Question no. 1(20 p)

Your research group is working on a type of B-cell lymphoma named Burkitt lymphoma. This type of cancer is often treated with Rituximab, which is a monoclonal antibody directed against the CD20 receptor found on the cell surface of Burkitt lymphoma cells. A primary goal of your research is to identify proteins that could serve as targets for drugs that could increase the efficiency of Rituximab treatment (adjuvants). In your laboratory you have access to Burkitt lymphoma cell lines that can be grown in cell culture.

a. Device a potential proteomics strategy to identify proteins that are differentially expressed as a result of Rituximab treatment.
b. Describe how proteins can be separated by 2-D PAGE. Can you name some advantages as well as some limitations of this technique? How can the method be modified to analyse two proteomes in one gel?
c. Describe how MALDI-ToF peptide mass fingerprinting (PMF) can be used to identify a human protein.
d. Sometimes the peptide data obtained in PMF are too scarce to yield reliable score-values in protein database searches. Describe how additional mass spectrometry data be obtained from the sample to increase the score-value?

Question no. 2 (15 p)

Describe the steps included in a typical Illumina gene expression protocol.

Question no. 3 (10 p)

When participating in medical research participants are presented with a document called the "informed consent form." This form is supposed to lay out all the information a person will need to make an informed decision as to whether or not he/she wants to participate in the research study. Discuss the pros and cons of the so called “broad consent” that is uses in connection with biobank research.

Question no. 4 (15 p)

A. Describe techniques used for the production of transgenic mouse models

B. Describe definition of phenotyping and discuss approaches to phenotyping

Question no. 5 (10p)

Explain briefly what we mean by CRM, proximal TFBS and distal TFBS, and how they may affect gene expression.

Question no. 6 (5 p)

Protein structures are stabilized by several types of interactions. Two such interaction types are disulfide bridges and hydrophobic interactions. Explain briefly about these two interaction types, and for each of them mention at least one type of amino acids that may participate in that interaction type.

Multiple choice questions (only one cross for correct answer). Correct answer gives 1 p

1.

In an electrophoresis system, using a native gel, proteins are separated due to differences in total charge.	
Which of the following decides the proteins' total charge?	
A	The voltage
B	The pH of the buffer
C	The protein size
D	The support medium

2.

The gene expression in tissue is the sum of gene expressions of several cell types	
It may be necessary to localize the gene expression to a specific cell type. Which one of these methods shows unequivocally from which cell the mRNA derives?	
A	Quantitative RT-PCR on the tissue homogenate
B	Western blot on the tissue homogenate
C	In situ hybridization on tissue sections
D	Immunohistochemistry on tissue sections

3.

A flow-cytometer can be used to detect the labelling intensity of several fluorochromes simultaneously.	
What properties of the fluorochromes are particularly important in such a setting?	
A	The photo-stability of the fluorochromes
B	Differences in emission/absorption maximum
C	The different dyes stains different cell surface markers
D	Differences in emission spectra
E	The different dyes have similar fluorescent intensity

4.

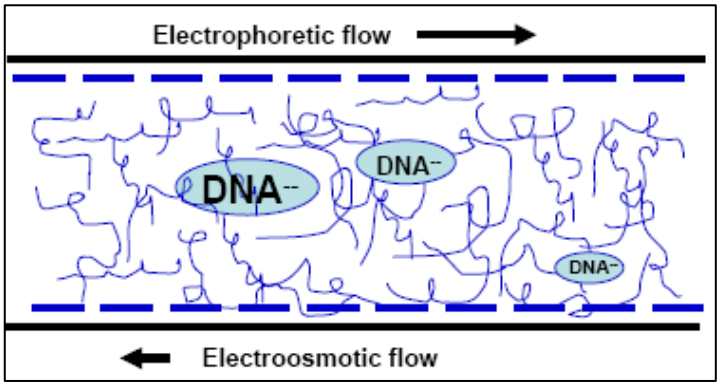
A population based biobank:	
A	Is established in relation to a population investigation
B	Include blood samples from a specific population
C	Include only specific parts of the population
D	Compare various populations

5.

Expression plasmids often contain the viral CMV immediate early promoter. The intention is to:	
A	Block the expression of all genes except for the inserted gene
B	Increase the expression of the N-terminal tag
C	Increase the expression of inserted gene
D	Assess the amount of control plasmid

6.

The schematic drawing shows separation of DNA fragments in a capillary electrophoresis system, where the capillary is filled with a polymer.



The separation is based upon the following principle?	
A	Differences in current during the electrophoresis run
B	Differences charge of the DNA fragments
C	Differences molecule size of the DNA fragments
D	Differences in electroendosmotic flow during the electrophoresis run

7.

Fluorescence recovery after photo-bleaching (FRAP) is a technique to study protein dynamics in live cells.	
What is this technique based on?	
A	The irreversible photo-bleaching of a fluorescent protein
B	The reversible photo-bleaching of a fluorescent protein
C	The intensity of green-fluorescent protein (GFP)
D	The mobility of a particular fusion protein
E	Rapid image acquisition of live cells

8.

Cis-trans isomerisation contributes to the conformation of the proteins:	
A	Cis-trans forms are equally expressed in proteins
B	Cis-forms are more stable and are dominating in proteins
C	Trans-forms are more stable and are dominating in proteins
D	Cis-trans forms influence the configuration of the protein

9.

Reporter gene studies are used in molecular cell biology to :	
A	Demonstrate the localization of genes
B	Demonstrate the localization of proteins
C	Examine transcriptional activation
D	Determine protein interactions
E	Assess mRNA levels

10.

Use of existing knowledge to describe genes or protein functions in Gene Ontology (GO) terms is called annotation with GO. "GO-annotation" implies:	
A	Each gene/protein may be annotated with several different terms from each of its sub-ontology (biologic process, cellular component, molecular function)
B	Each gene/protein may be annotated with only one GO-term
C	Each gene/protein may be annotated with only one GO-term from each sub-ontology (biologic process, cellular component, molecular function)
D	GO-annotation could only be performed by computers
E	All feasible GO-annotations for known genes is available in public databases

11.

Co-expression analyses of microarray data from Arabidopsis are often used to	
A	Verify quantitative RT-PCR results
B	Describe genomic position of inserted T-DNA in transgenic plants
C	Identify new and unknown genes linked to specific processes
D	Identify homologous genes present in other organisms

12.

The formula for estimating a Position Weight Matrix for transcription factor binding sites includes parameters for nucleotide count, sequence count, pseudocount and background nucleotide distribution.	
What would you use to get numbers for the nucleotide count?	
A	A set of co-regulated genes
B	A multiple alignment of known transcription factor binding sites
C	A set of core promoter regions
D	A multiple alignment of known transcription factor gene sequences
E	A Markov model

13.

Phylogenetic footprinting is often used in combination with motif discovery when analyzing transcription factor binding sites in gene promoter regions.	
What is the main purpose of using phylogenetic footprinting?	
A	Reduction of the number of false positive binding site predictions
B	Identification of active promoter regions
C	Identification of evolutionary relationships between transcription factors
D	Prediction of exonic genome regions
E	Mapping of suitable background sequences

14.

In evaluation of prediction methods for transcription factor binding sites we classify individual predictions as true positive, true negative, false positive or false negative.	
How would a predicted binding site that overlaps a real but unknown (un-annotated) binding site be classified?	
A	True positive
B	True negative
C	False positive
D	False negative
E	Unclassified

15.

The benchmark study of prediction methods for transcription factor binding sites that was published by Tompa *et al* showed a very low overall performance of the included methods.	
What is assumed to be the most important reason for the low performance?	
A	Lack of suitable score functions
B	Low quality of available position weight matrices
C	Lack of suitable background sequences with known binding sites
D	Lack of reference sequences where all real binding sites are known
E	Lack of well documented prediction methods

16.

Isoelectric focusing is a common method for separation of proteins	
In isoelectric focusing proteins are separated in the following gradient:	
A	A pH gradient
B	A salt gradient
C	A temperature gradient
D	A density gradient
E	A sucrose gradient

17.

Plasmid T-DNA vectors are used in transfer of foreign DNA into plant cells.	
After transformation of a plant cell, where is the T-DNA located?	
A	The T-DNA is integrated into the nuclear DNA
B	The circular T-DNA is replicated in the cytosol and passed on to new cells during cell division.
C	The T-DNA is integrated into the chloroplast DNA
D	The T-DNA is exclusively integrated into nucleolar DNA

18.

Chromatography can be used to estimate the size of a molecule.	
Which chromatographic principle is used for this purpose	
A	Partition
B	Affinity
C	Gel filtration (SEC)
D	Chiral
E	Ion exchange

19.

In Chromatography a highly efficient system is appreciated.	
An efficient chromatography matrix is most correctly characterized as a matrix that can:	
A	Separate compounds with short retention times
B	Separate compounds of large volumes
C	Produce large amount of results
D	Separate compounds with very similar properties
E	Separate compounds with very different properties

20.

Mass spectrometry (MS) is a very powerful technique	
Which is the most correct characterization of a mass spectrometer? The mass spectrometer:	
A	Separates compounds according to their molecular weight
B	Separates compounds according to their charge
C	Separates compounds according to their boiling point
D	Separates compounds according to their mass and charge
E	Separates compounds according to their mass

21.

A laser scanning (confocal) microscope allows us to obtain optical slices of the imaged sample.	
What particular component(s) is crucial for this?	
A	Lasers of different wavelengths
B	The pinhole
C	Fluorescent dyes with different emission wavelength
D	The digital detector(s)
E	Optical filters to discriminate excitation and emission light

22.

Auto-fluorescence can be a limiting factor in fluorescent imaging.	
What is causing auto-fluorescence?	
A	Unspecific binding of the primary antibody
B	Incomplete washing/removal of the added fluorochrome
C	The dye give rise to fluorescence without excitation
D	The emitted light from one fluororescent dye excites the second used dye
E	Endogenous factors in the tissue/cells with fluorescent properties

23.

Fluorescent imaging can be quantified in terms of differences in relative intensity	
What is this quantification based on?	
A	Relative intensity detected by the grey-scale detector(s)
B	The absolute intensity of the particular fluorochrome
C	The colour of the fluorescent dye
D	The relative intensity detected by the digital colour camera
E	The large Stoke`s shift

24.

Luciferase is used extensively in many different approaches in life science.	
What is luciferase?	
A	A fluorescent protein
B	A fluorescent dye
C	A fluorescently labelled secondary antibody
D	An enzyme
E	A reporter plasmid

25.

Monoclonal antibodies are important tools in many aspects of life science research and diagnostics	
What is a monoclonal antibody?	
A	An antibody made against a short peptide
B	An antibody that can bind only one antigen epitope
C	An antibody that recognize either a native or a denatured antigen
D	An antibody made in mice
E	An antibody made by one clone of B-cells