Amino Acids

[Study guide covering chapter 6]

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Structure.

- Phosphate group.
- Nitrogen/amino group: attached to the alpha carbon of the carboxylate.
- Carboxylate group.
- R-side chain.
- Concept of zwitterion.
- Amine group pH ~9.5
- Physiological pH ~7.5
- Alpha carbon is chiral except in glycine.
- Glycine, the carbon is achiral (has two H).
- Mammalian AA are L configuration (as opposed to D).
- Alpha aminos are AA attached to alpha carbon.
- Primary structure: sequence of AAs.
- AA joined via peptide bonds betw. COO- of one AA and the NH3+ of the other.
- Backbone >> carbolxylate, alpha carbon, and amino group.
- AA are the side chains.
- Binding sites.
- Ligand-receptor pairs.
- N-terminal (where the amino group is).
- C-terminal (where the carboxylate is).

Classification of Amino Acids.

- pKa
- Hydropathic index: a scale to describe hydrophobicity of the side chain.
- Glycine is a special case where its R-group is just H. Has the least steric hinderance. Can be found in the "nooks and crannies".
- Nonpolar: alanine, valine, leucine, isoleucine; aliphatic; very hydrophobic; typically form the hydrophobic cores.
- Proline is another special case as it's attached to the backbone twice. It has both an alpha carbon and alpha amino group. Proline is an imino acid. Rigid and forms kinks. Restricted conformations.

- Aromatic acids: 6-member ring of C and H; conjugated double bonds. H on the ring doesn't participate in H-bonding. The substituents on the ring influence side chains characteristics & determine what action takes place (e.g. hydrophilic or hydrophobic).
- Aliphatic, polar, uncharged AA: has amide group (asparagine, glutamine); or hydroxyl group (serine, threonine); form H-bonds with water. Typically found on surfaces.
- AA with sulfur: cysteine and methionine. Can form disulfide bridges via oxidation of the sulfhydral groups, but it doesn't always do that. The action/function depends on it's surrounding environment and "what else" there is.
- Acidic AA: carboxylic acid groups; e.g. aspartate and glutamate. Their negative charge can form ionic bonds with cations.
- Basic AA: have side chains containing N (+) and tends towards basicity; e.g. histidine, lysine, arginine. Their positive charges can form ionic bonds with anions. Lysine and arginine can form bonds to anionic compounds w/protein binding sites (i.e. those protein binding sites can become incorporated into a new compound as well as become altered). Those ligand-receptor sites can become "grandfathered in".
- Acidic/basic characteristics can allow AAs to participate in H-bonds and salt bridge formations.
- Carbon positions can be described using the Greek letters: alpha, beta, gamma, delta, epsilon).
- If pH < pKa then it favors the protonated form (-COOH, -NH3+). If pH>pKa, then it favors the deprotonated form (-COO- and -NH2).
- Imidazole ring. C3N2H4 (compound).
- In proteins, only the side chains, N-terminal, and C-terminal are dissociateable. Other C, N, H that form part of the backbone do not participate in acidic/basic characteristics.
- Electrophoresis: separate proteins via charge differences. Helps to identify proteins and components.

Variations in Protein Structure.

- Protein structure and characteristics can vary between different individuals and different ages. This variant nature is called variant regions.
- Hypervariable describes a situation where variation is tolerable within reason.
- Invariant regions, in contrast, do NOT vary between individuals, species, etc. Variation is NOT tolerated.
- Polymorphisms: when allele variations occur with great frequency.
- Homologous proteins: these belong to the same ancestral proteins.
- Paralogs: proteins that have similar structure and function that have evolved from the same gene after gene duplication.
- Divergent evolution: when one gene performs it's expected function yet a copy mutates into a different function or have different characteristics.
- Superfamily: large family of homologous proteins.
- Isoforms: 2+ functionally similar proteins with similar structure (but not identical) or AA sequence; isoforms of a protein have the same function.
- Isozymes: 2+ enZ w/similar functions but differ in structure; isozymes catalyze the same reactions.
- Developmental variation: structures and functions differ at different developmental stages.

- Tissue-specific isoforms: proteins that function "the same" but they vary in structure/characteristics from tissue group to another tissue group.
- Tissue-specific isozymes: enZ that function "the same" but they vary in structure/function from tissue group to tissue group.
- Species variation: proteins and enzymes (and their structure and function) can vary from species to species.

Modified Amino Acids.

- Post-translational modification. Post-protein synthesis, some AA residues in the primary sequence may be modified. These changes may or may not serve/enhance function or characteristics. Usu. occur after protein has already folded into its specific conformation.
- Glycosylation: the addition of carbohydrates to a molecule.
- Fatty acylation: the addition of lipid group(s) to a molecule. These types of changes (N- or O-) can enhance barrier/surface protection (e.g. N-linked oligosaccharides). O-linked oligosaccharides can enhance secretions.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4975971/
- https://www.nature.com/articles/nrm.2015.11
- Prenylation: the addition of farnesyl or geranylgeranyl groups via thioether linkate to specific cysteine residues of membrane proteins.
- Regulatory modifications. Phosphorylation, acetylation, and adenosine diphosphate (ADP)-ribosylation of some AAs can alter bonding characteristics of the AA.
- Other amino acid posttranslational modifications: can alter the activity of the protein.
- Selenocysteine: found in a few enZ and is required to activate those enZ.

Resources.

References.

Lieberman, M., & Peet, A. (2017). *Marks' basic medical biochemistry: A clinical approach*(5th ed.). Philadelphia, PA: LWW.