Semmelweis University

Department of Medical Chemistry Molecular Biology and Pathobiochemistry
and
Department of Medical Biochemistry

BIOCHEMISTRY, MOLECULAR AND CELL BIOLOGY I.

INFORMATION BOOKLET

2011-2012

Spring Semester

Semmelweis University
Department of Medical Chemistry, Molecular Biology and Pathobiochemistry and Department of Medical Biochemistry

Course: Medical Chemistry
Type: Compulsory

Course director: Prof. Veronika Adam
Teaching staff:

Prof. Mária Sasvári	Prof. József Mandl	
Prof. László Tretter	Dr. Beáta Törőcsik	
Dr. László Csanády	Dr. Nándor Müllner	Dr. Pál Bauer
Dr. Judit Bak	Dr. Éva Keresztúri	Dr. András Hrabák
Dr. Tatjana Szpaszokukockaja	Marta Stroe	Dr. Tamás Mészáros
Dr. Csaba Barta	Dr. Miklós Csala	Dr. László Szilák
Dr. Szabolcs Sipeki	Dr. Attila Ambrus	Dr. Zsolt Rónai
Dr. Éva Margittai	Dr. Gergely Krizsán	Dr. Miklós Végh
Dr. Judit Dóczi		

Teaching Secretary Dr. András Hrabák
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Student Affairs Secretary Mr. Zsolt Ozsváth
Tel: 459-1500/ext. 60061

Lab coordinator Dr. Gergely Keszler

Lab Staff Mrs Mária Kövecses
Mrs Márta Stroe
Mrs Kinga Pelczer

Course timing

Year:	1st		
Period:	2nd semester		
Total weeks:	lecture 14	, seminar -	, practical 14
Hours per week:	lecture 4	, seminar -	, practical 4

The aim of the course: Medical Biochemistry, Molecular and Cellular Biology I. gives a comprehensive description and understanding of chemical structures and processes important in human body and of the transfer of genetic information. These principles are necessary for the medical practice and for the learning of biochemistry. The informations also contribute to the learning of physiology, pathophysiology, pathology, pharmacology, numerous clinical topics and laboratory diagnostics.
Special emphasis is put on medical aspects. Skills in experimental work are also developed during laboratory programs.

Content:

Bioorganic chemistry

I. Amino acids, proteins and enzymes

II. Carbohydrates

III. Lipids

IV. Nucleotides, nucleic acids

V. Coenzymes, vitamins

VI. Molecular Biology

VII. Cell biology

Recommended books and handouts

Devlin: Textbook of Biochemistry

Sasvári-Müllner: Bioorganic compounds II. (manuscript)

Practical: Hrabák: Selected Collection of Chemical Calculations (manuscript)
Medical Chemistry and Biochemistry Laboratory Manual (manuscript)
Manuscripts can be bought in the shop of the Semmelweis Publisher (Nagyvárad tér)
Students' own lecture notes

Biochemistry lectures, dates, locations
Monday: 12.30-13.40; Wednesday: 12.10-13.20

Szent-Györgyi Hall, Theoretical Education Center (EOK) Semmelweis University, Budapest, 1094 Tűzoltó u. 37-47.

Lecturers: Prof. Mária Sasvári, Dr. Miklós Csala, Dr. Pál Bauer, Dr. Beáta Törőcsik, Dr. László Tretter, Dr. Csaba Barta.

Biochemistry, Molecular and Cellular Biology lectures

		Prof. Sasvári Mária
1	02-06	Amino acids. Amino acids as electrolytes. Structure and chirality of amino acids. Reactions of amino acids.
	02-08	Proteins. The peptide bond. Structure levels in proteins. Primary structure of proteins.
2	02-13	Steric structure of globular proteins. Conformation of proteins. Purification of proteins.
	02-15	Structural characteristics of fibrous proteins. Collagen.
3	02-20	Myoglobin and hemoglobin.
	02-22	Enzymes. Enzymes as proteins, enzyme activity. Isoenzymes. Coenzymes.
4	02-27	Enzyme kinetics. Mechanism of action of some important enzymes (serine proteases).
	02-29	Reversible and irreversible inhibitions of enzymes. Regulation of enzyme activity. Allosteric enzymes.
		Dr. Csala Miklós
5	03-05	Compartmentation in the eukaryotic cells. Membrane structure. Intracellular membranes. Cell nucleus.
	03-07	Movement of cellular organelles. Cytoskeleton, microfilaments, microtubuli, actomyosin. Mechanism of vesicular transport.
6	03-12	Metabolism and transport, the principle of metabolom. Metabolic profile of various organelles (endoplasmic retikulum, peroxisomes, lysosomes, mitochondria).
		Bauer Pál dr.
7	03-19	Nucleic acids – structure and function. Bases, nucleosides, nucleotides, DNA structure, DNA denaturation, hybridization.
7	03-21	DNA replication. Replication in procaryotes, leading and lagging strand. Okazaki fragments. DNA-dependent DNA polymerases. DNA ligase. Telomerase. topoizomerases. Replication in eucaryotes. Structure of eucaryotic chromosomes. Mitochondrial DNA. Nucleosome structure.
		Töröcsik Beáta dr.
8	03-26	DNA repair. Types of DNA damages; mutations, frame shift, nonsense mutations, mismatch repair. Coordination of repair and

	replication. Bauer Pál dr
8 03-28	Transcription in procaryotes. Structure of RNA; t-RNA, r-RNA, m-RNA, differences between the procaryotic and eucaryotic genomes. Transcription complexes, initiation, elongation, termination in procaryotes.
9 04-11	Transcription in eucaryotes, RNA polymerases, promoters, enhancers silencers. Processing of mRNA, mechanism of splicing. Alternative splicing.
1004-16	The genetic code. Activation of tRNA. Mechanism of translation, initiation, elongation, termination. Antibiotics. Posttranslation modifications.
1004-18	Protein transport into intracellular compartments. Proteolysis. Prof. Tretter László
1104-23	Regulation of gene expression in procaryotes. Operon model. Positive and negative regulation in the lac operon.
1104-25	Regulation of gene expression in procaryotes at transcryption level. Role of chromatine structure. DNS metilation. Enhancer sequences.
1205-02	Post-transcriptional regulation in eucaryotes. Regulation by the lifetime of mRNA. Translational regulation. Törőcsik Beáta dr
1205-02	Cell cycle in eucaryotes. Cyclins and cyclin dependent protein kinases. Proteases in the cell cycle. Regulation of G0/G1, G1/S and G2/M transitions. Integration of the repair into the cell cycle. Bauer Pál dr.
1305.07	The role of apoptosis in the cellular homeostasis. The apoptotic cell. Biochemical processes during apoptosis: role of mitochondria, activation of caspases, degradation of DNA. Prof. Tretter László
1305-09	Molecular biology of malignant tumors. Protooncogenes and cellular oncogenes. Tumor induction by retroviruses. Possible mechanisms of the activation of oncogenes. Anti-oncogens and their roles. Oncogenic effect of DNA viruses. Relationship between cell cycle and oncogenesis. Barta Csaba dr.
1405-14	Principles of gene technology. Cloning, genomic and cDNA libraries. Blotting techniques and their utilizations. PCR and its utilization in molecular biology. Vectors and endonucleases in the gene manipulation. Synthesis of recombinant proteins.
05-16	Expression of transgenes in mammalian cells. Transgenic, „knock out” animals in medical research. The Human Genome Project and its results. The DNA chip. Human gene therapy. Utilization of informatical methods in biological and medical research.

Medical Biochemistry, Molecular and Cellular Biology . Laboratory program and seminars 2011-2012 Spring Semester

• Week 1. 6-10 February	Carbohydrates (seminar)
• Week 2. 13-17 February	Proteins (experimental)
• Week 3. 20-24 February	Structure and function of proteins Amino acids as buffers (seminar).
• Week 4. 27 February – 2 March	Enzymology (seminar)
• Week 5. 5-9 March	Urease measurement (experimental)
• Week 6. 12-16 March	Gel filtration (experimental)
• Week 7. 19-23 March	Thin layer chromatography*
• Week 8. 26-30 March	Midterm exam I.
2-9 April	SPRING HOLIDAY
• Week 9. 10-13 April	Electrophoresis, western blot*
• Week 10.16-20April	Lipids (seminar/consultation)
• Week 11.23-27 April	Induction of β-galactosidase
• Week 12. 30 April- 4 May	Nucleic acids, vitamins, coenzymes (seminar/consultation)
• Week. 13. 7-11 May	Midterm exam II.
• Week 14. 14-18 May	Restriction digestion of pGL3 basic vector followed by gel electrophoresis (experiment) Laboratory exam (3rd midterm, written, 15')

* These programs are organized for various groups in different weeks according to a schedule.

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Laboratory programs are on the 1st floor, Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, "D" passage.

Medical Biochemistry, Mol. and Cell. Biology Laboratory programs, Date, locations, teachers – 2011-2012, Spring semester

- Group EM/1; Friday 8.00-11.00 Csaba BARTA
- Group EM/2; Thursday 8.00-11.00 Judit BAK
- Group EM/3; Friday 8.00-11.00 Mária SASVÁRI
- Group EM/4; Friday 12.00-15.00 Attila AMBRUS
- Group EM/5; Monday 8.00-11.00 Éva KERESZTÚRI
- Group EM/6; Tuesday 15.15-18.15 Erzsébet TÓTH
- Group EM/7; Monday 14.45-17.45 László CSANÁDY
- Group EM/8; Tuesday 14.45-17.45 Márta STROE
- Group EM/9; Monday 8.00-10.40 Zsolt RÓNAI
- Group EM/10; Friday 14.25-17.25 Tatjana SPASOKUKOTSKAJA
- Group EM/11; Friday 8.00-11.00 Tamás MÉSZÁROS
- Group EM/12; Monday 8.00-11.00 Szabolcs SIPEKI
- Group EM/13; Monday 14.40-17.40 Miklós CSALA
- Group EM/14; Wednesday 15.15-18.15 Pál BAUER
- Group EM/15; Friday 8.00-11.00 Nándor MÜLLNER

- Group ED/1; Tuesday 15.30-18.30 Gergely KRIZSÁN
- Group ED/2; Tuesday 15.30-18.30 Éva MARGITTAI
- Group ED/3; Monday 15.00-18.00 MIKLÓS VÉGH
- Group ED/4; Tuesday 8.30-11.30 JUDIT DÓCZI

Location: Student laboratories of Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, EOK Building, 1094 Budapest Tűzoltó u. 37-47., 1st Floor, Section „D"

Student Affairs Secretary: Mr Zsolt Ozsváth
EOK Building, 1st Floor, Section „C"**; Tel: 4591500/ext. 60061**

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Biochemistry, Molecular and Cell Biology, 2011-2012 Spring Semester Requirements of the Department

Semmelweis University

Name of the teaching unit:

Department of Medical Biochemistry

Faculty of Medicine

Name of the : Biochemistry, Molecular and Cell Biology I.

code: AOKOBI001_1A

credits: 7

Leader of the course:

Prof. Veronika Ádám

Content:

Bioorganic chemistry

I. Amino acids, peptides, proteins
Amino acids. Amino acids as electrolytes. Structure and chirality of amino acids. Reactions of amino acids. Proteins. The peptide bond. Structure levels in proteins. Primary structure of proteins. Steric structure of globular proteins. Conformation of proteins. Purification of proteins. Structural characteristics of fibrous proteins. Collagen. Myoglobin and hemoglobin.

II. Carbohydrates, lipids, nucleotides, vitamins, coenzymes
Description and structure of biologically important compounds (seminars, not lectures !)

III. Enzymology
Enzymes. Enzymes as proteins, enzyme activity. Isoenzymes. Coenzymes. Enzyme kinetics. Mechanism of action of some important enzymes (serine proteases). Reversible and irreversible inhibitions of enzymes. Regulation of enzyme activity. Allosteric enzymes.

IV. Cellular biology

Compartmentation in the eukaryotic cells. Membrane structure. Intracellular membranes. Cell nucleus. Movement of cellular organelles. Cytoskeleton, microfilaments, microtubuli, actomyosin. Mechanism of vesicular transport. Metabolism and transport, the principle of metabolom. Metabolic profile of various organelles (endoplasmic retikulum, peroxisomes, lysosomes, mitochondria).

V. Molecular Biology I. DNA, RNA and protein synthesis

Nucleic acids – structure and function. Bases, nucleosides, nucleotides, DNA structure, DNA denaturation, hybridization. DNA replication. Replication in procaryotes, leading and lagging strand. Okazaki fragments. DNA-dependent DNA polymerases. DNA ligase. Telomerase. topoizomerases. Replication in eucaryotes. Structure of eucaryotic chromosomes. Mitochondrial DNA. Nucleosome structure. DNA repair. Types of DNA damages; mutations, frame shift, nonsense mutations, mismatch repair. Coordination of repair and replication. Transcription in procaryotes. Structure of RNA; t-RNA, r-RNA, m-RNA, differences between the procaryotic and eucaryotic genomes. Transcription complexes, initiation, elongation, termination in procaryotes. Transcription in eucaryotes, RNA polymerases, promoters, enhancers silencers. Processing of mRNA, mechanism of splicing. Alternative splicing. The genetic code. Activation of tRNA. Mechanism of translation, initiation, elongation, termination. Antibiotics. Posttranslation modifications. Protein transport into intracellular compartments. Proteolysis.

Molecular Biology II. Regulation of gene expression

Regulation of gene expression in procaryotes. Operon model. Positive and negative regulation in the lac operon. Regulation of gene expression in procaryotes at transcription level. Role of chromatine structure. DNS metilation. Enhancer sequences. Post-transcriptional regulation in eucaryotes. Regulation by the lifetime of mRNA. Translational regulation. Cell cycle in eucaryotes. Cyclins and cyclin dependent protein kinases. Proteases in the cell cycle. Regulation of G0/G1, G1/S and G2/M transitions. Integration of the repair into the cell cycle. The role of apoptosis in the cellular homeostasis. The apoptotic cell. Biochemical processes during apoptosis: role of mitochondria, activation of caspases, degradation of DNA. Molecular biology of malignant tumors. Protooncogenes and cellular oncogenes. Tumor induction by retroviruses. Possible mechanisms of the activation of oncogenes. Anti-oncogens and their roles. Oncogenic effect of DNA viruses. Relationship between cell cycle and oncogenesis.

Molecular Biology III. Methods in molecular biology and gene technology

Principles of gene technology. Cloning, genomic and cDNA libraries. Blotting techniques and their utilizations. PCR and its utilization in molecular biology.

Vectors and endonucleases in the gene manipulation. Synthesis of recombinant proteins. Expression of transgenes in mammalian cells. Transgenic, „knock out" animals in medical research. The Human Genome Project and its results. The DNA chip. Human gene therapy. Utilization of informatical methods in biological and medical research.

Requirements

The participation on the laboratory programs is obligatory. In the case of more than three absences the semester will not be accepted. Replacement of the absence is possible only on the same week in another group. In this case the other laboratory teacher will certify the presence of the student. Other requirements see at Midterms.

Midterm examinations:

3 midterm exams will be organized during the semester (8th and 13th weeks and a laboratory midterm on the 14th week). For the acceptation of the semester (signature), students must get at least 1 point of each midterm (min. 2 points). Retakes are possible, organized by the laboratory teachers. The success on the laboratory midterm (i.e. at least 1 point) is not the condition for the signature, but it is the condition of the successful examination, independently on its result. Therefore, unsuccessful laboratory midterms must be repeated before the examination. 0-9 bonus points (3/each) can be obtained from the midterms. These bonus points will be included in the semifinal examination.

Type of the semifinal examination:

written, multiple choice + structure writing

Final mark:

31 points of 60 should be obtained from the written test to pass. In the case of this minimum, bonus points will be added to the exam points and the final marks will be determined by the total points:

less than 31 written points	fail (1)
31-39 points	: pass (2)
40-49 points	: satisfactory (3)
50-59 points	: good (4)
60-69 points	: excellent (5)

Registration and modification of the examination date:

Semmelweis University Neptun System

In the case of absence, please present medical certification according to the exam rules, or contact the teaching secretary.

Textbooks, manuscripts, handouts:

Lehninger-Nelson-Cox: Principles in Biochemistry
Devlin: Textbook of Biochemistry
Sasvári: Bioorganic compounds (manuscript)
Laboratory: Hrabák : Selected Collection of Chemical Calculations (manuscript)
Medical Chemistry and Biochemistry Laboratory Manual (manuscript)
Powerpoint files of seminars – www.biochemistry.sote.hu
Students' own lecture notes

Dates for semifinal exams.

Exams are held on Wednesdays (and an additional day in the last week) with maximal number of 50 students (Medical + Dentist) per day. Applications should be submitted through the University administration system Neptun. Unsuccessful exams can be repeated after 5 days.

Exemptions from semifinal exams.

Those students who would like to be being exempted from taking the biochemistry course on the basis of their previous studies are kindly asked to present their documents to the teaching secretary (or to dr. A. Hrabak) until 25 February. Students with the proper academic background are entitled to sit for a checking examination in written form (multiple choice test plus structures as in the chemistry exam). In case of successful examination the exemption will be granted by the department. The date of exam will be fixed later possibly at the end of February. For the material see the topic and structure lists.

LIST OF TOPICS FOR THE MIDTERMS ALSO INDICATING THE MATERIAL OF THE BIOORGANIC PART OF THE SEMIFINAL EXAMINATION.

Groups of questions: Group I. Amino acids, Proteins, Enzymes
Group II. Carbohydrates, lipids, nucleic acids,coenzymes
Group III. Molecular Biology

Please find enclosed the list of obligatory structural formulas as well.
These list serves as a help to prepare for the semifinal exam and also as a source for the questions for midterm examinations.

CHEMISTRY PRACTICAL QUESTIONS (for the laboratory midterm).

1. Reversible precipitation of proteins.
2. Irreversible precipitation of proteins.
3. Quantitative colorimetric determination of proteins (biuret, Ellmann).
4. Gel filtration. Separation of proteins from potassium iodide.
5. Paper and thin layer chromatography of amino acids.
6. Principle of gel electrophoresis and western blotting.
7. Electrometric titration of amino acids.
8. Construction of the saturation curve of urease.
9. Inhibition of urease activity.
10. Induction of β-galactosidase
11. Inhibition of transcription and translation by antibiotics.
12. Restriction digestion of pGL3 basic vector followed by gel electrophoresis

Bioorganic chemistry

Group I. Amino acids, proteins, enzymes (1-18.)

1. Neutral amino acids: Optical activity (enantiomers, diastereomers). Grouping principles (aliphatic and aromatic side chains, branched chain amino acids, sulfur containing amino acids). Hydropathy index. Acid-base character of neutral amino acids (protonic equilibria, isoelectric point, titration curve of alanine).

2. Neutral amino acids: polar side chains. Hydrogen bonds between side chains (examples!). Aromatic side chains in amino acids: their hydrophobic or hydrophilic character. Post-translational modification of amino acids (hydroxylation, phosphorylation). Biologically important derivatives of thyrosine (thyroxine, dopamine, noradrenaline, adrenaline). Biogen amines.

3. Acidic amino acids. Calculation of isoelectric point. Titration curve of aspartic acid. Comparison of acidity of different side chains and the □-carboxyl group. Amides of aspartic and glutamic acid.

4. Basic amino acids. Calculation of isoeletric point.. Comparison of basicity of amine and imine groups in amino acids. Titration curve of arginine. Which of common amino acids has buffering capacity at neutral pH?

5. Peptides. Formation and properties of the peptide bond (cis and trans configuration of a peptide bond). Ionic side chains, possible charges on a peptide, dependence of the net charge on pH. Isoelectric point of peptides and proteins. The structure of glutathion.

6. Proteins: conformation. Definition of primary, secondary, tertiary and quaternary structure, types of bonds and interactions at each level. Ramanchandran plot. □ helix, parallel and antiparallel □-sheets.

7. Fibrous proteins. a-keratin, silk fibroin and collagen. The collagen helix. Post-translational modification (hydroxylation). Defective hydroxylation in scurvy. Procollagen, tropocollagen, collagen fiber (nature of Lys cross-links).

8. Myoglobin. Structural features of the globin chain. Formula of heme, oxidation state of iron. Function of proximal and distal histidine.

9. Hemoglobin as an allosteric protein. Oxygen saturation curves for myoglobin and hemoglobin: a comparison. Function of BPG. The Bohr-

effect and its molecular mechanism. Conformational changes during oxygenation.

10. Effect of altered amino acid sequence on protein function. Normal human hemoglobin chains, comparison of fetal form to adult forms. Abnormal human hemoglobins: neutral and harmful mutation. HgM. HbS and the sickle cell anemia.

11. pH and temperature dependence of enzyme activity. Effect of charged groups in the active center on the pH profiles of enzymes. Definition of enzyme activity, specific enzyme activity and turnover number. Clinical importance of enzyme assays (nonfunctional plasma enzymes).

12. Effect of the enzyme on the equilibrium and on the activation energy. Transition states. The active center of the enzymes (lock and key model, induced fit model). Acid/base and covalent catalysis.

13. Serine proteases. Proteolytic activation of zymogens. Reaction mechanism: tetrahedral transition states. Specificity of proteases (chymotrypsin,trypsin, elastase). Specific inhibitor of Ser proteases (DIPF).

14. The Michaelis Menten model of enzyme kinetics. Initial rate. The Michaelis constant. Maximal velocity. Graphic evaluation of V_{max} and K_M.

15. Isoenzymes. Definition, examples (glucokinase-hexokinase, lactate dehydrogenases).

16. Reversible inhibition of enzymes. Competitive and non-competitive inhibition.

17. Control of enzyme activity by allosteric activation/inactivation. Kinetics of allosteric enzymes (K type and V type enzymes). Homotrope and heterotrop cooperativity (e.g. aspartate transcarbamoylase).

18. Control of enzyme activity by reversible covalent modification. Post-translational modification of proteins (phosophorylation). Protein kinases and protein phosphatases. Complex regulation (e.g. phosphorylase kinase).

Group II. Carbohydrates, lipids, nucleic acids (19-46.)

19. Monosaccharides: functional groups, hemiacetal formation, conformation of pyranose and furanose rings. Structural formula of some important aldose: D-L glyceraldehyde, erythrose, ribose, deoxyribose, glucose, mannose, galactose.

20. Asymmetric carbon atoms in monosaccharides, mutarotation, anomeric sugars. The structure of alfa-D-glucopyranose and beta-D-fructofuranose. Structural formula of important ketoses (dihydroxyacetone, ribulose, xylulose, fructose) and other sugars (L 301-306, lecture).

21. Derivatives of sugars: deoxy sugars, amino sugars and their N-acetyl derivatives. O- and N-glycosides. Structural formula of deoxyribose, fucose, N-acetyl-glucosamine, N-acetyl-D-galactosamine, sialic acid. Sugar phosphate esters .

22. Disaccharides: reducing and non-reducing disaccharides. Structure of sucrose, maltose, cellobiose and lactose.

23. Polysaccharides I. structure of important homopolysaccharides (glycogen, starch, dextran, cellulose).

24. Polysaccharides II. Structure of important heteropolysaccharides and their role in the living organism.

25. Fatty acids: nomenclature, function, classification. Saturated and unsaturated fatty acids. Essential fatty acids; function, physical properties Triacylglycerols, structure, function. Stereochemical numbering, prochirality.

26. Phosphoglycerolipids: structure, function. Selected representatives. Ether phospholipids. Plasmalogens.

27. Phosphosphingolipids: structure, function. Glycosphingolipids. Blood group antigens (ABO).

28. Cholesterol and its reduced derivatives, nomenclature, stereochemical structure. Bile acids (primary, secondary, conjugated bile acids): structure and function. Application of their detergent effect .

29. Steroid hormones. Structure, function. Vitamin D_3 and its biologically active derivatives.

30. Isoprene and its biologically active derivatives. Lipid soluble vitamins. Vitamin K_2, vitamin E. their functions. Vitamin A and its derivatives, function. Coenzyme Q: reduced and oxidized form. Dolichol phosphate, role in glycoprotein synthesis.

31. Arachidonic acid: structure. Eicosanoids: classification, functions(L. 258-259, lecture).

32. Membranes: fluidity, asymmetry, liposomes. Covalent lipid-protein conjugates: function, selected representatives.

33. Ribo- and deoxyribonucleosides and -nucleotides. Their structure and nomenclature.

34. Biological function of nucleotides (cyclic nucleotides, ATP, UDP-glucose cADP-ribose).

35. Base, nucleoside and nucleotide analogues, minor and rare bases and their importance.

36. Nucleic acids, their biological roles, general structural features. Primary structure of nucleic acids.

37. Three dimensional structure of DNA. Its role in the biological function.

38. Analysis of DNA(electrophoresis, blotting, sequencing).

39. Three dimensional structure of various RNAs. The genetic code, codons and anticodons.

40. Exo- and endonucleases and their role in DNA and RNA metabolism.

41. Compounds of B-vitamin complex, Vitamin C and their biological roles. Thiamine, riboflavine, pyridoxine, cobalamine and their coenzyme derivatives.

42. Vitamins belonging to nucleotides (CoA, NAD(P), FAD). Their role as coenzymes in the hydrogen or acyl group transfer. Other water soluble vitamins (folic acid, biotin). Their structure and function as coenzymes.

Group III: Cell Biology

1. Structure and function of biological membranes. Fluid mosaic model and lipid rafts.

2. Main characteristics and functions of the organelles belonging to the endomembrane system.

3. Which are the main components of the cytoskeleton? What kind of motor proteins are associated to the elements of cytoskeleton and what is their function?

4. The vesicle targeting. How do transport vesicles find their destination? Which proteins are involved and how?

5. The role of Rab cycle in vesicular transport.

6. The mitochondrial membranes and compartments. Main metabolic functions of mitochondria.

7. Nuclear membrane and the nuclear pore.

Group IV. Molecular Biology

Nucleic acid synthesis

1. The properties of DNA polymerases (I-II-III) and the reactions catalyzed by these enzymes.
2. The reaction catalyzed by DNA ligase, please mention several processes where this enzyme has an important role.
3. The initiation of DNA replication in prokaryotes, the replication fork, please characterize the leading and lagging strand!
4. Please describe the nascent Okazaki fragment, what kind of reactions (and enzymes) are necessary to form the final DNA strand from Okazaki fragments
5. The proteins participating in the replication of the prokaryotic genome, and their roles
6. The properties of the DNA polymerases present in eukaryotes. The time of DNA replication in the cell cycle

7. The replication bubbles (the movement of the replication forks: leading strand and lagging strand). The distribution of old and new histones
8. The organization of the eukaryotic genome (nucleosome structure, packaged nucleosomes, extended chromatin, condensed chromatin, chromatids in the metaphase chromosome.) The number of DNA molecules in G2 phase of the human cell
9. The most frequent lesions of DNA and the agents resulting these lesions. The significance of the presence of thymine in the DNA instead of uracil
10. The enzymes and reactions in the repair of depurination and deamination
11. The formation of thymine dimers and the enzymes and reactions in the repair of this lesion. The possibility of the correction of DNA lesions of both strands
12. Please, characterize the point mutations (substitutions and frame-shift mutations). What is the "nonsense-mutation"?
13. Please, describe the mechanism of spontaneous mutation (for example the transition from T-A to C-G)
14. What is a suppressor mutation? What is the principle of Ames' test?
15. Fundamental differences between the transcription of prokaryotic cells and the transcription of eukaryotes
16. The properties of the DNA directed RNA polymerase of E. coli
17. The promoter. The inhibition of transcription in prokaryotes. Strong and weak promoters. The elongation and termination of transcription in prokaryotes. The structure of polycistronic mRNA
18. Transcription of DNA in eukaryotic cells. The structure of the gene in eukaryotes, the eukaryotic promoter and the role of enhancers.
19. Eukaryotic RNA polymerases. Modifications of the primary transcript at the 5' end and at the 3' end
20. The mechanism of splicing. The components participating in this mechanism. The mechanism of alternative splicing.
21. Replication of bacteriophages. The lytic cycle of the replication of bacteriophages (T4 phage). The role of the restriction endonuclease-methylase pairs in the bacteria.

22. The replication of the retroviruses. The reactions catalyzed by the reverse transcriptase
23. Viral oncogenes and cellular protooncogenes. Oncogenic DNA viruses.

Protein synthesis and regulation of gene expression

24. The structure and function of tRNA. The formation of aminoacyl-tRNA. The specificity of aminoacyl-tRNA synthetases.
25. The structure, function, and assembly of ribosomes.
26. The direction of protein synthesis and the mRNA reading. The recognition of initiation codon(s) in prokaryotes. The role of IF1, IF2, IF3.
27. The recognition of translation start in eukaryotes The role of eIF2, eIF3, eIF4
28. Steps of elongation. The function of elongation factors in prokaryotes and eukaryotes. The termination of protein synthesis in pro- and eukaryotes.
29. The role and characteristics of signal sequences in direction of proteins. Transport of proteins across the endoplasmic reticulum membrane. The structure and role of the signal recognition particle.
30. Retention signal for endoplasmic reticulum resident proteins, quality control in the endoplasmic reticulum.
31. Anterograde and retrograde transport from ER to Golgi. Coat proteins, SNARES, G- proteins. Mechanism of exocytosis.
32. Lysosomes at the intersection of protein trafficking pathways. Receptor-mediated endocytosis. Protein degradation pathways.
33. Transport of proteins into the nucleus Nuclear import and export. Sorting of proteins into the mitochondria. The role of heat shock proteins in targeting proteins into different intracellular compartments.
34. The lac operon.Induction of beta galactosidase activity. The function of lac operon. The role of CAP-protein and cAMP in dual control of lac operon.
35. The control of gene expression in eukaryotes. Transcriptional control. The components (signal, level, mechanism) and purpose of gene control in eukaryotic organisms. Gene regulatory sequences (enhancer,

upstream promoter element) and gene regulatory proteins.

36. Processing control, Transport control, mRNA degradation conttol. Alternative RNA splicing, changes of poly-A addition. Control of mRNA degradation.
37. Translational control in eukaryotes. Translational repressor protein. Translational enhancer. Translational frameshifting. Control by phosphorylation of eIF2.

Biology of cancer. Methods in molecular biology and gene technology

38. The molecular genetics of cancer. Mechanisms by which retroviruses can cause cancer. Major classes of protooncogenes in the intracellular control network
39. Transformation of cells, detection of oncogenes. The conversion of protooncogenes to oncogenes. Tumor suppressor genes.
40. General procedure for detecting and isolating DNA regulatory sequences. Gel retardation, footprinting. DNA binding proteins.
41. Recombinant plasmids. Expression vectors, reporter genes (CAT, luciferase)
42. Genomic and cDNA libraries. Screening of DNA libraries with colony hibridization. Southern, Northern and Western blotting. DNA chip technology.
43. PCR as a new tool in medical diagnosis. Amplification of specific DNA fragments by PCR. Prenatal diagnosis of 21OH-ase deficiency by allele specific PCR. Prenatal diagnosis of DF508 deletion in cystic fibrosis by PCR
44. The Human Genome Project. Mapping strategies (genetic and physical maps, markers, ordered chromosomal libraries). Automatic DNA sequencing, DNA and protein databases. The polymorphic nature of the human genome (SNP, STR, VNTR)
45. Recombinant DNA technology in medical industry. Insulin production in bacteria and its regulation by IPTG. Production of secretory proteins in bacteria and in higher animals. Transgenic animals (the giant mouse)
46. Cystic fibrosis (CF): Diagnosis and treatment by recombinant DNA technology. RFLP as a marker of genetic diseases. RFLP markers of CF. The structure and the function of CFTR protein.

47. Human gene therapy. NeoR/TIL gene marking. ADA gene therapy. Cancer gene therapy. Prospects for CF gene therapy.
48. Eukaryotic cell cycle I. Cyclins and cdk-s. Control of G1/S transition, restriction point. Control of G2/M transition.
49. Proteolysis in the cell cycle. Oncogenes and cell cycle. The retinoblastoma protein (p105) cycle. p53 and the regulation of proliferation/apoptosis.
50. Apoptosis. Function of apoptosis in tissue homeostasis. Morphological and biochemical characteristics of apoptosis. Different pathways for activating caspases

<u>The structures of the following compounds are highly recommended to know at the semifinal exam:</u>

Aromatic rings: benzene, naphtalene, phenantrene, pyrrole, thiophene, furane, thiazole, oxazole, imidazole, pyrazole, pyridine, pyrane, pyrazine, pyrimidine, purine, indole, pteridine, acridine.

Basic organic compounds: methanol, ethanol, propanol, butanols, ethylene glycol, glycerol, inositol, phenol, diethylether, formaldehyde, acetaldehyde, acetone, mercaptoethanol, aniline, urea, guanidine.

Organic acids: formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, oxalic acid, malonic acid, succinic acid, glutaric acid, adipic acid, maleic acid, fumaric acid, lactic acid, β-hydroxybutyric acid, pyruvic acid, acetoacetic acid, citric acid, cis-aconitic acid, isocitric acid, α-ketoglutaric acid, malic acid, oxaloacetic acid, tartaric acid.

Amino acids and derivatives: glycine, alanine, valine, leucine, isoleucine, phenylalanine, tyrosine, tryptophane, cysteine, methionine, serine, threonine, lysine, arginine, histidine, aspartic acid, asparagine, glutamic acid, glutamine, proline, cystine, β-alanine, ornithine, citrulline, homocysteine, homoserine, ethanolamine, choline, histamine, epinephrine, serotonin, thyroxine.

Lipids: palmitic acid, stearic acid, palmitoleic acid, oleic acid, linoleic acid, linolenic acid, arachidonic acid, diacyl- and triacylglycerols, phophatidic acid, phosphatidyl-ethanolamine, phosphatidyl-choline, phosphatidyl-serine, phosphatidyl-inositol, platelet activating factor, sphingosine, sphingomyelin, cholesterol, cortisol, aldosterone, estradiol, testosterone, progesterone, cholic acid, taurocholic acid, isoprene, β-carotene, prostaglandin E_2.

Carbohydrates: D- and L-glyceraldehyde, dihydroxyacetone, erythrose, treose, ribose, deoxyribose, glucose, mannose, galactose, fructose, ribulose, xylulose, maltose, cellobiose, lactose, sucrose, N-acetyl-glucosamine, L-fucose, sialic acid, aldonic and uronic acids, UDP-glucose, structural unit of starch and glycogen, structural unit of hyaluronic acid, chondroitin-sulfates and heparine.

Nucleotides: adenine, guanine, cytosine, uracil, thymine, hypoxanthine, xanthine, uric acid, nucleosides and nucleotides formed of the bases mentioned previously, a structural unit of ribo- and deoxyribonucleic acid, pseudouridine, 5-fluorouracil, 5-bromouracil, 6-mercaptopurine.

Vitamins and coenzymes: thiamine (and its pyrophosphate), riboflavine (FAD), nicotinamide (NAD, NADP and their reduced forms), pyridoxal phosphate, coenzyme A, coenzyme Q, vitamin A, vitamin D_3, ascorbic acid, folic acid, tetrahydrofolic acid, biotin, porphyrine backbone.