

**Exam MOL3000  
Introduction to Molecular Medicine**

**Monday December 6<sup>th</sup> 2010, 9.00 am - 1.00 pm**

ECTS credits: 7.5

Number of pages (included front-page and MCQ answers sheets): 15

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Examination results are announced on <http://studweb.ntnu.no/>

### Question 1 (10p).

Cells have to react upon a wide variety of signals. The term “signal transduction” describes the overall process how cells convert an extracellular signal into a specific cellular response and includes a plenty of different intracellular signalling pathways. However, there are intracellular signalling molecules which are found in almost all signal transduction pathways.

- a) Define the term “2nd messenger”, name at least five of them and describe for three 2nd messengers the molecular mechanism how they are generated or released during signalling (5p).
- b) Describe how protein kinases and phosphatases change the activity of downstream proteins and explain what is meant by “kinase cascade” by using the mitogen-activated protein kinase (MAPK) pathways as example (2.5p).
- c) Explain how G-proteins act as molecular ON/OFF switches in signalling and what accessory factors are needed. Which two classes of G-proteins do we find in signal transduction pathways? Give one specific example for each class (2.5p).

### Question 2 (2.5p).

Input sequences to Blast and PSI-Blast are often given in the Fasta format. Give an example of a protein sequence in Fasta format. The name of the protein is “trypsin”, it has been isolated from “Mus musculus”, and the sequence starts with “MRALLFLA...” and ends with “...IQNTIAAN”.

### Question 3 (7.5 p).

Coronary heart disease (CHD) is caused by a partial or complete block of a coronary artery. A complete block is usually the end result of a thrombotic event in an arteriosclerotic coronary artery. An arteriosclerotic plaque is frequently found near (under) the thrombus.

- a) Describe the composition of an arteriosclerotic plaque (2.5p).
- b) Describe how the arteriosclerotic plaque develops (different stages) and how it may lead to coronary infarction (2.5p)
- c) Make a list of major risk factors for coronary heart disease (2.5p).

**Question 4 (5 p).**

Describe how dietary iron is taken up in the intestine, including the proteins that are vital in regulation of iron metabolism

**Question 5 (5 p).**

Gene expression can be controlled by epigenetic mechanisms. Describe the most common epigenetic modification of DNA in human cells, and explain how this modification is supposed to affect gene expression.

**Question 6 (5p)**

Receptor down regulation is a process where signaling receptors are targeted for lysosomal degradation.

- a) Given that a signaling receptor is located at the plasma membrane, what is the first step in receptor down regulation? (0.5p)
- b) What is the result of receptor down regulation? (1p)
- c) What is the sorting signal for lysosomal targeting of signaling receptors? (0.5p)
- d) Three enzymes collaborate in this process, which enzymes? (1p)
- e) Which of these enzymes controls target protein (target receptor) specificity? (1p)
- f) If lysosomal targeting of a signaling receptor fails, what is the outcome? (1p)

**Question 7 (5p)**

- a) Explain the terms “mutation” and “genetic polymorphism” (1p)
- b) Explain the terms “point mutation”, “deletion”, “insertion” and “silent mutation” (1p).
- c) Explain on a general basis why some types of point mutations have more serious consequences than others (2p).

- d) Give examples of endogenous (inside the cell) and exogenous (environmental) factors that can cause mutations (1p).

**MCQ, each question 1p. One answer is the most correct. Answer the questions on separate MCQ answers sheets enclosed. Only one cross for each question (the best alternative).**

1.

Which of the following is the best description of “the central dogma”?	
A	All RNA is made by transcription of DNA, and tRNA, rRNA, mRNA and other RNA molecules are translated to protein
B	All RNA is made by transcription of DNA, and mRNA and tRNA are the keys to understand the link between DNA and protein
C	All RNA is made by transcription of DNA, and mRNA is translated to protein

2.

Prokaryotic and eukaryotic genes have many common features, but also important differences.	
What is the best description of three important differences between prokaryotic and eukaryotic genes?	
A	Prokaryotes genes are often larger, are poly-cistronic and often contain enhancers
B	Eukaryotic genes are often larger, are poly-cistronic and contain enhancers
C	Eukaryotic genes are often larger, are mono-cistronic and contain enhancers
D	Prokaryotic genes are often larger, are poly-cistronic and contain introns

3.

Transcribed RNA is processed prior to translation in eukaryotic cells.	
What is the correct order of these processes?	
A	Pre-RNA is 5` capped, spliced, a polyA tail is added and transported out of the nucleus
B	Pre-RNA is 5` capped, a polyA tail is added, spliced and transported out of the nucleus
C	Pre-RNA is 5` capped, transported out of the nucleus, a polyA tail is added and spliced.

4.

What does it mean that a cell is polyploid?	
A	That is contains more than 2 copies of one or a few of its chromosomes
B	That is contains more than 2 copies of a full set of homologous chromosomes
C	That is contains more than 2 copies of its sex chromosomes
D	That is contains more than 2 copies of its autosomal chromosomes

5.

Parkinson disease is one of the most common movement disorders. It is caused by deterioration of neurons.	
Which signaling molecule is missing in Parkinson disease?	
A	PACAP
B	Dopamine
C	Acetylcholine
D	Norepinephrine
E	Oxytocin

6.

UV radiation can introduce pyrimidine dimers in DNA. XP patients lack the ability to repair these DNA damages.	
What kind of repair pathway repairs this DNA damage?	
A	Homologous recombination and translesion synthesis
B	Nucleotide excision repair and translesion synthesis
C	Base excision repair and translesion synthesis
D	Nucleotide excision repair and Base excision repair

7.

In the development into cancer, both caretaker and gatekeepers are mutated.	
Which genes are characterised as caretaker genes?	
A	Genes involved in transcription, DNA replication and cell cycle control
B	Genes involved in DNA repair, transcription and cell cycle control
C	Genes for protooncogenes and tumour suppressor genes.
D	Genes involved in DNA repair, DNA replication and detoxification of carcinogens

8.

The ERK MAPK pathway typically involves the activation of the small G protein Ras downstream of the activated receptor. The activation of Ras is mediated by the two cytosolic proteins GRB2 and Sos	
What type of protein is GRB2?	
A	Kinase
B	Guanine nucleotide exchange factor
C	GTPase activating protein
D	Adaptor protein
E	Small G-protein

9.

One important player in various cellular stress responses is NF- $\kappa$ B.	
Which statement does most accurately describe the molecular mechanism of classical NF- $\kappa$ B activation?	
A	The NF- $\kappa$ B dimer is phosphorylated, activated and released into the nucleus
B	The inhibitor I- $\kappa$ B is phosphorylated, degraded and NF- $\kappa$ B is released
C	The I- $\kappa$ B kinase is phosphorylated, activated and NF- $\kappa$ B is released
D	The I- $\kappa$ B kinase is activated, and phosphorylates and activates NF- $\kappa$ B
E	The inhibitor I- $\kappa$ B is phosphorylated, inhibited and NF- $\kappa$ B is released

10.

The tumor suppressor protein p53 can be activated in response to various cellular stress.	
What describes most precisely the mechanism of p53 activation after DNA damage?	
A	ATM and ATR phosphorylate p53 and disrupt the p53-MDM2 interaction
B	Chk1 phosphorylates p53 and disrupts the p53-MDM2 interaction
C	p14ARF phosphorylates p53 and disrupts the p53-MDM2 interaction
D	p14ARF binds MDM2 and disrupts the p53-MDM2 interaction
E	ATM and ATR bind MDM2 and disrupt the p53-MDM2 interaction

11.

The extent to which circulating levels of glucose stimulate glucose metabolism in beta cells is coupled to glucose sensing ,i.e. the affinity and Vmax of enzymes of glucose metabolism	
Which one of the following enzymes is <i>best</i> documented as a glucose sensor?	
A	Glukokinase
B	Phosphofruktokinase
C	Pyruvate dehydrogenase
D	Glucose transporter (GLUT) 2
E	Pyruvate carboxylase

12.

C-peptide is used to estimate beta cell function in humans in vivo	
Which is <i>one</i> rationale for measuring C-peptide rather than insulin?	
A	C-peptide is part of the insulin molecule in the circulation
B	C-peptide measurements reflect insulin secretion also in subjects treated with insulin
C	C-peptide is degraded less easily than insulin in blood samples
D	C-peptide measurements are cheaper than insulin
E	C-peptide can be measured in lesser amounts of blood (plasma) than insulin

13.

Intrauterine conditions can affect risk of getting type 2 diabetes	
Which of the following conditions imparts <i>the most recognized</i> risk?	
A	Higher than normal birth weight
B	Lower than normal birth weight
C	Delivery by Caesarean section
D	Prolonged vaginal delivery
E	Overweight in the mother during pregnancy

14.

ClustalW and ClustalX are programs that are used for simultaneous alignment of several sequences (protein, DNA). In the output from the program completely conserved positions are marked with a star (“*”).	
What does it mean that a position is completely conserved in a ClustalW or ClustalX sequence alignment?	
A	It means that the amino acids in that position are protected against mutations.
B	It means that all sequences in the alignment have conservative changes in that specific position.
C	It means that the program is using that position as a reference point.
D	It means that all sequences in the alignment have the same amino acid in that specific position.
E	It means that the position is part of (or is coding for) the active site of the protein.

15.

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

16.

The similarity score between two protein sequences in a sequence alignment is based on a scoring matrix. Important matrices are PAM and BLOSUM.	
What is the basis for making a scoring matrix?	
A	Counts of mutations observed in reference alignments between protein sequences



B	Similarities between different amino acids based on e.g. size and charge
C	Codon similarities of amino acids
D	How frequent different amino acid types are observed in proteins
E	Scoring matrices are based on protein structures

17.

When comparing sequences by sequence alignment we need to estimate the significance of the similarity. The E-value is often used for this.	
What does the E-value indicate?	
A	Expected number of identical sequence positions in alignment
B	Expected number of identical sequences in database
C	Estimated number of significant digits in score value
D	Expected number of sequences that give same score value or better if database is probed with random sequences
E	Estimated alignment length

18.

We can use sequence alignment tools to compare related protein sequences by sequence alignment. Such alignments may be either local or global	
What is characteristic of global alignments, compared to local alignments?	
A	Global alignments are made against all sequences in a database
B	In a global alignment the full length of both sequences is aligned
C	Global alignments use score matrices estimated from a global sequence set
D	In a global alignment protein-coding DNA sequences are aligned based on their protein sequences
E	In a global alignment a DNA sequence is aligned against a protein sequence

19.

When Blast or PSI-Blast is used for comparing sequences we have to take sequence properties into account, in particular regarding level of complexity.	
Why may a low-complexity protein sequence give problems in Blast?	
A	It will give too few hits in the score matrix
B	Only high-complexity sequences may cause problems
C	The sequence is often short, and will therefore return few significant hits
D	It will give a complex sequence alignment that is difficult to interpret
E	The sequence may have a very atypical distribution of amino acids

20.

Huntington`s disease is caused by an autosomal dominant mutation in the <i>Htt</i> gene	
The disease seems to appear more severe in successive generations likely due to	
A	Expansion of triple repeats within the coding sequence

B	Deletion of triple repeats within coding sequences
C	Chromosomal translocation of <i>Htt</i>
D	Transposons; i.e. sequences of <i>Htt</i> move themselves to new positions within the genome

21.

Inheritance of one deficient allele for a tumour suppressor gene may predispose for cancer	
Why is this?	
A	The tumour suppressor gens are present in only one copy
B	One deficient allele destroy the expression of other genes
C	Only one healthy allele increases the risk for loss of gene function
D	The mutated allele suppresses the healthy allele

22.

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

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 increase the risk for oxidation of LDL and foam cell formation.
C	The mutations inhibit cellular uptake and processing of cholesterol.
D	The mutations increase formation of xanthoms that contain cholesterol.

E	The mutations cause inflammation of intima and thereby attract monocytes.
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25.

At the early endosome (EE) receptors targeted for lysosomal degradation are recognized by HRS.	
What is the name of the chemical compound that is enriched on EE and vital for HRS function in guiding lysosomal degradation?	
A	Phosphatidylinositol 4,5 bi-phosphate, PI(4,5)P <sub>2</sub>
B	Phosphatidylinositol 3-phosphatase PI3-phosphatase
C	Phosphatidylinositol, PI
D	Phosphatidylinositol 3-kinase, PI3-kinase
E	Phosphatidylinositol 3-mono-phosphate, PI(3)P
Abbreviations: HRS - Hepatocyte Growth Factor-regulated Tyrosine Kinase Substrate.	

26.

The Toll-like receptors (TLRs) utilize leucine-rich repeat motifs in the extracellular domain for ligand binding; and a shared intracellular domain called the Toll/interleukin-1 receptor domain (TIR)-domain for the recruitment of TIR-domain containing signaling adapters for the initiation signaling.	
What is the name of the TIR-adapter used for signaling by most of the TLRs?	
A	TRAM
B	TRIF
C	MYD88
D	TIRAP
Abbreviations: MYD88 (Myeloid differentiation primary response gene (88)) TRAM (TRIF-related adaptor molecule) TRIF (TIR-domain-containing adapter-inducing interferon- $\beta$ ) TIRAP (TIR- domain-containing adaptor protein)	

27.

The Toll-like receptors (TLRs) utilize leucine-rich repeat motifs in the extracellular domain for ligand binding; and a shared intracellular domain called the Toll/interleukin-1 receptor domain (TIR)-domain. The recruitment of TIR-adapters to TLR4 upon receptor activation initiates two major signaling pathways.	
What is the name of the TIR-adapter pair used for the initiation of type I interferon upon activation of TLR4?	
A	TRAM and MYD88
B	MYD88 and TRIF

C	TIRAP and MyD88
D	TRAM and TRIF
	Abbreviations: MYD88 (Myeloid differentiation primary response gene (88)) TRAM (TRIF-related adaptor molecule) TRIF (TIR-domain-containing adapter-inducing interferon- $\beta$ ) TIRAP (TIR- domain-containing adaptor protein)

28.

Communication between cells has to be terminated after cellular response. What is the mechanism for termination of hormonal signals?	
A	Excretion through the urine
B	Apoptosis
C	Specific enzyme-catalyzed reactions
D	Binding to carrier protein

29.

Hormones are produced in internal secretory glands and cells. What are the major hormones produced by the adrenal cortex?	
A	Estrogens and progesterone
B	Aldosterone, glucocorticoids and androgens
C	Thyroxine and triiodothyronine
D	Corticotropine, thyroid stimulating hormone and antidiuretic hormone
E	Epinephrine and norepinephrine

30.

Hormones are produced in internal secretory glands and cells. Which modifications must some hormones gain after their secretion to become activated?	
A	Covalent modifications
B	Glycosylations
C	Binding to carrier proteins
D	Cleavage by proteolytic enzymes

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## MCQ svar / MCQ answers

## Eksamen/Exam MOL3000 "Introduction to molecular medicine" 06.12.2010.

MCQ, each question 1p. One answer is the most correct. Answer the questions on separate MCQ answers sheets enclosed. Only one cross for each question (the best alternative).

**NB! Very important: use black or dark blue pen!**

If you make a mistake, shade the entire square, and put a new cross in the correct square.

The exam must be answered on this sheet. **Remember to write your candidate number on all the pages!**

(If you have less than 6 digits in your candidate number, leave the first squares blank.)

Question 1    ☐ A    ☐ B    ☐ C

Question 2    ☐ A    ☐ B    ☐ C    ☐ D

Question 3    ☐ A    ☐ B    ☐ C

Question 4    ☐ A    ☐ B    ☐ C    ☐ D

Question 5    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 6    ☐ A    ☐ B    ☐ C    ☐ D

Question 7    ☐ A    ☐ B    ☐ C    ☐ D

Question 8    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 9    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 10    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 11    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 12    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E



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Question 13    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 14    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 15    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 16    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 17    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 18    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 19    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 20    ☐ A    ☐ B    ☐ C    ☐ D

Question 21    ☐ A    ☐ B    ☐ C    ☐ D

Question 22    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 23    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 24    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 25    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 26    ☐ A    ☐ B    ☐ C    ☐ D

Question 27    ☐ A    ☐ B    ☐ C    ☐ D



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Question 28    ☐ A    ☐ B    ☐ C    ☐ D

Question 29    ☐ A    ☐ B    ☐ C    ☐ D    ☐ E

Question 30    ☐ A    ☐ B    ☐ C    ☐ D

