FACULTÉ DE PHARMACIE
DE Paris-Saclay

Biotechnology mock exam
(format/questions/topic may change depending on the year)

EXAM INSTRUCTIONS

- DURATION : **2H**

- THIS EXAM HAS A TOTAL OF **20** POINTS

- FILL IN THE HEADINGS ON THIS FIRST PAGE VERY CAREFULLY SO THAT YOUR COPY REMAINS ANONYMOUS.

- NO MENTION OR SIGN OF RECOGNITION MUST BE MADE ON THE FOLLOWING PAGES, OTHERWISE, THEY WILL BE DEEMED INVALID.

- NO COMPLAINTS ABOUT THE TEST WILL BE ACCEPTED AFTER THE FIRST 15 MINUTES OF THE TEST.

- WRITE YOUR ANSWERS LEGIBLY IN THE SPACES PROVIDED.

- IF YOU HAVE ANY PROBLEMS, PLEASE CONTACT THE INSTRUCTORS IN THE ROOM.

- ANY COMMUNICATION OR ATTEMPT TO CHEAT WILL RESULT IN THE FAILURE OF THE TEST.

GOOD LUCK !

A) Multiple choice questions, circle the right(s) answer(s), (1 point per question)

1) About somatic cell therapy, what is/are the <u>correct</u> sentence(s):

A) Autologous cell therapy induces frequent immune reactions

B) Somatic cell is any cell of the body except germ line cells

C) Embryonic stem cells are multipotent stem cells

D) Cell-based therapies consists in administration of living cells

E) Autologous cell therapy is most of the time well tolerated

2) Protein separation techniques are often based on the following properties **except**:

A) Solubility of the protein   B) Viscosity of the protein

C) Charge of the protein   D) Specific binding affinity of the protein

B) Short answer questions

Question 1

- Please describe 3 strategies possible to improve a therapeutic protein by acting on its glycosylation, please illustrate each strategy by an example (2 points*)*

Question 2
Your company has been asked to develop a new version of an interferon-gamma protein with a prolonged blood half-life. Please propose and present shortly **2** possible strategies. (2 points)

Question 3
Quickly explain what the peptide mapping control method is. (1 point)

Question 4

When producing a therapeutic protein, what are the 4 main characteristics that need to be controlled (1 point)

C) case study (please answer with 2/3 sentences)

Erythropoietin (EPO) is a glycoprotein cytokine secreted by the kidneys that stimulates red blood cell production in the bone marrow. Recombinant erythropoietin (rEPO) is used as a treatment against insufficiency of endogenous production of erythropoietin leading to renal failure, inflammatory anaemia, anaemias associated with cancer and chemotherapy, and anaemias associated with chronic diseases.

a) What host cell(s) can be chosen to produce the rEPO protein? Justify and give an order of choice according to the quality of glycosylation. (1.5 points)

b) What are the different steps that are needed to create from a commercial plasmid, a plasmid that will allow rEPO expression? (1.5 points)

The schematic overview of the production of EPO is presented below.
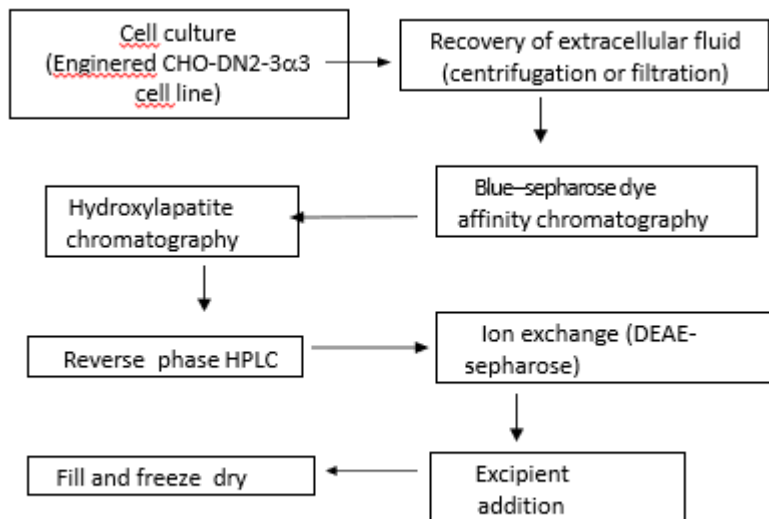
Adapted from G Walsh. Biopharmaceuticals 2d edition. 2003. Wiley

c) At which step does the downstream process start? (1 point)
d) Explain why no cell lysis steps are present in the purification process. (1 point)
e) What are the possible contaminants/impurities present after the bioproduction step? (1 point)
f) What is the principle of the ion exchange step in the purification scheme? (1 point)

Once the protein is produced and purified, a quality control is performed by denaturing electrophoresis (SDS-PAGE), with the addition of a reducing agent. The revelation of the gel is done by staining it with Coomassie Blue. The result of the analysis is shown in the figure below: (1) crude culture supernatant, (2) intermediate purification step, (3) after purification
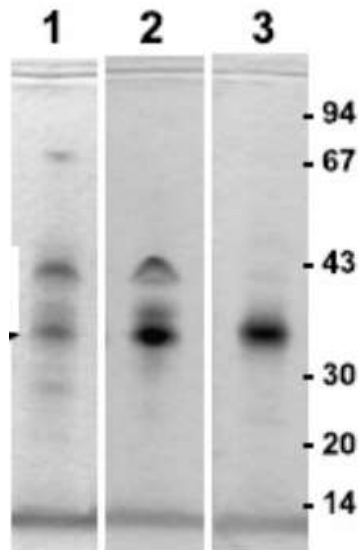
g) Describe the SDS-PAGE technique and explain how it can be used to monitor the purity of EPO during its production (1 point)
h) Describe the results obtained and conclude (1 point)
i) How could you verify that a batch of EPO is not contaminated with a given microorganism ? (1 point)

j) How could a RNA-based product could be used as an alternative to rEPO ? (1 point)

Some scientists have tested the effect of EPO on obesity. In one experiment they used groups of mice, on high fat died (HFD) or on normal control diet (NC) while treating them with a placebo (con) or rEPO. During this experiment the scientist monitored the animal body weight (figure A) and the calory (food) intake (figure B).
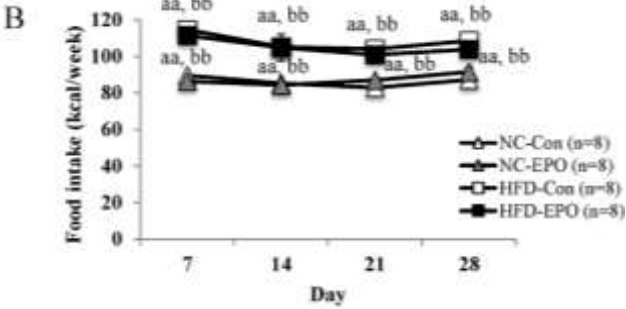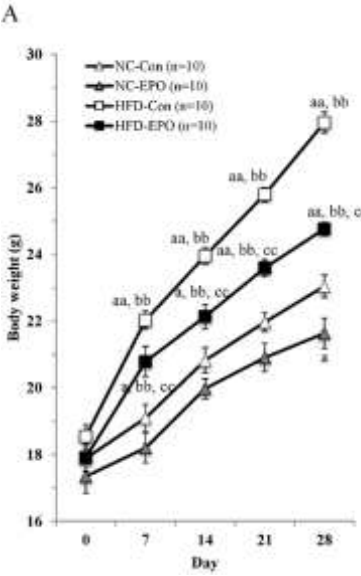
e) Quickly describe the results of the experience and conclude. (1 point)

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