LECTURE 3:

COENZYMES AND **COFACTORS**

- Types
- Roles/ Biochemical functions

Molecular Components of an enzyme

- Simple enzymes: consists of only one peptide chain

- Conjugated enzymes:

holoenzyme = apoenzyme + cofactor

(protein) (non-protein)

Molecular Components…

- In addition to enzymes, other chemical species often participate in the catalysis

- Cofactors: molecules required for an optimum enzyme function
- Include prosthetic groups-(metal ions) and coenzymes (small organic molecules)

Salient features of Coenzymes

1. The protein part of the enzyme gives the necessary three dimensional infrastructure for chemical reaction; but the group is transferred from or accepted by the co-enzyme.

2. The co-enzyme is essential for the biological activity.

3. Co-enzyme is a low molecular weight organic substance. It is heat stable.

4. Co-enzymes combine loosely with the enzyme molecules. The enzyme and coenzyme can be separated easily by dialysis.

5. When the reaction is completed, the co-enzyme is released from the apo-enzyme.

6. One molecule of the co-enzyme is able to convert a large number of substrate molecules with the help of enzyme.

7. Most of the co-enzymes are derivatives of vitamin B complex group of substances.

Cofactors often function as transient carriers of specific (functional) groups during catalysis

table 8–1

Some Inorganic Elements That Serve as Cofactors for Enzymes

Cu^{2+}	Cytochrome oxidase
Fe^{2+} or Fe^{3+}	Cytochrome oxidase, catalase, peroxidase
K^{+}	Pyruvate kinase
Mg^{2+}	Hexokinase, glucose 6-phosphatase, pyruvate kinase
Mn^{2+}	Arginase, ribonucleotide reductase
Mo	Dinitrogenase
Ni^{2+}	Urease
Se	Glutathione peroxidase
Zn^{2+}	Carbonic anhydrase, alcohol dehydrogenase, carboxypeptidases A and B

Coenzymes can be classified by their source:

1) Metabolite coenzymes

- synthesized by common metabolites
- include nucleoside triphosphates
- most abundant is ATP, but also include uridine diphosphate glucose (UDP-glucose) and S-adenosylmethionine
- ATP can donate all of its three phosphoryl groups in group-transfer reactions
- S-adenosylmethionine can donate its methyl group in biosynthetic reactions
- UDP-glucose is a source of glucose for synthesis of glycogen in animals and starch in plants

2) Vitamin-derived coenzymes

- Vitamins are required for coenzyme synthesis and must be supplied in the diet

- they are derivatives of vitamins, and can only be obtained from nutrients.

  NAD and $NADP^+$, FAD and FMN, lipid vitamins, …

Coenzymes

For transfer of groups other than hydrogen

- Sugar phosphates
- CoA-SH (Coenzyme A)
- Thiamine pyrophosphate
- Pyridoxal phosphate
- Folate enzymes
- Biotin
- Cobalamine ($VitB_{12}$) coenzymes
- Lipoic acid

For Transfer of hydrogen

- NAD+, NADP+
- FMN, FAD
- Coenzyme Q

table 8–2

Some Coenzymes That Serve as Transient Carriers of Specific Atoms or Functional Groups*

Coenzyme	Examples of chemical groups transferred	Dietary precursor in mammals
Biocytin	CO_2	Biotin
Coenzyme A	Acyl groups	Pantothenic acid and other compounds
5′-Deoxyadenosylcobalamin (coenzyme B_{12})	H atoms and alkyl groups	Vitamin B_{12}
Flavin adenine dinucleotide	Electrons	Riboflavin (vitamin B_2)
Lipoate	Electrons and acyl groups	Not required in diet
Nicotinamide adenine dinucleotide	Hydride ion ($:H^-$)	Nicotinic acid (niacin)
Pyridoxal phosphate	Amino groups	Pyridoxine (vitamin B_6)
Tetrahydrofolate	One-carbon groups	Folate
Thiamine pyrophosphate	Aldehydes	Thiamine (vitamin B_1)

Cosubstrates

- The substrates in nature.
- Their structures are altered for subsequent reactions.
- Shuttle mobile metabolic groups among different enzyme-catalyzed reactions.

Prosthetic groups

- Supply the active sites with reactive groups not present on the side chains of amino acid residues
- Can be either covalently attached to its apoenzyme or through many non-covalent interactions
- Remain bound to the enzyme during the course of the reaction

Metal ions

- Metal-activated enzyme: ions necessary but loosely bound
- Often found in metal-activated enzyme

Functions of metal ions

- Transfer electron
- Linkage of S and E；
- Keep conformation of E-S complex
- Neutralize anion

Metalloenzymes

- Are metalloproteins that perform catalytic functions)
- Ions tightly bound
- Found particularly in the active site, transfer electrons, bridge the enzyme and substrates, stabilize enzyme conformation, neutralize the anions

- Examples????

Table 5.2. Metallo-enzymes

Metal	Enzyme containing the metal
Zinc	Carbonic anhydrase, carboxy peptidase, alcohol dehydrogenase
Magnesium	Hexokinase, phospho fructo kinase, enolase, glucose-6-phosphatase
Manganese	Phospho gluco mutase, hexokinase, enolase, glycosyl transferases
Copper	Tyrosinase, cytochrome oxidase, lysyl oxidase, superoxide dismutase
Iron	Cytochrome oxidase, catalase, peroxidase, xanthine oxidase
Calcium	Lecithinase, lipase
Molybdenum	Xanthine oxidase

Next lecture

Enzymes