled genes in Eukaryotes (not by operon)

Eukaryotic genes that co-expressed : scattered over different chromosomes

- have specific combination of control elements (Transcription activator)

⇒ Promoting simultaneous transcription of gene - NO matter where they are.

OR by chemical signals from out of cell. (Steroid Hormone)

Nuclear architecture and gene expression.

Territory of each chromosome, divided into region of chromatin loops.

Loops of chromatin, extends from that chromosomal territory into specific sites in nucleus.

Transcription factory - Different loops may congregate in such sites (rich in RNA Pol and transcription associated proteins)



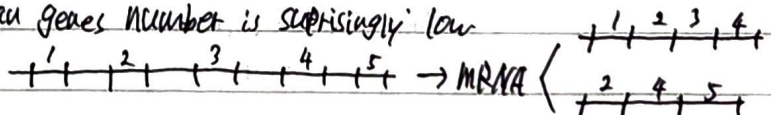
Post-transcriptional Regulation : fast respond to environmental changes.

RNA Processing : alternative RNA splicing - depend on which RNA segments treated as exons, introns.

Regulatory proteins specific to cell type control intron/exon choices by bind to regulatory sequence within Primary transcript.

⇒ This is reason why human genes number is surprisingly low

ex) Primary RNA transcript → mRNA



Initiation of translation and mRNA Degradation.

Some mRNA, initiation of translation blocked by regulatory proteins - bind to specific sequences or untranslated region (UTR) at 5', 3' end. → prevent attachment of ribosome.

All mRNAs in cell's translation may regulated simultaneously - global control.

ex) starting translation of mRNAs that stored in eggs.

After fertilization, translation triggered by sudden activated of translation initiation factors
Lifespan of mRNA.

Bacterial cells: few minutes later, degraded by enzymes - 빠르게 분해될 수 있음

Some mRNA in Multicellular Eukaryotes: much longer.

→ 3' end UTR에 mRNA 생길 때 어떤 영향을 Nucleotide sequence에 따라서 다름.

Protein Processing and degradation. (after translation)

↳ for functional protein molecules ex) regulatory proteins are activate/inactivate by reversible addition of phosphate groups.

by selective degradation, protein degradation (function time)

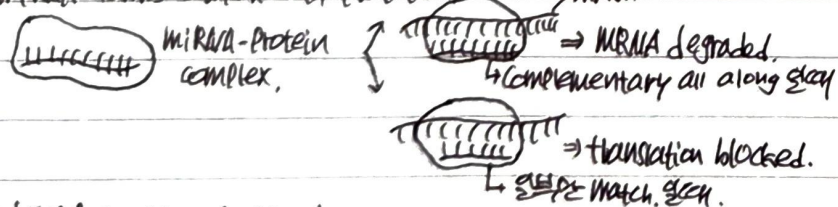
- protein of Ubiquitin (small protein) 통해 protein destruction by Proteasome recognize Ubiquitin tagged proteins and degrade them.

Noncoding RNA (ncRNA) play multiple roles in controlling gene expression.

Effect on mRNAs by microRNAs and small interfering RNAs.

2 types of ncRNAs: microRNA (miRNA) - small (21 nucleotide size), single stranded RNA. bind with mRNA.
longer RNA precursor processed by enzymes to miRNA.

miRNA forms complex with proteins.



: small interfering RNAs (siRNAs)

miRNA와 siRNA blocking gene expressions (RNA interference) RNAi

miRNA와 siRNA의 차이점 difference in structure of precursor. (siRNA double stranded RNA / miRNA single stranded RNA)
subtle

Chromatin Remodeling and Effects on Transcription by ncRNA.

ncRNA can cause remodeling of chromatin structure.

이것은 어떻게?

ex. Piwi-interacting RNAs (piRNAs) : induce formation of heterochromatin blocking expression of parasitic DNA in genome known as transposons /

ex. long noncoding RNAs (lncRNAs) : $\frac{5\%}{\text{유전자 발현}} > \frac{1\%}{\text{ex}}$ lncRNAs bind back to and coat chromosomes

leads to condensation of entire chromosome into heterochromatin

Program of differential gene expression leads to different cell types in multicellular organisms

zygotes (fertilized egg) $\rightarrow$ cell division $\rightarrow$ cell differentiation $\rightarrow$ morphogenesis (shape of organism)

$\rightarrow$ not randomly distributed but are organized into tissue and organs in 3-dimensional arrangement.

결론 differential gene expression results from genes being regulated differently in each cell type.

$\Rightarrow$ how different sets of activators come to be present in two cells?

1. cells that arise from early embryonic mitosis develop the differences that start each cell along its own differentiation pathway.

2. Cellular differentiation leads to one particular cell type.

Cytoplasmic determinants and Inductive Signals

Two source of information, used to varying extents in different species, tell cell which genes to express at any given time during embryonic development.

1. Cytoplasmic determinants in the egg. (containing RNAs and proteins encoded by mother's DNA)

Cytoplasm of unfertilized egg : not homogeneous (distributed unevenly)

each fertilize 되면 distribute zygote's cytoplasm into separate cells.

$\rightarrow$ After fertilize + mitotic division, cell nuclei of embryo exposed to different combination of cytoplasmic determinants and express different genes

2. Induction by nearby cells : signals conveyed to embryonic cell from other embryonic cells in vicinity

$\rightarrow$ It cause changes in target cells. Process called "Induction"

Sequential Regulation of gene expression during cellular differentiation

Point of determination : Point of which embryonic cell is irreversibly committed to become particular cell type.

과정 differentiation : Process of cell attains its determined fate.

First sign of differentiation = appearance of mRNAs for 'tissue-specific protein'

Later, differentiation is observable by microscope as changes in cellular structure.

In molecular level, different sets of genes sequentially expressed when their precursor divide.

In fully differentiated cell, transcription remains principal regulatory point for maintaining appropriate gene expression.

⇒ Differentiated cell = specialist at making tissue-specific proteins

ex) Skeletal muscle cell: develop from embryonic precursor cells $\xrightarrow{\text{particular condition}}$ Myoblast (2B39N15)

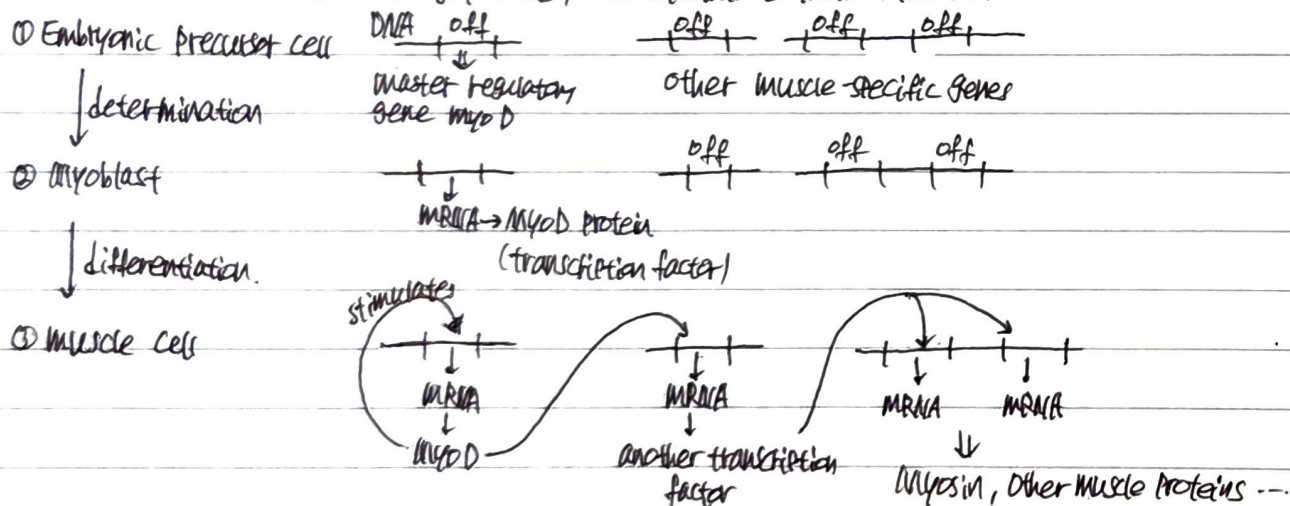
Myoblast start to churn out large amount of muscle-specific proteins.

molecular level during muscle cell determination → master regulatory genes.

⇒ Protein products commits cells to becoming specific cells.

ex) MyoD gene make MyoD Protein - can change "Some of" fully differentiated non muscle cells into muscle cells $\downarrow$ But need combination of regulatory proteins etc.

MyoD Protein: transcription factor bind to specific control elements in enhancers of various target genes, and stimulate their expression.



Pattern formation: setting up body plan (*Drosophila melanogaster*)

Cytoplasmic determinant + inductive signals both contribute to stationary organizing tissues and organs of the organism in their characteristic places = pattern formation.

3 major body axes (x, y, z) → set up before organs appear.

"molecular cues" that control pattern formation ⇒ "positional information" provided by

→ Life cycle of *Drosophila*.

Cytoplasmic determinant + inductive signals.

Cytoplasmic determinants that localized in unfertilized egg provide positional information.

Developing egg with nurse cells (nutrient, mRNA ... supplied to egg) → fertilized egg and laid →

Segmented embryo → larva → pupa → adult.

Genetic analysis: "homeotic gene": regulatory genes that control pattern formation in the fly (25 of 41 Head, Thorax, Abdomen 3 5/21/11)

Axis establishment

- cytoplasmic determinant : initially establish axes. → These substances are encoded by genes of mother ⇒ "maternal effect gene"

→ 동소 주변에서 세포 분열을 정하는 신호 분자. Also called "egg-activity genes"

Bicoid : morphogen that determines head structure.

- bicoid : one of maternal effect gene determine body axis (anterior end을 결정)

Morphogen gradient hypothesis - mother's bicoid gene is essential for setting anterior end. Concentrated at anterior end.

bicoid mRNA highly concentrated at extreme anterior end of mature egg.

If egg fertilized, mRNA translated to protein, diffuse from ant → posterior.

[정자의 nurse cell 및 여정에서 bicoid transcript to bicoid mRNA → Egg로 이동 및 anterior 쪽으로]

→ bicoid RNA is translated when fertilized → 이 단백질이 gradient 형성

Cancer result from genetic changes that affect cell cycle control.

Type of genes associated with cancer

Oncogenes : cancer-causing genes → Proto-oncogenes : code for proteins that stimulate normal cell growth and division.

Epigenetic changes : abnormal chromatin condensation.

Translocation : translocated proto-oncogenes ends up near an active promoter.

Gene amplification : increase number of copies of proto-oncogenes.

Point mutations : mutation in the promoter, enhancer or code sequence

Tumor-suppressor gene → proteins they encode help prevent uncontrolled cell growth.

↳ 이 단백질도 낮은 mutation rates contribute to onset of cancer.

Interference with normal cell-signaling pathways → 2 key genes (has proto-oncogene, p53 tumor suppressor gene)

- ras gene → Ras protein (rat sarcoma) : G protein that relays signal from growth factor receptor on plasma membrane to cascade of protein kinases → cellular response of cell : protein that stimulate cell cycle.

Mutation of ras gene - lead to production of hyper active ras protein that trigger kinase cascade even in absence of growth factor.

- Intracellular signal lead to synthesis of protein that suppresses the cell cycle
- DNA damage is intracellular signal that passed via protein kinases, lead to activate p53.

p53 block cell cycle until damage repaired.

p53 gene = tumor suppressor gene → encodes specific transcription factor that promotes synthesis of cell cycle-inhibiting protein.

Activated p53 protein : activate p21 → p21 protein halts cell cycle by binding to cyclin-dependent kinase.

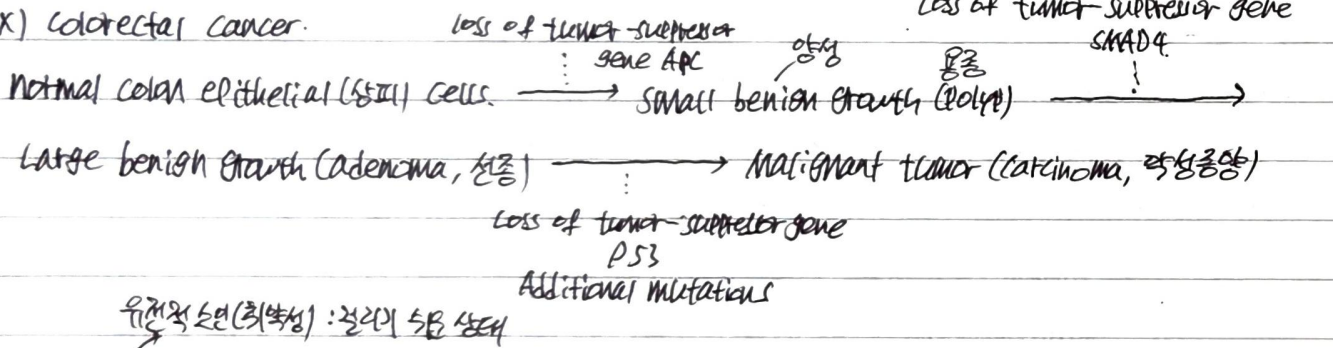
p53 also activate expression of group of miRNAs that inhibit cell cycle.

p53 protein also turn on gene that directly involved in DNA repair.

If DNA damage is irreparable, p53 activate "suicide" gene.

Multistep Model of Cancer Development

ex) colorectal cancer.



Inherited Predisposition and Environmental Factors contribute to cancer.

↳ exposure to DNA damaging agents

The Role of viruses in cancer. → tumor viruses

15% of cancer cases → virus play a role

Virus can interfere with gene regulation in several ways if they integrate their genetic materials into DNA of cell. (Viral integration)

Virus can produce proteins inactivate p53 or other tumor-suppressor ~~genes~~ proteins.

19. DNA Technology

Variable tools for genetic engineering and biological inquiry. { chemical tech enable to identify which of the 4 nucleotide is added. } Minuscule & interesting

DNA sequencing: dideoxy sequencing → sequencing by synthesis (single template strand of each fragment immobilized, and complementary strand synthesized, one nucleotide at a time) →

(amplify) third-generation sequencing → DNA molecule that carry foreign DNA into host cell.
DNA cloning: Plasmid - Gene inserted into plasmid (cloning vector) (Host cell)
→ Recombinant DNA (Plasmid) → 여기 박테리아에 넣어주면 Recombinant bacterium
여기 Cloning 하면 Gene cloning.

⇒ obtain Particular Genes or Proteins expressed from inserted gene.

Using Restriction Enzymes to make Recombinant DNA Plasmid. (cleave sugar-phosphate backbone)

restriction enzymes recognize "restriction site", cutting both DNA strand.

↳ 스스로는 Afla coyl methyl group 추가해서 자신들 "recognize sequence" 이 작용하지 못함.

같은 enzyme 이면 항상 같은 set of "restriction fragments"

Sticky end: short extensions that can form hydrogen bonded base pairs 

둘이 붙으면 DNA ligase & sugar phosphate backbone 연결해서 양쪽으로 만듦

To make sure fragment가 제대로 inserted into plasmid → 다시 같은 enzyme으로 잘라서 gel electrophoresis

Amplifying DNA: PCR (Polymerase chain Reaction) - have high specificity (least 15 nucleotides long Primers)

1. heated to denature (separate) Double strands → 2. cooled to allow binding DNA Primers

→ 3. special DNA polymerase extends primers. (special: 열안타는 enzyme denatured. Pfu polymerase, Taq polymerase)

PCR Primer 가 애초에 designed at each end. restriction site.

⇒ error test: plasmid (with gene of resistance on antibiotic) 과 PCR로 만든 DNA fragment 을 섞어서
잘라 붙여 bacteria에 넣고 antibiotic 넣기. - 이때 PCR에 오류 있으면 die. (Plasmid에 DNA
fragment 연결 안됨) : error free selection.

Expressing cloned Eukaryotic Genes.

Bacterial expression system 으로서 전작 DNA 를 Expression 하는것이 문제.

① Difference in Promoters and DNA control system ⇒ solve by "expression vector" = cloning vector that contains highly active bacterial promoter.

② Eukaryotic Geneon Intron 의 존재 → cDNA (complementary DNA), only have exon 을 활용.

Eukaryotic DNA cloning and Expression system ⇒ Using eukaryotic cell (Yeast cell ...)

- 근데 또 포유동물 cell 과 Yeast cell 차이는 극심하다 함

electroporation: 전기장 보내서 cell membrane on temporary hole 생성후 DNA 삽입 (또는 그냥 주사기로)
Virus 같은 DNA 삽입 infect to cell.

Biologists use DNA technology to study gene expression and function.

Analyzing Gene Expression.

Nucleic acid probe: Synthesized short single strand nucleic acid, complementary to mRNA interest.

In situ hybridization: allows to see mRNA in place in intact organism. (labeled by fluorescent dyes)

RT-PCR (Reverse transcriptase Polymerase chain reaction) → for comparing the amounts of specific mRNA in several samples at the same time.

1. cDNA (complementary DNA) 만들기: Reverse transcriptase로 mRNA를 따라서 상보적인 DNA 가닥 생성
→ mRNA 분해하고 그자리 따라서 상보적 DNA 형성 → double stranded DNA 생성
2. PCR로 수많은 종류의 cDNA 중 원하는 것만 amplify by using specific primer that hybridized. → gel electrophoresis 하면 band 보는데 보면 해당 mRNA가 있었다는 것.

qRT-PCR (quantitative RT-PCR): gel electrophoresis 쓰지 않고 빛을 감지해서 measure PCR product and provide quantitative data.

Identify Networks of gene expression across entire genome.

어떤 gene 이 발현되었는지, 생성된 mRNA를 cDNA로 다시 제작해서 읽어냄 → RNA-seq (Sequencing)

cutted mRNA를 reverse-transcribed into cDNA. → 이를 컴퓨터로 sequencing 해서 전체 sequence mapping
↳ 시퀀싱 장비의 한계, 정확도 향상, 역전사 효소, 정확한 매핑을 위한 것.

- 이 방법은 hybridization 이 기반하지 않아서 knowing genomic sequences 에 의존 X.

다른 방법: DNA Microarray assays. → 각 점의 형광색을 보고 어떤 reverse transcribe 된 DNA 가 어디서 발현되고 있는지 알 수 있다.

Determining Gene function.

in vitro mutagenesis - mutation introduced into cloned gene. it disable (knock out) normal cellular gene (by altering, destroying function of gene product)

Gene drive - engineered new allele, much more highly favored for inheritance than wild type allele.

RNA interference (RNAi) - doesn't alter genome: 특정 mRNA 표적 분해, 번역 차단
→ 비영양만 줄일 뿐 아예 knockout (disable) 은 아님.

Genome-wide association study: 유전물질 희미 위해 자연적으로 유전적 변이 있는 사람들 찾아 씀.

look for genetic markers - DNA sequence that vary in population.

Polymorphism: Variation in coding or noncoding DNA sequences among population.

Single nucleotide polymorphism (SNP): single base pair site variation, found in at least 1% of the population.

detect by microarray assays, RNA-seq, PCR

→ 이 위치로 disease 가 밀어넣어 있음, gene that cause disease locates very close to SNP crossing over 이 disease gene과 SNP 사이에서 거의 발생 X, 한계 유전물질

∴ 해당 SNPs 는 해당 유전병의 표적이 될 수 있다. (genetic marker)

Cloned organisms and stem cells are useful for research.

differentiation 과정 중에 gene loss 발생할까? → If differentiated cell can generate whole organism, X.

Cloning plants - single cell cultures. : Successful cloning of whole plants from single differentiated cell

Plant의 Matured cell can dedifferentiate (Totipotent : 전능성)

Cloning Animals - Nuclear transplantation. : Remove nucleus of egg (enucleated, 핵제거) and replace it with nucleus of differentiated cells.

(Somatic Cell Nuclear Transfer)

Donor level ↑ : lower the Percentage of normal tadpoles.

⇒ Nuclear potential tends to be restricted more as embryonic development and cell differentiation progress

Reproductive cloning of mammals. ex. dolly, a lamb.

Cloned animals of the same species are not always identical.

ex. cat named CC (Carbon copy) - different color by random X chromosome inactivation

⇒ Environmental influence + random phenomena. modification

Epigenetic (후생 유전) differences in clones Animals (DNA 메틸화, 히스톤 아세틸화, noncoding DNA, 리스톤... 아세틸화)

Stem cells of Animals.

Embryonic and Adult stem cells.

Totipotent (전능성) : 전분화 가능
X

- Embryonic stem cell (ES) : Pluripotent (만능성) : 태반 형성 불가, 혼자서 완전한 개체로 성장 불가.

Can differentiate into wide variety of specialized cells.

- Adult stem cell : can generate several defined types. (limited to certain tissues)

Induced Pluripotent Stem cells (iPS) - turn back clock in fully differentiated cells

differentiated cell → ES cell by using modified retrovirus to introduce cloned copies of

4 stem cell master regulatory genes DNA가 아니라 RNA를 넣어, RNA를 DNA로 역전사 하는 virus

→ 이 deprogrammed 된 세포가 iPS cell, but 완전한 ES cell X. (유전자 표현 및 세포 기능에 차이)

유리 모세관 통과.

Practical applications of DNA-based biotechnology affect our lives in many ways

Medical applications : diagnosis and treatment of disease (PCR, labeled nucleic acid probes) + 유전자 발현 분석 가능

Personal genome Analysis : 개인도 질병 예측 가능 by PCR and sequencing for SNP that correlated with disease.

유전자 발현 분석 가능 (예: Mitochondrial DNA, 남자: Y)

Personalized medicine. : Individual's genomic information으로 predict benefit, risk of particular medication (Pharmacogenetics, 약물 유전학)

Human Gene therapy and Gene editing

Gene therapy: introduction of genes into afflicted individual for therapy.

→ 적은 수의 defective gene의 replacement: insert normal allele of defective gene into somatic cells of tissue affected by disorder.

: Permanent 해야 해서 주로 stem cell 포함 tissue에 행한다.

Issue: 어떻게 삽입된 유전자를 조절할 것인가, 삽입으로 다른 것에 영향을 받지 않나.

To avoid complications of using viral vector → direct gene editing by CRISPR-Cas 9

Pharmaceutical Products

✓ Synthesis small molecules for drugs - for Disease that molecular basis is fairly well understood.

ex. 암 치료에 필요한 단백질의 합성을 막는 분자

but 내성 (Drug resistance) 문제: 암세포에서 약물에 내성을 가진 것이 자연선택의 결과로 나타나 진화.

✓ Protein Production in cell cultures: 세포의 단백질을 생산 시스템을 활용, 정제 후 사용 (Insulin, GH, TPA-)

✓ Protein Production by Pharm Animals: use not cell, whole organisms.

transgene - gene that transferred into one organism from another.

egg 세포 from recipient species's female, and fertilized them in vitro (체외)

replicate desired gene from donor organism, fertilized egg에 직접 주입, incorporated.

이후 대리모 (surrogate female)에 이식 → transgenic organism 탄생 (생체 공장. ex. 젖은 약물이 나오게)

Forensic evidence and genetic profiles → determining individual's unique set of genetic markers (genetic profile)

gel electrophoresis + nucleic acid hybridization using markers ⇒ Short tandem repeats (STRs)

⇒ 매우 sensitive: specific region of genome that tandemly repeated units of 2~5 nucleotide sequences

(highly variable from person to person) ⇒ polymorphic

PCR로 STR amplify - fluorescent tag 붙은 primer로 증폭 후 / electrophoresis로 길이 파악

Environmental clean up - chemicals 분해하거나, 분해할 수 있는 능력으로 gene 삽입해서 증

Genetically engineered microorganism

Agricultural Applications - ex. improve agricultural productivity, improve flavor or nutritional value

C₃ rice → C₄ rice, GMOs

20. The Evolution of Genomes

Metastatic tumors 전이성 종양

Human Genome Project fostered development of faster, less expensive sequencing techniques.

Reference genome: full sequence that best represents the genome of a species.

Whole-genome shotgun approach: Cut DNA from many copies of entire chromosome into overlapping fragments short enough for sequencing → clone the fragments in plasmid or other vectors → sequence each fragments → order the sequences into one overall sequence by computer software

———— → — — — — — → —————

Metagenomics: DNA from entire community of species is collected from environmental sample and sequenced.

advantage-ability to sequence the DNA of mixed microbial populations (no need to culture each species separately in lab)

Scientists use bioinformatics to analyze genomes and their functions.

Centralized Resources for Analyzing Genome Sequences.

ex) NLM, NIH, NCBI에 방대한 데이터 - can analyze using software from NCBI → BLAST

by them, Identifying protein-coding genes and understanding their functions.

Gene annotation: To identify all protein-coding genes in the sequence and ultimately their functions.

- Structural annotation: computer에서 pattern (유전자에 있는 코딩을 드러내는 것), ex. start, stop signals, RNA splicing site, ... 또는 이미 알려진 mRNA 패턴을 찾).

Expressed sequence tags (ESTs): 현재 세포 안에서 활발히 만들어지고 있는 mRNA
→ cDNA 합성, cataloged. ⇒ unknown gene을 알 수 있다.

- functional annotation: 이미 알려진 gene과 비교, predicted 한 것과 비교, knocking out 해서 기능 파악...

Understanding genes and gene expression at the system level.

System biology: Proteomics (Proteome: entire set of proteins expressed by cell or group of cells)

↳ Proteins가 언제 어디서 생성되어 어떻게 상호작용하고 기능하는지

Aim to model the dynamic behavior of whole biological systems based on the interactions among system's parts

ex) Gene A, B 둘다 mutate or 둘 중 하나씩만 mutate 해서 예상을 벗어나면

A-B interaction 있다고 분.

Pan-Cancer Atlas: 암 발생 기원 패턴과 발암 경로로 통합 분석, 서로 다른 암이라도 동일한 패턴이나 분자적 특성을 가질 수 있음을 알고, 암종 불명 항암제 처방기 위한 기반

Genomes vary in size, number of gene, and gene density.

tandemly 3, 4번으로 반복되는

genome size만으로 아무것도 알 수 없다.

Number of genes : human ↓ 이유 - extensive alternative splicing of RNA transcripts.

Post-translational modifications (cleavage, addition of carbohydrate groups -)

miRNA 같은 regulatory RNA의 작용.

Gene density and Noncoding DNA (Gene per Mb (million base pair)) : intron의 존재, regulatory sequences, noncoding DNA, repetitive DNA.

Multicellular eukaryotes have a lot of noncoding DNA and many multigene families

unique noncoding DNA : gene fragments + pseudogene (유전자) → accumulates mutations that no longer produce functional proteins.

(보아 갖다든 뜻)

repetitive DNA : DNA 대부분 차지, but Junk DNA 처럼 high level of sequence conservation than exon

Transposable (전이성) Elements and Related Sequence

(전이성)

Transposable elements : DNA that can move from one location to another within genome

X entirely detach from DNA, original and new DNA site brought very close together by bending DNA. by enzyme or other proteins.

Movement of Transposons and Retrotransposons.

Eukaryotic transposable elements { Transposons : DNA를 Cut-Paste or copy-paste.

Retrotransposons : DNA → RNA → DNA → Paste
reverse transcriptase

Sequences related to Transposable elements → dispersed copies are similar but not identical.

→ retrotransposon.

lose ability to move altogether : related sequences.

Alu elements : large portion of transposable element-related DNA, consist of family of similar sequences transcribed into RNA, and some help regulate gene expression

L1NE-1 (L1) : retrotransposon; crucial for development of early embryos.

→ 대부분의 transposable elements는 단백질을 만들지 않는다는 점에서 기능적이지 않기에 noncoding DNA category.

Other repetitive DNA, including simple sequence DNA (not related to transposable elements)

Probably arisen from mistakes during DNA replication or recombination.

원래는 duplication of long stretches of DNA. / 또는 simple sequence DNA (many copies of tandemly repeated short sequences) ex. GTTAC의 반복.

한개 2~5 nucleotides 단위면 STR (short tandem repeat). 사람마다 반복횟수 차이 매우 뚜렷.

대부분 telomere, centromere에 분포.

"genetic profile (유전자 지문)"

이것 때문에 DNA 분석 활용

Genes and Multi-gene Family.

Gene related DNA : exon + intron + regulatory sequence.

- Unique sequence to species 안됨. 나머지 : Multi-gene families : collection of two or more identical or similar genes.

Identical : ex) family of identical DNA sequences that each include genes for 3 largest rRNA.
~~~~~ ~~~~~ ~~~~~ ... → 같은 ribosome 만들 수 있는 이유.

NonIdentical : ex) two related families of genes that encode globins. ( $\alpha$ ,  $\beta$  globin)

Various forms of  $\alpha$ ,  $\beta$  globins : 변하는 환경에 적응 하기 함.

Duplication, Rearrangement, Mutation of DNA contribute to genome evolution.

Duplication of entire chromosome sets : Failure to separate homologs during meiosis I. (Polyploidy, 15%)

Alterations of chromosome structure

→ rarely facilitate evolution of gene

ex) fusion of two ancestral chromosomes in chimpanzee (L2, L3) → human chromosome 2.

Chromosome 2 on sequence for telomere-like 3' extra, unusual centromere-like 4' 포함.

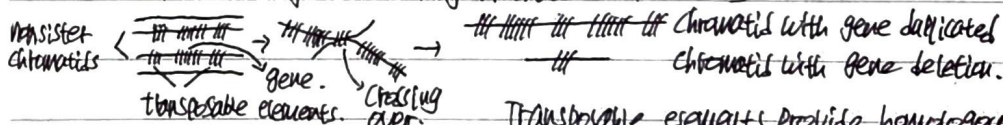
→ could still normal, mutates can mate and produce offspring? - would have two non-equivalent sets of chromosomes → If it make meiosis impossible, lead to separate species.

Medical 3, 3'는 frequently break and rearrange 2'는 point 돌 변 : Hot spots.

→ associated with congenital disease (선천성)

Duplication and Divergence of Gene-sized Regions of DNA

By unequal crossing over during Prophase I of meiosis



Transposable elements provide homologous site : non-sister chromatids can cross over.

slippage : template (주형) shifts (오르 내리) respect to the new complementary strand.

→ part of template strand is either skipped by replication machinery or used twice as template

Simple sequence DNA 여러 종 있다 : globin family

Evolution of genes with related functions : Human globin genes

Ancestral globin gene → duplication → mutation in both copies  $\alpha$   $\beta$  → transposition to different chromosomes

→ further duplication and mutations :  $\alpha$  globin gene family on 16  
 $\beta$  globin gene family on 11.

Evolution of genes with Novel Function (신기능 '기능')

ex) gene for lysozyme and  $\alpha$ -lactalbumin (우유 치즈 만들기 위해)

Lysozyme gene duplicated, one of them evolved into gene of  $\alpha$ -lactalbumin (milk production)



Rearrangement of parts of Genes - Exon duplication and Exon shuffling.

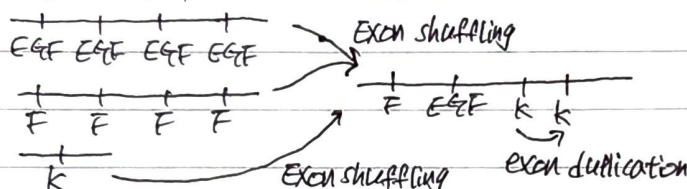
augment 강화, 확장  
owe (기원하다, 의존하다)  
underscore 강조하다

- existing DNA sequence of rearrangement & genetic evolution > 10.

ex) extracellular matrix protein, collagen encoding gene.

exon shuffling (owing to errors of meiotic recombination) → lead to new proteins.

ex) gene for tissue plasminogen activator (tPA) - It helps control blood clotting : 4 domains of 3 types.



How Transposable Elements contribute to genome Evolution.

- Transposable elements of similar sequence scatter : facilitate recombination between nonhomologous chromosomes by providing homologous region for crossing over.

- Transposable elements Jump into Protein-coding sequence, regulatory sequence. ex) Alu transposable elements

- Transposable elements may carry group of genes ex)  $\alpha_1, \beta$  globin gene family.

exon of intron이 끼면 Protein have new domain ⇒ new Protein.

Comparing genome sequences provides clues of evolution and development.

ARB 더 비슷하면 more closely related.

- Comparing distantly related species : determining which gene remained similar can help clarify evolutionary relation ship  
ex) Yeast gene 47% can be replaced by corresponding human gene : common origin & 2H.

- Comparing closely related species : only small number of gene differences are found - Phenotypic difference.

→ help answer what genomic information defines human or chimpanzees.

인간에서 빠르게 evolving 하는 것들 - genes that code for transcription factors ex) Fox P2 (Vocalization and speech)

- Comparing genomes within a species.

대부분 Human's diversity seems to be in the form of SNPs (Single nucleotide polymorphisms)

SNP : single base-pair sites where genetic variation is found in at least 1% of population

It occurs on average about once in 100-300 base pairs

CNVs : copy number variants 유전자 개수 차이, SNPs PH 변이, CNVs 유전자 증감, 여러개의 copy, deletion

CNV, SNP, STR... : useful genetic markers for studying human evolution.

more likely to have phenotypic consequences and role in disease and disorder.

Widespread conservation of developmental genes among animals

homeotic genes (called Hox gene in animals) - encode transcription factor that regulate gene expression and specify body segments in fly  
include 130 nucleotide sequence Homeobox - codes for 60 amino acid Homeo domain in encoded proteins  
→ Vertebrate, Invertebrate 둘다 유사한 nucleotide sequence / Homeobox containing sequence & Plan. Yeast animals & 2H

homeobox encoded homeodomain is the part of protein that binds to DNA when protein function as transcription factor.

Elsewhere in protein, domains that are more variable interact with other transcription factors like enhancers. Different combination of homeobox genes are active in different part of embryo.