School of Biosciences

WRITTEN EXAMINATION

Course: Biomarkers in Molecular Medicine

Sub-course

Course code: BV705A

Credits for written examination 4 hp

Date: 28/2 2025

Examination time: 8:15 – 12:30

Examination responsible: Andreas Tilevik

Teachers concerned

Aid at the exam/appendices: calculator

Write your answers directly in the exam sheets!

No negative points for the multiple-choice questions will be given. You can only get two or zero points on these questions. To get points on these questions, all correct statements must be selected and all incorrect statements must be unselected.

Grade points 40 p.

Examination results should be made public within 18 working days

Good luck!

Describe how biomarkers are currently used in medicine, drug discovery, and environmental health (23 p)

1. Which of the following statements are correct regarding the biomarker discovery process (zero, one or several statements can be correct)? (2p)

   ☐ The identification phase usually involves more subjects (samples) than the validation phase.
   ☐ The identification phase usually involves more variables that are measured (for example more proteins or more genes) than the validation phase.
   ☐ The validation phase should include the same subjects (e.g. people) as the ones that were included in the verification phase.
   ☐ The qualification phase usually involves a different experimental technique compared to the identification phase.

2. Which of the following methods can be considered as high-throughput technologies to identify new biomarkers (zero, one or several statements can be correct)? (2p)

   ☐ RNA-sequencing
   ☐ Mass spectrometry (Mass spec)
   ☐ ELISA
   ☐ Protein arrays

3. Study the two different definitions of biomarkers below:

   "A biomarker is a biological molecule found in blood, other body fluids, or tissues that can be used as a sign for the presence of a disease".

   "A biomarker, or biological marker, is a measurable indicator of some biological state or condition"

   Describe two distinct differences between these two definitions. (2p)

4. One can use the clinical skin prick test to detect allergies against certain allergens. Explain the molecular and cellular process that needs to take place in order to generate a red spot on the skin within a few minutes. (4p)

5. Explain how the erythrocyte sedimentation rate (ESR) test works as an indication of inflammation. (2p)

6. Name two molecular biomarkers on T helper cells that can be used to diagnose AIDS by flow cytometry (to count the number of T helper cells). Explain how these measurements are used to diagnose AIDS. (3p)

7. Explain briefly what may cause a decrease (1p) or an increase (1p) in the total serum protein level. Your answer should include examples of proteins that may be altered during certain conditions.

8. You have done a cohort study where you have followed smokers and non-smokers over 20 years to test if there is an increased risk to get Alzheimer's disease for smokers. Calculate the relative risk (RR) to get Alzheimer's disease for the smokers and draw a conclusion based on this RR. **Show your calculations**. (2 p)

Patient ID	Survival time (years)	Event (0=censored, 1 = event)	SUM
Smoker	200	9800	10000
Non-smoker	20	9980	10000
SUM	220	19780	20000

9. Which of the following statements are correct regarding the biomarkers for autoimmune diseases (zero, one or several statements can be correct)? (2p)

☐ CRP is a general marker for inflammation and is sometimes used as a supportive marker for autoimmune diseases.
☐ IgE antibodies are commonly used as a general marker for autoimmune diseases.
☐ The proteins albumin and gp120 are common markers for Rheumatoid arthritis (RA).
☐ Glucose concentration is used as a biomarker to adjust insulin therapy in patients with type 1 diabetes.

10. Which of the following statements are correct regarding the biomarker CRP (zero, one or several statements can be correct)? (2p)

☐ CRP can be detected from a blood sample.
☐ The CRP level is usually lower in patients with bacterial infections compared to patients with viral infections.
☐ CRP can differentiate between all types of autoimmune diseases with high accuracy.
☐ CRP is a general biomarker for detecting inflammatory diseases such as autoimmune diseases and sepsis.

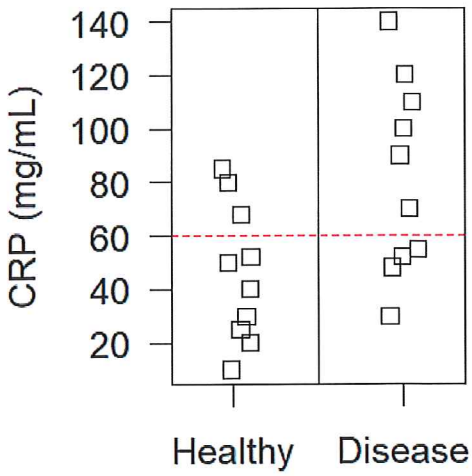
Describe how bioinformatics tools can be used for biomarker discovery (17 p).

1. Imagine that you have measured the concentration of PSA to detect prostate cancer. You have collected the following data: (3p)

Subject	State	PSA concentration (ng/ml)
1	Healthy	5
2	Healthy	2
3	Healthy	3
4	Prostate cancer	3
5	Prostate cancer	4

   Show the calculation that you need to do for the first round of iteration when using the Leave-One-Out Cross-validation method. You therefore only need to show the calculations of the cutoff value and the prediction you make when you leave the first person out.

2. In a study, one has evaluated the blood CRP concentration as a biomarker for a certain autoimmune disease. In total, 10 healthy controls and 10 patients with the disease were included in the study. The research group decided to use a cutoff value of 60. Values above this cutoff value are associated with a positive test result, whereas values below this cutoff are associated with a negative test result. (8p)



a) How many false negative results are there? (1p)

b) How many true negative results are there? (1p)

c) How many false positive results are there? (1p)

d) Given the cutoff value, what is the sensitivity of the test? **Show your calculations.** (1p)

e) Given the cutoff value, what is the specificity of the test? **Show your calculations.** (1p)

f) Given the cutoff value, what is the positive predictive value? Assume the same prevalence as observed in the sample. **Show your calculations.** (1p)

g) What is the positive likelihood ratio (LR+)? **Show your calculations.** (1p)

h) What is the negative likelihood ratio (LR-)? **Show your calculations.** (1p)

3. Let's say that the area under the ROC curve is equal to 0.55, with a 95% confidence interval that is equal to [0.4 0.7] for a certain biomarker. Is this biomarker significantly better than chance? Explain why or why not. You need a motivation to get points. (2p)

4. Which of the following statements are correct regarding the negative/positive predictive value (NPV/PPV) and accuracy (zero, one or several statements can be correct)? (2p)

☐ The PPV is the probability that you have the disease, given a negative test result.
☐ The accuracy is the sum of the true negatives and true positives divided by the sum of all positives and negatives.
☐ The accuracy is the sum of the true positives divided by the sum of all positives and negatives.
☐ The NPV is the probability that you are healthy, given a positive test result.

5. Which of the following statements are correct regarding validation methods (zero, one or several statements can be correct). (2p)

☐ By using the leave-one-out cross-validation (LOOCV) method, only one data point is set aside to be used in the test data in every iteration.
☐ By using the LOOCV, about half of the data points are used in the test set.
☐ 4-fold cross-validation means that each data point participates four times in the test data set.
☐ In the holdout method, the data points participate in either the training data set **or** the test data set (not both).