UNIVERSITETET I OSLO

Det matematisk-naturvitenskapelige fakultet

Exam in: MBV4230 and MBV9230 Eukaryotic transcription factors
– structures, function, regulation
Day of exam: Friday 1 Nov 2013
Exam hours: 10:00 – 13:00
This examination paper consists of three pages.
Permitted materials: None

Make sure that your copy of this examination paper is complete before answering.

All questions are given in English, but you may choose yourself in which language (Norwegian or English) you prefer to answer. This exam consists of two parts. The first part is a set of questions, where you are supposed to provide brief and concise answers through a few phrases only (less than 10 phrases). The second part consists of questions that may require slightly more elaborate answers, although you should still try to keep the text volume limited and the style concise.

Part I: Short questions

1. The expression of a gene is controlled by promoter sequences. Some core promoter elements are recognized by general transcription factors. Which factor recognizes the TATA-box, the INR-region and the DPE, respectively?

2. Below is shown a short sequence from the core-promoter (called P2) in the beginning of the *MYC* gene. Indicate the most probable position for a TATA-box, an INR-region and the transcription start site (TSS) in this sequence:
`GGCATCGCGA CGCGCTGAGT ATAAAAGCCG GTTTTCGGGG CTTTATCTAC TCTGCTGTAG TAATTCCAGC GAGAGGCAGA`

3. RNA polymerase II (RNAPII) is the key enzyme in the process of transcription. The largest subunit of RNAPII contains a particular repeat-structure. Describe briefly its amino acid composition or sequence, and how it becomes modified in several positions of each repeat?

4. Describe briefly the functions of the two factors DSIF and NELF?

5. When studying chromatin-associated proteins, one encounters a long list of names in the form of abbreviations. Below is a list of eight such proteins (1-8) as well as different activities (A-H). Place each protein together with its respective chromatin activity.

Protein	Activity
1. PADI4	A. *De novo* methyltransferase
2. LSD1	B. Deimination
3. DNMT3	C. Histone chaperone
4. MOF	D. Histone acetyltransferase
5. HIRA	E. FeII- and 2-ketoglutarate-dependent oxidases
6. TET1	F. Tandem acetyl-lysine binder
7. $TAF_{II}250$	G. FAD-dependent amine oxidases
8. SirT1	H. Histone H1K26 deacetylation

For simplicity you may answer by a list of the form 1A, 2B etc (examples are not correct combinations). Only one combination is in principle the correct answer per protein.

6. A large part of the human genome is transcribed, but not coding for proteins. Explain in few words what classifies lincRNAs. Describe briefly where the locus of Xist lincRNA is found, the activity of this lincRNA and whether it has a role in *cis* or *trans* regulation.

7. Laminopathies is a description of 17 distict diseases caused by mutations in lamins. Describe briefly the function of lamins, what types of lamins exist, and which type of lamin is primarily mutated in laminopathies.

8. Enhancers are important elements regulating transcription. Describe briefly the difference between active, primed and poised enhancers?

Part II: Full questions

A

TFIIB is one of the general transcription factors with key roles in the assembly of the preinitiation complex (PIC) and promoter escape. Describe in more details:

1. How TFIIB interacts with DNA at early stages of PIC assembly.
2. How TFIIB interacts with RNA polymerase II and the functional implications of this interaction.
3. The role of TFIIB in early elongation and promoter escape

B

S-adenosyl-methione (SAM, AdoMet) is a substrate for different enzymes and the byproduct of the reaction is S-adenosyl-homocysteine (AdoHcy). Two families of enzymes use this substrate to modify two different amino acid residues in the histone tails and also in the histone core region.

1. Describe briefly the different modification products generated by these enzyme families on these two amino acid residues.
2. How is the specificity of these enzyme families toward different amino acid positions in histones?

3. Give two types of domains that are required for the enzymatic activity of these two enzyme families.
4. Describe briefly one enzyme from each family, their modification product and the transcriptional activity associated with their induced modifications in histones.
5. Different reader proteins are able to bind to these two histone modifications. Give an example of two different domains that bind to each of these modifications described above.

C

Several types of signalling reflecting cellular stress (DNA damage, hypoxia, oncogenic activation etc) may lead to activation of p53.

1. p53 is frequently mutated in human cancers. In which part of the protein do we find cancer hotspot mutations. Explain how such mutations may destroy p53 function.
2. Focusing on alterations related directly to the p53 protein, what kind of changes are taking place when p53 is undergoing activation.
3. As part of the p53 activation process, the interaction of p53 with another key protein (here called X) is modulated. Describe this X protein and how its interaction with p53 is modulated as a result of signalling. Include also the consequences of such altered interaction.
4. In some cancers this protein X is overexpressed. Explain why this change may have similar effect as mutants in p53.
5. A drug has been developed that counteracts the effect of overexpressed protein X. What is its name and where does it bind?
6. One of the downstream effects of activated p53 is cell cycle arrest. Explain briefly the link between p53 and Rb in generating this effect.