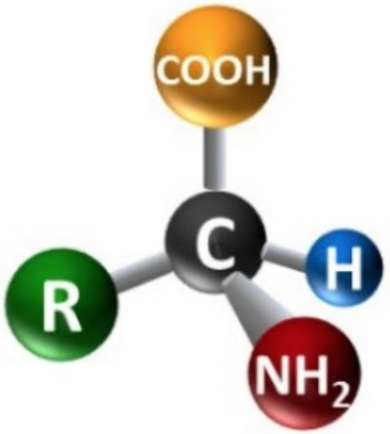
Amino Acids 1



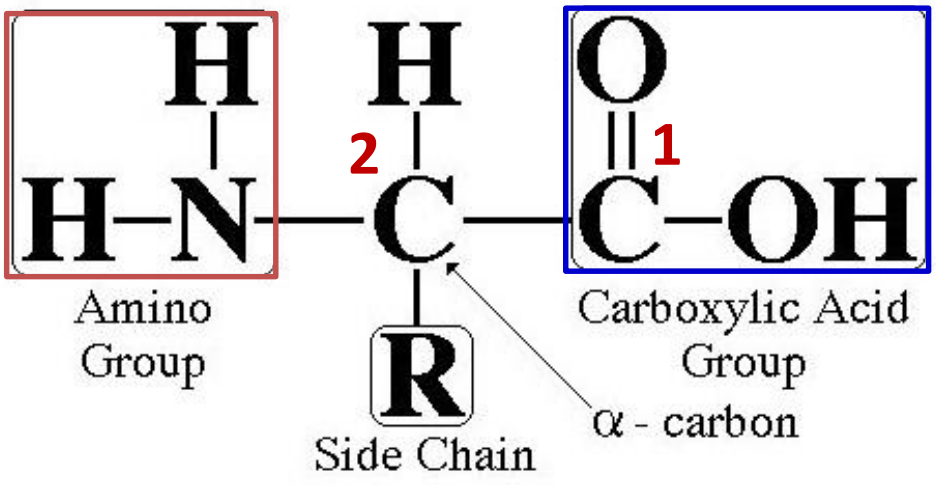
Dr. Nesrin Mwafi

Biochemistry & Molecular Biology Department

Faculty of Medicine, Mutah University

Amino Acid Structure

- Amino acids are biologically important organic molecules that contain both carboxylic acid (-COOH) as well as amine ($-NH_2$) groups
- The side-chain also called "**R**" group is specific to each amino acid



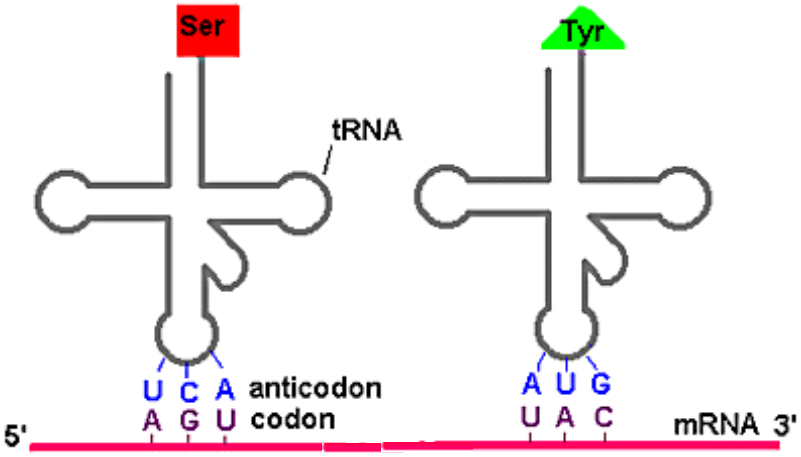
- Amino group is attached to α-carbon (C2)
- C, N, O and H are the key elements of amino acids

Biological significance of Amino Acids

1. Amino acids are N-containing molecules
2. The basic structural building units (monomers) of proteins
3. Precursors of many biomolecules like neurotransmitters (non-protein role)
4. They are also utilized as an energy source

- There are **20 standard** (canonical) amino acids which are encoded directly by triplet codons in the universal genetic code during in vivo protein synthesis process (mRNA translation)

Genetic Code Table



- **The 20 standard** amino acids are known as proteinogenic or natural amino acids

2nd base in codon

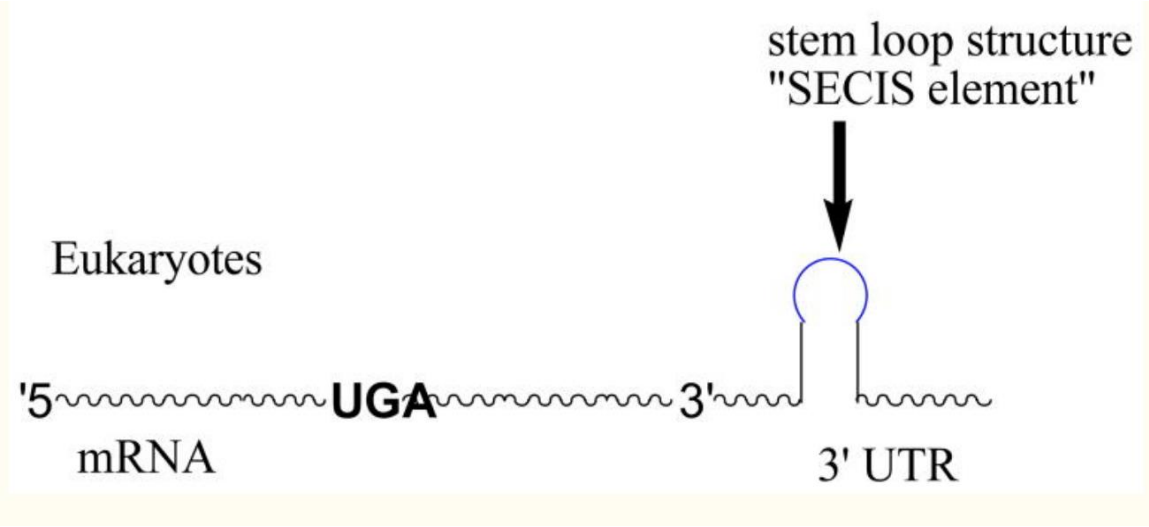
1st base in codon	U	C	A	G	3rd base in codon
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	STOP	STOP	A
	Leu	Ser	STOP	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Standard Amino Acids List

Histidine	Arginine	Alanine
Isoleucine	Asparagine	Asparatate
Leucine	Glutamine	Cysteine
Methionine	Glycine	Glutamate
Phenylalanine	Proline	
Threonine	Serine	
Tryptophan	Tyrosine	
Valine		
Lysine		

Standard Amino Acids

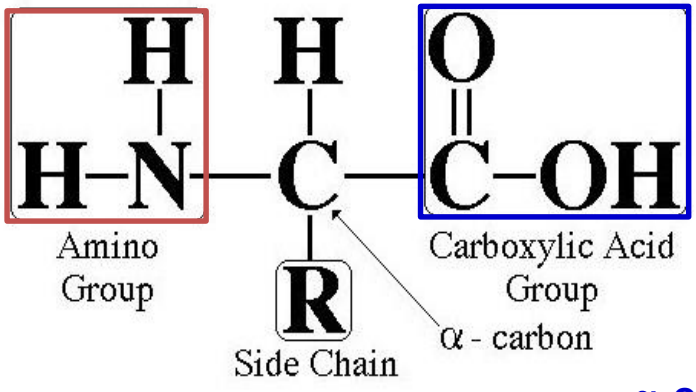
1. They are proteinogenic and natural amino acids (the other proteinogenic amino acids N-formyl methionine, pyrrolysine and selenocysteine are called non-standard or non-canonical amino acids)

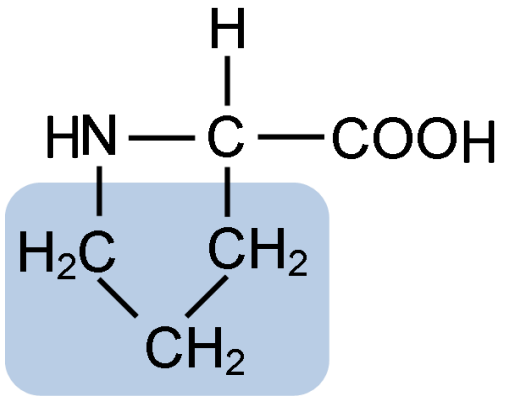


Incorporation of selenocysteine in protein structure by unique mechanism

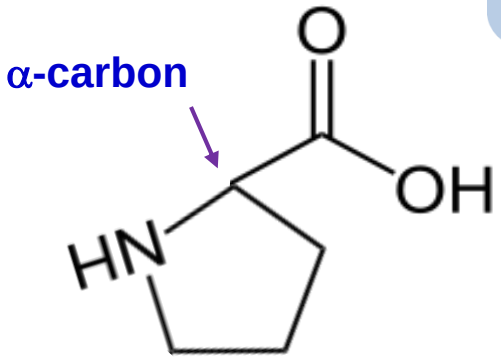
Standard Amino Acids

2. Known as 2-, alpha- or **α-amino acids** as the primary amino group ($-NH_2$) is attached to α-carbon (the carbon next to –COOH group). Proline is an exception which has a secondary amino group (-NH-)



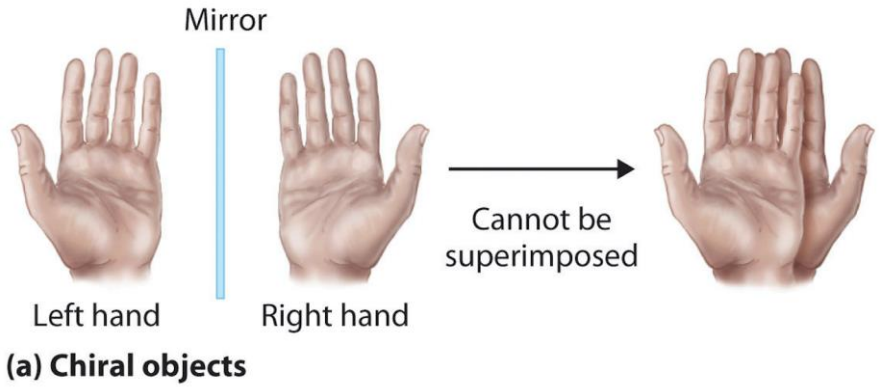


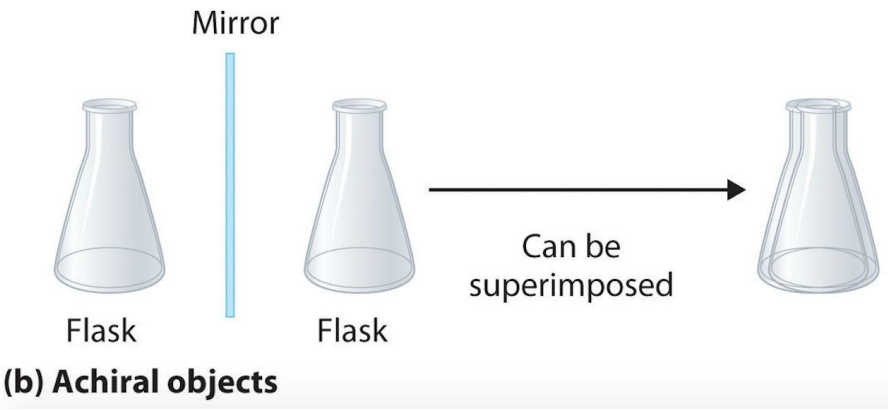
proline



Standard Amino Acids

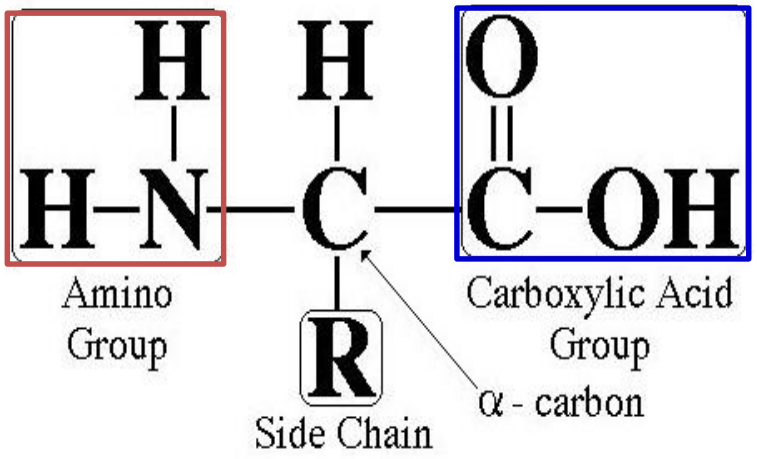
3. They are all chiral molecules (except glycine which has **achiral** C) with **L**- stereochemical configuration (left-handed isomers)

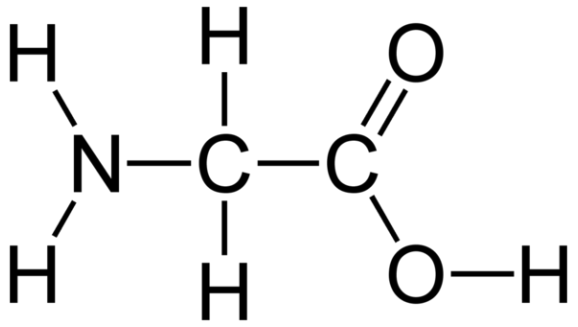




Standard Amino Acids

- Chiral molecules should contain at least one chiral center (**usually a carbon atom**)
- **Chiral carbon**: asymmetric carbon atom attached to 4 different groups of atoms





Glycine

Isomerization

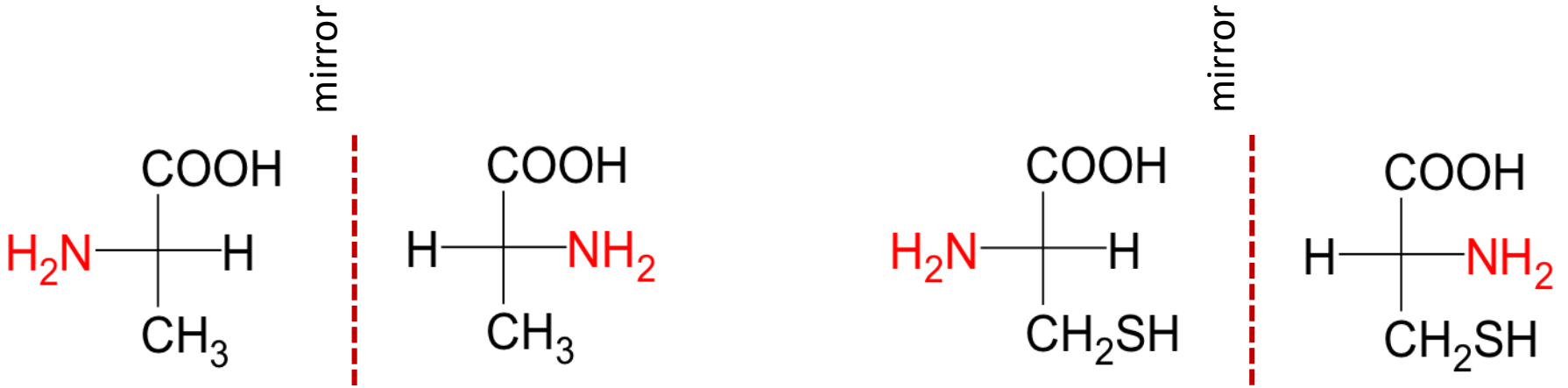
- Isomers: are molecules with same molecular formula but different chemical structures

  1. Constitutional (structural) isomers: atoms and functional groups bind together in different ways
  2. Stereoisomers (spatial isomers): differ in the configuration of atoms rather than the order of atomic connectivity

D/L Amino Acids

- Enantiomers: are two stereoisomers that are mirror images to each other but not superimposable
- **D-** (dexter)/**L-** (laevus) Nomenclature system: commonly used to assign the configurations in sugars (carbohydrates) and amino acids
- As a rule of thumb: if the amino group is on the right-hand side of α-carbon at Fisher projection, the configuration is D. If it is on the left-hand side, the configuration is assigned as L.

Fischer Projections of Amino Acids



L-alanine **D**-alanine **L**-cysteine **D**-cysteine

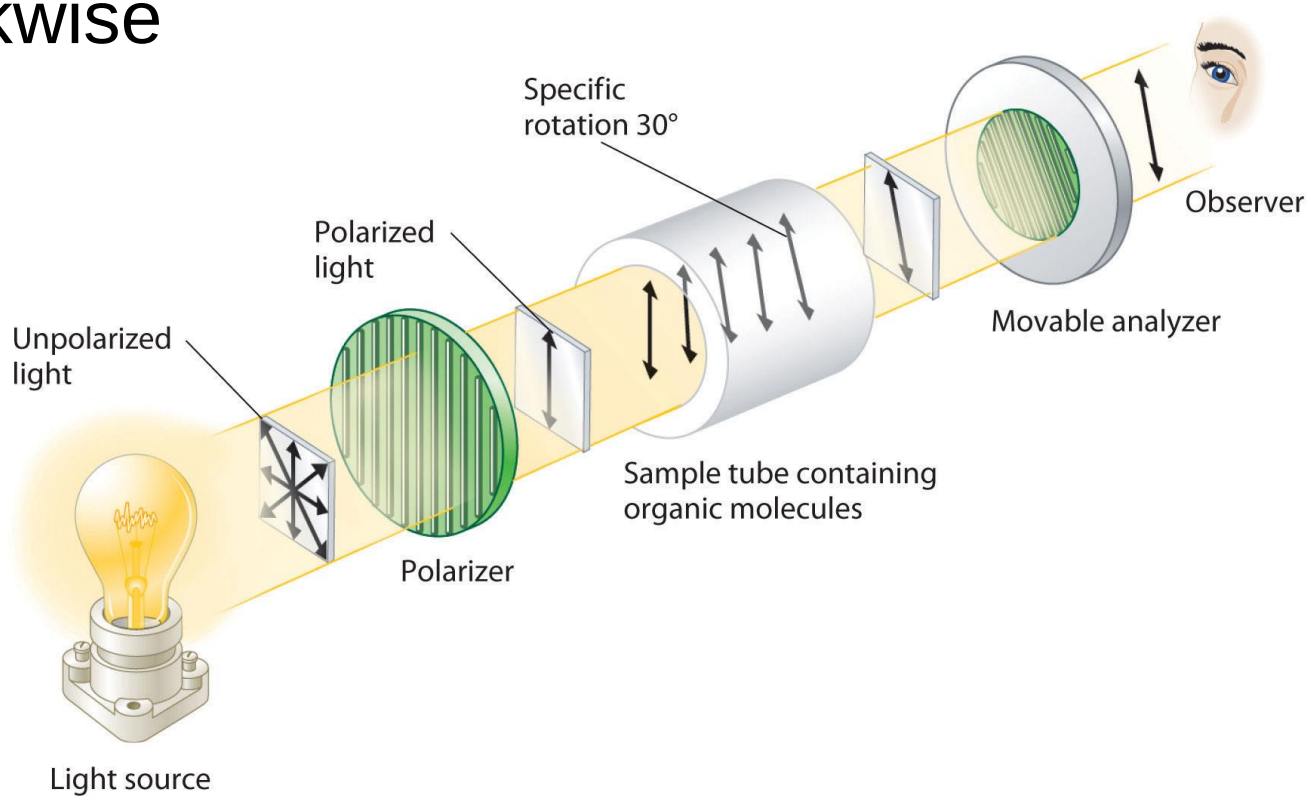
Fisher Projection: is one way commonly used to represent the structure of chiral molecules like carbohydrates and amino acids

D/L Amino Acids

- Most naturally occurring sugars are D-isomers while most naturally occurring amino acids are L-isomers (amino acids of protein)
- D-amino acids polypeptides (right-handed isomers) are components of bacterial cell walls to resist digestion by other organisms

Optical Activity

- Enantiomers are optically active and can rotate the polarized light plane either clockwise or counterclockwise



Polarimeter is used to measure optical rotation

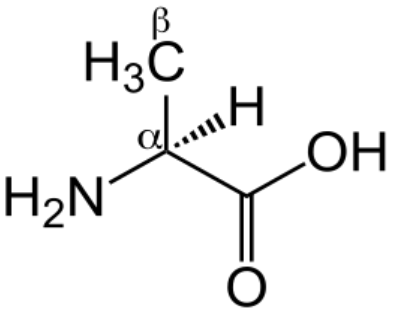
Optical Activity

- **(+)/(-) nomenclature system**: if one enantiomer rotates the light clockwise, it is labeled (+) or (*d*) (dextrorotatory). The second mirror image enantiomer is labeled (-) or (*l*) laevorotatory
- D/L system should not be confused with +/- or *d*/l system. For example, D-isomer might be levorotatory
- 9 of 19 L-amino acids commonly found in proteins are dextrorotatory
- **Racemic mixture** contains equal amounts of each enantiomer (net rotation is zero)

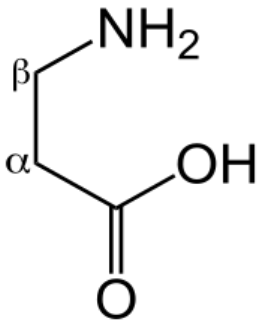
Classification of Amino Acids

- >300 amino acids classified in many ways:

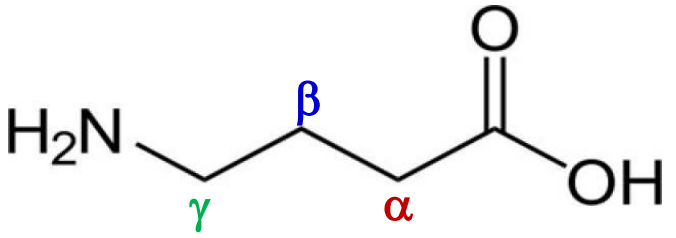
1) Proteinogenic and non-proteinogenic amino acids (either have non-protein role like GABA and carnitine or formed by post-translational modification of protein like hydroxyproline)
2) Standard and non-standard amino acids
3) α, β, γ and δ amino acids



α-alanine



β-alanine

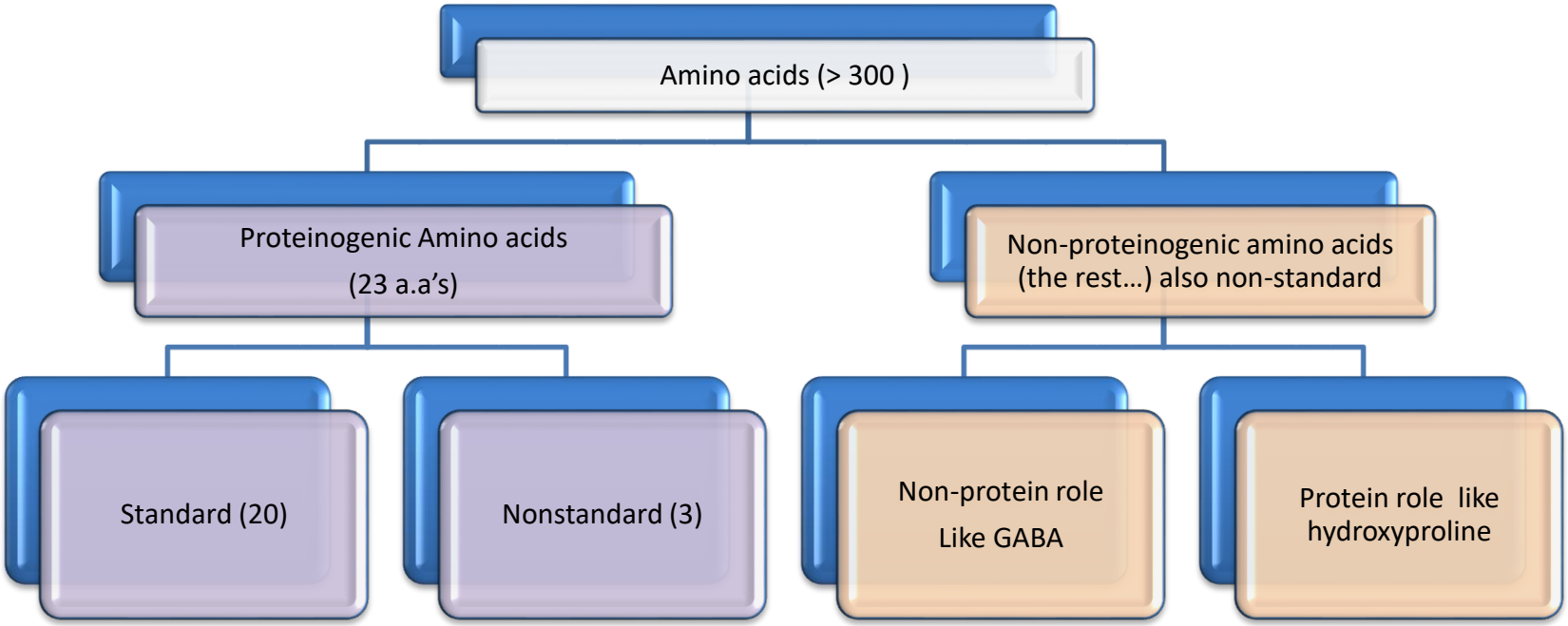


γ-aminobutyric acid (GABA)

Classification of Amino Acids

- β-amino acids are non-proteinogenic with β-alanine is the only common naturally occurring β-amino acid. β-alanine is used in plants and microorganisms in the synthesis of pantothenic acid (vitamin B_5)
- Unlike α-peptides, The β-peptides are artificial peptides used in some antibiotics to counter resistance as they are more stable against proteolytic degradation

Classification of Amino Acids



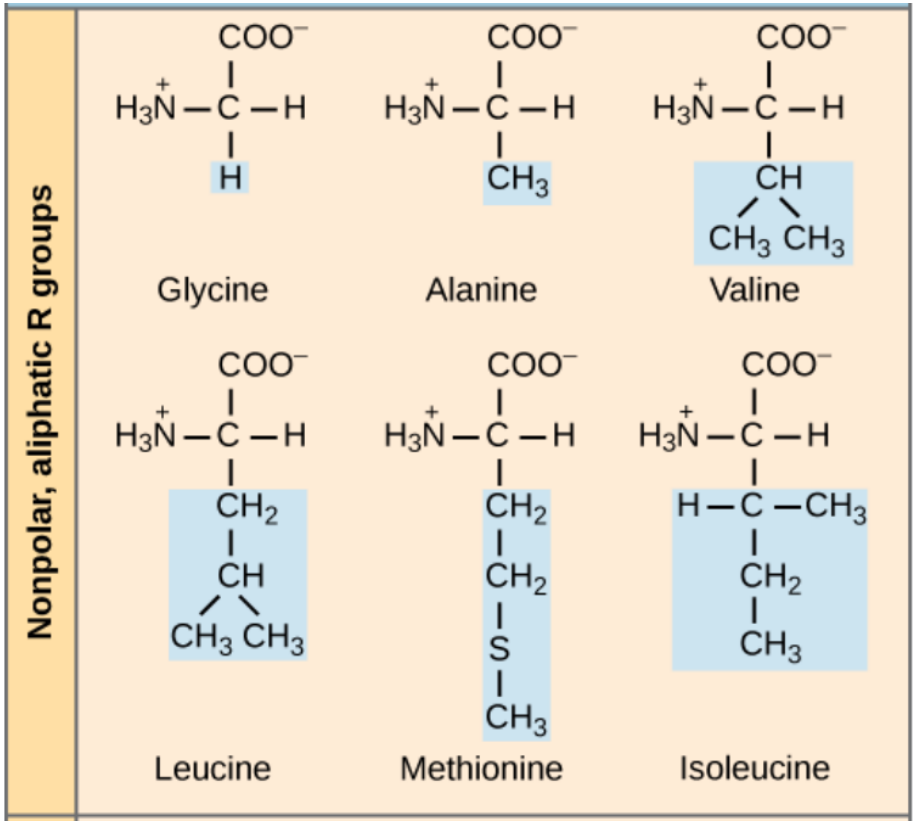
Categories of Standard Amino Acids

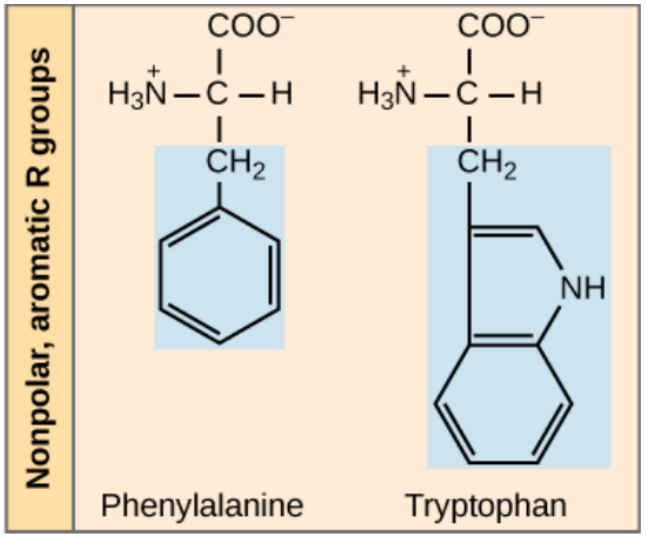
- The 20 standard amino acids are classified into 3 major categories according to the polarities of their "R" groups:

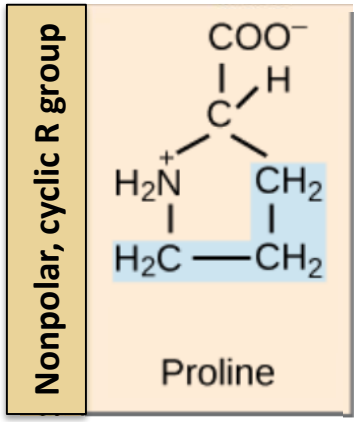
1) **Amino acids with non-polar R groups**
2) **Amino acids with charged polar R groups**
3) **Amino acids with uncharged polar R groups**

Amino acids with non-polar R groups

- 6 amino acids with aliphatic, 2 with aromatic and one with cyclic side chains





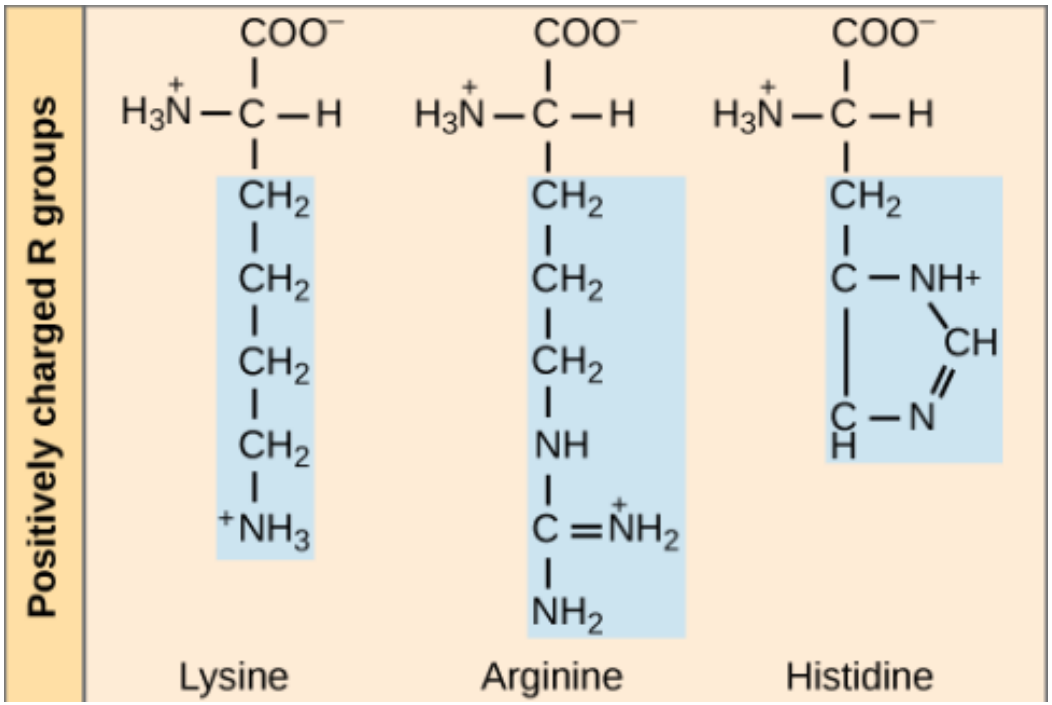


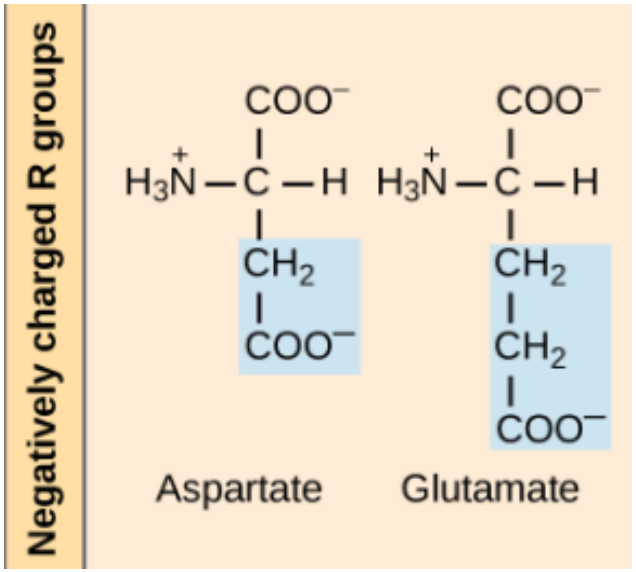
Amino acids with non-polar R groups

- Glycine has the simplest side chain: H atom
- Alanine, valine, leucine and isoleucine have aliphatic hydrocarbon side chains
- Methionine has a thioether side chain (sulfur atom)
- Proline has a cyclic pyrrolidine side chain
- Phenylalanine has a phenyl moiety
- Tryptophan has an indole group

Amino acids with charged polar R groups

- 3 amino acids are positively charged (basic) and 2 amino acids are negatively charged (acidic)



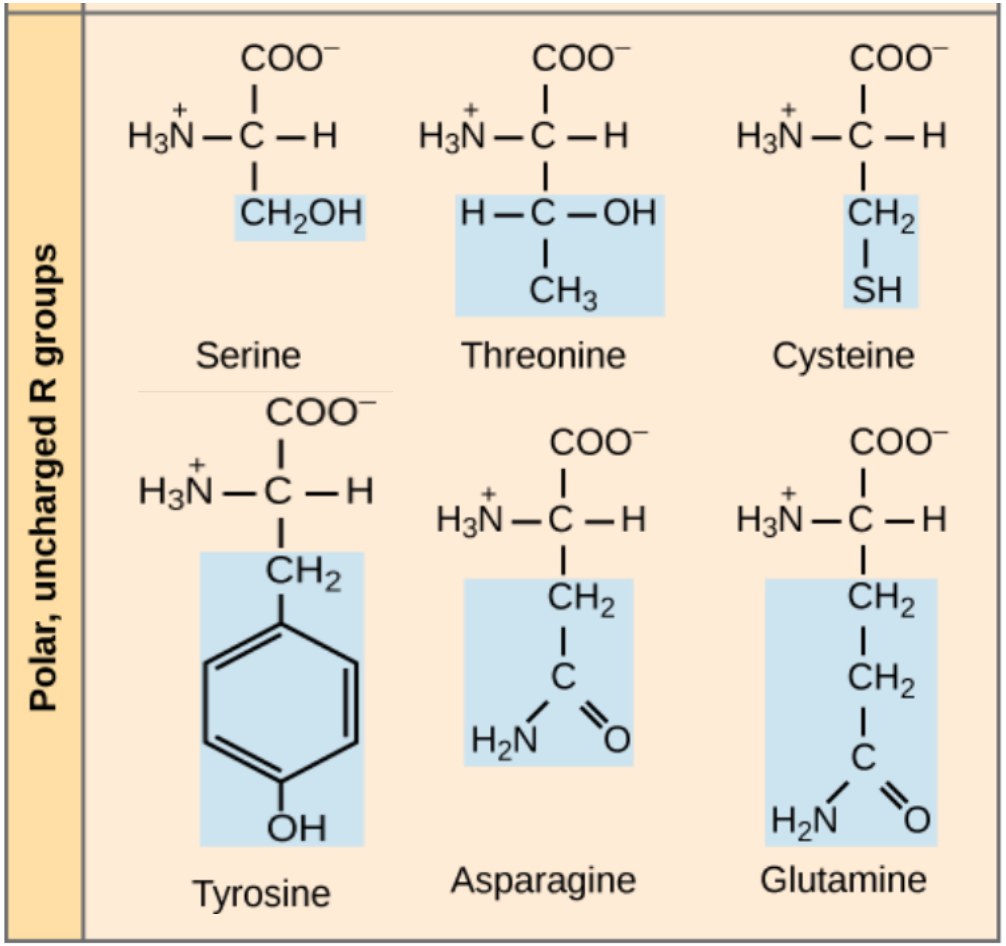


Amino acids with charged polar R groups

- Arginine has a guanidine group
- Lysine has a butyl ammonium side chain
- Histidine has imidazole group
- Aspartic and glutamic acids in their ionized state are called aspartate and glutamate, respectively

Amino acids with uncharged polar R groups

- 6 amino acids with hydroxyl, amide or thiol groups

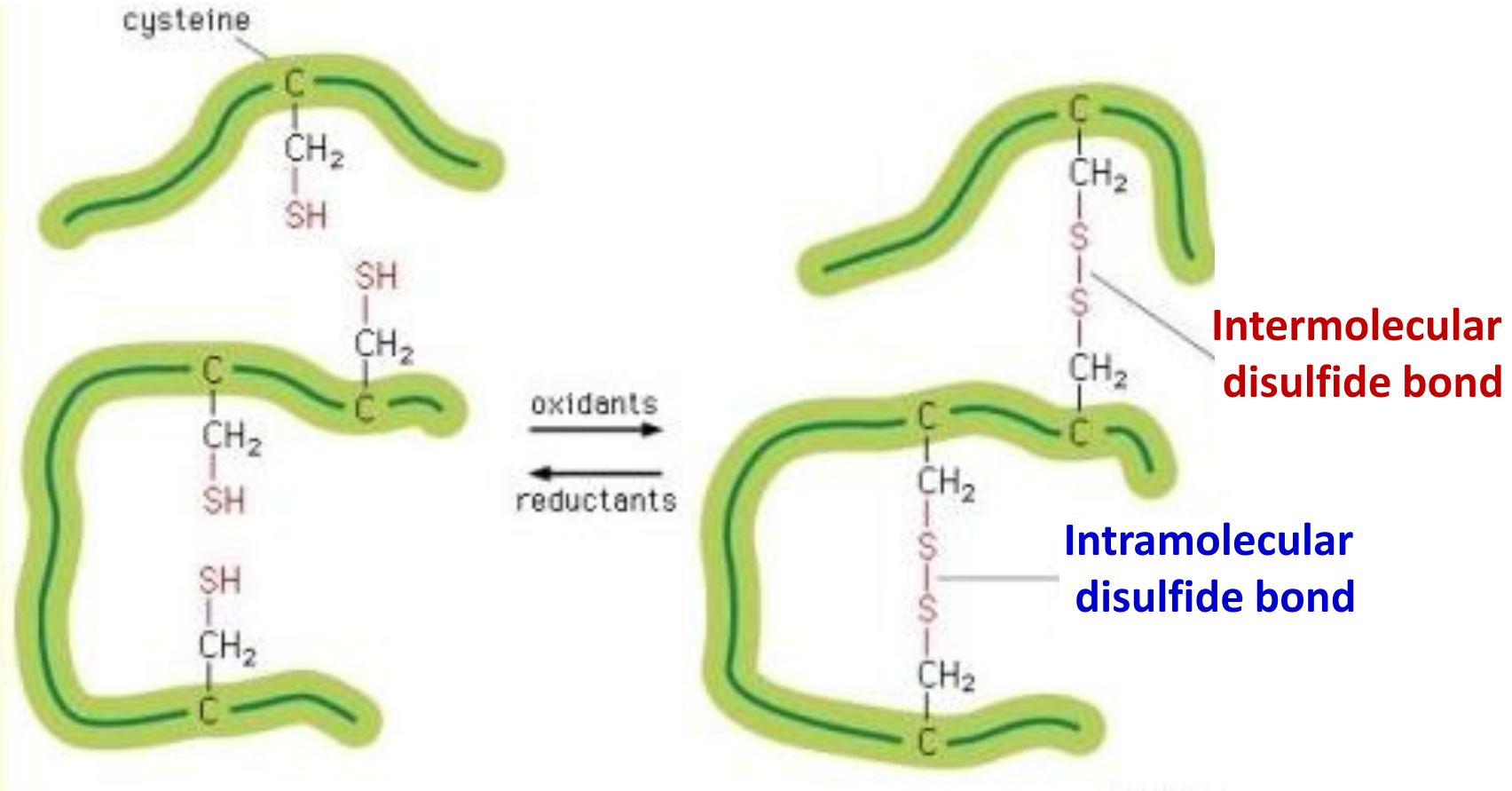


Amino acids with uncharged polar R groups

- Serine and threonine bear hydroxyl (-OH) R group
- Asparagine and glutamine have amide bearing side chains. They are the amide derivatives of aspartic and glutamic acids
- Tyrosine is aromatic and has a phenolic group
- Cysteine has a thiol group that can form a disulfide bond (-S-S-) with another cysteine through the oxidation of 2 thiol groups (cystine is the oxidized **dimeric** form). The disulfide bridge in proteins contributes to the stability and overall shape of a protein

Amino acids with uncharged polar R groups

- **Disulfide bond** is a covalent linkage formed between the sulfhydryl groups (SH) of **two cysteine residues (**after oxidation) to produce a **cystine** residue



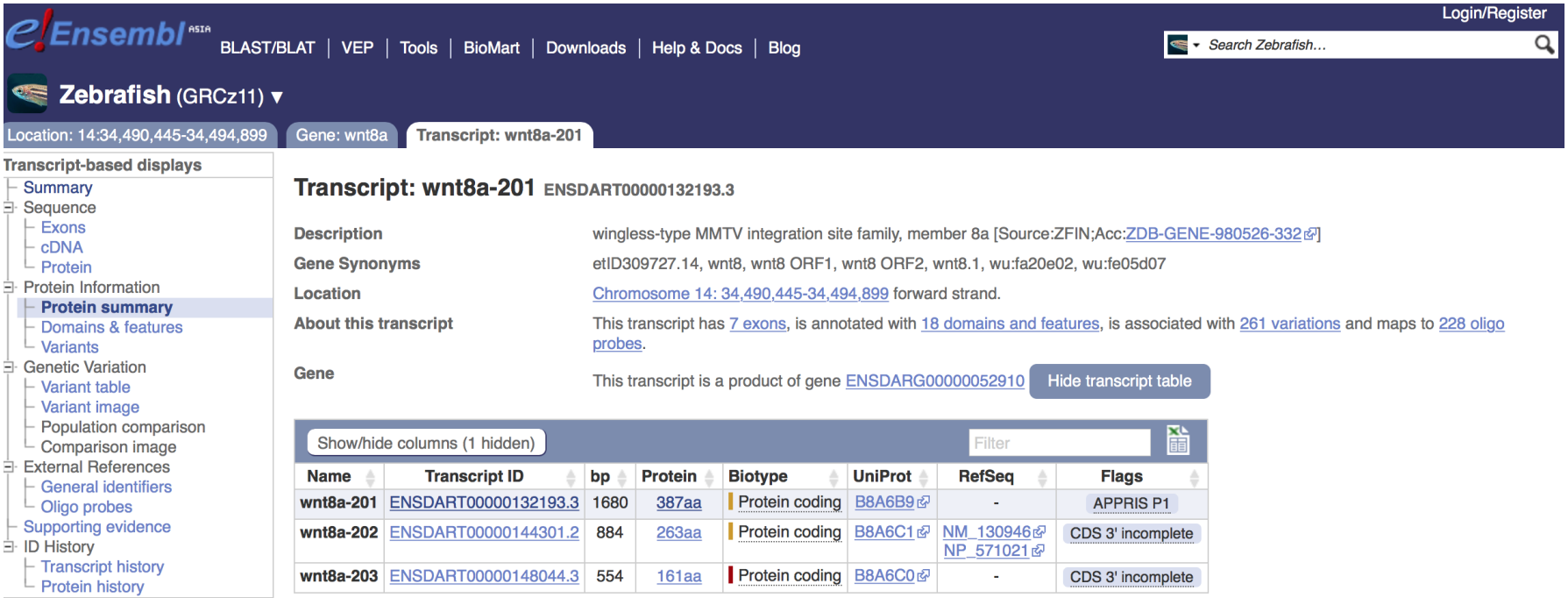
Amino acids with uncharged polar R groups

- Cysteine residues may be separated from each other by many amino acids in the primary sequence of a polypeptide or may even be located on two different polypeptides. The folding of the polypeptide chain(s) brings the cysteine residues into proximity and permits covalent bonding of their side chains.
- Disulfide bond could be **intramolecular** (2 cysteine residues on the same polypeptide chain) or **intermolecular** (2 cysteine residues on two separate/ different polypeptide chains)

Amino Acids Abbreviations

3-letters	1-letter	Amino acid
Ala	A	Alanine
Arg	R	Arginine
Asn	N	Asparagine
Asp	D	Aspartic acid (Aspartate)
Cys	C	Cysteine
Gln	Q	Glutamine
Glu	E	Glutamic acid (Glutamate)
Gly	G	Glycine
His	H	Histidine
Ile	I	Isoleucine
Leu	L	Leucine
Lys	K	Lysine
Met	M	Methionine
Phe	F	Phenylalanine
Pro	P	Proline
Ser	S	Serine
Thr	T	Threonine
Trp	W	Tryptophan
Tyr	Y	Tyrosine
Val	V	Valine

Ensembl Genomic Browser



Ensembl Genomic Browser