COURSE PROGRAM

Biological chemistry subject– compounds forming biological organisms and chemical processes taking place within biological organisms. Biopolymers as borderline living matter organization. Biocatalysis – Enzymes as essential components of biochemical processes.

Biopolymers. Monomers forming biopolymers. Bifunctional nature of monomers. Linear polymers. Branched polymers. Linked polymers. Regular polymers. Polyaminoacids and homopolynucleotides as regular polymers. Diversity of monomer sequence in irregular polymers. Diversity of proteins and nucleic acids as a basis for variety living forms. Direction of polymer sequence.

Molecular characteristics of biopolymers. Molecular weight. Centrifugation and sedimentation equilibrium.

Aminoacid composition of proteins. Aliphatic aminoacids: glycine, alanine, valine, leucine, isoleucine. Aminoacid – proline. Aromatic aminoacids – phenylalanine, tryptophan. tyrosine. Oxiamnoacids – serine and threonine. Bicarbonic aminoacids and amides – glutamic and asparagine aminoacid, glutamine and asparagine. Basic aminoacids – lysine, arginine and histidine. Sulfur-containing aminoacids – cysteine, methionine, Peptide chain. Spectral characteristics of peptide chain, sidechains and terminal end groups of proteins and peptides.

Nucleosides and nucleotides – low molecular weight components of nucleic acids. Ribose and deoxyribose. Major heterocycles – adenine, guanine, cytosine, thymine or uracil. Ribonucleosides – adenosine, guanosine, cytidine, uridine. Deoxyribonecleosides – deoxyadenosine, deoxyguanosine, deoxycytidine, thymidine. Minor components as a products of monomer transformation in the nucleic acids. Nucleotides – phosphates of nucleosides. Mono-, di-, trinucleotides. Intranucleotide bond. Ribonucleic acids (RNA). Deoxyribonucleic acids (DNA). spectral properties of nucleosides and nucleotides.

Noncovalent interactions in biopolymers. Electrostatic interactions. Hydrogen bonds. van-der-Waals interactions. Hydrophobic and hydrophilic groups in biopolymers. Specific interactions between hydrophobic regions in aqueous systems (hydrophobic interactions). Intraplanar interactions of aromatic and conjugated heterocyclic systems (stacking interactions). Secondary structure of proteins. Alpha-spiral conformation of polypeptide chains. Beta-sheet conformation of polypeptide chains. Stacking interactions as a basis for spiral structure formation of polynucleotide.

Complementation of heterocycles and nucleic acids. Complementary nucleic acid sequences. Specific interactions between complementary strands of nucleic acid as a example of specific interactions. Structure of native DNA (Watson-Crick model). Intrastrand complementary interaction. Tertiary structure of biopolymers as a result of intermolecular interactions. The role of disulfide bonds in tertiary structure formation in proteins.

Specific intermolecular interactions of biopolymers. Quaternary structure of proteins/ Protein subunits. Phospholipids. Lipoproteins in biological membranes. Membrane protein receptors and its interaction with effectors.

Conformational lability of biopolymers. Native and denatured state. Denaturation-induced loss of specific interactions. Reversibility of native-denatured states. Diversity of functionally significant fixed biopolymer conformations. Regulation of enzymes activity by directed conformational changes.

Primary structure of biopolymers. N- to C- direction in proteins and 5'- to 3'- direction in nucleic acids. Decomposition of proteins into aminoacids and nucleic acids

hydrolysis to free heterocycles. Enzymatic digestion. Methods of separation and analysis of monomer mixtures.

Phenyl isothiocyanate method of step-by-step cleavage of polypeptides from N-terminus (Edman method). Automatic protein sequencing systems. Enzymatic digestion of proteins by specific proteases – trypsin, chymotrypsin, pepsin etc. Disulfide bond cleavage. Method of blocks overlay for the analysis of fragment sequence in the original polypeptide chain. Specific ribonucleases. Digestion of DNA by restriction enzymes. Sanger methods.

Enzymatic catalysis. Structure of enzymes. Metal ions and specific organic molecules (prosthetic groups) involvement in the catalysis performed by some enzymes. Mechanism of enzymatic action. Sorption of substrates in specific (adsorption) centers of enzymes as first stage of enzymatic process. Chemical interaction of substrates with enzymes as intermediate stage of some enzymatic processes. Enzyme catalytic center. Kinetic equation for the description of single-substrate enzymatic reaction (Michaelis equation). Maximal velocity of the reaction, Michaelis constant. pH-dependence. Competitive inhibition of enzymes. Allosteric effects (activators/inhibitors). Multisubunit enzymes.

Enzyme reaction types. Oxidoreductases. Transferases. Co-enzyme A (CoA-SH). Transfer of phosphor-containing residues, Kinases. Adenosinetriphosphate – major donor of phosphor-group. Hydrolases. Proteases. Hydrolysis of nucleic acids. Lyases. Isomerase. Racemases and epimerases. Ligase (synthetase). Synthesis associated with hydrolysis of ATP and GTP.

Catabolic and anabolic processes. Cellular bioenergetics and catabolism. ATP pool – major energy storage in the cell. Energy-rich bonds.

NAD.H oxidation by oxygen and formation of energy-rich bonds. Citric acid cycle – major source of NAD.H formation from NAD+. Synthesis of citrate and its isomerization to isocitrate. Oxidative decarboxylation of isocitrate. Thiaminepyrophosphate-dependent decarboxylation of ketoglutarate. Succinyl-CoA formation and its transformation into succinate (associated phosphorylation of GDP). Oxidation of succinic acid to fumarate. Malate formation and its oxidation to oxaloacetate.

Carbohydrate oxidation. Glycolysis. Major reactions. Glucoso-6-phosphate formation from glucose and glycogen. Glucoso-6-phosphate isomerization into levuloso-6-phosphate. Formation of levuloso-1,6-diphosphate. Cleavage of levuloso-1,6-diphosphate into glyceroaldehyde-3-phosphate and dihydroxiacetonephosphate. Triosophosphates conversion. Oxidation of glyceroaldehyde-3-phosphate to 3-phosphoglycerate, associated with phosphorylation of carboxyl group. Formation of high-energy bond. Phosphoryl residue transfer onto ADP. Isomerization of 3-phosphoglycerate into 2-phosphoglycerate. 2-phosphoglycerate dehydration and formation of high-energy molecule – phosphoenolpyruvate. Pyruvatekinase and formation of ATP from ADP. Pyruvate as terminal product of glycolysis. Anaerobic pyruvate transformation. Bioenergetic balance of anaerobic glycolysis.

Pyruvate dehydrogenase complex. Thiaminpyrophosphate-dependent decarboxylation of pyruvate. Acetyl-CoA formation. Energy balance of glucose to acetyl-CoA transformation.

Electron transfer chain. Mitochondrial localization. 4 complexes of submitochondrial system of electron transfer chain. Oxidation of NAD.H by ubiquinone (complex I). Oxidation of succinate by ubiquinone (complex II). Oxidation of reduced ubiquinone by cytochrome C (complex III). Oxidation of reduced cytochrome C by molecular oxygen (complex IV). ADP phosphorylation with formation of ATP associated

with electron pair transfer in complexes I, III, IV. Total bioenergetics profile of citric acid cycle.

Oxidation of fatty acids. Stage 1 metabolism of lipids: a) stomach digestion of lipids, b) intestinal digestion of lipids. Triacylglycerols hydrolysis. Absorbtion of lipids. Triacylglycerol resynthesis. Chylomicrons. Fatty acids activation by attachment to CoA (connected with ATP-hydrolysis). Carnitine – inner mitochondrial membrane transfer protein of activated fatty acids with long chain. Dehydrogenation of CH_2-CH_2-group acyl-CoA. Hydration of double bond and formation of hydroxyacyl-CoA. Oxidation of fatty acid. Acyl-residue transfer to CoA. Total bioenergetics balance of fatty acids oxidation to acyl-CoA. Odd chain fatty acid oxidation. Eventual formation of propionyl-CoA. Fate of propionyl-CoA: carboxylation and transformation to succinyl-CoA. Fate of succinyl-CoA.

Catabolism of aminoacids. Stage 1 metabolism of aminoacids: a) gastric digestion of proteins, b) pancreatic digestion of proteins, c) intestinal digestion of proteins. Absorption of aminoacids. Protein recycling in the body. Transport of aminoacids in the body in fed state and fasting state. Aminoacids metabolism: fate of nitrogen atom. Transamination reactions between aminoacids (role of ketoglutarate and pyruvate in the reaction). Glutamate- and alanine- aminotransferases. Transdeamination of aminoacids: complex mechanism involving oxidative deamination and involvement of alpha-ketoglutarate. Dehydrogenase of glutamic acid. Other common deamination ways: by L-amino acid oxidases, D-aminoacid oxidases, dehydratases, desulfhydrases. Detox of ammonia: trapping by glutamic acid and aspartic acid.

Urea cycle – pathway of ammonium excretion from the mammalian organisms. Transformation of ammonium into urea. Carbamoylphosphate synthesis. Attachment of carbamoyl residue to ornithine and formation of citrulline. Interaction of citrulline with aspartate with formation argininesuccinate Fumarate cleavage and formation of arginine. Hydrolytic splitting of urea from arginine. Fumarate synthesis – interconnection between urea cycle and citric acids cycle (“bicycle”). Energy expenditures of urea bicycle.

Utilization of glycine and formation of 1-carbon unit intermediate with THFA. Catabolism of proteins in the muscle: interconnection with liver by alanin/glucose flow. Similarity to Cori’s cycle: replenishment of glucose in muscle by interconnection with liver by lactate/glucose flow.

Gluconeogenesis. Common reaction of gluconeogenesis and glycolysis. Replacement of irreversible steps in glycolysis. Localization of gluconeogenesis and malate-aspartate shuttle. Formation of phosphoenolpyruvate via intermediate oxaloacetate. Phosphoenolpyruvate transformation into hexosephosphate via reversed glycolysis pathway. Significance of gluconeogenesis and energy profile. Glucose synthesis from non-hydrocarbon precursors (lactate, aminoacids, glycerol, propionyl-CoA entry).

Biosynthesis of macromolecules precursors. Oligo- and polysaccharides biosynthesis. Biosynthesis of glycogen (glycogenesis). Role of UDP-glucose. Regulation of glycogen metabolism.

Biosynthesis of lipids and fatty acids. Difference between catabolism and anabolism of fatty acids. Localization of these processes. Acetyl-CoA – major biosynthesis precursor. Fatty acid synthase complex. ACP protein. Formation of acetyl-ACP and malonyl-ACP from acetyl-CoA and malonyl-CoA. Acetyl transfer from acetyl-ACP to malonyl-ACP with release of CO_2. 3-ketogroup reduction in 3-ketoacyl-ACP with NADPH. Dehydration of 3-oxiacyl-ACP. Double bond reduction by NADPH. Cycling. Release of fatty acid (palmitic as an example). Bioenergetic balance of fatty acids synthesis. Coenzymes and source of NADPH. Regulation of synthesis. Triacylglycerol synthesis.

Interaction of glycerol-3-phosphate/dyhydroxyacetonephosphate with acyl-CoA and formation of phosphatidic acid. Metabolism of adipose tissue. Liver-adipose tissue axis: transport of lipids in the organism. Steroids. Major structural block of steroids. Cholesterol. Scheme of cholesterol synthesis via mevalonic acid: production of aceto-acetyl-coA/HMG-CoA/reduction into mevalonate. Production of 5 carbon units and stepwise condensation into 30C unit. Cyclization and further refurbishment.

Aminoacids biosynthesis. Essential and nonessential aminoacids. Fate of carbon skeleton. Introduction of NH_4 into aminoacids via glutamate and glutamine. 6 biosynthetic families. Glucogenic/ketogenic acids. Biosythesis of non-essential aminoacids. Biosynthesis of phosphoserine and serine. Reaction of serine and THFA (removal of single-C intermediates) with formation of glycine. Transamination of oxaloacetate with formation of aspartic acid and pyruvate with formation of alanine. Transformation of methionine to homocysteine through S-adenosylmethionine. Formation of cysthatione from serine and homocysteine and its transformation into cysteine and homoserine. Glutamic acid synthesis from ketoglutarate/aspartic acid from oxaloacetate (interconnection with TCA). Formation of aminodicarbon acids amides. Asparagine and glutamine synthetases. Arginine biosynthesis. Precursors for histidine biosynthesis. Tyrosine relation to phenylalanine. Phosphorylation-dehydrogenation-cyclization of glutamic acid with formation of proline.

Nucleotides biosynthesis.

Source of nucleotides in the body. Peculiarities of purine nucleotides. Source of atoms and groups in the purine nucleotides. Interaction of PRPP with glutamine and formation of 5-phosphorybosil-1-amine. Attachment of glycine residue and addition of single-C group. Substitution for NH. Cyclization of small penta-cycle. Carboxylation with CO_2 subsequent interaction with aspartic acid. Release of fumarate. Addition of single-C moiety. Big cycle cyclization with formation inosin-5'-monophosphate. Source of purine cycle atoms: aminoacids, tetrahydrofolate derivatives. Transformation pathways of 5'-IMP to 5'-AMP and 5'-GMP. Phosphorylation by kinases.

Synthesis of pyrimidine nucleotides: synthesis of carbomoylphosphate and carbamoyl-aspartate, formation of dihydroorotate, transformation to orotate. Cyclization of pyrimidine ring and attachment of PRPP and formation of orotidine-5'-phosphate. Formation of UMP. Transformation of 5'-NMP to 5'-NDP and 5'-NTP. Synthesis of CTP from UTP. Reductive methylation of dUMP with formation of TMP by N^5,N^{10}-metylene-TGF.