UNIVERSITY
OF SKÖVDE

School of Biosciences

Course: Biomarkers in Molecular Medicine

Sub-course

Course code: BV705A

Date 9/1 2024

Available teacher
Andreas Tilevik

Credits for written examination: 4 hp

Examination time: 8:15 – 12:30

Available on phone number: 076-7701257

Visiting the examination   ☐   Yes, at:

  ☒   No

Aids and other information for invigilators:

Calculator	☒	Provided by the University	Writing paper	☒	Lined
	☒	Student's own calculator		☐	Squared
	☐	Not allowed			

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School of Biosciences

WRITTEN EXAMINATION

Course: Biomarkers in Molecular Medicine

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Date: 9/1 2024

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Examination responsible: Andreas Tilevik

Teachers concerned: Andreas Tilevik

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 qualification phase in the biomarker discovery process. Focus on the differences and similarities in sample size and experimental technique used in the two phases. (2p)

2. What is the erythrocyte sedimentation rate (ESR)? Explain how it can be used as a biomarker for inflammation (2p).

3. Name the five main types (groups) of biomarkers that exist and briefly describe how they are used in the medical care system (5p):

4. 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	5	1
4	10	0
5	10	0
6	10	0
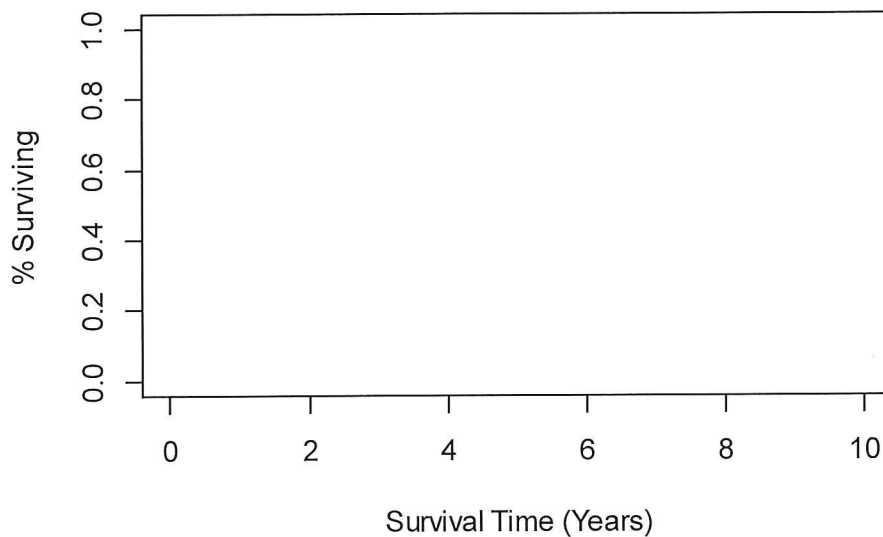
5. Which of the following statements are correct regarding biomarkers for kidney failure (zero, one or several statements can be correct)? (2p)

☐ Creatinine level is low in serum during kidney failure
☐ Creatinine level is very high in urine during kidney failure
☐ Albumin level is relatively high in urine during kidney failure
☐ A certain allele of the APOE gene can be used to predict kidney failure

6. Which of the following statements are correct regarding personalized medicine for treating breast cancer (zero, one or several statements can be correct)? (2p)

☐ If the HER2 receptor is present on the surface of the cancer cell, this is an indication that the drug Herceptin (Trastuzumab) will be beneficial for the patients
☐ The FISH method can be used to stain the HER2 gene
☐ The level of Albumin in the blood can be used to monitor possible toxic effects on the liver during drug therapy
☐ The level of Albumin in blood is used to determine the dose of the Herceptin (Trastuzumab) for the patients

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

☐ The risk of developing Alzheimer's disease can be predicted based on the type of allele the person has for the BRCA1 or BRCA2 gene
☐ The B-type natriuretic peptide (BNP) is released from myocytes in response to increased wall stress
☐ High levels of bilirubin in the blood can be an indication of liver diseases
☐ Total tau and phosphorylated tau (p-tau) are commonly measured in cerebrospinal fluid (CSF) or blood samples to aid in the diagnosis of Alzheimer's disease (AD)

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

☐ The glucose level is an example of a biomarker for monitoring
☐ The HER2 receptor is an example of a predictive biomarker
☐ The CRP can be used to distinguish viral from bacterial infections
☐ Specific IgE antibodies are diagnostic biomarkers for allergy

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 cerebrospinal fluid show better accuracy than biomarkers collected from blood
☐ Creatinine and APOE levels in serum are commonly used as biomarkers for Alzheimer's
☐ The concentration of Amyloid-beta proteins and Tau proteins in cerebrospinal fluid are used as biomarkers for Alzheimer's
☐ A certain allele of the APOE gene can be used as a risk biomarker for Alzheimer's disease

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

1. Name three differences between the hold-out method and the cross-validation method when it comes to validating a biomarker. (3p)

2. In a study, one has evaluated the blood CRP concentration as a biomarker for a certain autoimmune disease. In total, 11 healthy controls and 10 patients with the disease were included in the study. The research group decided to use a cutoff value of 75. 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)
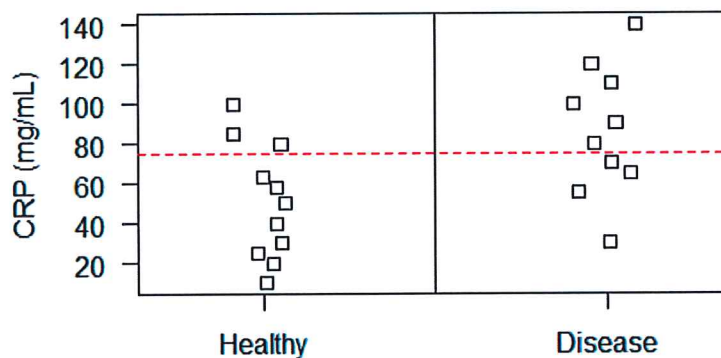
a) How many false negative results are there? (1p)

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

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

d) Given the cutoff value, what is the specificity 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 positive 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. Study the ROC curve below. Which of the following statements are correct regarding this curve (zero, one or several statements can be correct)? (2p)
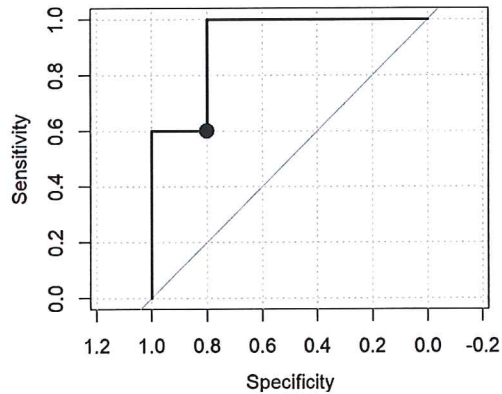
☐ The area below the ROC curve is greater than 0.95
☐ The point on the curve (marked with a filled circle) tells us that the cutoff value, associated with this point, results in a sensitivity of 60% and a specificity of 80%
☐ The point on the curve (marked with a filled circle) tells us that the cutoff value, associated with this point, results in a sensitivity of 80% and a specificity of 60%
☐ The area below the diagonal line (the reference line in grey color) is 0.5

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 proportion of correct predictions
☐ The accuracy is the sum of the true positives divided by all negative results
☐ The NPV is the probability that you are healthy given a negative test result

5. Describe how the method of K-nearest neighbor (KNN) works in order to predict if a person has the disease or not (2p)