School of Biosciences

WRITTEN EXAMINATION

Course: Biomarkers in Molecular Medicine

Sub-course

Course code: BV705A

Credits for written examination 4 hp

Date: 1/3 2024

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. Explain the difference between the identification phase and the verification phase in the biomarker discovery process. Focus on the differences and similarities in sample size and techniques used in the two phases. (2p)

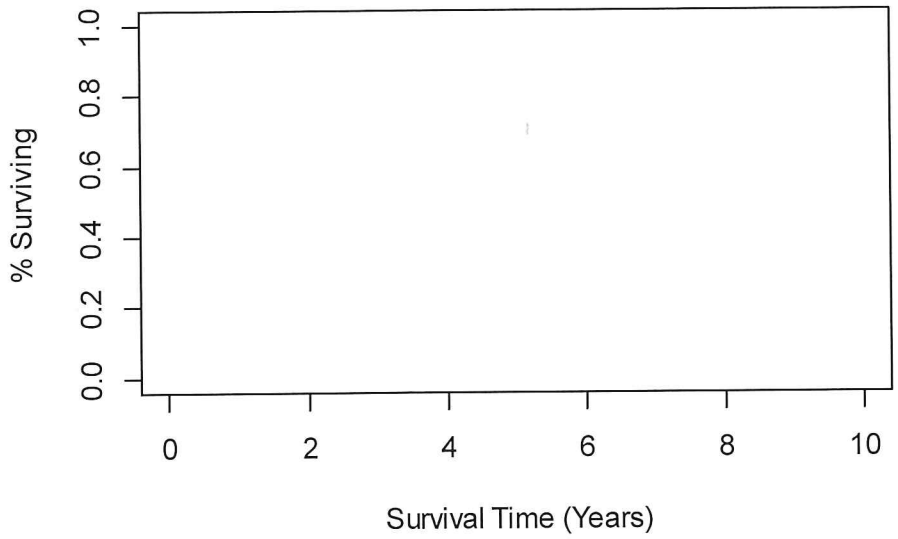
2. Name at least two biomarkers that can be used to predict kidney failure and describe the underlying process that causes different levels of these biomarkers in blood and/or urine. (4p)

3. Describe the differences between prognostic and predictive biomarkers and name an example of such a biomarker for each type. (3p)

4. Explain 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.

5. Draw a survival curve in the plot below based on the data in the following table. (4p)

Patient ID	Survival time (years)	Event (0=censored, 1 = event)
1	2	1
2	4	1
3	4	1
4	10	0



6. 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 that is also partly used as a marker for autoimmune diseases.
☐ The IgE antibody is a common marker for type 1 diabetes.
☐ The proteins gp120 and gp41 are common markers for Rheumatoid arthritis (RA).
☐ The glucose concentration can be used as a biomarker to regulate insulin therapy for patients with type 1 diabetes.

7. 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 much lower in patients with bacterial infection compared to patients with viral diseases.
☐ CRP is a common biomarker for inflammation.
☐ CRP is a biomarker for detecting inflammatory diseases such as autoimmune diseases and sepsis.

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

☐ Bilirubin is a waste product of the breakdown of white blood cells.
☐ A high level of bilirubin in the serum is an indication of reduced liver function.
☐ A low level of albumin in the serum is an indication of reduced liver function.
☐ A high level of unconjugated bilirubin in the serum is an indication of Gilbert's syndrome.

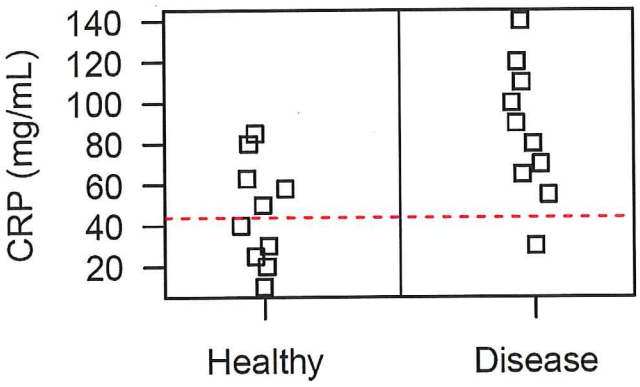
9. Which of the following statements are correct regarding biomarkers for Alzheimer's (zero, one or several statements can be correct)? (2p)

☐ Biomarkers collected from the blood show better accuracy than biomarkers collected from the cerebrospinal fluid.
☐ The concentration of Amyloid-beta proteins and Tau proteins in the cerebrospinal fluid are used as biomarkers for Alzheimer's.
☐ Creatinine and APOE levels in serum are commonly used as biomarkers for Alzheimer's.
☐ Albumin and APOE levels in serum are commonly used as biomarkers for Alzheimer's.

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

1. Explain how the hold-out method works to validate a biomarker. Also, discuss the sample size you need for this method in comparison to the cross-validation method. (3p)

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 44. Values above this cutoff value are associated with a positive test result, whereas values below this cutoff are associated with a negative test result.



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

b) How many true positive 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? (1p)

e) Given the cutoff value, what is the accuracy of the test? (1p)

f) Given the cutoff value, what is the negative predictive value? Assume the same prevalence as observed in the sample. (1p)

g) What is the positive likelihood ratio (LR+)? (1p)

h) What is the negative likelihood ratio (LR-)? (1p)

3. Suppose that one has validated a biomarker and calculated the positive likelihood ratio to 5.0. Explain what this value means (show that you can interpret such a value). (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 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 negative test result.

5. Which of the following statements are correct regarding computational methods that can combine biomarkers (zero, one or several statements can be correct)? (2p)

☐ LDA combines variables in a way that maximizes the separation between the groups.
☐ The KNN method is based on the distance between the unknown (new) observation and data points with a known class (e.g. known disease or healthy).
☐ The KNN method determines the class of the unknown (new) observation based on the majority class of its K closest neigbours of known class.
☐ The KNN method and the LDA method work in the exactly same way and will therefore result in the same accuracy.