12

BIOCHEMISTRY

faculty of medicine - JU2017

ketone starch lipid protein amine carbohydrates isomers

◉ Sheet ○ Slides

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Membrane Proteins

- The cell membrane usually consists of 45% Lipids, 45% Proteins and 10% Carbohydrates.

- Membrane proteins vary, and they are distributed unequally and not randomly in the membrane. (They are concentrated in one region more than the other)

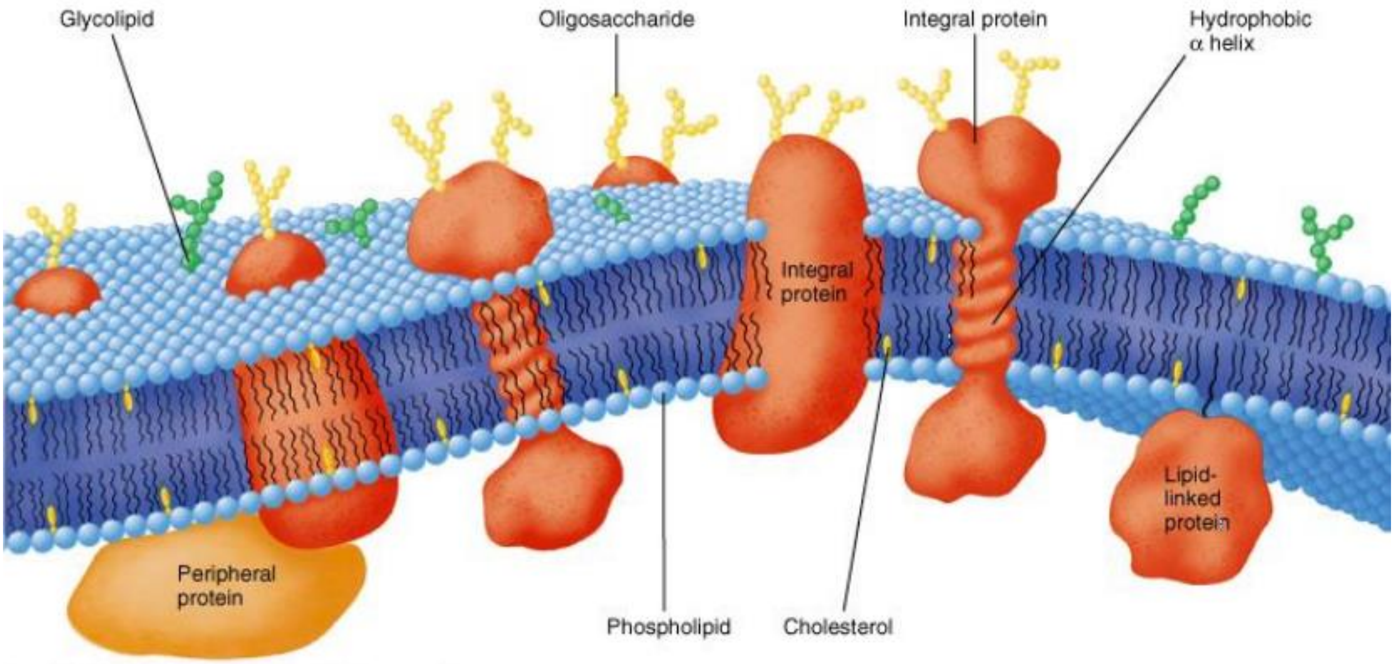
- on each membrane, we don't have only one protein molecule that functions as a receptor, or one protein molecule than functions as a channel for example. We have hundreds of thousands of proteins on the membrane for each function.

- Due to how the proteins are arranged in the membrane, the shape/ arrangement of the membrane is called The Fluid Mosaic Model (Fluid: The membrane is not static. /Mosaic: Proteins decorate the membrane).

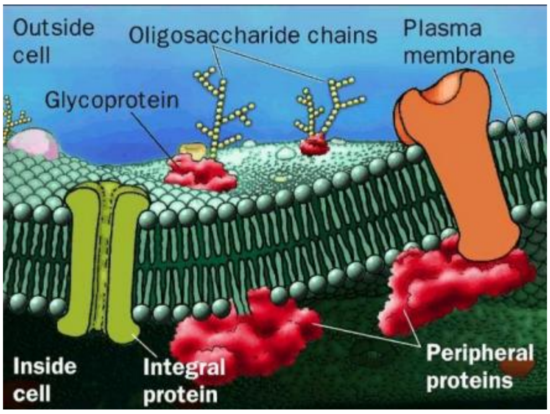
Types of Protein Association with the Membrane

Proteins can attach to the membrane in different ways. They either attach only exteriorly, fully or are anchored to the membrane by lipid groups.

1) **Peripheral Proteins:**



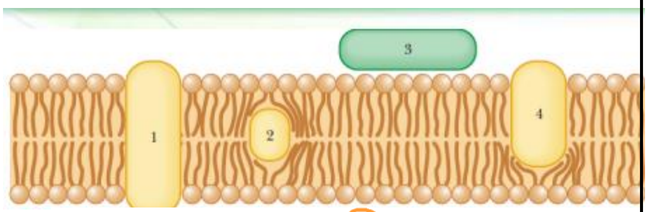
- When proteins are associated with the exterior of membranes via non-covalent (electrostatic) interactions with the phosphate head of the phospholipid , they are called peripheral proteins.



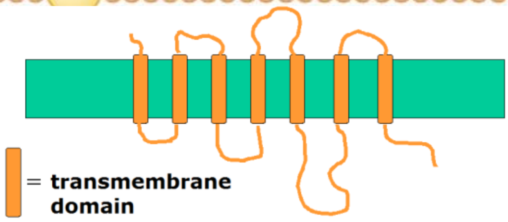
- They are associated with the membrane, but do not penetrate its hydrophobic core.
- They are often associated with integral proteins.
- Peripheral proteins are not strongly bound to the membrane, thus can be removed without disrupting the membrane structure. A mild detergent removes them by breaking non-covalent(electrostatic) interactions between them and the membrane.

2) Integral proteins:

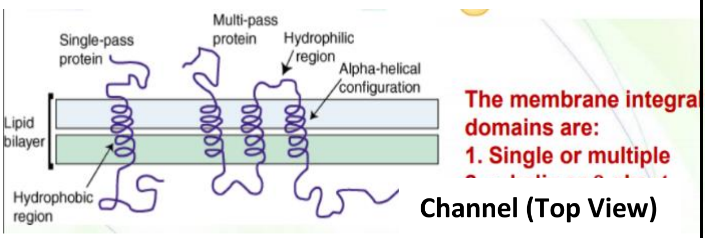
When proteins pass through/are inserted into the membrane, or partially inserted (enter one side of the membrane but don't exit the opposite side) they are called integral Proteins.



- They can be associated in different ways. (Proteins 1,2 and 4 in the picture)

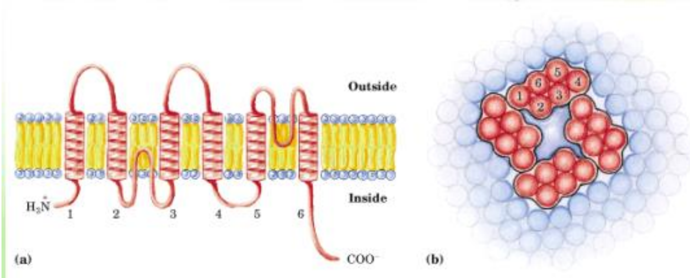


- These Proteins have trans-membrane domains. Trans-membrane domains are the parts of the protein that are actually inserted into the membrane (in the hydrophobic region of the membrane)
- They can be exposed to: *__both the inside and outside of the cell__* (in this case, they enter one side and exit the opposite one, such as **protein number 1** in the picture), *__only one side of the cell__*(**protein 4**) or *__not exposed at all__* (**protein 2**).
- An integral protein may be inserted in the membrane once, and is called a single pass protein in this case, which has one trans membrane region. It may insert into the membrane multiple times



(just like a thread goes through a button) and is called a multi-pass protein, which has more than one trans-membrane region.

- Some of them can form channels. In this case, they are multi-integral (multi-pass proteins).



- Some of them are carriers, like glucose carriers, which carry glucose from one side of the membrane to the other.
- In order to separate integral proteins from the membrane, we have to disrupt the whole membrane.

3) Lipid Anchored proteins:

When proteins are anchored to the membrane via a lipo-moiety (pronounced: lipo-mo-yee-tee), they are called lipid anchored proteins.

- Lipo-moieties are a type of lipoproteins (a protein that has a lipid chain anchored to it). These lipid chains insert into the membrane, anchoring the membrane protein.

Main Functions of Membrane Proteins

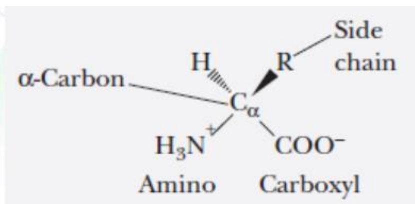
1)Transport: since membranes are impermeable barriers.
i.e.: Channels, carriers

2) Signaling: Protein receptors and other small molecules (like lipids) work in signal transformation.

3) Catalysts: enzyme linked receptors.

Amino acids

An amino acid (often referred to as AA), is an organic molecule which consists of an α-carbon (also called a central carbon). This α-Carbon makes 4 bonds, 3 of which are with mandatory groups that do not differ from one AA to the other:

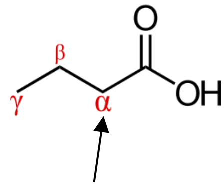


1) A carboxyl group (-COOH).
2) An amino group ($-NH_2$).

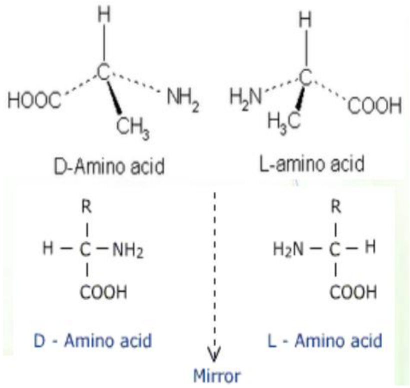
3) A hydrogen atom.

And an organic side group (R-group) which is unique to each amino acid.

- The α-Carbon is the carbon which is exactly beside the carboxyl group carbon. (in other words, it is carbon number 2, since the carboxyl group carbon is number 1).

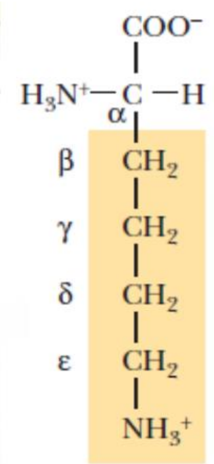


- The α-Carbon is a chiral carbon. It is connected to 4 different groups in all amino acids, hence each amino acid has its own enantiomer and thus D and L configurations. (except one amino acid that doesn't have a chiral α-carbon: glycine). If the ($-NH_2$) is on the **left**, the AA is in **L**-configuration, and if it's on the **right**, the AA is in **D**-configuration.



- In our bodies, the L-Configuration AAs are the ones that are present, whereas sugars are naturally present in the D-configuration in our bodies.

- Sidechain carbon atoms are designated with letters of the Greek alphabet, counting from the α-Carbon. These carbon atoms are, in order, β (spelled Beta), γ (spelled Gamma), δ (spelled Delta) and ε (spelled Epsilon).
- The terminal carbon (the last one in the chain) is referred to as the ω (spelled Omega) carbon, exactly like in fatty acids. (the photo on the right for example, does not have an ω-Carbon, instead, it has an NH_3^+ group attached to the ε-Carbon).



Variation of Amino Acids

Amino acids differ in 6 main characteristics according to the differences in their R-groups:

1) Size: Since R-groups differ in size, AAs will differ as well.
2) Shape: could be ring shaped, branched or any other shape.
3) Charge: the R-group charge (+ve, -ve, or neutral) determines the charge of the AA.
4) Hydrogen bonding capacity: some are hydrogen bond donors, others are acceptors,

the rest are neither donors nor acceptors.
5) Hydrophobic Characteristics: some are polar, others are not.
6) Chemical reactivity: some are reactive, others are not.

Classification of Amino Acids

Amino acids can be classified in many ways. For the sake of this course, we are using the simplest method to classify them.

Non-polar	Polar (Uncharged)	Basic Charged (positive)	Acidic Charged (negative)
Alanine	Serine	Lysine	Glutamate
Valine	Threoeine	Arginine	Aspartate
Leucine	Glutamine	Histidine	
Isoleucine	Asparagine		
Mehionine	Cysteine		
Tryptophan	Tyrosine		
Phenylalanine			
Proline			
Glycine			

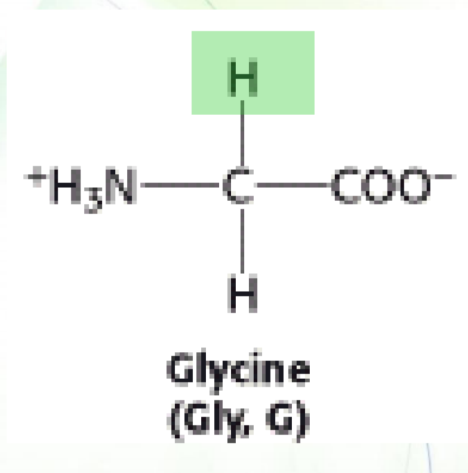
*Note: For each amino acid, you have to know its name, function, 3-letter abbreviation, structure and characteristics.

1) Nonpolar amino acids:

- Can be *aliphatic* (have a chain), *non-aliphatic* (don't have a chain) or *aromatic* (R-group contains a ring structure).
- They are all hydrophobic (except for Glycine, which will be explained later on).

A) Non-Aliphatic:

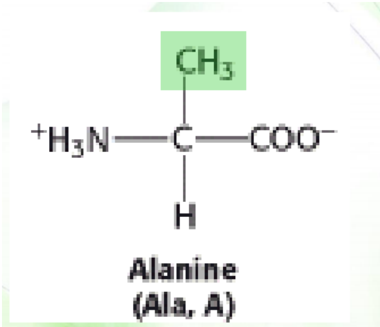
1) Glycine (Gly):



- R-group is a Hydrogen atom.
- It is the simplest Amino Acid.
- It is the ONLY achiral AA.
- It is a derivative (مشتق) of acetic acid.
- Could also be considered a derivative of aminoethane.
- It is the only hydrophilic AA that is non-polar.

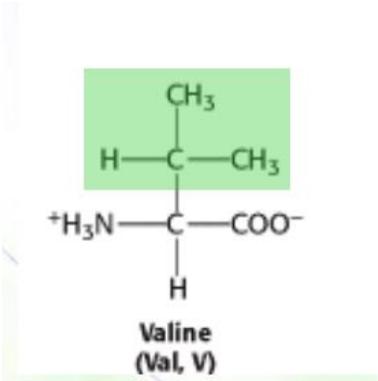
B) Aliphatic:

1) Alanine (Ala):



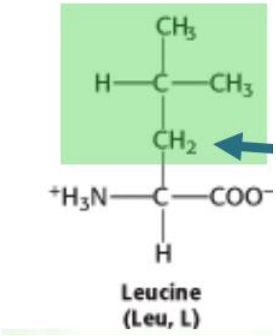
- R-group is a methyl group ($-CH_3$).
- It is the second simplest AA.

2) Valine (Val):



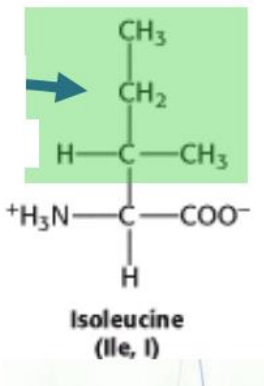
- R-group is branched, making the AA branched at the β-Carbon.
- Essential AA, since the body can't synthesize it.
- In its protein structure, it makes a steric hindrance (hindrance: obstruction), since it's branched at the β-Carbon, affecting the protein structure.

3) Leucine (Leu):



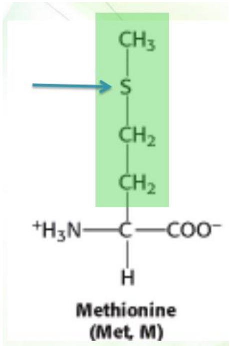
- R-group is branched, making the AA branched at the γ-Carbon.
- Essential AA, since the body can’t synthesize it.
- The branch at the γ-Carbon does not cause steric hindrance.

4) Isoleucine (Ile):

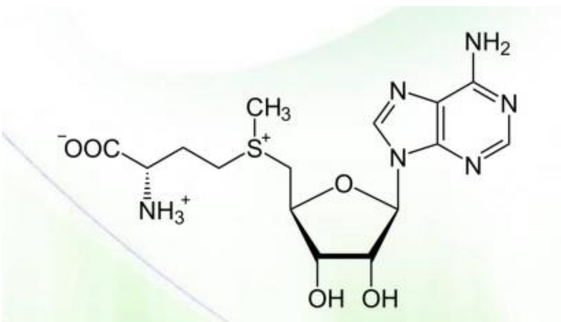


- R-group is branched, making the AA branched at the β-Carbon.
- Essential AA, since the body can’t synthesize it.
- In its protein structure, it makes a steric hindrance (hindrance: obstruction), since it’s branched at the β-Carbon, affecting the protein structure.

5) Methionine (Met):

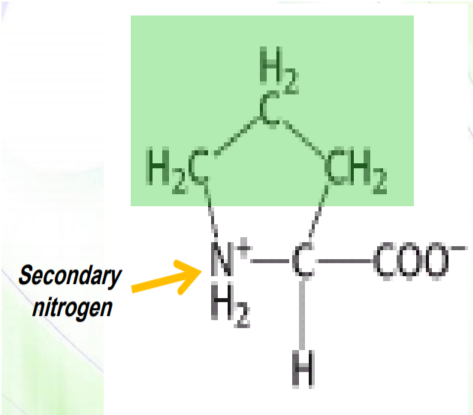


- R-group contains sulfur.
- It is one of two AAs which has a sulfur-containing R group.
- It is a thioether, meaning it has almost an ether formula (R-O-R’) but with a sulfur molecule instead (R-S-R’).
- The sulfur atom is **internal** and not terminal, making the molecule **inactive**.
- It can react to make S- Adenosyl -L- Methionine (SAM) which serves as a methyl donor (single carbon donor) in reactions.



S- Adenosyl -L- Methionine (SAM)

6) Proline (Pro):

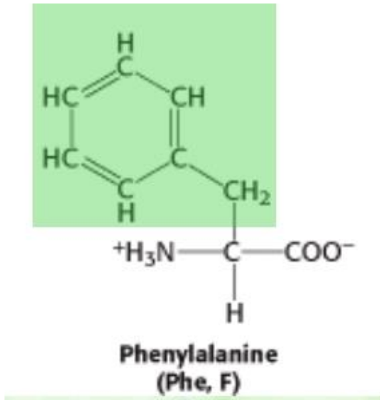


- R-Group has a semi ring shape.
- It's an imino acid
- This is the only AA which has a ring within its structure (not attached to it, but from the structure itself). The ring involves the α-Carbon and the nitrogen molecule, making the AA a rigid one (not flexible).
- It plays a major role in protein structure because of its rigidity.
- When it makes a peptide bond, the nitrogen will form 3 bonds **not** containing hydrogen. Thus, it will **not** be a hydrogen bond donor.

C) Aromatic:

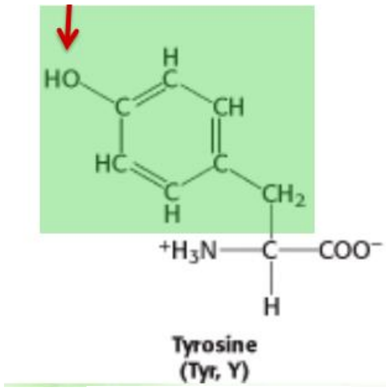
1)Phenylalanine (Phe):

- R-group contains a Phenyl group (-C_6H_5).
- It is similar to Alanine, but with a substituted phenyl group.
- It is highly hydrophobic.



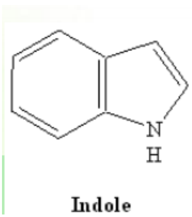
2)Tyrosine (Tyr):

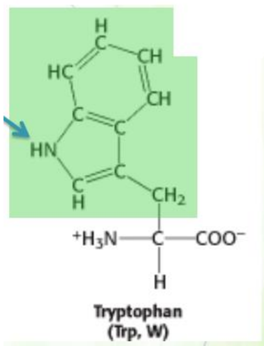
- R-group contains a phenyl and a hydroxyl group.
- Looks like Phenylalanine, but with an (-OH) group added.
- The hydroxyl group makes the molecule reactive due to its capacity to form hydrogen bonds.



3)Tryptophan (Trp):

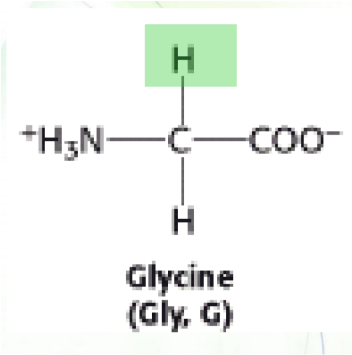
- R-group contains a double ring structure (<u>**indole**</u>).
- It is the bulkiest, most hydrophobic structure in all AAs.





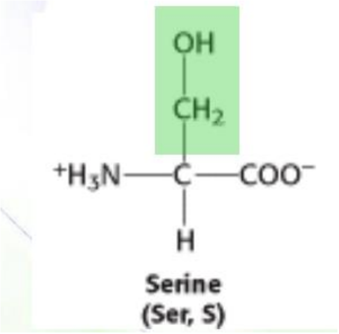
2) Polar (Uncharged) Amino Acids:

1)Glycine (Gly) again:



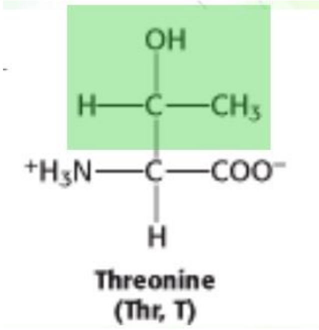
- R-group is a hydrogen atom.
- It is polar. Looking at the R-group itself (H Bond), it is not polar, but the AA as a whole is polar, as it contains a carboxyl group (-COOH) and an amino group ($-NH_2$).
- This makes glycine both hydrophilic for the reason just mentioned, and hydrophobic for the reason in page 6.

2) Serine (Ser):



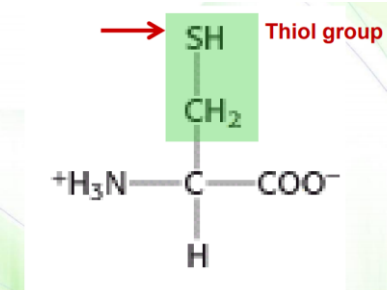
- R-group contains a hydroxyl group(-OH).
- It is close to Alanine in structure.

3) Threonine (Thr):



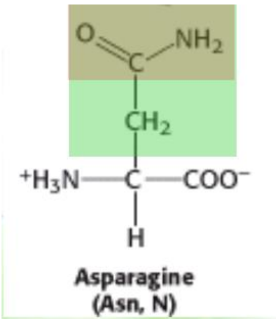
- R-group contains a hydroxyl group (-OH)
- It is close to valine in structure.

4) Cystine (Cys):



- R-group contains Sulfur (Thiol group).
- The second out of 2 AAs containing Sulfur.
- The sulfur atom is terminal, making the AA reactive unlike methionine.
- If we have two Cystine AAs, they would form a disulfide bond, due to the sulfur atom being terminal. This bond is important in stabilizing protein structures.

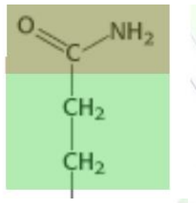
5) Asparagine (Asn):



- R-group contains an Amide group.

6) Glutamine (Gln):

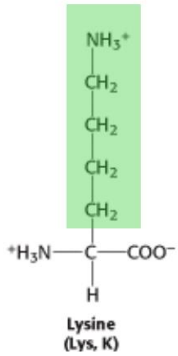
- R-group contains an Amide group.



C) Positively Charged Amino Acids (Basic):

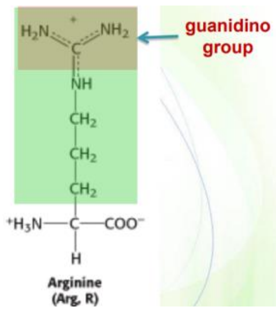
All the AAs in this group have basic properties, and they are:

1) Lysine (Lys):



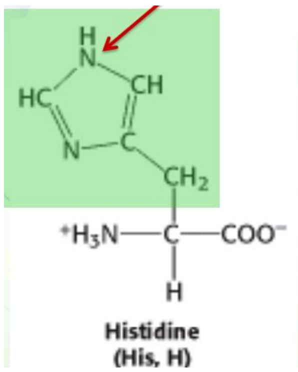
- R-group contains an amino group which is positively charged at physiological pH.

2) Arginine (Arg):

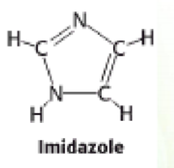


- R-group contains am amino group which is positively charged at physiological pH.
- Contains a **guanidino** group.

3) Histidine (His):



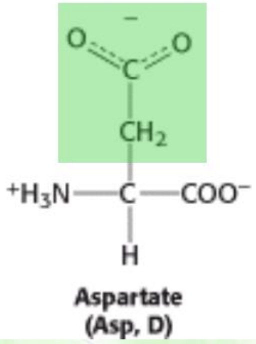
- R-group contains the ring structure, imidazole.
- The nitrogen atom can be positively charged.
- This AA is important, since the nitrogen atom can donate and accept protons near physiological pH.



D) Negatively Charged Amino Acids (Acidic):

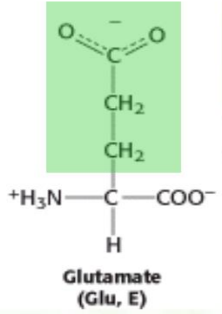
1) Aspartate (Asp):

- R-group contains a ($-COO^-$).
- Precursor of asparagine.
- Also known as aspartic acid.



2) Glutamate (Glu):

- R-group contains a ($-COO^-$).
- Precursor of glutamine
- Also known as glutamic acid.



Summary of Amino Acids and Their Common Characteristics

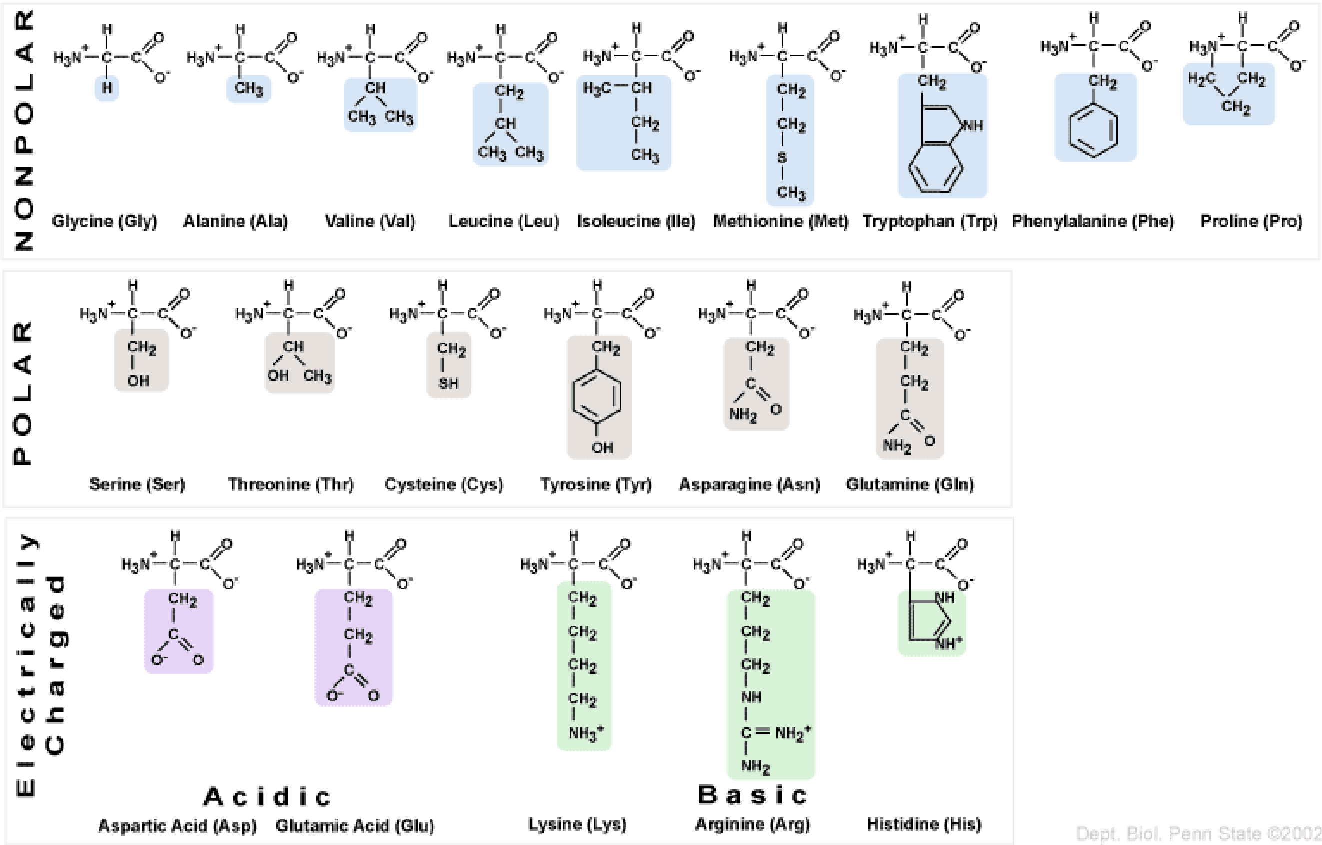
- Glycine is the only achiral AA amongst the rest. Glycine also is hydrophilic and hydrophobic at the same time.
- Valine, leucine and isoleucine all contain branched R-group sidechains and cannot be synthesized by the body.
- Valine and isoleucine are branched at the Beta carbon. This causes steric hindrance in their protein structures.
- Methionine and cystine are the only AAs with a sulfur atom in their structures.
- Serine and threonine are the two AAs with a hydroxyl group in their R-side chains. This makes them polar and reactive.
- The non-polar aromatic AAs are the most hydrophobic ones. Tryptophan is the most hydrophobic of all AAs.
- Asparagine and glutamine have amide groups in their R-side chains.
- Lysine and arginine contain amino groups in their R-side chains.
- Aspartate and glutamate contain a ($-CO_2^-$) group in their R-side chains.

General Characteristics of Amino Acids

1) Amino Acids are the building blocks of proteins.
2) All AAs are chiral, because they connect to 4 different groups. One AA on the other hand is not. Glycine is connected to two hydrogen atoms, making it the only AA with an achiral α-Carbon.

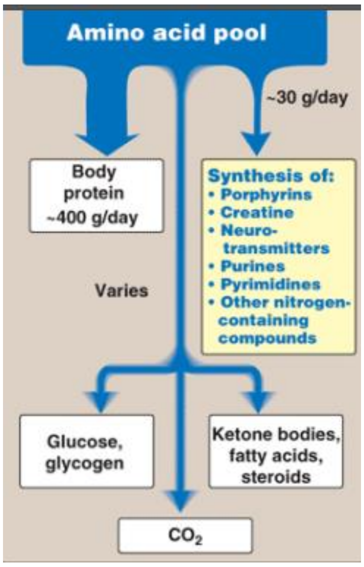
3)Acid-Base Properties: Another important feature of free amino acids is the presence of both a basic (-NH_2) and an acidic (-COOH) group at the α-carbon. Compounds such as amino acids that can act as either an acid or a base are called amphoteric.

4) Amino acids are found only in L-form in proteins in the human body. If the D-form is present, it is converted into the L-form.



* you can revise all the AAs and their structures from this picture after studying them.

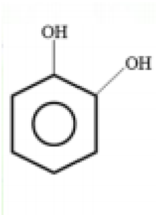
Biological Significance of Amino Acids



- Amino acids are functional by themselves, since they are the building blocks of proteins.
- AAs can also be present in other molecules. The α-nitrogen atom of amino acids is a primary source for many nitrogenous compounds, such as: hormones, neurotransmitters and biologically active peptides.
- We can also derive other molecules from AAs such as porphyrins, creatine, purines, pyrimidines and other nitrogen containing compounds (mentioned in the point above).

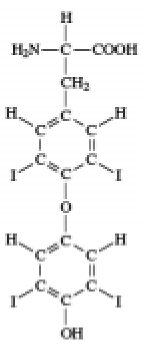
Some Amino Acids that have derivatives are:

1) Tyrosine:



catechol

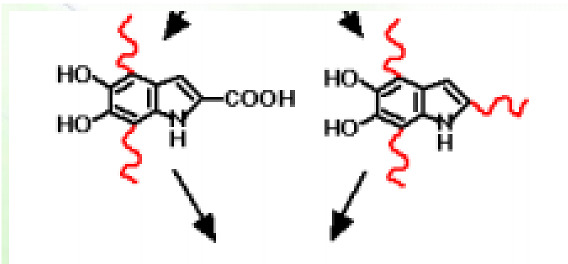
- It is the precursor of neurotransmitters known as catecholamines (catechol ring containing structures). These neurotransmitters are responsible for the fight-or-flight reactions, and they are: dopamine, norepinephrine and epinephrine (also known as adrenaline).

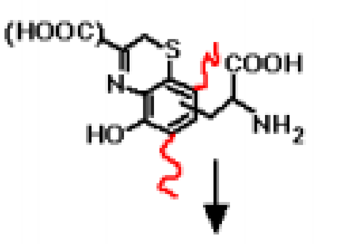


thyroxine (Thy)
occurs only in the hormone protein thyroglobulin: I= iodine

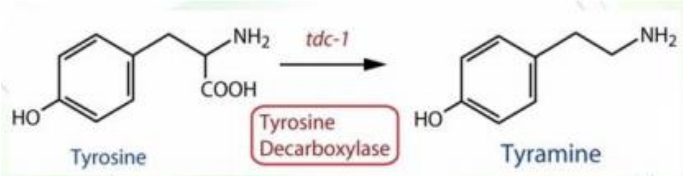
- It is also a precursor of other molecules such as:

1)Thyroxine: which is the thyroid gland hormone.
2) Melanin: Melanin is the pigment which gives color to our skin. It has two types: Eumelanin, which gives our skin the dark color, and pheomelanin which gives the red color.





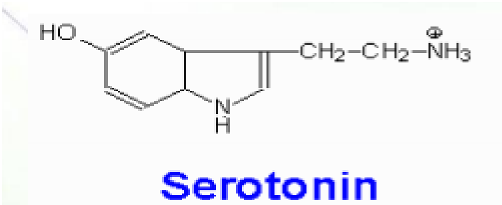
- It can also be converted to tyramine, which functions just like epinephrine. Tyramine is found in cheese.

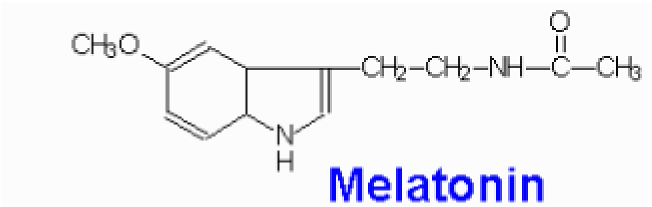


2) Tryptophan:

- Tryptophan is a relaxant that is mainly found in milk.

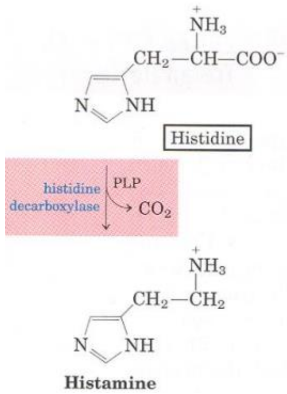
- It serves as the precursor for the synthesis of two neurotransmitters: serotonin (neurotransmitter-sedative) and melatonin (which is responsible for your day-night cycle, meaning it tells your body when to sleep and when to wake up.)





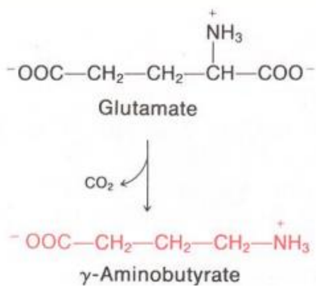
3) Histidine:

One main biological molecule derived from histidine is histamine. Histamine:



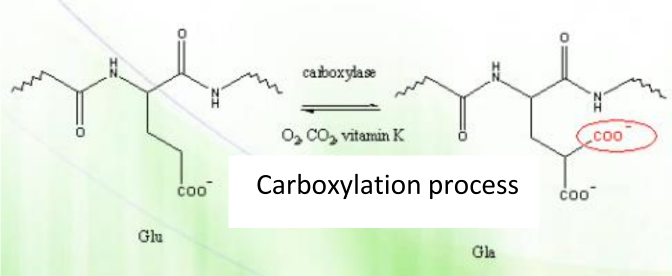
- Regulates physiological function in the gut.
- Acts as a neurotransmitter.
- Causes allergic symptoms (a major cause for asthma).
- Contributes to the inflammatory response.
- Causes constriction of smooth muscles.

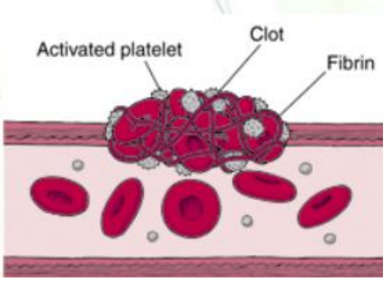
4) Glutamate:



- Is a precursor of γ- aminobutyric acid (GABA), which is an inhibitory neurotransmitter in the CNS.

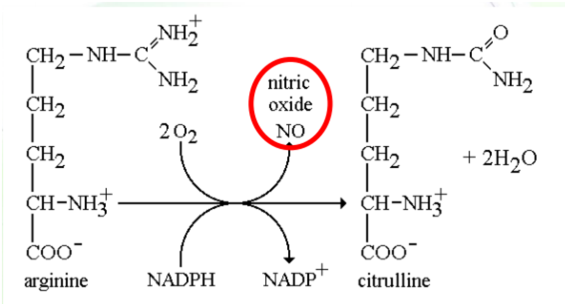
- The glutamate residues of some clotting factors are carboxylated (addition of carboxyl group) to form γ-carboxyglutamate (Gla) residues. Vitamin K is essential for the process. This carboxylation is essential for the function of clotting factors.





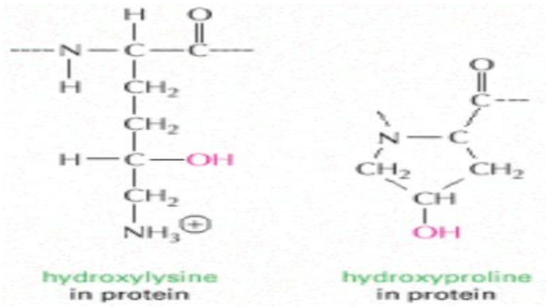
5) Arginine:

- L-arginine is the precursor of nitric oxide (NO). NO has several functions including: vasodilation, inhibition of platelet adhesion, inhibition of leukocyte adhesion, antiproliferative action. It is also a scavenging superoxide anion (anti-inflammatory).



6) Lysine and Proline:

- Both are hydroxylated and are part of collagen structure.



The End!

Thank you for bearing!

*Some good resources to read from are: https://www.britannica.com/science/amino-acid
2) https://www.khanacademy.org/test-prep/mcat/biomolecules/amino-acids-and-proteins1/a/chemistry-of-amino-acids-and-protein-structure