PROTEINS

Standard Amino Acids

- Building blocks of proteins
- More then 300 AA have been described
- Only 20 AA are found in mammalian tissue
- These 20 AA are called primary or standard AA

Standard Amino Acids

- Each AA contain a amino group (NH2), carboxyl group (COOH) and a distinct side chain exception to this rule is Proline which contains Imino group (NH) instead of amino group

Standard Amino Acids

- Phenylalanine
- Tryptophan
- Valine
- Threonine
- Leucine
- Isoleucine
- Methionine
- Serine

Standard Amino Acids

- Histidine
- Arginine
- Lysine
- Leucine
- Alanine
- Cysteine
- Glutamic acid
- Aspartic acid

Non Standard Amino Acids

- These Amino acids do not take part in the protein synthesis but play important role in the body.

Non Standard Amino Acids

- Citrulline
- Ornithine
- Taurine
- DOPA
- GABA

Classification of Standard Amino Acids

- Amino acids with Aromatic side chain
- Amino acids with aliphatic side chain
- Amino acids with side chain containing Sulphur atom
- Amino acids with Acidic side chains
- Amino acids with Basic side chains
- Amino acids with side chain having OH group
- Imino Acid

Amino acids with Acidic Side Chains

- These are mono amino dicarboxylic
- Aspartic acid
- Glutamic acid

Amino acids with Basic Side Chains

- These are diamino monocarboxylic
- Arginine
- Histidine
- Lysine

Amino Acids with Aliphatic Side Chain

- Glycine
- Alanine
- Valine
- Leucine
- Isoleucine

Amino Acids with Side Chain Having OH Group

- Serine
- Threonine

Amino Acids with Side Chain Containing Sulphur Atom

- Cysteine
- Cystine
- Methionine

Amino Acids with Aromatic Side Chain

- Phenylalanine
- Tyrosine
- Tryptophan

Classification of Proteins

- **Simple Protein**
  - Albumin
  - Globulin
  - Prolamin
  - Histone
  - Protamine

Albumins

- These are water – soluble proteins
- Occur in both plant and animal kingdoms.
- Coagulated by heat
- Examples:
  - Serum albumin
  - Ovalbumin
  - Lactalbumin

Globulins

- Insoluble in water
- They are found in animals
- E.g.
  - Lacto globulin
  - Serum globulins
  - Legumin

Globulins

- Globulins are more easily precipitated than albumins and this can be done by only half- saturation with ammonium sulfate.
- Thus half-saturation with ammonium sulfate can be used to separate globulins from albumin; this process is called salting out.

Globins

- These are rich in histidine but are not basic.
- They unite with heme to form hemoglobin
- Hemoglobin of different species differs only with respect to goblin, but the heme part is the same in all cases.

Prolamins

- These are soluble in 70 to 80% ethanol but insoluble in water and absolute alcohol
- Examples are gliadin of wheat and zein of maize.
- These are rich in the amino acid praline but deficient in lysine.

Histones

- These are very strongly basic proteins
- They are rich in arginine
- In combination with deoxyribonucleic acid (DNA) they form Nucleoproteins or Nucleohistones which occur in nuclei forming chromatin material

Histones

- The association of DNA and Histone gives rise to complex called nucleosomes, 10nm in diameter, in which DNA strands wind around a core of Histone molecules.
- Histones are soluble in water but not in ammonium hydroxide.
- These proteins contain little or no tryptophan

Protamines

- These are present in sperm cells
- They are of relatively smaller size
- They are basic protein and resemble but unlike them are
- Soluble in ammonium hydroxide
- Like Histone they form nucleoproteins with nucleic acids and are rich in arginine. These proteins lack in both tyrosine and tryptophan

Functions of Proteins

- Catalytic Proteins, e.g. Enzymes
- Regulatory Proteins
- Structural Proteins, e.g. hairs, Nail etc
- Transport Proteins, e.g. Albumin

Functions of Proteins

- Defensive Proteins, e.g. Immunoglobulin
- Contractile Proteins, e.g. Actin, Myosin
- Genetic Proteins, e.g. Nucleoproteins
- Storage Proteins

Structural Classification of Proteins

- Derived Proteins
- Primary derived proteins (denatured proteins)
- Secondary derived proteins (hydrolytic proteins)

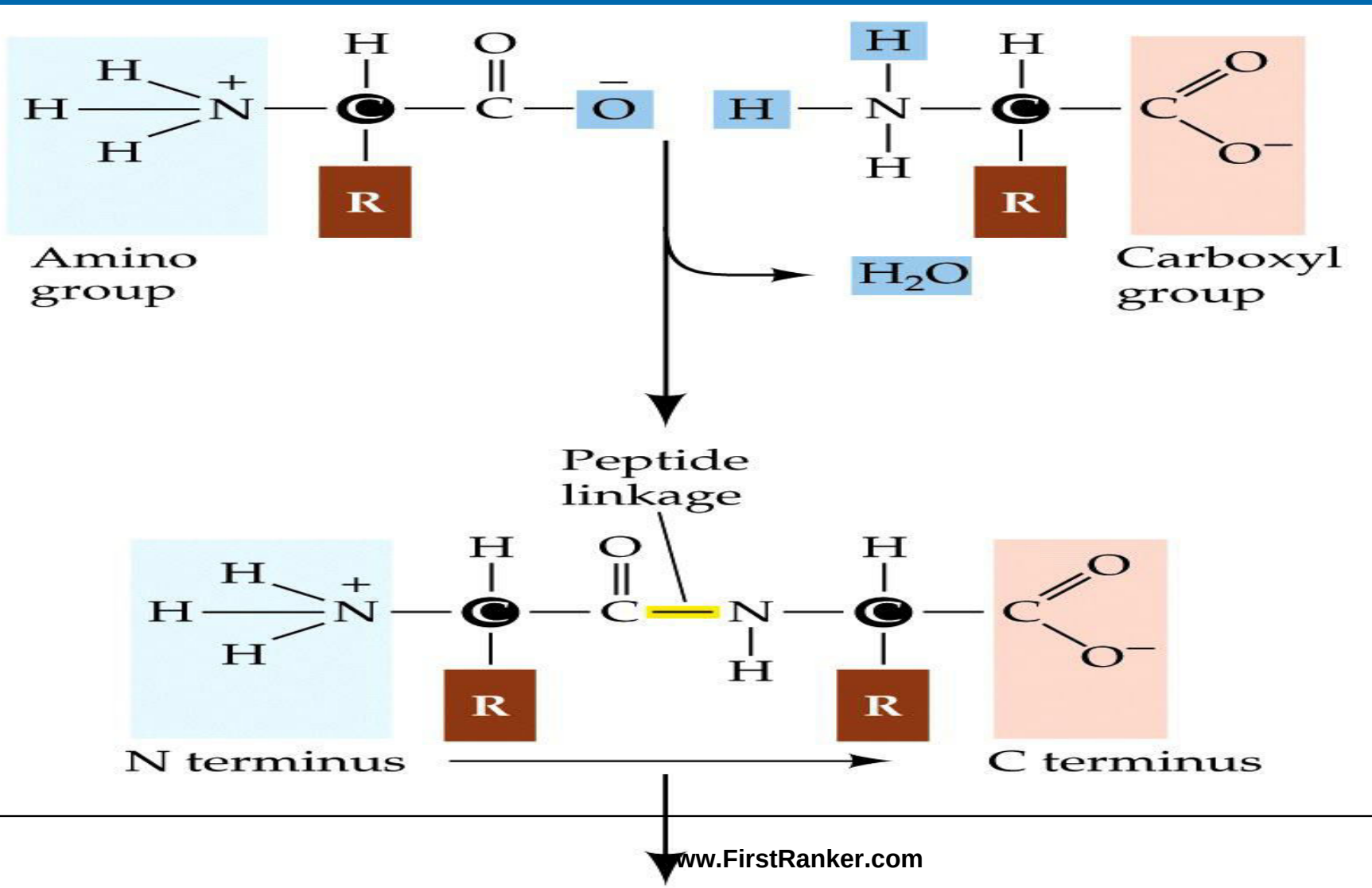
Primary Structure

- The sequence of amino acids in a protein.
- Peptide bond

Primary Structure

- Peptide bond
  - Amide linkage between the α-carboxyl group of one AA & the α-amino group of another.
  - It is a very stable bond.
  - Not broken by conditions that denature proteins such as heating or high concentration of urea.

Primary Structure
Peptide Bond (Cont.)



Primary Structure

- **Peptide bond (Cont.)**
  - Non enzymatically hydrolyzed by prolong exposure to strong acid or base at elevated temperature.
  - All AA sequences read from amino terminal to carboxyl terminal of the peptide bond.

Primary Structure

- **Peptide bond (Cont.)**
- Polypeptide chain
  - Linkage of many AA through peptide bond results in un branched chain.
  - Each AA in a polypeptide chain is called as a residue or moiety.

Primary Structure

- **Peptide bond (Cont.)**
  - Trans-configuration
  - Uncharged but polar
  - Partial double bond
  - Lack of rotation around the bond

Primary Structure

- Peptide bond (Cont.)
  - Trans-configuration

Primary Structure

- Peptide bond (Cont.)
  - Uncharged but polar
  - - C=O & - NH groups of the peptide bond neither accept nor give proton over the pH range of 2 to 12
  - So charge is present only on N-terminal amino group and carboxyl group on C-terminal & any ionized group present in R.

Primary Structure

- Peptide bond (Cont.)
  - Partial double bond
  - Because it is shorter in length then single bond.

Primary Structure

- Peptide bond (Cont.)
  - Lack of rotation around the bond.
  - This is a rigid bond prevents ant rotation around carbonyl carbon and the nitrogen of the bond.

Secondary Structure of Proteins

- Alpha Helix
- Beta sheets
- Beta bends (reverse turns)
- Non-repetitive secondary structure
- Super-secondary structures (Motifs)

Secondary Structure of Proteins

- Alpha Helix
  - A spiral structure
  - Consist of coiled polypeptide chain back bone core with the side chains extending outward from the central helix.
  - E.g. keratin

Secondary Structure of Proteins

- Alpha Helix
  - Hydrogen bond
  - Between carbonyl oxygen & amide hydrogen's .
  - Function of Hydrogen bond.
  - Individual Hydrogen bond is weak but collectively serve to stabilize the helix.

Secondary Structure of Proteins

- Alpha Helix
  - AA per turn 3.6 AA.
  - AA that disrupts the Alpha Helix
  - Proline (Imino gp)
  - Glutamate, Aspartate, Histidine, Lysine, arginine (charged)
  - Tryptophan (bulky side chain)
  - Valine, Isoleucine (branch at beta carbon)

Secondary Structure of Proteins

- Beta sheets
  - Contain 2 or more peptide chains or segments of polypeptide chains that are fully extended.
  - There may be a single polypeptide chain which is folding on itself.
  - Arrangement of the polypeptide chains may be parallel of anti-parallel.

Secondary Structure of Proteins

- Beta sheets (Cont.)
  - All peptide bond components are involved in the hydrogen bonding.
  - Hydrogen bonds are perpendicular to the polypeptide back bone core.
  - Hydrogen bond may be inter-chain or intra chain.

Secondary Structure of Proteins

- Beta bends (reverse turns)
  - Generally composed of 4 AA
  - Mostly contain Proline & Glycine
  - Stabilized by the Hydrogen & ionic bonding.
  - Connect the successive strands of anti parallel Beta sheets

Secondary Structure of Proteins

- **Non-repetitive secondary structure**
  - Less regular structure usually in the shape of a coil.

Secondary Structure of Proteins

- Super-secondary structures (Motifs)
  - Produced by packing side chains from adjacent secondary elements close to each other.

Motifs

- Proteins that binds to DNA contains one or more of a limited number of motifs.
- The zinc motif is common, found in number of proteins that functions as transcription factor.

Domains

- Fundamental functional & three dimensional structural units of polypeptides.
- Those polypeptide chains which contains more then 200 AA in length generally consists of 2 or more Domains.
- Folding of peptide chain within a Domain is independent of folding in other Domains.

Tertiary Structure

- The structure of a globular protein in the aqueous environment is compact.
- High density atoms in the core of the molecule.
- Hydrophobic side chains are buried in the interior.
- Hydrophilic groups are usually present on the exterior or surface.

Tertiary Structure

- Stabilized by:
  - Hydrophobic interactions
  - Hydrogen bonds
  - Electrostatic interactions
  - Disulfide bonds

Tertiary Structure

- Hydrophobic interactions
- If the protein molecules is present in the aqueous environment.
- AA with the Hydrophobic side chains are buried in the interior.
- AA with the Hydrophilic groups are usually present on the exterior or surface.

Tertiary Structure

- Disulfide bonds
- A covalent linkage formed from the sulphydryl group (- SH) of each of the 2 cysteine residues.
- Immunoglobulins contains many Disulfide bonds.

Tertiary Structure

- Hydrogen bond:
- AA side chain having O2 or N-bound H2 (alcohol group of serine & Threonine) can form H-bond with electron rich atoms (O2 of a carboxyl group)

Tertiary structure

- **Ionic interactions:**
  - Negatively charged groups, such as the carboxyl group (-COO-) in the side chain of aspartate or glutamate can interact with the + charged groups such as Amino groups ($-NH_3+$) in the side chain of lysine.

Protein Folding

- Information needed for the folding is located in primary structure of polypeptide.
- Folding begin along with the synthesis instead of waiting for synthesis of entire chain to be completed.
- Factors which contribute to the folding include,

Protein Folding (Cont.)

- Charge on the side chains of AA.
- Hydrophobic interactions
- Hydrogen bonds
- Electrostatic interactions
- Disulfide bonds
- Chaperones

Protein Folding (Cont.)

- Chaperones:
- Also known as Heat shock proteins.
- Assist folding
- Protect
- Some times keep protein unfolded until synthesis is complete.

Quaternary Structure

- Stabilized by:
  - Hydrophobic interactions
  - Hydrogen bonds
  - Electrostatic interactions

Denaturation

- Loss of secondary and tertiary structure.
- This lead to loss of function.
- Denaturant include,
- Urea, extremes of pH, organic solvents.

Denaturation (Cont.)

- **2 types of Denaturation.**
  - Reversible Denaturation
  - Irreversible Denaturation
  - Some proteins can refold upon removal of denaturant.
  - Other can’t refold upon the removal of denaturant.