Chapter 4

Expression of Genetic Information

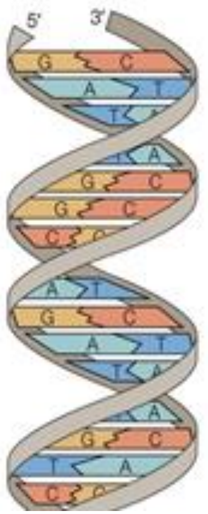
목 차

1. 중심 원리 (Central Dogma)

Central Dogma

by F. Crick

DNA → RNA → Protein (단백질)



4 종류의 염기로 구성

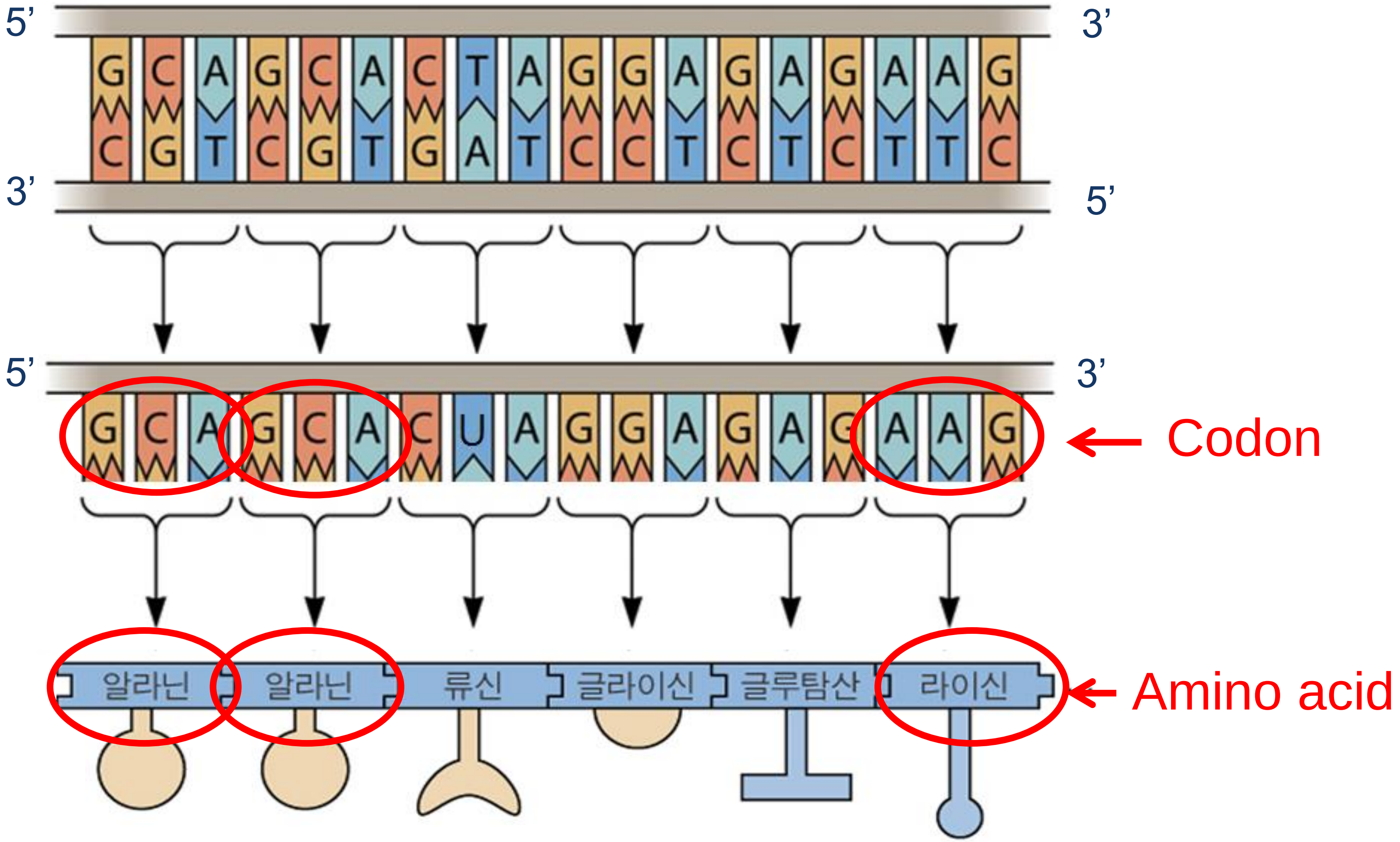
20 종류의 아미노산으로 구성

Central Dogma

DNA	RNA	Protein **(단백질)**
(4개 염기)	(4개 염기)	(20개 아미노산)
A, T, G, C	**U, A, C, G**	

단위암호당 염기의 개수	표시 가능 아미노산 개수
1 (A, T, G, C)	4
2 (AA, AT, AG,…)	4 x 4 = 16
3 (AAA, AAT, AAG,…)	4 x 4 x 4 = 64

Genetic Code



DNA
(ATGC)

RNA
(AUGC)

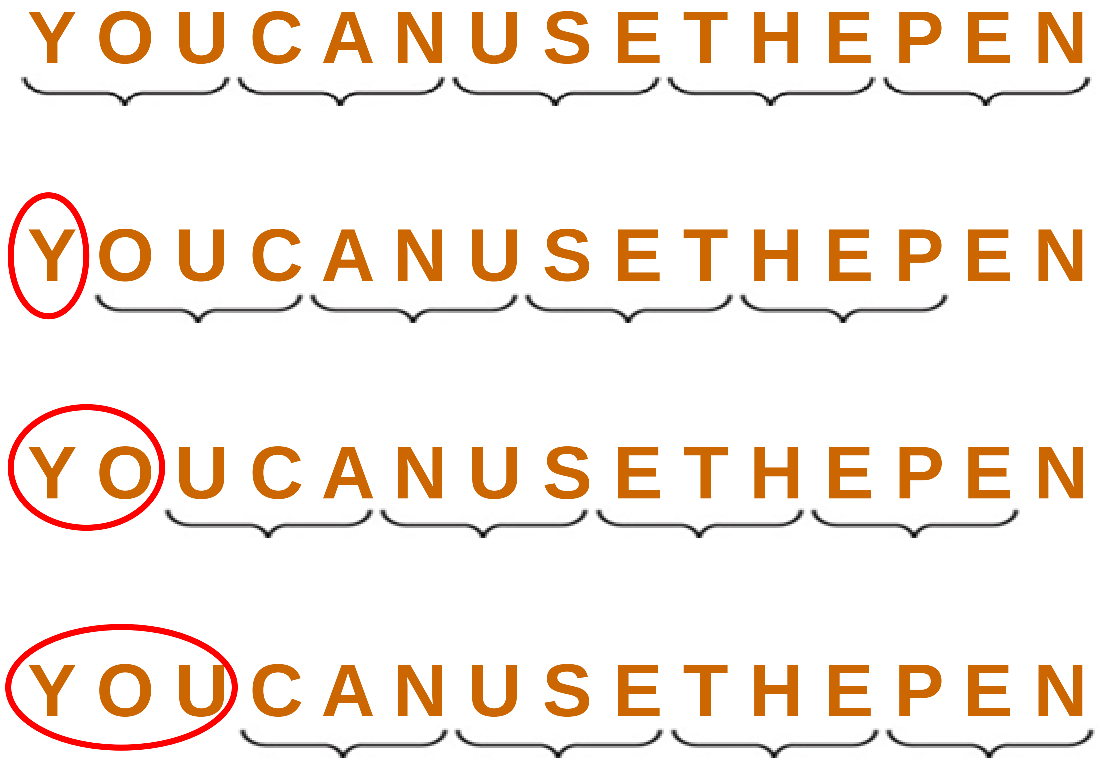
Protein

← Codon

← Amino acid

Triplet of Bases

Triplet



YOUCANUSETHEPEN

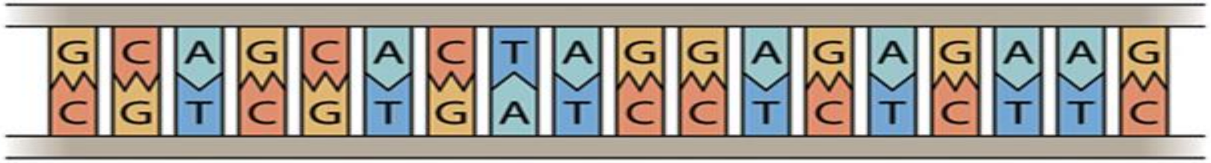
YOUCANUSETHEPEN

YOUCANUSETHEPEN

YOUCANUSETHEPEN

Decoding

<DNA>



<Amino acid>

Ala Ala Leu Gly Glu Lys

<Protein>

Ala – Ala – Leu – Gly – Glu – Lys

<Letter>

Y O U C A N U S E T H E P E N

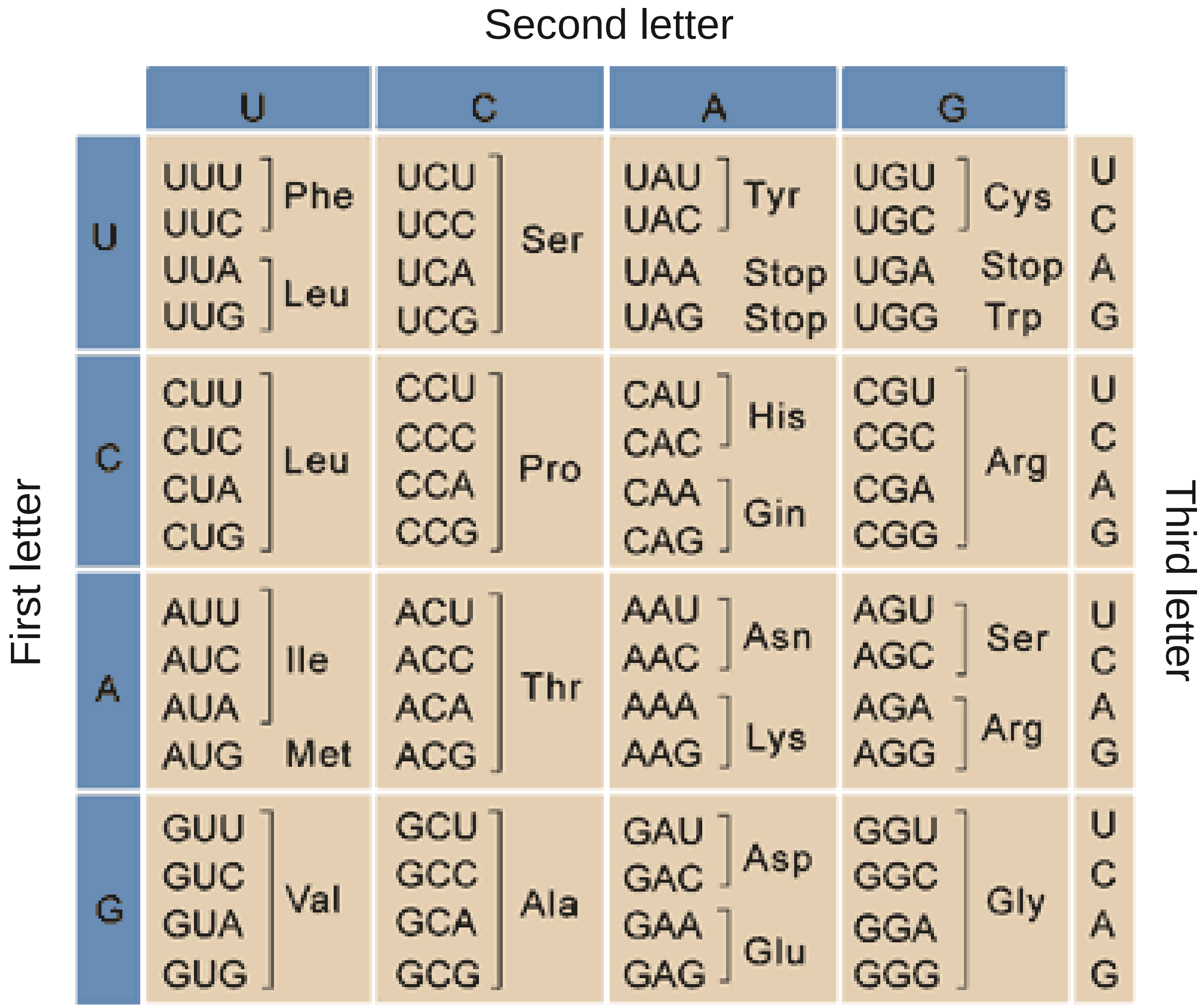
<Word>

YOU CAN USE THE PEN

<Sentence>

You can use the pen.

Genetic Code



Second letter

First letter	U	C	A	G	Third letter
U	UUU Phe UUC UUA Leu UUG	UCU UCC Ser UCA UCG	UAU Tyr UAC UAA Stop UAG Stop	UGU Cys UGC UGA Stop UGG Trp	U C A G
C	CUU CUC Leu CUA CUG	CCU CCC Pro CCA CCG	CAU His CAC CAA Gin CAG	CGU CGC Arg CGA CGG	U C A G
A	AUU AUC Ile AUA AUG Met	ACU ACC Thr ACA ACG	AAU Asn AAC AAA Lys AAG	AGU Ser AGC AGA Arg AGG	U C A G
G	GUU GUC Val GUA GUG	GCU GCC Ala GCA GCG	GAU Asp GAC GAA Glu GAG	GGU GGC Gly GGA GGG	U C A G

※ 출처 : commons.wikimedia.org

RNA Tie Club

(Gamow & Watson)

- 20 members for 20 amino acids

- Designed club tie

  Designed tie pins for 20 amino acids

RNA Tie Club

1) ALA - George Gamow
2) ARG - Alexander Rich
3) ASN - Paul Doty
4) ASP - Robert Ledley
5) CYS - Martynas Ycas
6) GLN - Robley Williams
7) GLU - Alexander Dounce
8) GLY - Richard Feynman
9) HIS - Melvin Calvin
10) ISO - Norman Simmons
11) LEU - Edward Teller
12) LYS - Erwin Chargaff
13) MET - Nicholas Metropolis
14) PHE - Gunther Stent
15) PRO - James Watson
16) SER - Harold Gordon
17) THR - Leslie Orgel
18) TRY - Max Delbrück
19) TYR - Francis Crick
20) VAL - Sydney Brenner

George Gamow

(Physicist)

"Alpher, Bethe, Gamow"
(Paper about the chemical elements in space)

"αβγ" paper (April 1, 1948)

※ 출처 : George Gamow, https://en.wikipedia.org

2. 게놈 (Genome)

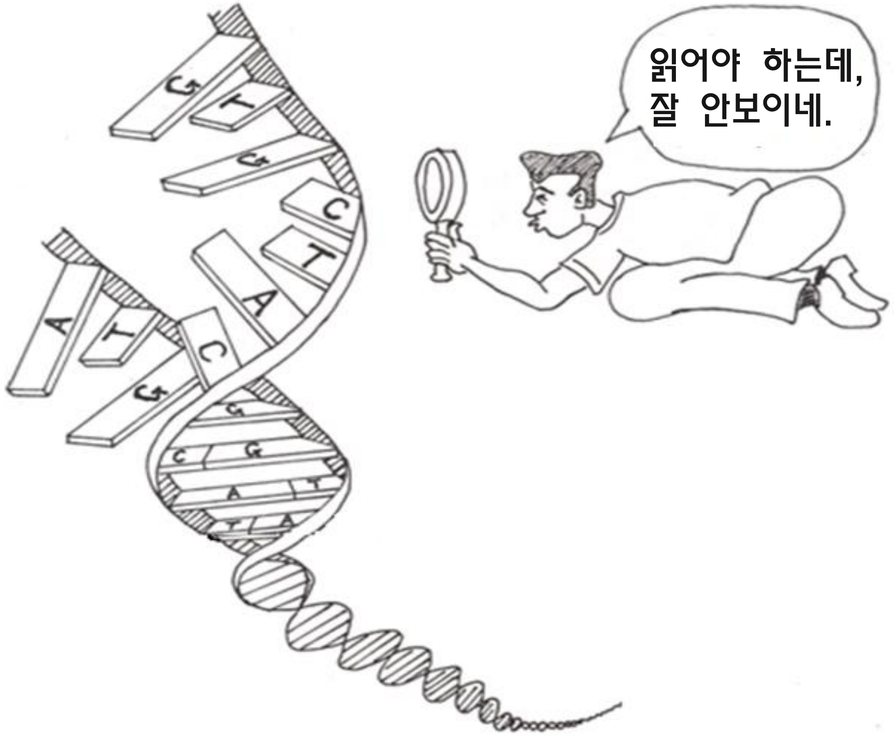
Gene & Genome

- DNA
- 염색체 (chromosome)
- 유전자 (gene)
  - 어떤 단백질의 아미노산 서열을 결정하는데 필요한 완전한 정보를 가진 DNA
- 게놈 (genome, 유전체)
  - 한 생물체 내에 존재하는 유전물질의 완전한 세트

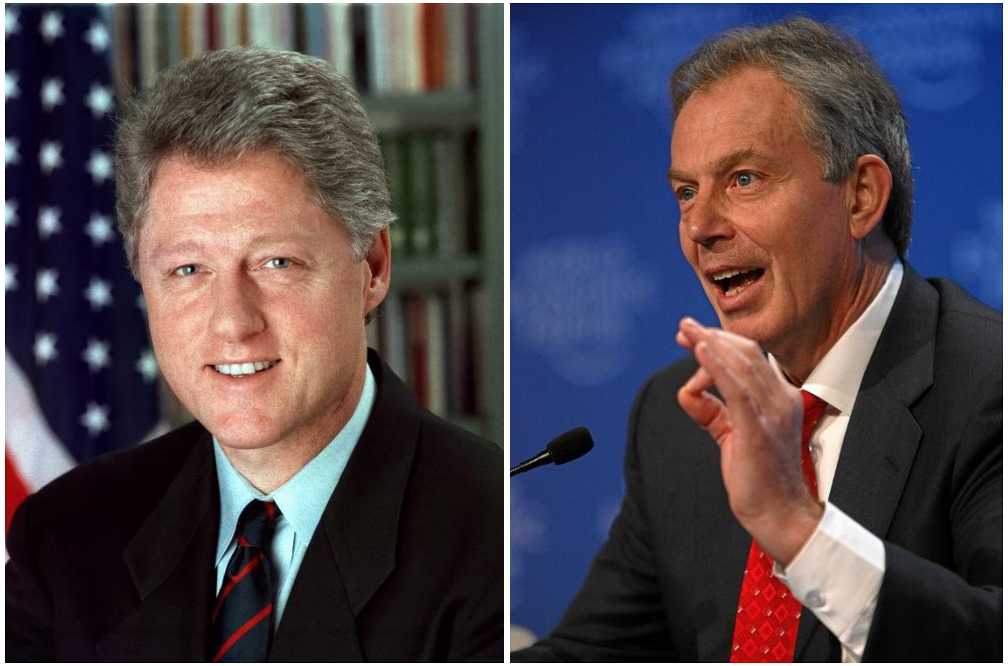
인간 게놈 프로젝트

(Human Genome Project)

- 1988, Watson이 National Center for Human Genome Research **초대 소장을 맡으며 출범**
- 3.2 x 10^9 bp



First Draft of HGP



- **2000. 6. 26.**
- **B. Clinton**

  (White House)
- **T. Blair**

  (10 Downing St.)
- **Clinton**

  “Today, we are learning the language in which God created life.”

※ 출처 : Bill Clinton, https://en.wikipedia.org,
Tony Blair, https://www.wikidata.org

Toward one thousand genome
(게놈 해독 비용 1000달러를 향하여)

- 2000년 당시

  30억불(3조원), 10년
- 2007년

  100만불, 수개월
- 2009년

  4,400불, 십수주
- 2015년

  1,000불

개인 유전정보 분석 서비스(2011년 상반기 기준)

디코드미 (deCODEme)

2,000불

내비지닉스 (Navigenics)

999불

23앤드미 (23andMe)

499불

개인 유전정보 분석 서비스

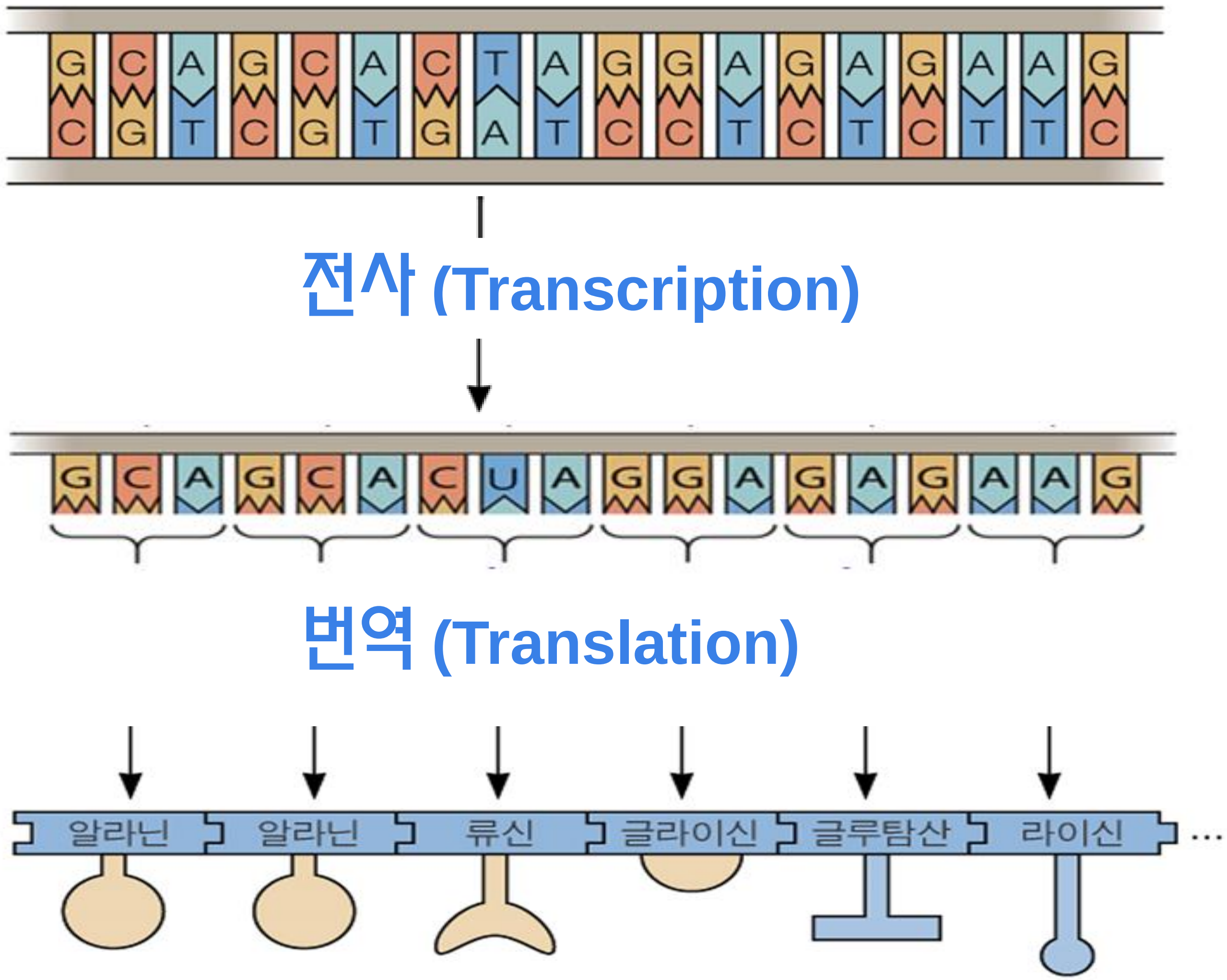
- 침을 튜브에 담아 서비스 회사로 배송

- DNA 유전코드 판독
  질병과의 연관성 분석
  분석완료 통보

- 웹에 접속하여 결과 확인
  지속적인 업데이트 정보 제공 받음

3. 전사 (Transcription)

Central Dogma



DNA

전사 (Transcription)

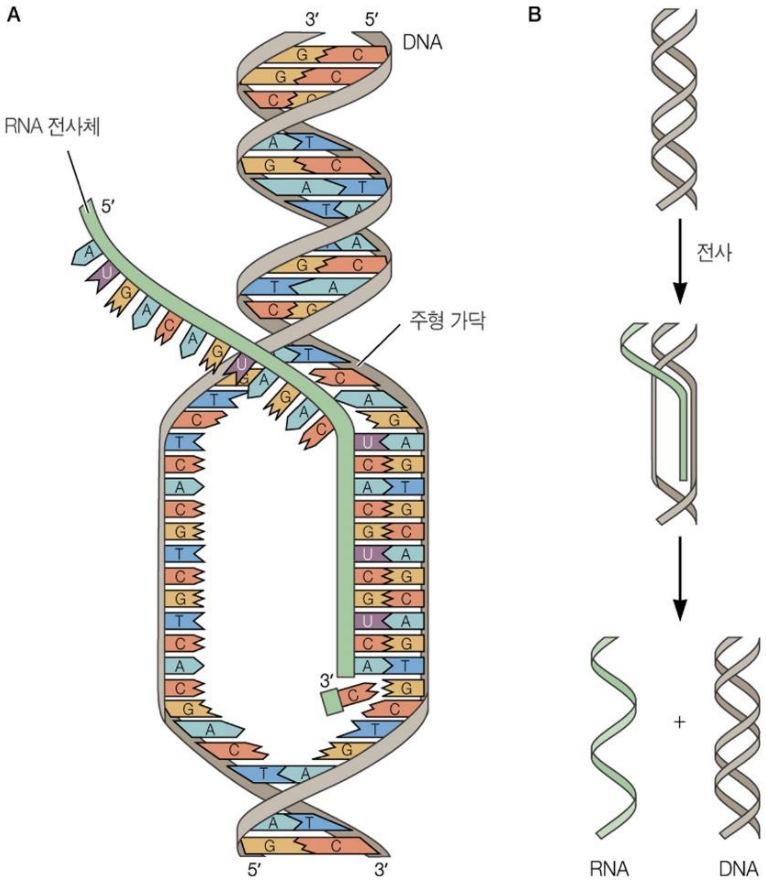
mRNA

번역 (Translation)

Protein

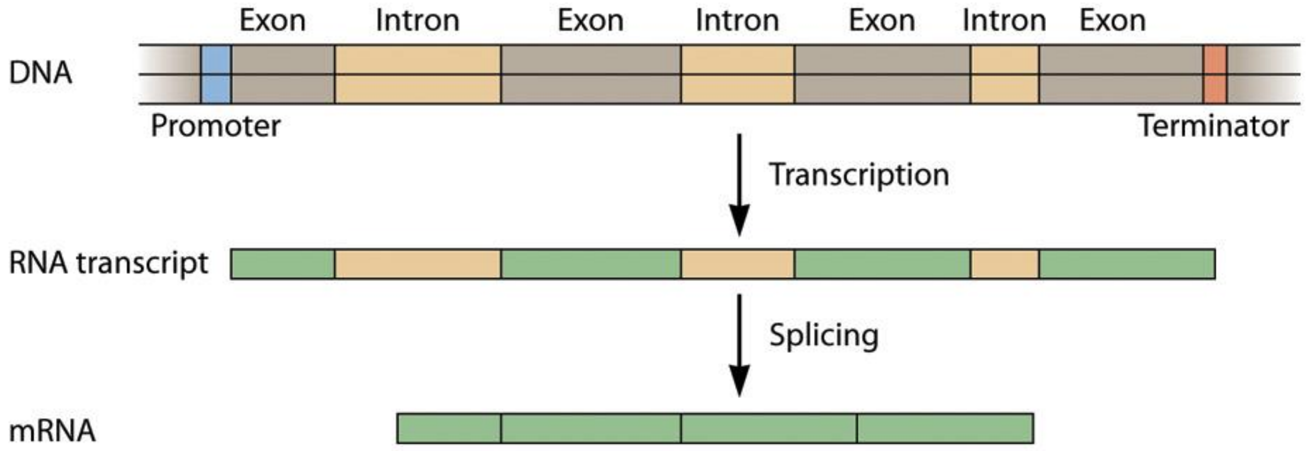
Transcription

- mRNA synthesis by RNA polymerase



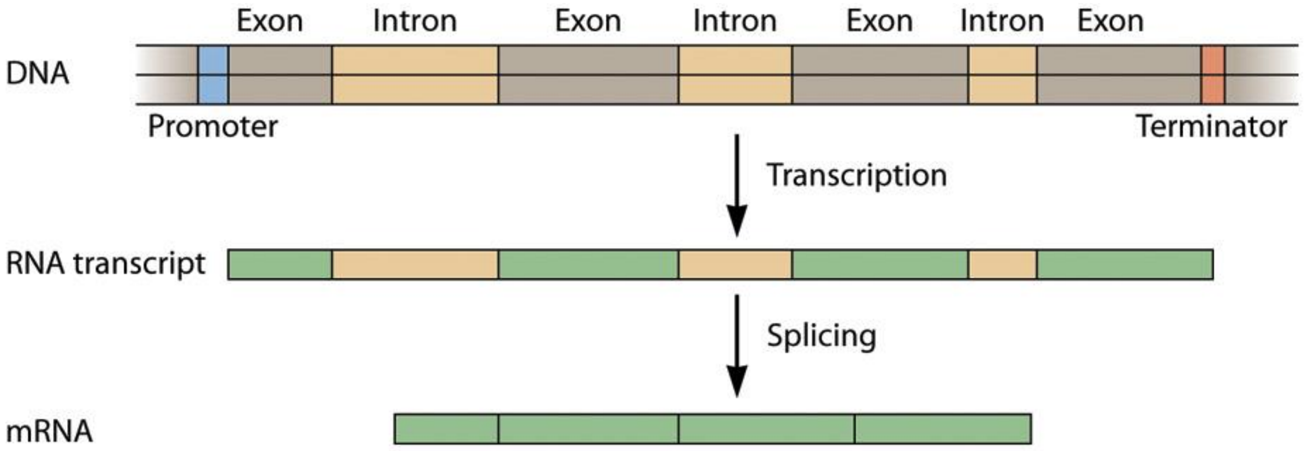
Regulation of Transcription

- Promoter
  - Binding site of RNA polymerase and regulatory proteins (transcriptional regulator; activator or repressor)
- Terminator
  - The site where transcription stops



Regulation of Transcription

- Processing of eukaryotic RNA
  - Splicing : joining of exons

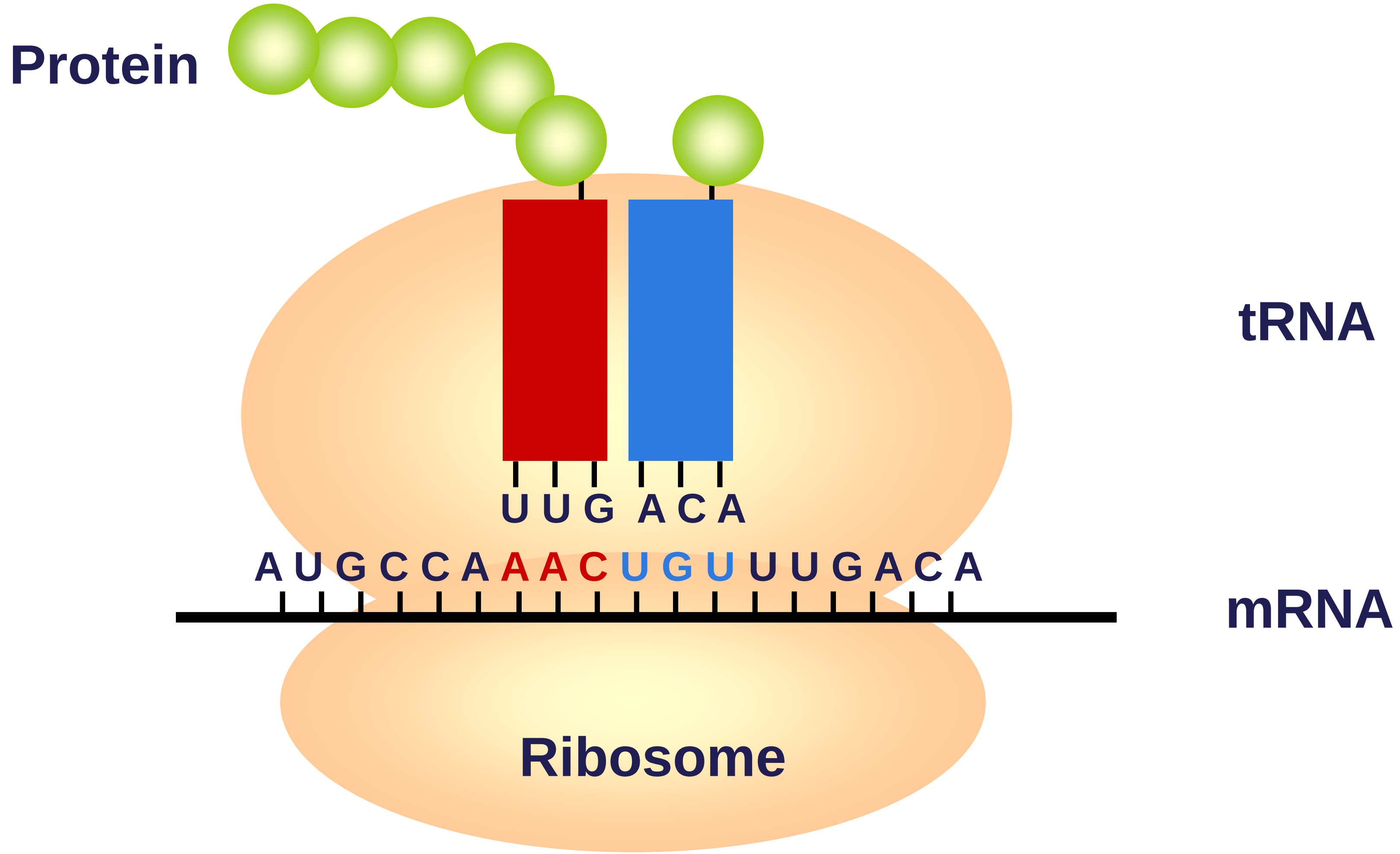


RNA

- mRNA (messenger RNA)
  - 단백질로 번역되는 정보 제공
- rRNA (ribosomal RNA)
  - 라이보솜 구성성분
- tRNA (transfer RNA)
  - 번역 과정에서 아미노산 운반

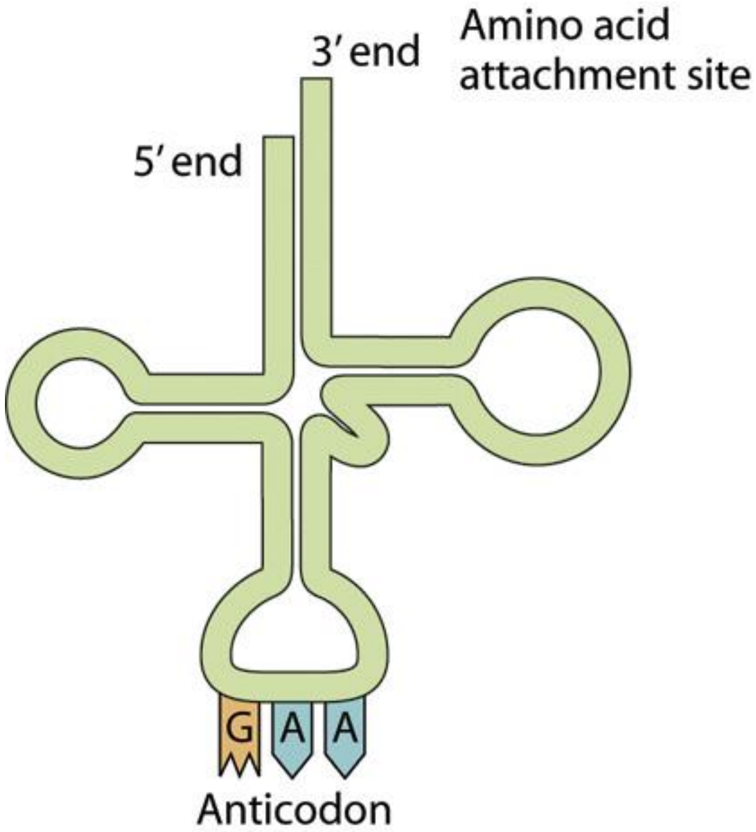
4. 번역(Translation)

Translation



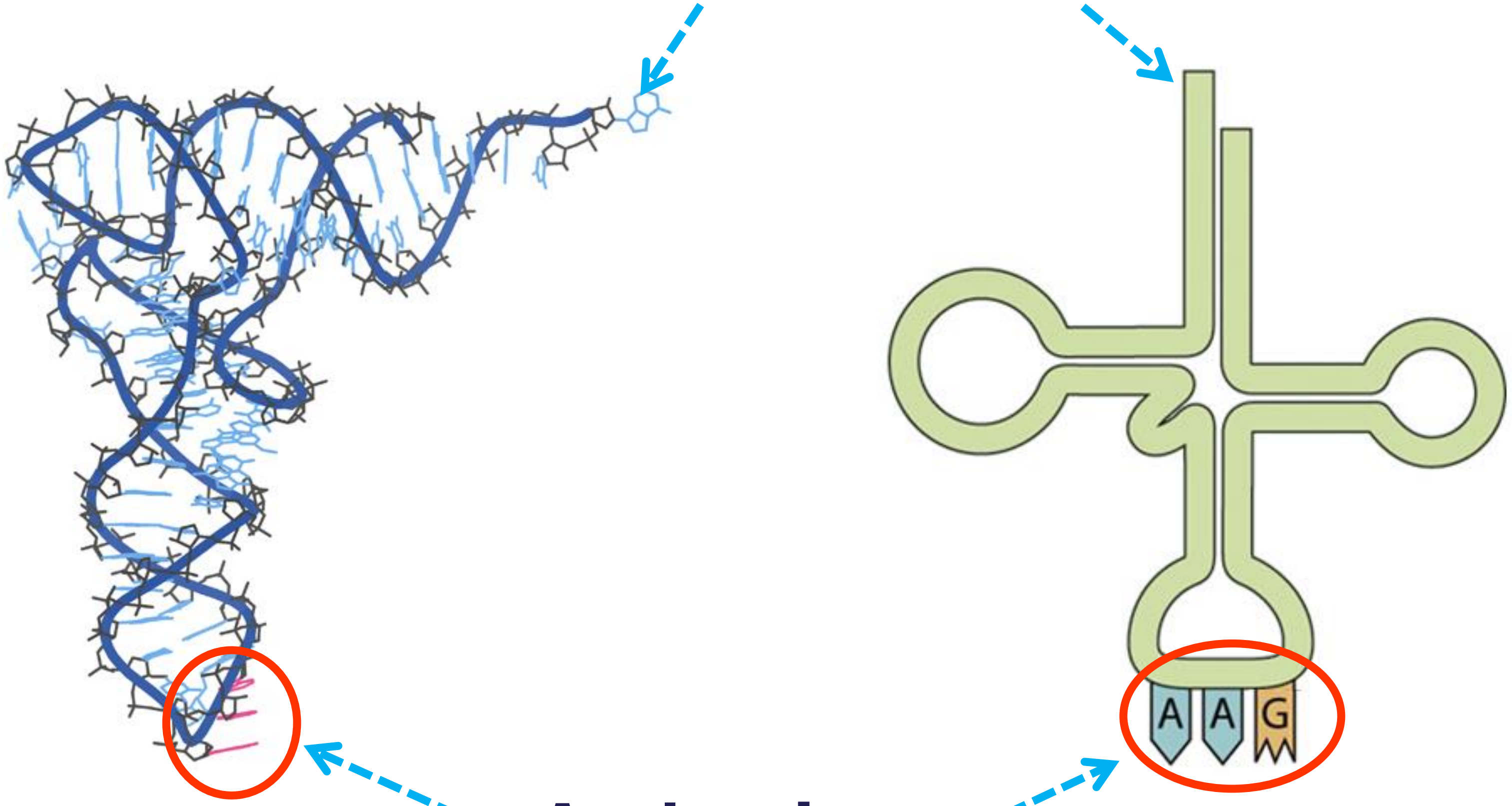
Translation

- tRNA
  - Cloverleaves shaped folding
  - Anticodon: complementary to codon
  - 3’ end: amino acid attachment



tRNA

Amino acid attachment site

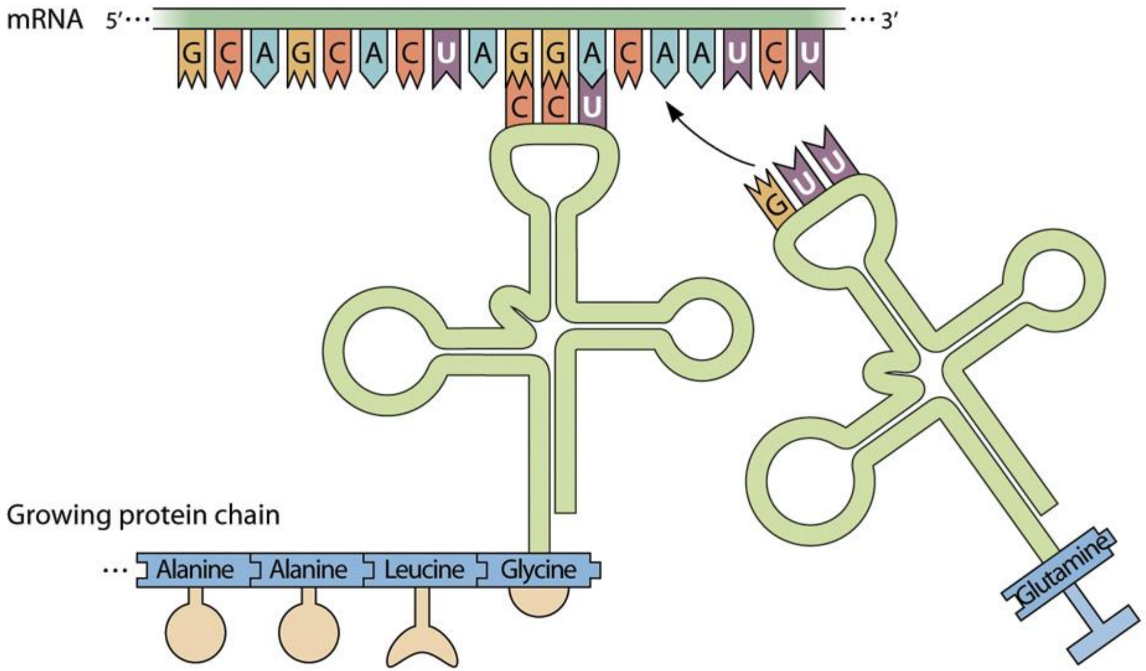


Anticodon

※ 출처 : commons.wikimedia.org

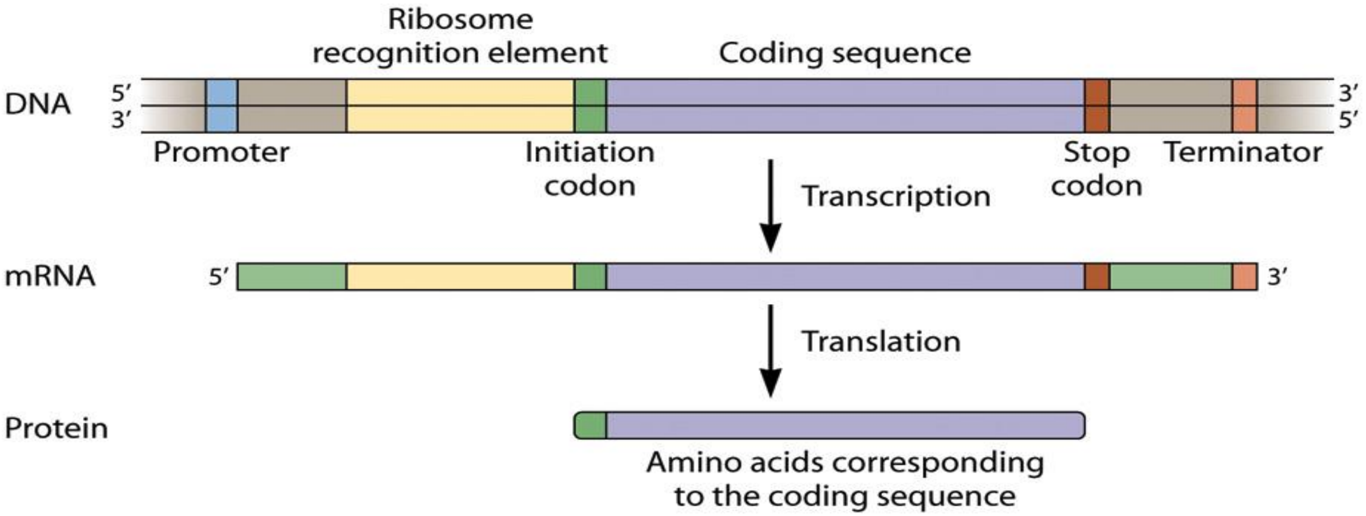
Translation

- Assembly of ribosome and mRNA
- Binding of tRNA
- Peptide bond formation
- Release of tRNA



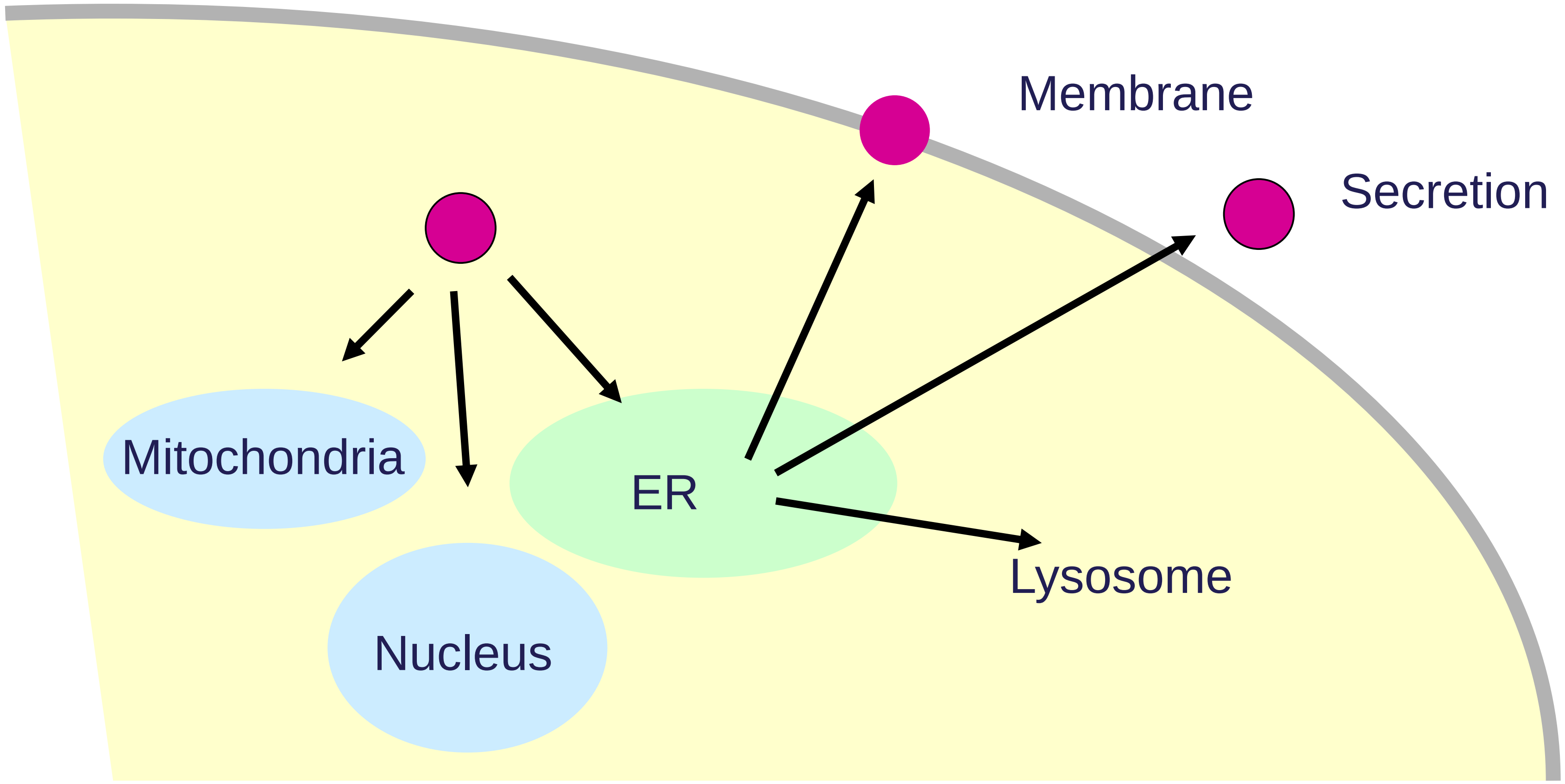
Translation

- Ribosome binding site in mRNA
  - Shine-Dalgarno Sequence
- Initiation codon
  - AUG for methionine
- Stop codon
  - UGA, UAA, UAG : no corresponding tRNA



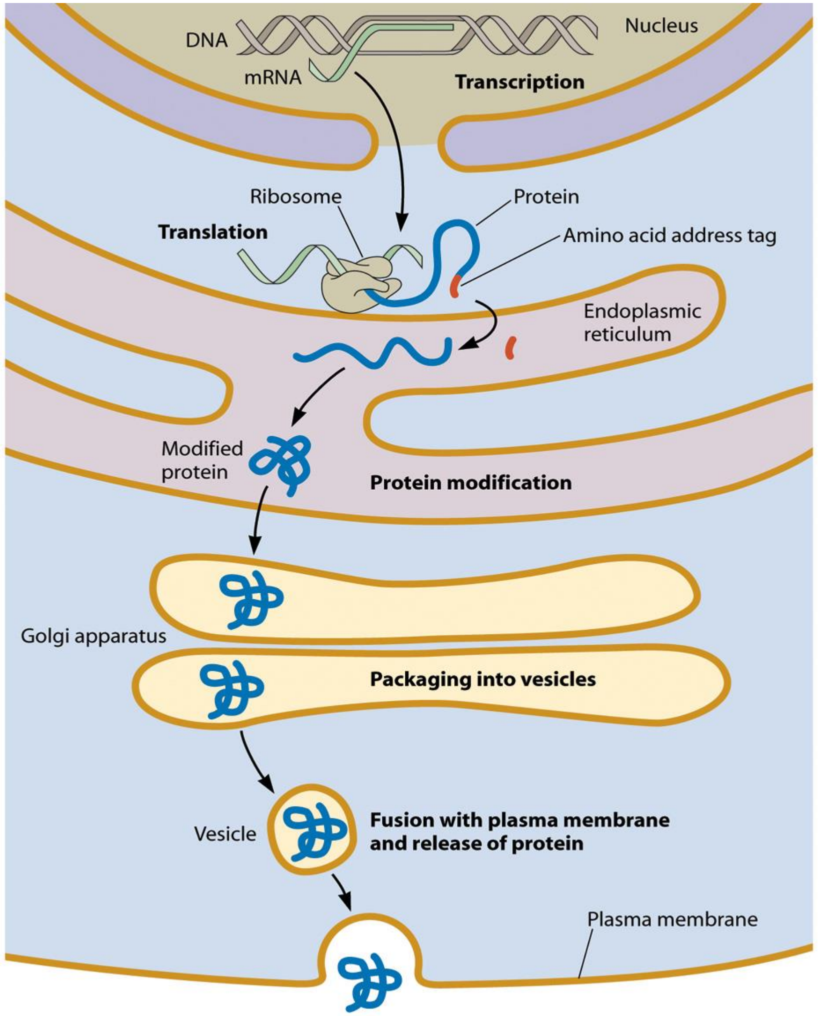
Cellular Fate of Proteins

- Protein Targeting to specific compartment (ER, Nucleus, Mitochondria) is guided by **signal peptide (tags)**



Protein Targeting to ER

- Proteins with signal peptide
  - Secretory proteins
  - Membrane proteins
  - Proteins in ER, Golgi, and lysosome
- Modification during transport from ER to Golgi apparatus
  - Glycosylation



Chapter 5

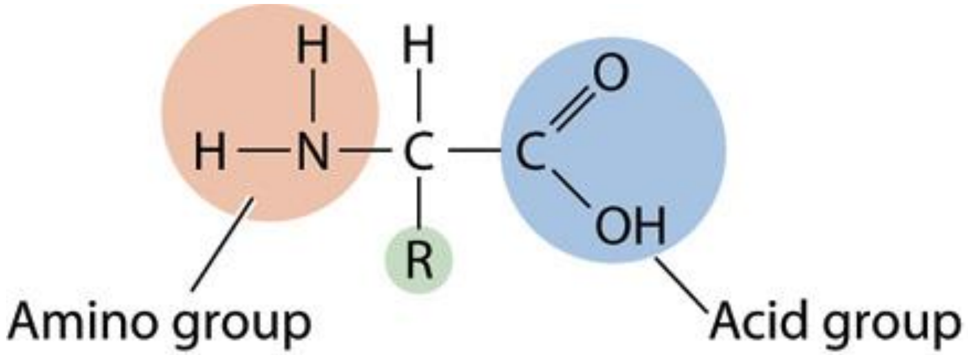
Protein Structure and Function

목 차

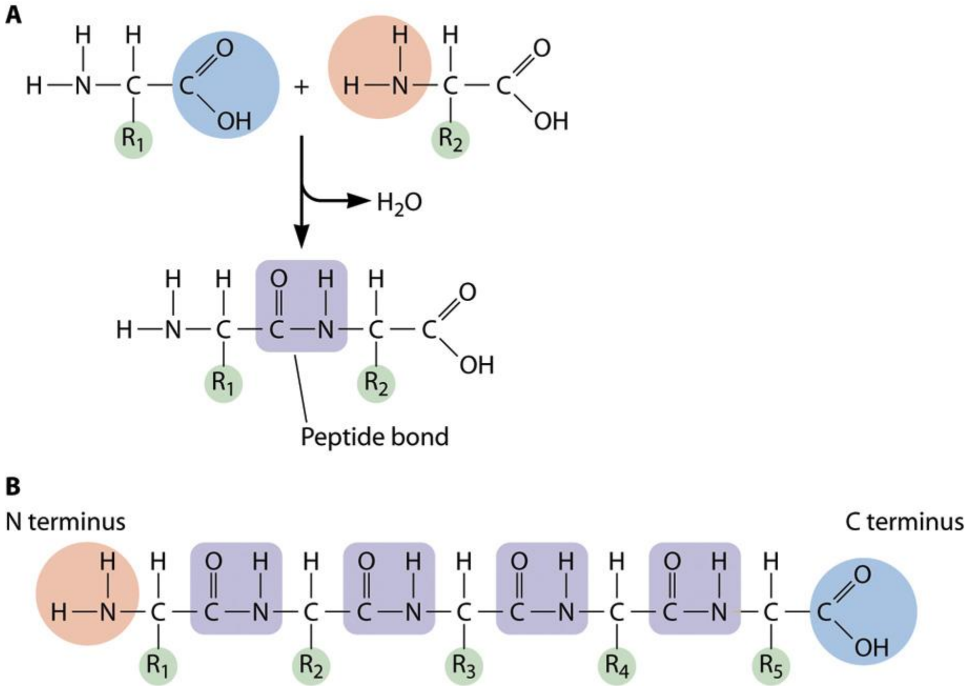
1. 아미노산 (Amino acid)

Amino Acids and Primary Structure

- Amino acids
  - Amino group
  - Carboxyl group
  - R group; 20 Side chains

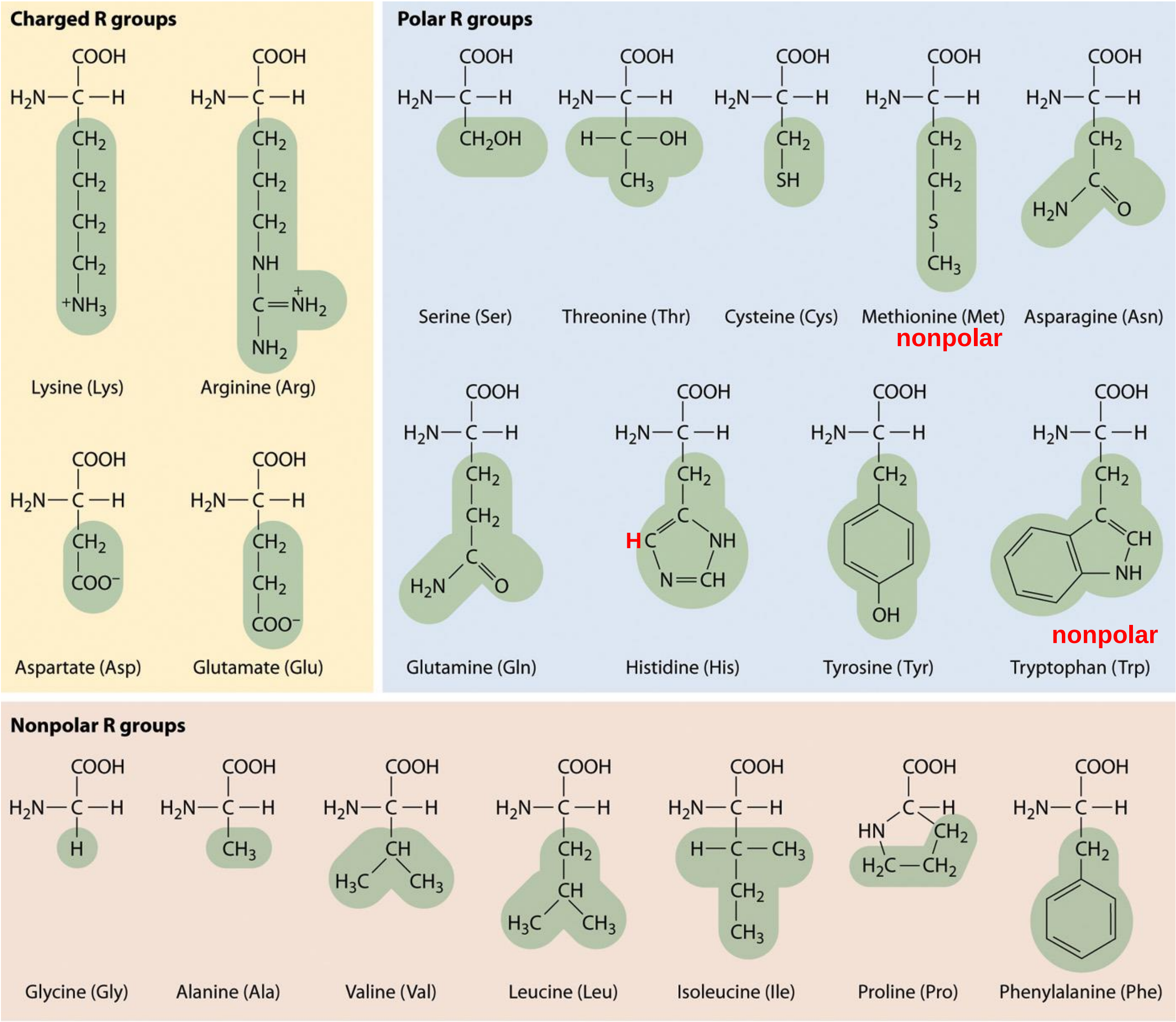


Amino Acids and Primary Structure



- Peptide bond
  - Between NH_2 and COOH
- Polypeptide
  - A chain of amino acids
  - N terminus and C terminus
- Primary structure
  - Linear arrangement (sequence) of amino acids

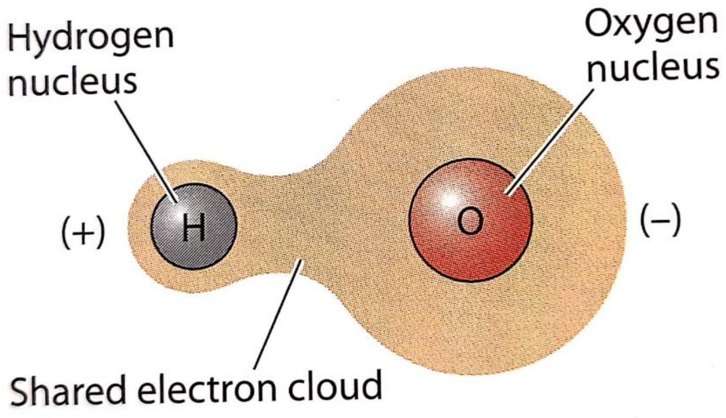
Amino Acids

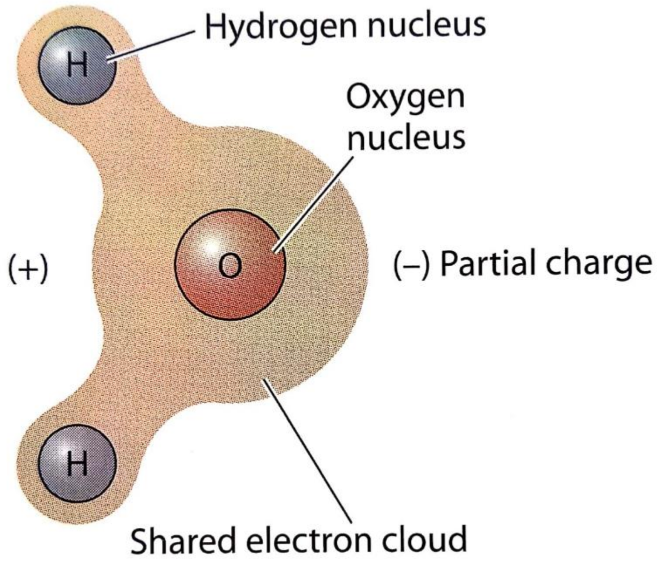

Charged R groups
Lysine (Lys)
Arginine (Arg)
Aspartate (Asp)
Glutamate (Glu)
Polar R groups
Serine (Ser)
Threonine (Thr)
Cysteine (Cys)
Methionine (Met)
nonpolar
Asparagine (Asn)
Glutamine (Gln)
H
Histidine (His)
Tyrosine (Tyr)
nonpolar
Tryptophan (Trp)
Nonpolar R groups
Glycine (Gly)
Alanine (Ala)
Valine (Val)
Leucine (Leu)
Isoleucine (Ile)
Proline (Pro)
Phenylalanine (Phe)

2. 수소 결합 (Hydrogen bond)

Polar

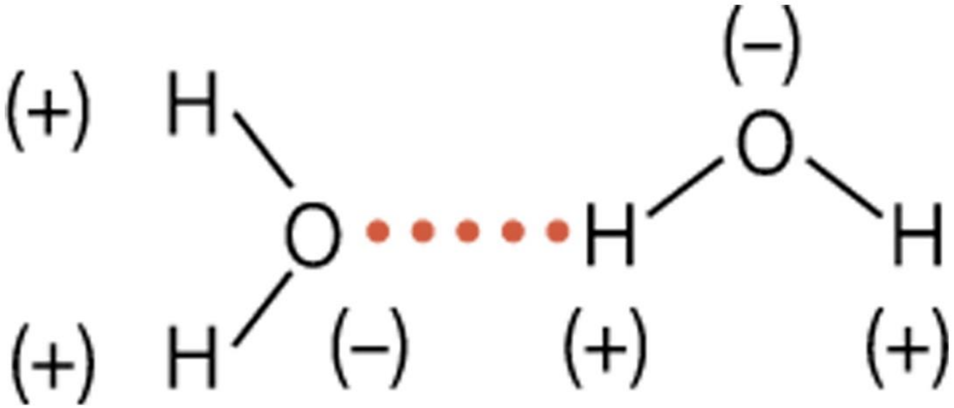
- Polar
  - Hydrophilic



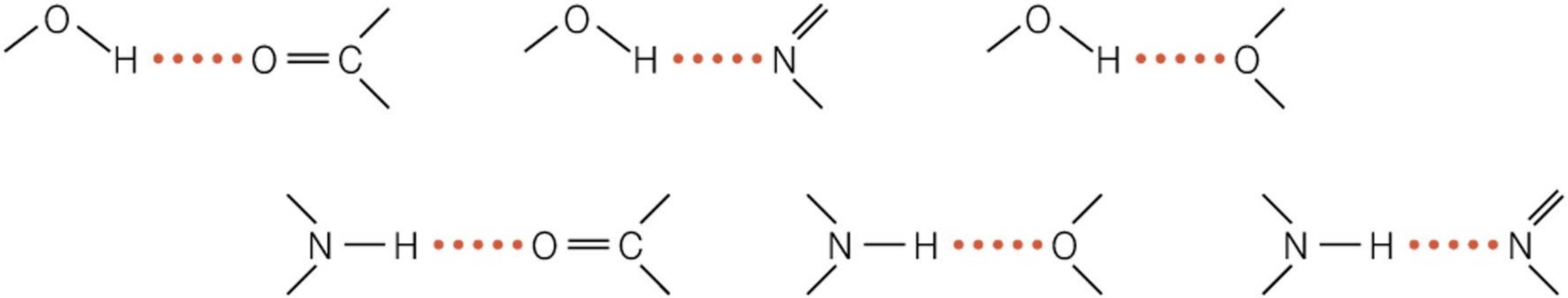


Hydrogen bond

- High electronegativity
  - F, O, N



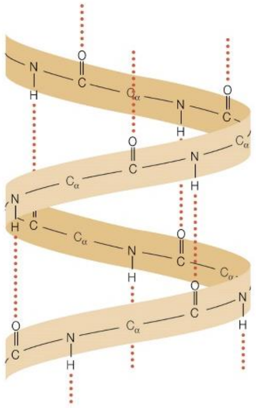
Hydrogen bond

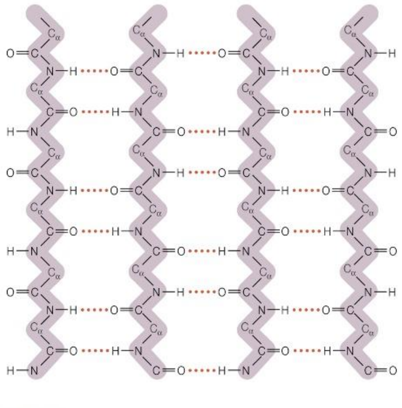


3. 단백질 구조 (Protein structure)

Primary and Secondary Structure

- Primary structure
  - Linear arrangement (sequence) of amino acids
- Secondary structure
  - Core elements of protein architecture
  - Neutralization of partial charges of the peptide backbone by hydrogen bonding
  - Local folding of polypeptide chain
    - α helix, β sheet : 60% of the polypeptide chain
    - Random coils and U-shaped turn



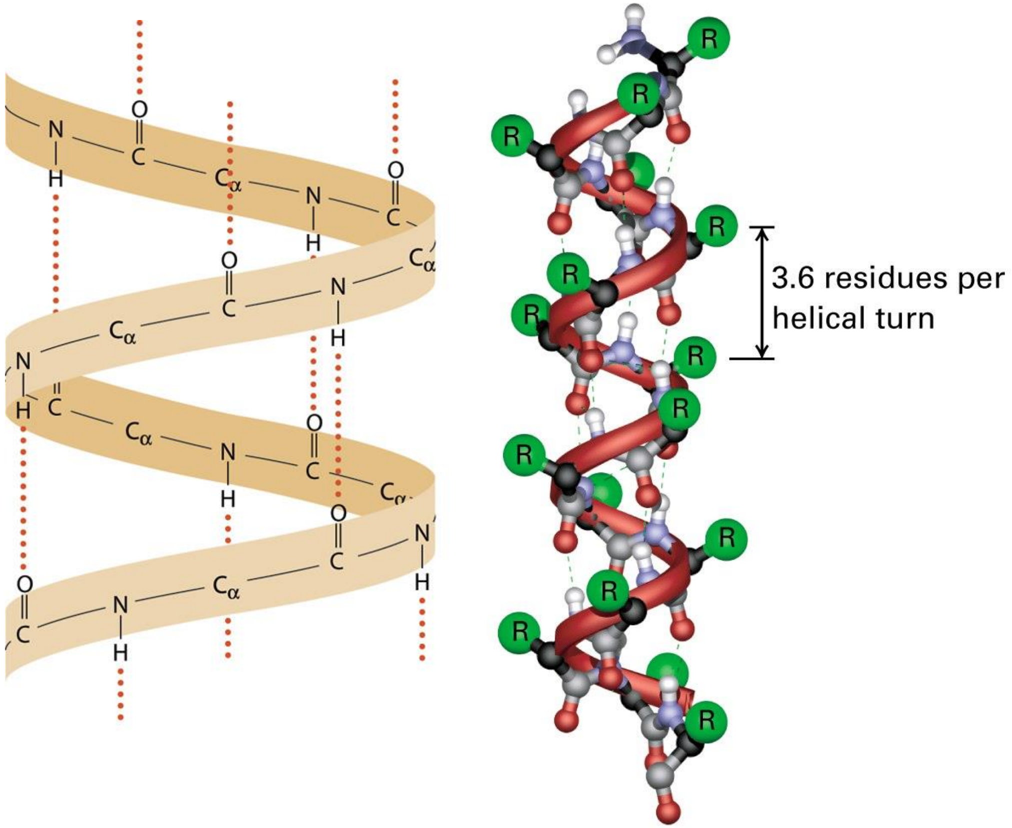


α-Helix

- Hydrogen bond between carbonyl O (n) and amid H (n+4)
- Directionality on the helix : The same orientation of H bond donor
- Side chains point outward :

  Determine hydrophobic or

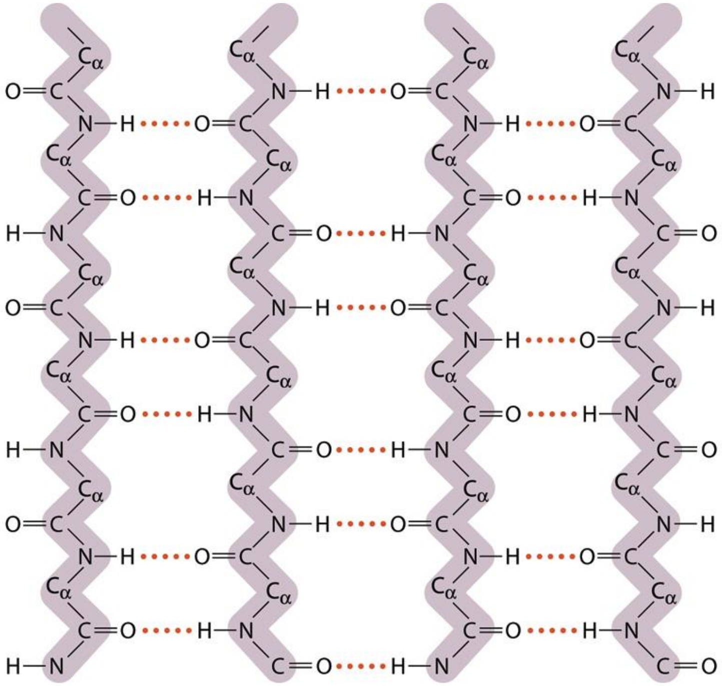
  hydrophilic quality



β-Sheet

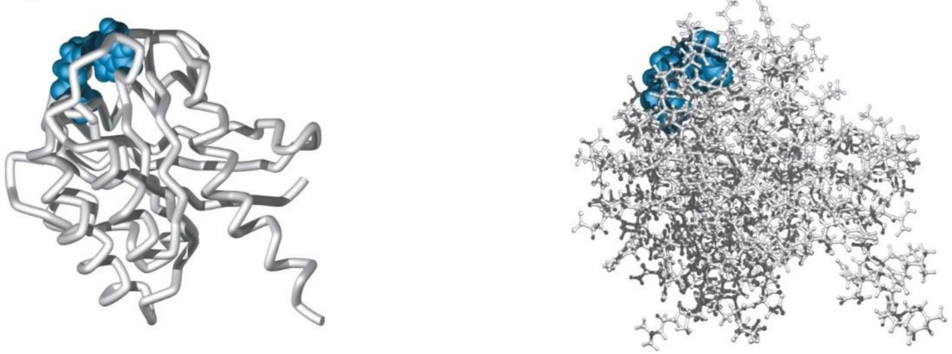
- Hydrogen bonding between β strands → β sheet,
  pleated sheet

- Usually not flat,
  but twisted



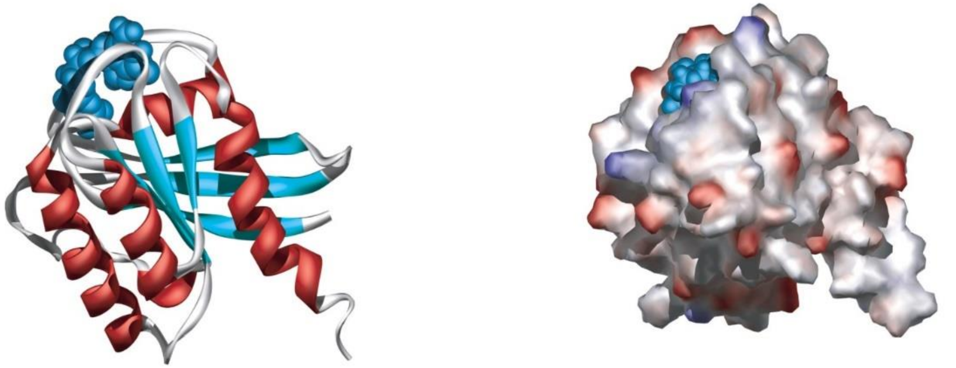
Tertiary Structure

- Overall folding of a polypeptide chain



(a) C_α backbone trace

(b) Ball and stick

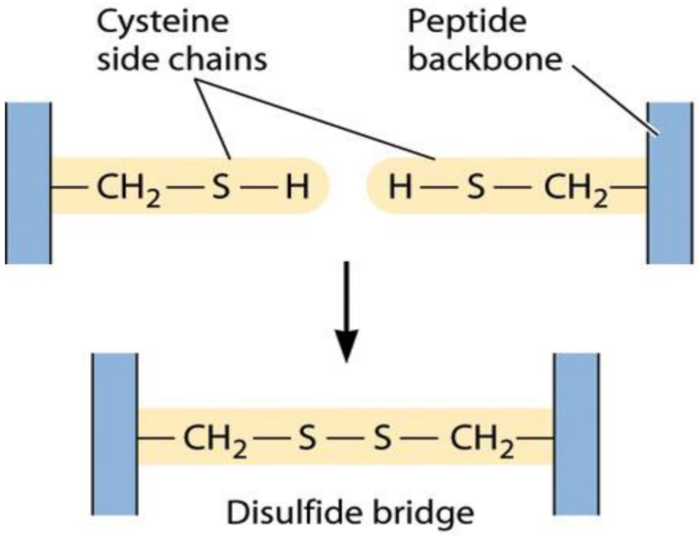


(c) Ribbons

(d) Solvent-accessible surface

Tertiary Structure

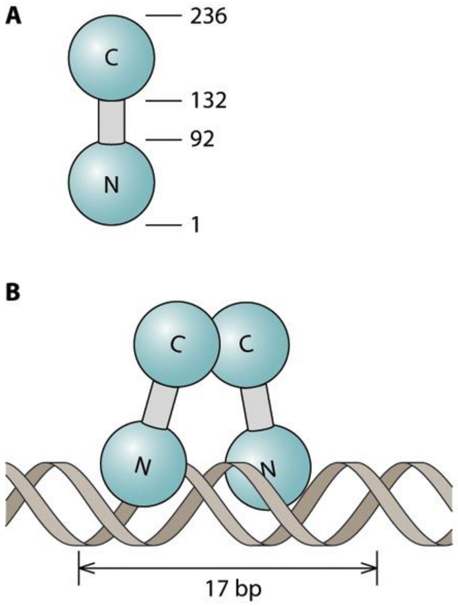
- Stabilization
  - weak interaction
    - Hydrophobic interaction between nonpolar side chains
    - Hydrogen bond between polar side chains and peptide bonds
  - Disulfide bond formation



Higher Levels of Structure

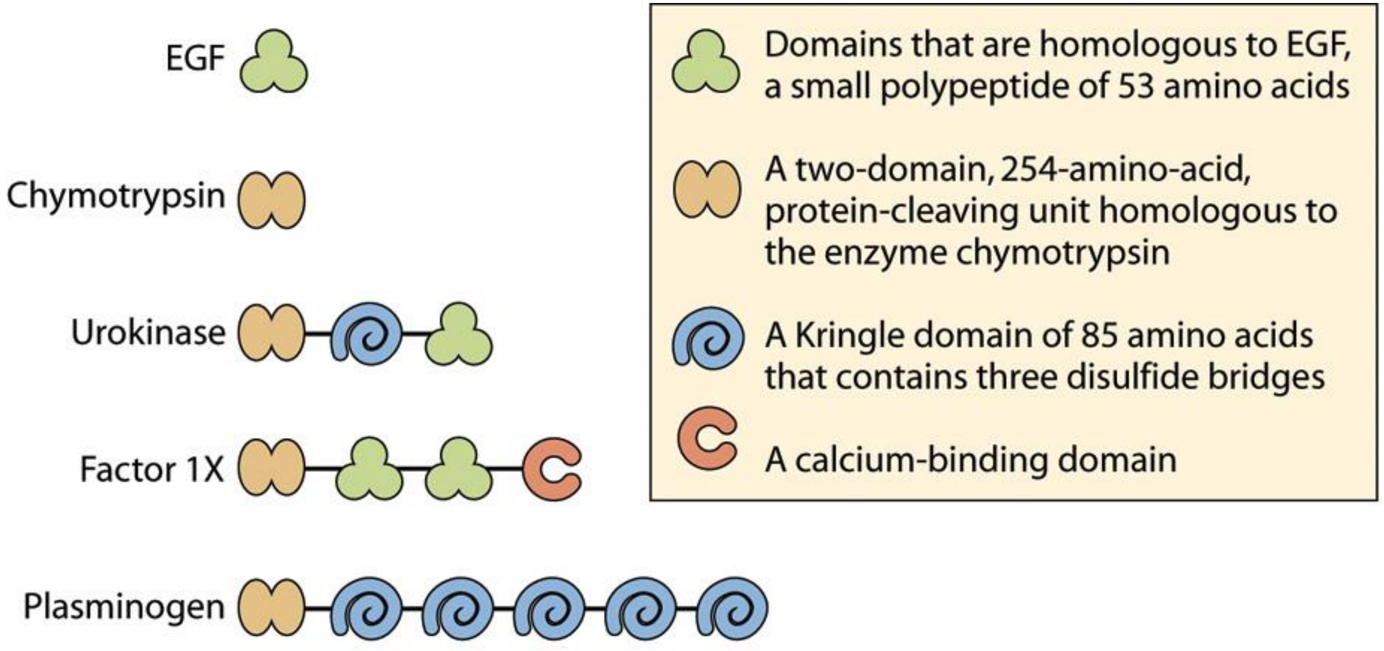
- Domains
  - One stable, compact, three-dimensional shape
  - Fundamental units of protein structure and function
    - DNA binding domain, transmembrane domain

  - e.g. lambda repressor (236 aa)
    - N terminal domain : DNA binding
    - C terminal domain :
      Interaction with C terminal domain
      of another molecule (dimerization)



Modular Proteins

- New proteins by combination of functional domains
- Biotechnological application using recombinant DNA technology



Domains that are homologous to EGF, a small polypeptide of 53 amino acids

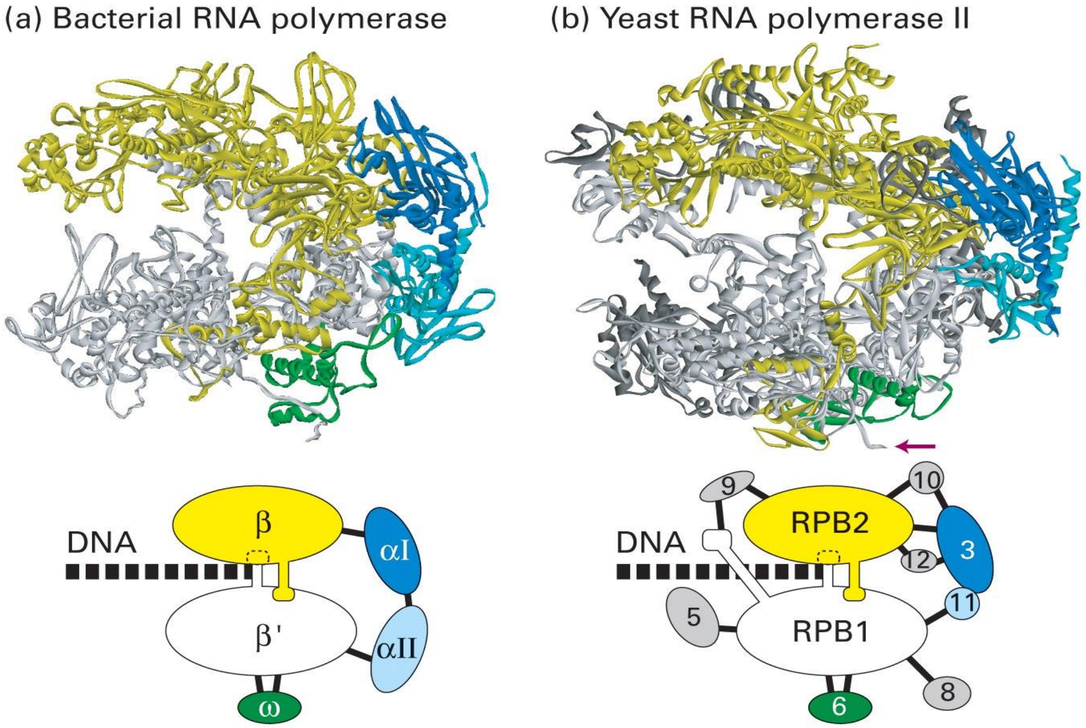
A two-domain, 254-amino-acid, protein-cleaving unit homologous to the enzyme chymotrypsin

A Kringle domain of 85 amino acids that contains three disulfide bridges

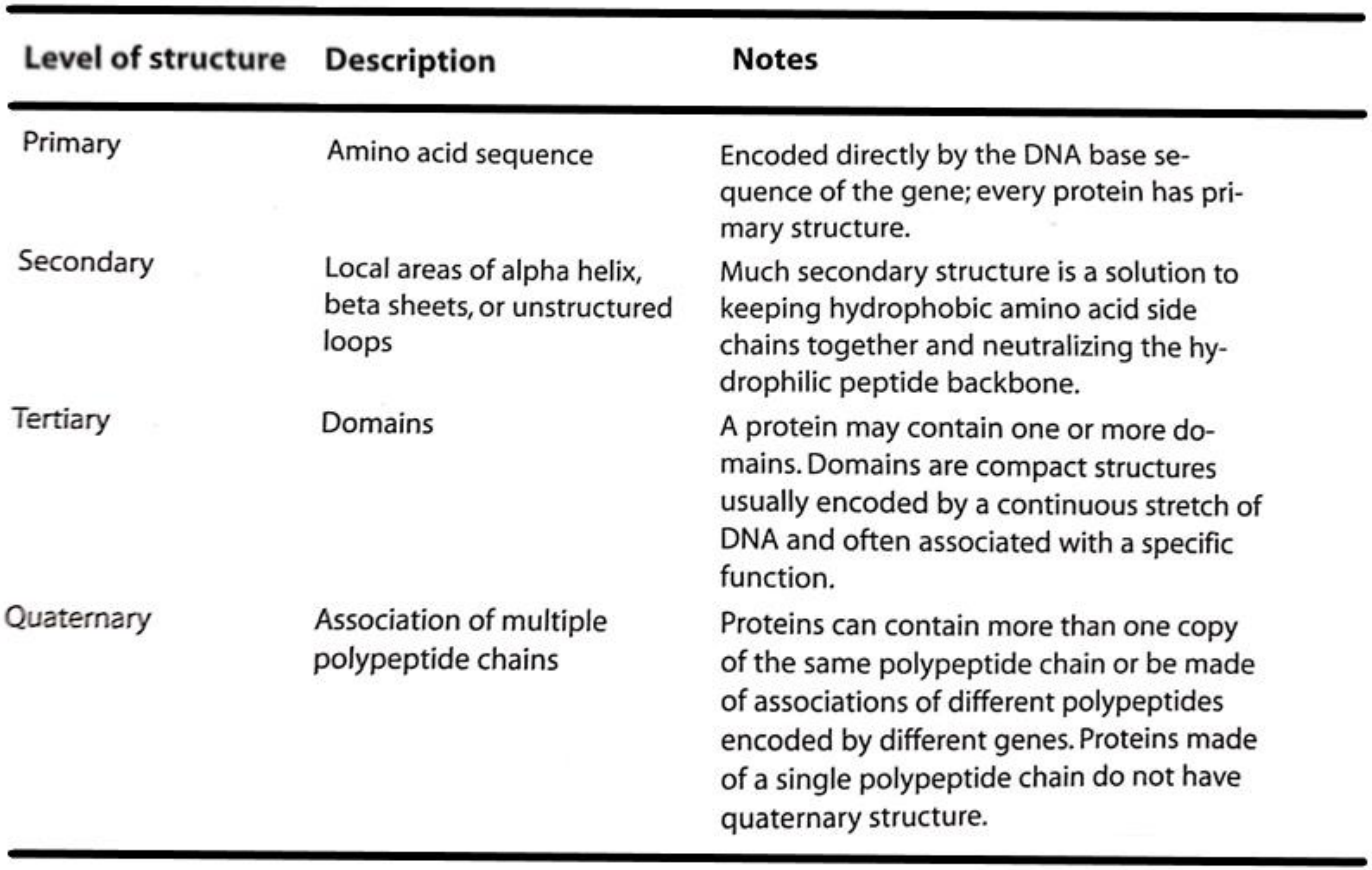
A calcium-binding domain

Quaternary Structure

- Association of multiple polypeptide chains
  - Lambda repressor : dimer
  - *E. coli* RNA polymerase : Five polypeptide chains



Levels of Protein Structure



Level of structure	Description	Notes
Primary	Amino acid sequence	Encoded directly by the DNA base sequence of the gene; every protein has primary structure.
Secondary	Local areas of alpha helix, beta sheets, or unstructured loops	Much secondary structure is a solution to keeping hydrophobic amino acid side chains together and neutralizing the hydrophilic peptide backbone.
Tertiary	Domains	A protein may contain one or more domains. Domains are compact structures usually encoded by a continuous stretch of DNA and often associated with a specific function.
Quaternary	Association of multiple polypeptide chains	Proteins can contain more than one copy of the same polypeptide chain or be made of associations of different polypeptides encoded by different genes. Proteins made of a single polypeptide chain do not have quaternary structure.

4. 단백질 구조와 기능 (Structure and Function)

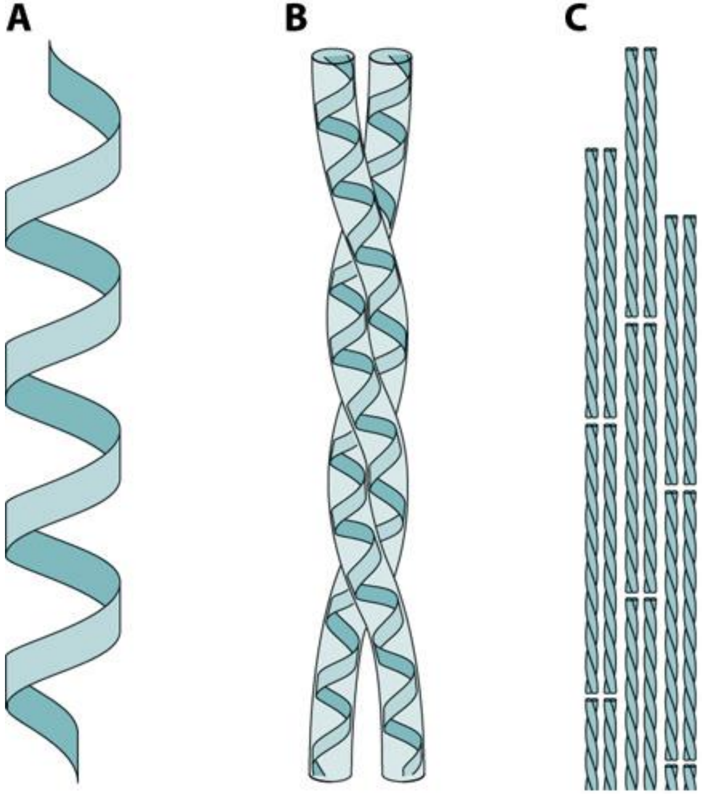
Disruption of Protein Structure

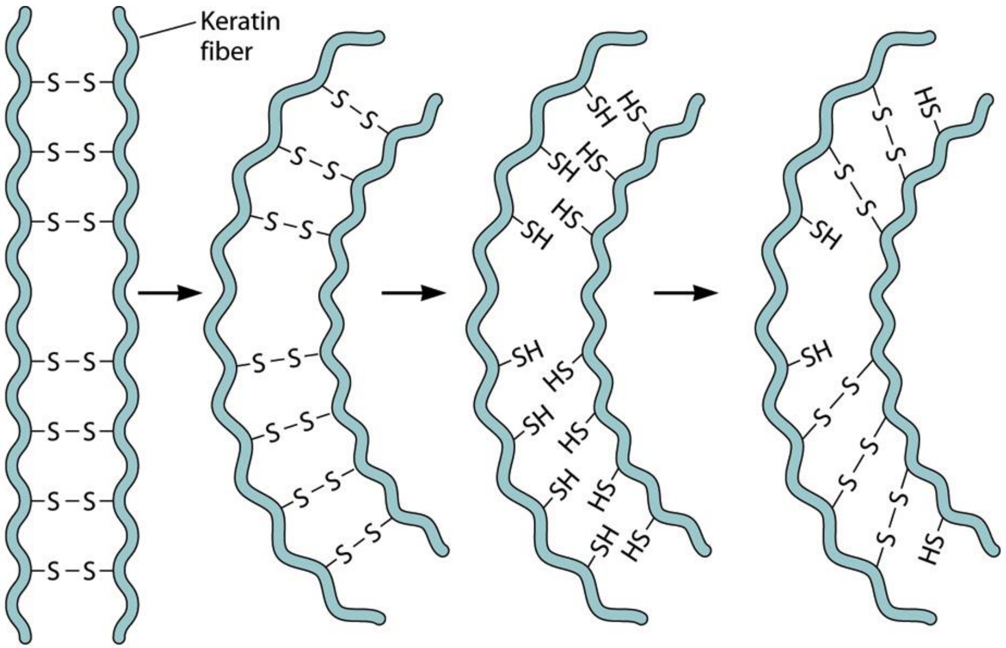
- Factors disrupting protein structure
  - Heat, extreme pH, organic solvent, detergent
- Denaturation
  - Complete unfolding of amino acid chain
  - Sometimes irreversible : e.g. boiled egg
  - Melting temperature (T_m)
    - Denaturation temperature for a given protein
    - Depending on protein structure
      - Proteins from organisms living at high temperature
      - Disulfide bridge increases protein stability

Examples of
Protein Structure and Function

- Keratin
  - Structural protein for hair, wool, feathers, nails, scales, hooves, horns, skin
  - Very strong and water insoluble
    - Hydrophobic alpha helices
      - Long α-helix with hydrophobic amino acids
      - Forming fibers by hydrophobic interactions
    - Disulfide bonds
      - The more S-S bonds the harder the structure
      - Permanent hair wave
        - Reducing of disulfide bond → Generation of new disulfide bond

Examples of
Protein Structure and Function

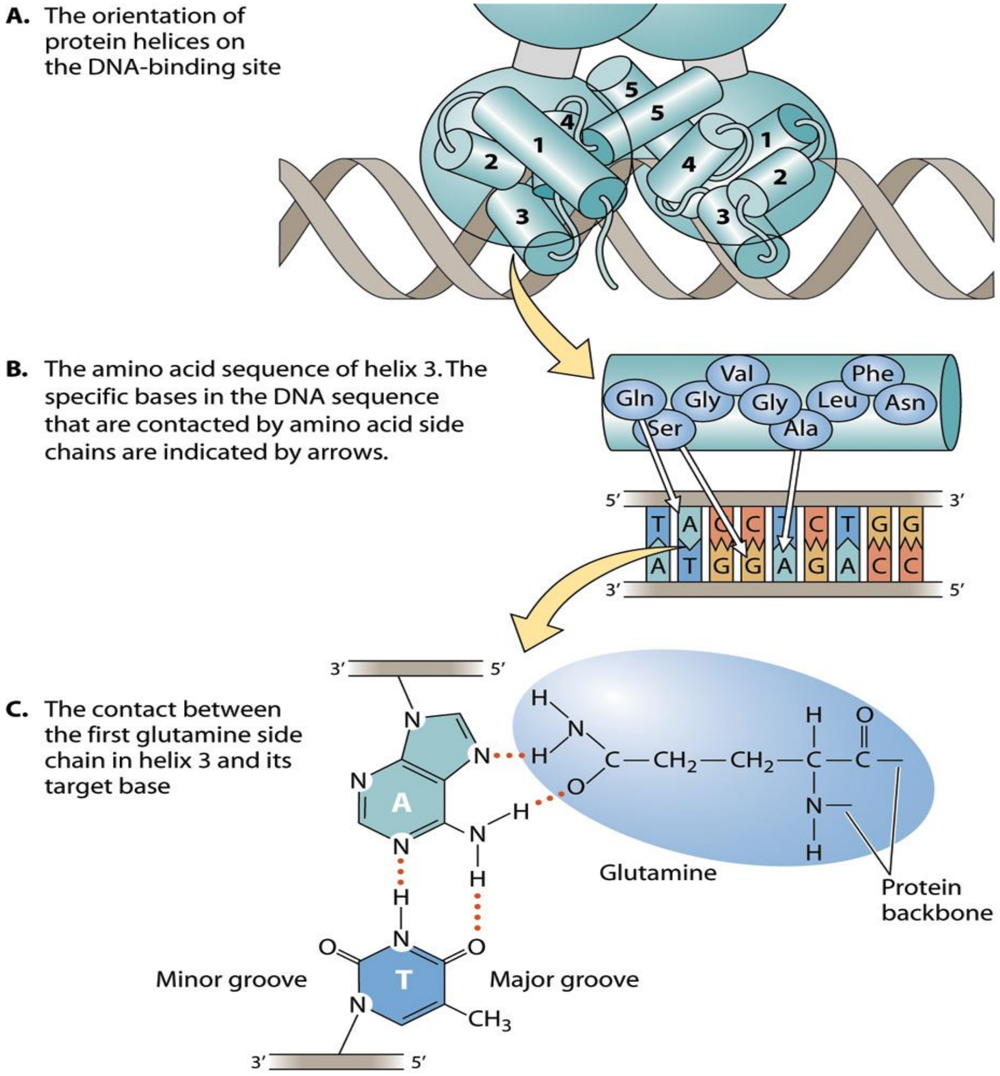




1. Normal hair
2. Hair is wrapped around curling rod.
3. Reducing agent breaks disulfide bonds.
4. Neutralization allows disulfide bridges to re-form; new disulfide bonds hold hair in a wavy conformation.

Lambda Repressor

- Binding of N-terminal domain helix 3 to specific bases within the DNA sequence



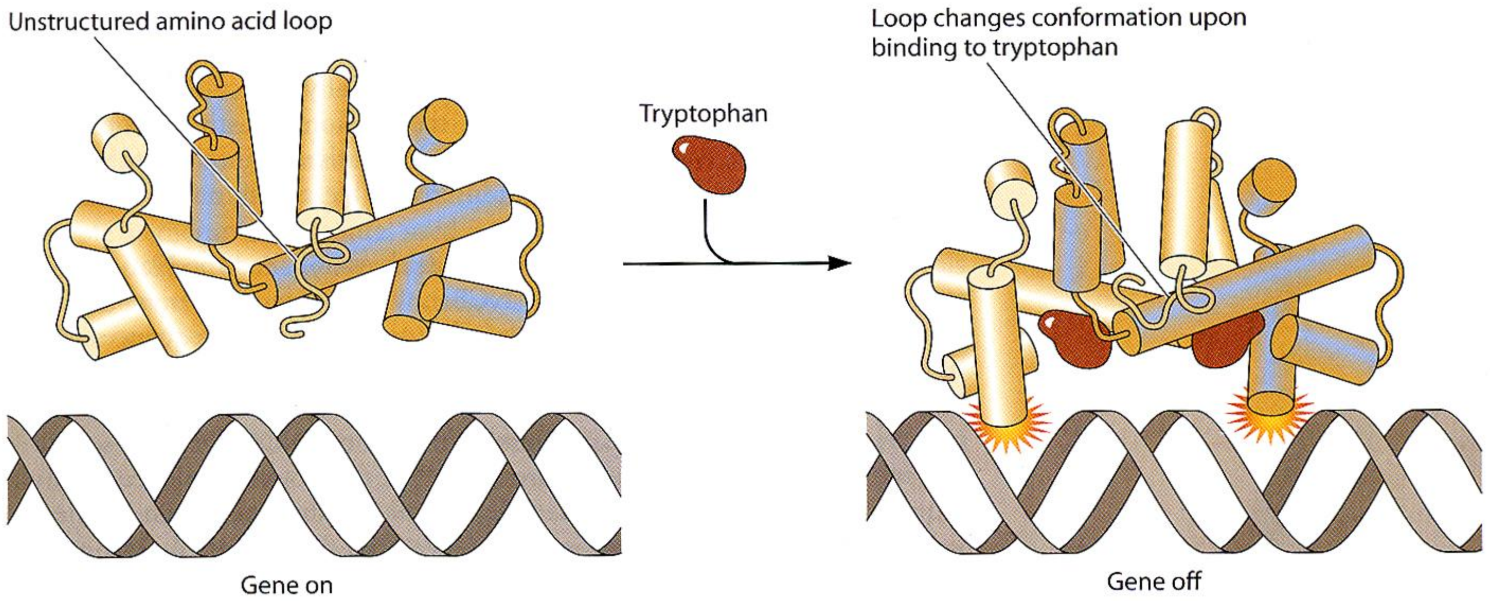
A. The orientation of protein helices on the DNA-binding site

B. The amino acid sequence of helix 3. The specific bases in the DNA sequence that are contacted by amino acid side chains are indicated by arrows.

C. The contact between the first glutamine side chain in helix 3 and its target base

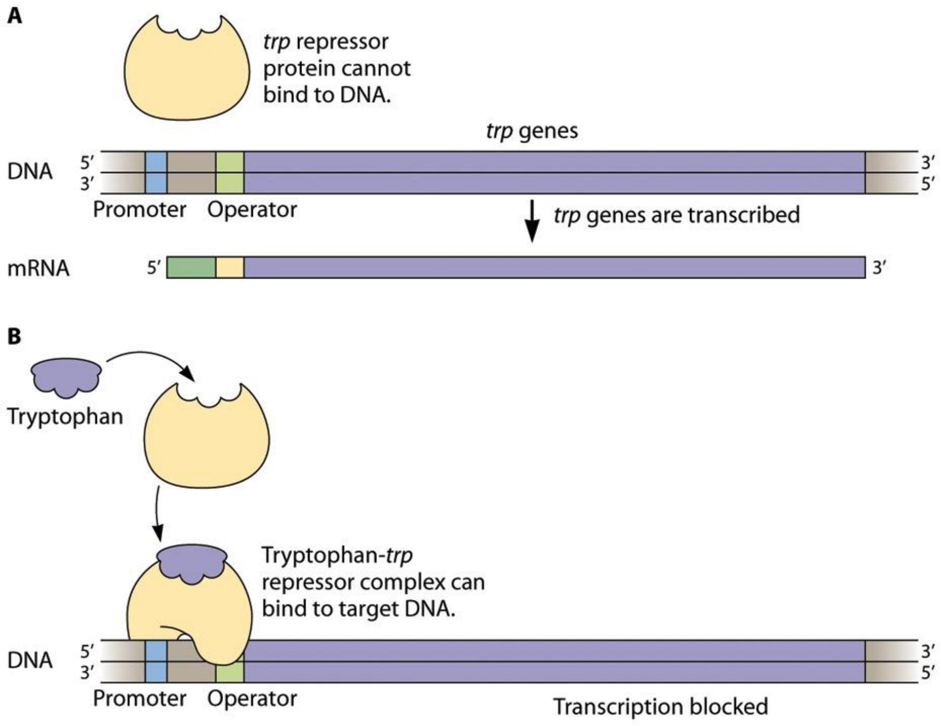
Trp Repressor

- If plenty of Trp in the cytosol
- Binding of Trp into Trp Repressor and change the conformation
- Trp repressor binds to DNA and represses the expression of genes involved in Trp synthesis



Regulation of Tryptophan Synthesis

- Trp synthesis in *E. coli*
  - Turn off transcription of Trp genes in the presence of Trp
- Hormonal regulation in higher eukaryotes



Predicting Protein Structure

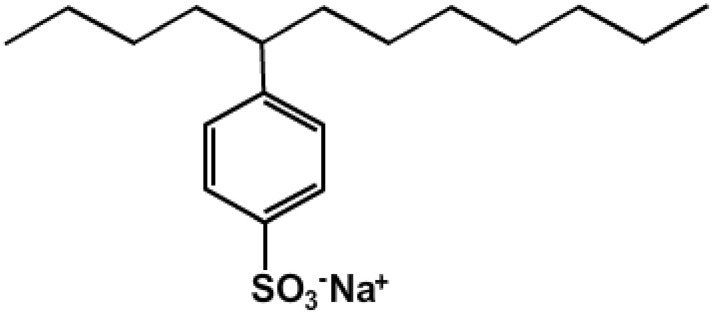
- It is difficult to predict three dimensional structure from the amino acid sequence
- Compare to other proteins with known function or structure
  - Easy access of information through public database
    - NCBI (National center for Biotechnology Information) run by National Institutes of Health (NIH)
    - http://www.ncbi.nlm.nih.gov
  - Testing structure-function prediction
    - Using molecular biological tools
    - Introduction of mutations into protein

      →change of protein function

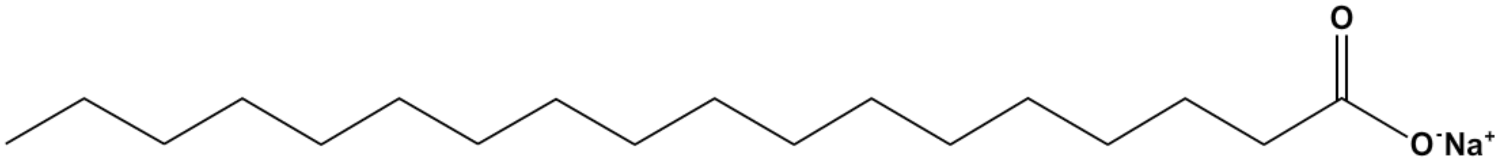
Protein Engineering

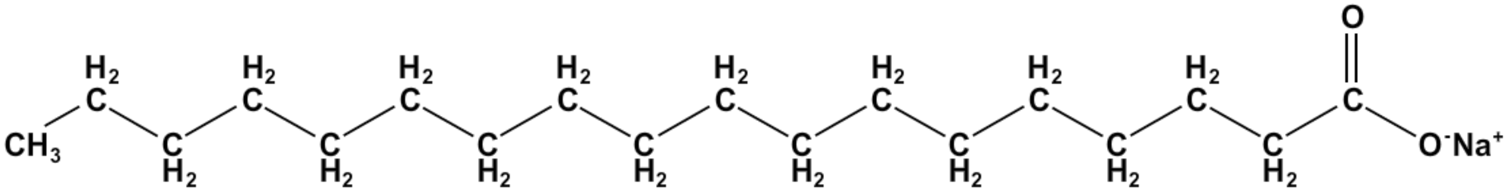
- Manipulation of protein’s amino acid sequence to change its function or properties
- Chemical manufacturing
  - Develop enzymes more suitable for industrial applications
  - Increasing enzyme stability
    - e.g. bacteriophage lysozyme: introduce S-S bond to increase heat resistance
    - Proteases in detergent

Detergent

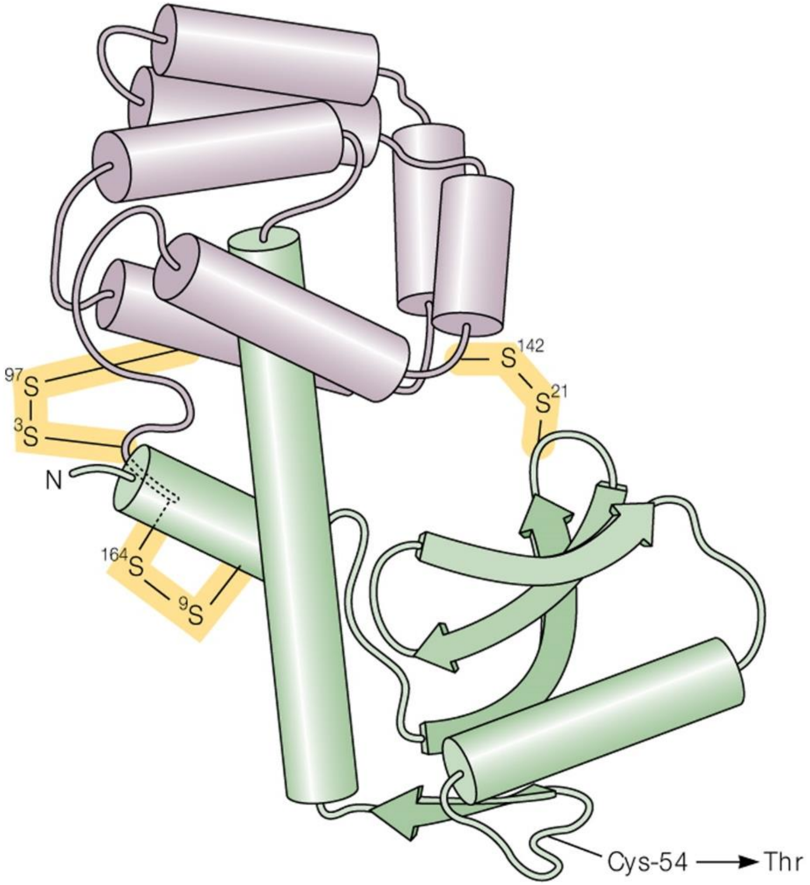


- Soap





Protein Stability Engineering



- Bacteriophage T4 Lysozyme
- To increase the stability
  - Three S-S bonds
  - Cys-54 → Thr