NTNU

Faculty of Medicine
Department of Cancer Research and Molecular Medicine

Exam MOL3007

Functional Genomics

Tuesday May 29th 9.00-13.00

ECTS credits: 7.5
Number of pages (included front-page): 5

Supporting materials: None

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

NOTE THAT SINGLE QUESTIONS ARE WEIGHTED DIFFERENTLY (INDICATED BY NUMBER OF POINTS (p) PER QUESTION).

PLEASE START ANSWERING EVERY QUESTION (1-7) ON A NEW SHEET OF PAPER!

Question 1 - (25p)

Contemporary governmental biotechnology strategies (for example the Norwegian National Biotechnology Strategy released December 2011) convey expectations to functional genomics to contribute to improved diagnosis and treatment in health care.

a) Describe and discuss how transcriptomics can be used to improve diagnosis and treatment of disease. (10p)
   - What is transcriptomics?
   - Chose one of the central methodologies used to measure the transcriptome and explain its main principles
   - Discuss strategies in ongoing research where transcriptomics is used to improve understanding of disease mechanisms and to improve on disease diagnosis. Give examples.

b) What is the role of knowledge management in functional genomics? Give examples of types of publicly available resources used in current research.(5p)

c) How is functional genomics expected to contribute to systems medicine and personalized medicine? Give examples of applications of personalized medicine. Discuss societal aspects of the given examples of personalized medicine. (10p)

Question 2 - (20p)

In your research project you are trying to identify proteins involved in multiple myeloma- a cancer of the bone marrow that is characterized by abnormal proliferation of plasma cells (antibody-producing B-cells). One characteristic of these cells is that they express high levels of the surface antigen CD138.

a) Describe a method to enrich for plasma cells from blood samples.

b) After plasma cells have been isolated from both myeloma patients as well as healthy controls, you want to compare the respective proteomes by running 2-dimensional polyacrylamide gel electrophoresis (2D-PAGE). Describe the underlying principles for protein separation and visualization by 2D-PAGE

c) During the analyses you experience problems of gel-to-gel variation that makes it difficult to pairwise compare spots between the patient- and control gels. Describe an alternative method in which two proteomes can be separated and independently visualized within the same gel.

d) After a series of experiments, you identify a protein spot that is consistently overexpressed in the myeloma cells compared to the normal plasma cells. You aim at identifying this protein by using MALDI-TOF MS (matrix assisted laser desorption/ionization time-of-flight mass spectrometry). Briefly explain the principles of protein identification by peptide mass fingerprinting by using MALDI TOF MS and make a schematic drawing of the MALDI ion source.

e) A peptide identified in the MALDI MS spectrum has a molecular weight of 2547 Da. At which m/z values would you expect to see ion signals in MALDI MS and in ESI MS, respectively? Draw the predicted MALDI MS spectrum and the predicted ESI MS spectrum, indicating the m/z values for all predicted ion species.

Question 3 - (15p)

a) «Informed consent» is used in biomedical research. Explain what «Informed consent» is and discuss the purposes of using «Informed consent» in biomedical research

b) The uses of whole genome sequencing or exome sequencing methods are rapidly increasing in genomic research.
   - Briefly describe 3-4 ethical concerns raised in connection with genomics or genetics.
   - Discuss the issue of "return of research results" to individual research participants from genomic or genetic research. Identify what is at stake here and present various arguments used in the debate.

Question 4 - (10p)

a) Phylogenetic footprinting can be used to eliminate spurious or false positive predictions of transcription factor binding sites. Explain what we mean by false positive predictions, and how phylogenetic footprinting can reduce this problem.

b) The performance of a motif discovery method may be assessed by benchmarking. Explain how benchmarking can be done, and how the performance quality can be estimated from the benchmarking results. You do not need to give formulas, but explain briefly the four prediction categories used in many formulas.

Question 5 - (10p)

a) It is essential to have high-quality crystals in X-ray crystallography. Explain the typical set-up for the hanging drop vapor-diffusion experiment.

b) Structure determination by NMR is based on restraints that can be generated from the NMR data. Describe briefly three different types of NMR-based restraints and how they can be used for structure determination.

Question 6 - (10p)

Virtually all human genes have mouse equivalents. This makes the mouse a useful model for research into human development, physiology, disease, therapies and drug discovery.

Describe and discuss common approaches that change genes in mice in order to create the mouse model of human disease.

Question 7 - (10p)

The discovery of fluorescent proteins has revolutionized our understanding of cell biology. Using recombinant DNA technology we can easily make chimeras of a protein serving a cellular function and a fluorescent protein.

a) You are setting up an experiment to image cells expressing fluorescent protein chimeras to obtain the best possible optical resolution.
   - What type of microscope is best for this purpose?
   - How can 3D-data be obtained?
   - Name two different GFP variants
   - How do the GFP variants differ?

b) In the next experiment your goal is to investigate protein-protein interaction.
   - What microscope based technique would you choose for this study?
   - In how close proximity must the two proteins be to allow this method to work?

c) You are using mice to image the spreading of a bacterial infection after injecting the bacteria into the peritoneum (body cavity)
   - How would you engineer the bacteria's to allow detection in the whole -animal model?
   - How would you monitor the bacterial spreading?
   - Discuss the difference between the principles of this method and the principles of fluorescense microscopy.