Faculty of Medicine
Department of Cancer Research and Molecular Medicine

Exam MOL3000
Introduction to Molecular Medicine

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Question 1 (7p).

Intracellular signal transduction cannot be described by a linear model, rather it is a complex network made up of several signalling pathways which are activated by the same or different stimuli. The integration of several signal transduction pathways is necessary for the cell to coordinate the different incoming signals and to create a specific response. However, it also requires a high degree of regulation. The MAPK pathways are conserved signal transduction mechanisms that are activated by various stimuli and coordinate diverse cellular processes.

Dysregulated signal transduction pathways can have serious consequences for the single cell but also for the whole organism. One example is a mutated B-Raf (B-Raf is one specific isoform of the Raf kinase) which is found in human cancer. The most common mutation is an amino acid substitution at position 600 from valine to glutamic acid (V600E) which leads to an increased activity of B-Raf.

a) Name the MAPK pathway in which B-Raf is acting and at which step. Describe briefly what is thought to be the main activating stimulus and cellular outcome of this pathway and based on this, explain why mutated B-Raf (V600E) is cancer-promoting (3.5p).

b) Explain how the relation between deregulated signaling and disease can be exploited in therapy using melanoma patients with mutant B-Raf (V600E) as example (3.5p).

Question 2 (10 p)

The general function of lipoproteins is to transport fat by the vascular system using mainly the blood vessels, and to minor extent the lymph vessels.

a) Explain briefly the general chemical and physiological reasons why it is necessary to transport lipids by specific transport systems rather than dissolved it in blood and lymph (1p).

b) Describe the general composition and general structure of a lipoprotein (3p)

c) Name the 5 main groups of lipoproteins and explain which property has given rise to the names (3p).

d) Explain briefly the function of chylomicron and HDL (3p).

Question 3 (2.5p)

Explain why PSI-Blast may be more sensitive than ordinary Blast for finding related protein sequences in a database.

Question 4 (5p)

The Toll-like receptors (TLRs) are transmembrane receptors that are expressed by cells of the innate immune system and report the presence of invading pathogens.

a) How many distinct TLRs are known in humans? (1p)

b) How is the limited number of TLRs able to recognize the relatively large number of pathogens? (1p)

c) Which TLR does not use the TIR-adapter MYD88 for signaling? (1p)

d) Which TIR-adapter is used by this TLR (in c)? (1p)

e) What is the result of TLR signaling? (1p)

Abbrivations:

MYD88 - Myeloid differentiation primary response gene (88)

TIR-domain - Toll/interleukin-1 receptor domain

Question 5 (12p)

Based on the principles of Mendelian inheritance one can say in general that a character (or disease) is dominant if it is manifested in heterozygotes and recessive if it is not.

a) Explain briefly why particularly autosomal dominant inherited characters (or disease) vary greatly in their phenotype. (5p)

b) Why does the varying phenotype create ethical challenges concerning genetic testing? (2p)

c) Explain briefly the inheritance of Hemophilia A and the molecular mechanisms underlying the disease. (5p)

Question 6 (3.5p)

It is now well recognized that endocrine cells do not, as previously believed, release only a single hormone, that hormones can bind to a number of different receptors and receptors can bind to a number of different hormones. New results are challenging many other long-held beliefs in endocrinology.

Describe how new molecular techniques can be used to aid the discovery of the physiological functions of hormones/receptor systems.

MCQ, each question 1p.

Make one (1) cross for each question (the best alternative). Set a cross in front of the correct answer

1.

We often use sequence alignment for the analysis of sequence data (DNA, RNA, protein). An alignment is an optimal comparison of sequences showing regions where the sequences are similar to each other. Often we distinguish between pair-wise and multiple sequence alignment.	
What do we mean by multiple sequence alignment?	
A	Sequence alignment with several equivalent solutions.
B	Iterative sequence alignment with several iterations.
C	Simultaneous sequence alignment of more than two sequences.
D	Simultaneous sequence alignment of all DNA reading frames for a protein.
E	Sequence alignment of repetitive regions in DNA.

2.

Blast and PSI-Blast are typically used for searching with a given sequence in a data base to find significantly related sequences, often expressed as an E-value.	
How can the size of the data base affect the estimate of significance?	
A	Results from small data bases require smaller E-values to be significant.
B	Large data bases can easier cause errors in E-value estimates.
C	Size of the data base does not matter.
D	Results from small data bases require larger E-values to be significant.
E	Small data bases contain too little information to give correct E-values.

3.

A dotplot may be used to compare two sequences (protein, DNA).	
What kind of information can we read from a dotplot?	
A	A dotplot will directly give us the optimal alignment between two sequences.
B	A dotplot visualizes similar regions in two sequences as diagonal stripes of dots.
C	A dotplot shows regions with similar secondary structure in two proteins.
D	A dotplot shows were the sequences have sequencing errors.
E	A dotplot is just a tool for explaining how to find an optimal alignment of two sequences.

4.

All receptors are proteins that upon binding trigger a biological response.

What is the name of a compound that binds a receptor and inhibits its biological response?	
A	Competitive agonist
B	Agonist
C	Ligand
D	Competitive antagonist

5.

Inflammasomes are molecules that are responsible for IL-beta and IL-18 production.	
What caspase takes part in the assembly of the inflammasomes?	
A	Caspase 3
B	Caspase 8
C	Caspase 1
D	Caspase 9
E	Caspase 6

6.

Cyclic AMP (cAMP) is an important 2nd messenger in signal transduction pathways.	
Which enzyme catalyzes the generation/accumulation of cAMP after a receptor-ligand interaction?	
A	Protein kinase A
B	cAMP phosphodiesterase
C	Phospholipase C
D	Adenylyl cylcase
E	Guanylyl cyclase

7.

G-proteins are important signaling molecules and act as molecular ON/OFF switches.	
Which accessory factor accelerates the switch to the ON confirmation?	
A	GTPase-activating protein
B	Guanine nucleotide exchange factor
C	Kinase
D	Phosphatase
E	Receptor

8.

The mitogen-activated protein kinase (MAPK) pathways are conserved signal transduction mechanisms in eukaryotes.	
Which MAPKs are typically activated in response to cellular stress?	
A	JNK and p38 MAPKs
B	Erk1/2 and JNK MAPKs

C	Erk1/2 and p38 MAPKs
D	Erk1/2, JNK and p38 MAPKs

9.

High-risk human papilloma viruses are associated with cancer, particularly cervical cancer. Two of the early viral proteins, E6 and E7 interfere with the cellular p53 signaling network.	
What describes most precisely the molecular mechanisms of E6 and E7 in the host cell?	
A	E6 binds the tumor suppressor p53 leading to p53 degradation, and E7 binds the Rb protein leading to Rb inactivation
B	E6 binds the Rb protein leading to Rb inactivation, and E7 binds the tumor suppressor p53 leading to p53 degradation
C	E6 forms an ubiquitin ligase leading to p53 degradation, and E7 binds the Rb protein leading to the release of E2F
D	E6 forms an ubiquitin ligase leading to p53 degradation, and E7 phoshorylates the Rb protein leading to the release of E2F
E	E6 interacts with MDM2 leading to p53 degradation, and E7 binds the Rb protein leading to the release of E2F

10.

p53 is a transcription factor that regulates the expression of various protein-coding genes. Furthermore p53 regulates the expression of selected microRNAs (miRNAs).	
How do miRNAs regulate gene expression?	
A	miRNAs bind to target mRNAs leading to degradation of the mRNA
B	miRNAs bind to target promoters leading to degradation of the mRNA
C	miRNA bind to target mRNAs leading to inhibition of the transcription
D	miRNAs bind to target promoters leading to inhibition of the transcription
E	miRNA bind to target mRNAs leading to inhibition of nuclear export

11.

What do we call all kinds of molecules that have the ability to trigger a response in another cell?	
A	Hormones
B	Signaling molecules
C	Neurotransmitters
D	Cytokines

12.

The endocrine system consists of many different organs and tissues.	
In which organ/tissue is leptin produced?	
A	Heart

B	Thyroid gland
C	Gonads
D	Adipose tissue
E	Kindney

13.

There are different types of inheritance.	
What is characteristic for an X-chromosome linked inherited disease?	
A	One or several children will inherit the disease when both parents are carriers
B	The children inheriting the disease is independent on gender
C	There is no transfer of the disease from father to son
D	All children inheriting the disease will become ill

15.

What is the purpose of gene therapy?	
A	Increase the expression of a particular gene in order to produce normal proteins
B	Change the expression of a particular gene in order to produce normal proteins
C	Introduce a particular gene into cells in order to produce normal proteins
D	Knock-down a particular gene in order to produce normal proteins

15.

The classical defect in hereditary hemochromatosis is a mutation (C282Y) in the HFE (hereditary hemochromatosis protein) gene.	
What are the known / postulated functions of this gene product?	
A	Interaction with transferring-receptor 1 (TfR1) and 2 (TfR2) and a cofactor of hepcidin synthesis
B	Uptake of iron-bound transferrin in hepatocytes and a cofactor of hepcidin synthesis
C	Downregulation of iron efflux from macrophages and interaction with beta-2-microglobulin
D	Transcriptional regulator of hepcidin synthesis and interaction with beta-2-microglobulin

16.

Colorectal cancer is the most common cancer in Europe.	
Which genes are most often mutated in hereditary non-polyposis colon cancer (Lynch syndrome)?	
A	Genes involved in cell cycle
B	Genes involved in DNA mismatch repair

C	Genes involved in ER stress and apoptosis
D	Genes involved in maintaining epithelial structure

17.

Defects in a single gene may sometimes lead to hereditary predisposition for cancer. Which of the following statements about this kind of cancer inheritance is the most correct?	
A	Hereditary cancer usually involves inheritance of an oncogene
B	Hereditary cancer usually involves inheritance of a defect tumor suppressor gene
C	Hereditary cancer is a typical example of recessive mode of inheritance
D	Hereditary cancer is a typical example of dominant mode of inheritance

18.

Oncogenes are genes that due to modified properties can contribute to cancer development. Which of the following statements is correct?	
A	Oncogenes code for proteins that contribute to cancer development due to loss of protein activity.
B	Oncogenes code for proteins that contribute to cancer development due to increased or altered activity
C	If oncogenes mutate, but without becoming active, they are called proto-oncogenes
D	If oncogenes mutate and gain an activity that promotes cancer development, they are called proto-oncogenes

19.

Tumor protein p53 (tp53) is important for the protection against cancer and is mutated in more than 50 % of all cancers.	
Which of the following statements best describes the role of tp53 in normal cells?	
A	Tp53 is a kinase that upon DNA damage will phosphorylate and activate DNA repair proteins
B	The amount of tp53 increases in cells after damage to DNA and inhibits further cell division
C	Tp53 is a transcription factor that, when active, will increase the level of BCL2 in cells.
D	Tp53 is a proto-oncogene

20.

Complications of diabetes can occur after many years of disease	
Which of the following conditions is most closely associated with complications?	
A	Hyperglycemia

B	Elevated fatty acids
C	Age at onset of disease
D	Genetic factors

21.

Mutations in the glukokinase gene can cause diabetes by effects on insulin-producing beta cells.	
Which mechanism is the primary one?	
A	Decreased uptake of glucose
B	Decreased phosphorylation of glucose
C	Decreased oxidation of glucose
D	Decreased binding of glucose to an extracellular receptor

22.

High density lipoprotein (HDL) is one of the lipid transporters in mammals.	
The major function of HDL is to:	
A	Transport cholesterol and triglycerides from peripheral tissues to liver.
B	Transport cholesterol from peripheral tissues to liver.
C	Transport cholesterol from liver to peripheral tissues.
D	Transport cholesterol and triglycerides to peripheral tissues
E	Transport cholesterol and phospholipids from liver to peripheral tissues.

23.

Low density lipoprotein (LDL) is one of the lipid transporters in mammals.	
The major apoprotein(s) in LDL is/are:	
A	ApoE
B	ApoB48 and ApoC
C	Apo CI and ApoCII
D	ApoE and ApoB58
E	ApoB100

24.

LDL receptor mutations are associated with increased risk of coronary heart disease.	
Why is this?	
A	The mutations increase activity of LDL scavenger receptors.
B	The mutations inhibit cellular uptake and processing of cholesterol.
C	The mutations increase the risk for oxidation of LDL and foam cell formation.
D	The mutations increase formation of xanthoms that contain cholesterol.
E	The mutations cause inflammation of intima and thereby attract monocytes.

25.

Free fatty acids are poorly soluble in water due to their long aliphatic chain.	
They are transported in the blood mainly by:	
A	IDL
B	VLDL
C	Albumin
D	Chylomicron
E	Lipoprotein (a)

26.

Dietary factors may modulate risk for cardiovascular disease (CVD).	
Saturated fatty acids increase the risk of CVD. Which statement is best documented?	
A	Saturated fatty acids inhibit fibrinolysis.
B	Saturated fatty acids selectively increase cholesterol in the blood.
C	Saturated fatty acids increase blood platelet aggregation.
D	Saturated fatty acids activate blood coagulation by binding to prothrombin.
E	Saturated fatty acids increase both cholesterol and triglycerides in the blood.

27.

There are indications from animal studies and epidemiology that antioxidants may prevent cardiovascular disease, particularly coronary heart disease (CHD).	
Which statement is best reflecting the present-day view on antioxidants?	
A	Antioxidants most likely do not prevent CHD.
B	Diets rich in antioxidants, such as fruit and vegetables, reduce risk of CHD.
C	Defined antioxidants, like vitamin E if high enough dose is given.
D	Antioxidants have been proved to prevent CHD.
E	Flavonoids that can be isolated from fruits reduce risk of CHD.

28.

Long term effects of inflammatory disorders may result in anemia.	
The molecular mechanism underlying this phenomenon is usually due to	
A	Reduced Hepcidin expression
B	High Hepcidin expression
C	Iron depletion from macrophages
D	Iron depletion from intestinal cells
E	Excess iron secretion via perspiration

29.

TLR9 signals from the endosomal compartments (early and late endosomes).
What is the ligand for TLR9?

A	LPS derived from Gram-negative bacteria
B	Double stranded RNA from viruses
C	Peptidoglycan degradation products
D	CpG DNA from bacteria's and viruses
E	Single stranded RNA
	Abbrivations: TLR9 - Toll-like Receptor 9 LPS - Lipopolysaccharide

30.

Many different diagnoses belong to the group of cancer diseases. Still, there are some common features on the molecular level that seem always to be present in cancers, e.g. alterations in gene expression.	
Which of the following statements is most in accordance with our current understanding of cancer development?	
A	Mutations are the only molecular events that can lead to cancer
B	Epigenetic events are the only molecular event that can lead to cancer
C	Mutations and epigenetic event can both individually lead to cancer
D	Mutations are necessary for cancer development, but epigenetic events can promote such development