NTNU

Faculty of Medicine
Department of Cancer Research and Molecular Medicine

Exam MOL3007

Functional Genomics

Thursday December 20th 9.00-13.00

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

Supporting materials: None

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Exam results: January 25th
Examination results are announced on http://studweb.ntnu.no/

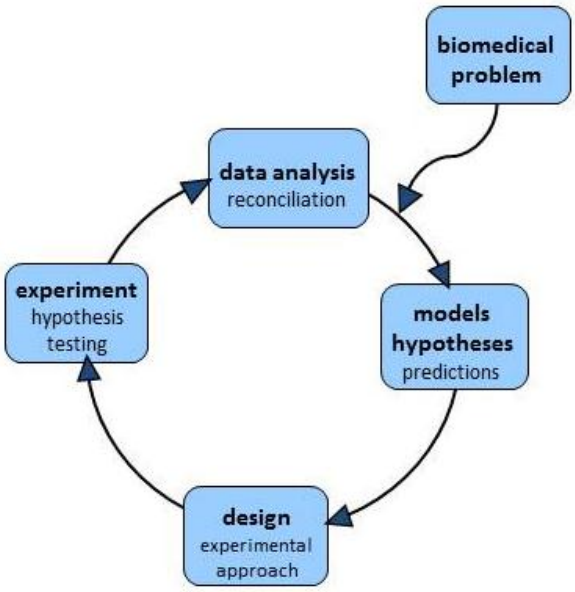
NOTE THAT SINGLE QUESTIONS ARE WEIGHTED DIFFERENTLY (INDICATED BY NUMBER OF POINTS (p) PER QUESTION).

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

Question 1 - (25p)

Discuss central elements of the functional genomics/systems biology research process and how it is applied.

a) Explain each of the four steps in the cycle. What is the aim of the actions taken? What are the main actions?
Give examples related to a biological or biomedical problem for each of the steps. 15p



b) Discuss <u>two examples</u> of the use of a functional genomics approach to improve either understanding of a biological phenomenon, or disease diagnosis or disease treatment. Which type of genome-wide screening (-omics) was used? How were the results analysed and interpreted? 10p

Question 2 - (20p)

In your research project, you are studying a protein known to be embedded in the lysosomal membrane, and that is phosphorylated at a yet uncharacterised amino acid residue.

a) With purified lysosomes in hand, you want to enrich your protein by ion exchange chromatography. Which additive is essential to the buffer in this case?
b) You run SDS-PAGE for all the fractions after the ion exchange column, in some of the fractions you see proteins with corresponding molecular weight to your protein. Which mass spectrometry based method would you use to confirm in which fraction the correct protein is? Describe the principle of this method

c) You find the protein in one fraction and you know the protein is phosphorylated. You now want to find which amino acid is phosphorylated. Explain which techniques you would use, biochemical and mass spectrometry based?

d) A tryptic peptide VKEGMNIVEAMER (Monoisotopic molecular mass = 1504.7) was analysed by MALDI MS. What do you expect the mass spectrum to look like? Draw the mass spectrum and indicate the m/z values and the approximated isotope distribution for the peptide ion species.

e) The doubly charged (i.e. doubly protonated) peptide VKEGMNIVEAMER was sequenced by ESI MS/MS. Draw the mass spectrum as you expect it to appear. Indicate the types of fragment ion series that you expect to see. Explain the appearance of the MS/MS spectrum, including assignments of peaks. A Table of amino acid residue masses is provided below.

Amino Acid Residues

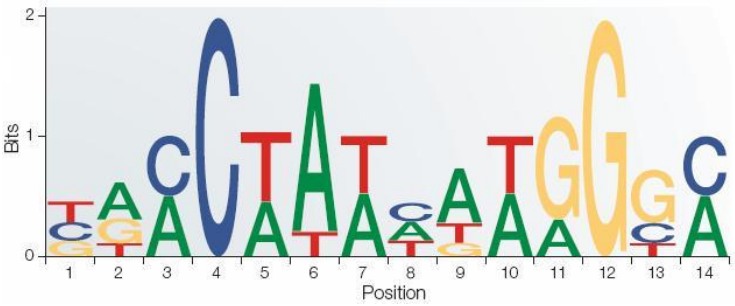
Amino acid	Three (one)-letter code	Monoisotopic mass	Average mass
Glycine	Gly (G)	57.021	57.052
Alanine	Ala (A)	71.037	71.079
Serine	Ser (S)	87.032	87.078
Proline	Pro (P)	97.053	97.117
Valine	Vat (V)	99.068	99.133
Threonine	Thr (T)	101.048	101.105
Cysteine	Cys (C)	103.009	103.145
Isoleucine	Ile (I)	113.084	113.160
Leucine	Leu (L)	113.084	113.160
Asparagine	Asn (N)	114.043	114.104
Aspartic acid	Asp (D)	115.027	115.089
Glutamine	Gln (Q)	128.059	128.131
Lysine	Lys (K)	128.095	128.174
Glutamic acid	Glu (E)	129.043	129.116
Methionine	Met (M)	131.040	131.199
Histidine	His (H)	137.059	137.142
Phenylalanine	Phe (F)	147.068	147.177
Arginine	Arg (R)	156.101	156.188
Tyrosine	Tyr (Y)	163.063	163.176
Tryptophan	Trp (W)	186.079	186.213
Homoserine lactone	—	83.037	83.090
Homoserine	—	101.048	101.105
Pyroglutamic acid	—	111.032	111.100
Carbamidomethylcysteine	—	160.031	160.197
Carboxymethylcysteine	—	161.147	161.181
Pyridylethylcysteine	—	208.067	208.284

Question 3 - (15p)

Genetic testing for several traits and diseases are now offered directly to consumer via the internet, and can therefore be done relatively easily. Identify and discuss challenges and benefits that an increasing focus on genetic testing can have on individuals and on society.

Question 4 - (10p)

A set of transcription factor binding sites can be represented with a sequence logo, similar to the one shown below. Describe the individual steps that are needed to make this type of logo. No formulas are needed.



Question 5 - (10p)

X-ray crystallography can give you the three-dimensional structure of a protein molecule. Describe how this can help you to predict function of novel proteins, understand the mechanism of enzymes and receptors, and design or modify inhibitors.

Question 6 - (10p)

Discuss why the mouse is an attractive model for a functional genomics approach to human biology.

Question 7 - (10p)

Fluorescent proteins are used in confocal microscopy to study intracellular trafficking patterns of the proteins of interest.

a) How do we make the protein of interest fluorescent?

b) Define the term Stokes shift.

c) We are about to study how two different proteins co-traffic within the cell and want to make them both fluorescent. What should be the characteristics of the fluorescent proteins of choice?

d) We are about to perform Fluorescence Resonance Energy Transfer (FRET). Give an example of a FRET pair.

e) What do we study when we are performing FRET?