UNIVERSITETET I OSLO

Det matematisk-naturvitenskapelige fakultet

Exam in: MBV4230 Eukaryotic transcription factors – structures, function, regulation
Day of exam:. Thursday 20 May 2010
Exam hours: 09.00 – 12.00
This examination paper consists of 6 pages.
Appendices: 1 answer sheet
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 multiple-choice questions, where you are supposed to answer by filling in the correct options in the enclosed answer sheet. This sheet (last page) should be handed-in together with the rest of your paper.
The second part consists of questions where the answers should be given in free form writing style. For this second part, try to provide brief and concise answers.

Part I: Multiple-choice questions

1. The phosphorylation status of CTD of RNA Polymerase II changes during the transcription cycle. Which of these enzymes has specificity towards serine 5 of CTD? *(only one correct answer)*

1. P-TEFb (CDK9)
2. TFIIH (CDK7)
3. SCPs
4. Fcp1
5. Ssu72
6. Srb10 (CDK8)

A) Alternatives 1,4 and 5 are correct
B) Alternatives 2, 4, 5 and 6 are correct
C) Alternatives 2, 3 and 5 are correct
D) Alternatives 1, 3 and 6 are correct
E) Alternatives 2, 3, 5 and 6 are correct

2. Which of the statements are true for TFIIB? Choose one of the alternatives following the statements (A-E) *(only one correct answer)*

1) TFIIB has helicase and kinase enzymatic activities
2) TFIIB is an adaptor between TBP and RNAP II
3) TFIIB has a N-terminal B-finger that is involved in RNAP II interaction
4) TFIIB functions as a contact point for activators
5) The B-finger of TFIIB occupies the same location as the DNA-RNA hybrid
6) The C-terminal core domain of TFIIB contacts DNA prior to TBP-binding

A. 1,3,4, and 5 are correct
B. 2,3, and 5 are correct
C. 2,3,4, and 5 are correct
D. 1,3, and 4 are correct
E. 2,3,5 and 6 are correct

3. Combine the different general transcription factors (left column) with the corresponding functions (right column). Fill in the answer sheet by providing the correct number associated with each letter.

A. TFIIH	1) ...remains associated with Pol II during transcription
B. TFIIA	2) ...functions as a bridge between TBP and Pol II
C. TFIIF	3) ...is required for activator response
D. TFIID	4) ...binds TATA box
E. TFIIE	5) ...has both helicase and kinase activities
F. TFIIB	6) ...regulates the activity of TFIIH

4. Which of these factors/complexes do <u>not</u> activate gene transcription?

A) ARC-L
B) CRSP
C) Sin3
D) TAF2
E) SAGA
F) MYST
G) GNAT
H) LEF1

5. Chromatin I

Histones may be modified by post-translational modifications of several types and at several specific positions.

A) H3 R2 methylation
B) H3 K4 methylation
C) H3 K9 acetylation
D) H3 K9 methylation
E) H3 S10 phosphorylation
F) H3 K14 acetylation
G) H3 R17 methylation
H) H3 K27 methylation
I) H3 K36 methylation
J) H3 K79 methylation
K) H4 R3 methylation
L) H4 K20 methylation
M) H2B K120/123 ubiquitination

Post-translational modifications of histone tails are one of the mechanisms to control chromatin access for the transcription apparatus. Which of the modifications above (A-M) correlate with the active state of genes?

6. Chromatin II

Referring to the list of histone post-translational modifications in question 5, which of the histone patterns above are modified/catalyzed by SET-domain containing proteins?

7. Chromatin III

Referring to the list of histone post-translational modifications in question 5, which of the histone patterns above are modified/catalyzed by PRMT-domain activity?

8. Chromatin IV

Referring to the list of histone post-translational modifications in question 5, which of the histone patterns above are linked to HP1 binding and subsequent heterochromatin formation?

9. Architectural transcription factors

Which of the following statements is NOT true for architectural transcription factors / HMG proteins?

A. HMG-proteins lack a transactivating domain.
B. HMG-proteins have extensive post-transcriptional modifications.
C. HMG-proteins have a function in establishing active or inactive chromatin domains.
D. HMG-proteins lack a DNA binding domain.
E. HMG-proteins have a function in bending DNA.
F. HMG-proteins facilitate nucleosome-remodeling.
G. HMG-proteins can stabilize transcription factor binding to chromatin.

10. Homeodomain transcription factors

What is true about homeodomain transcription factors?

A. Homeodomain transcription factors harbour an N-terminal arm in the homeodomain that confers specificity upon DNA binding

B. The DBD of homeodomain transcription factors is made up of a helix-turn-helix motif where the recognition helix contacts DNA in the minor groove

C. The DBD of homeodomain transcription factors contains two protruding α-helical loops contacting DNA directly in the major groove.

D. Homeodomain transcription factors work as homodimers, and contact inverted repeat DNA half sites.

E. The homeodomains are able to assume a variety of conformations dependent on the DNA element.

11. STATs

Which of the statements are true for the STAT-family of transcription factors?

A. The STATs belong to the steroid receptor superfamily
B. The STATs belong to the signal-dependent nuclear factor superfamily
C. The STATs belong to the regulatory cell-specific superfamily of transcription factors
D. The STATs belong to the constitutive family of transcription factors
E. The STATs belong to the latent cytoplasmic factor superfamily

12. Various signal dependent transcription factors

In the list below, combine each of the transcription factors in the first column with the correct DNA-binding statement (second column) and with a relevant signalling molecule (third column). Fill in the answer sheet by providing the correct combinations of letter-number-letter.

TF	DNA binding	Signal
A. RXR heterodimer	1. …works as a dimer. The dimer is kept together by reciprocal SH_2-Tyr^P interactions.	F. TGFβ-related factors
B. Steroid receptor	2. …requires a partner transcription factors with strong DNA binding capacity that determine the gene to be activated.	G. Cytokines, growth factors, peptides
C. SMAD	3. …binds as homodimers to inverted repeat DNA half sites	H. LPS, IL-1, TNF-α
D. NF-κB	4. …usually binds as heterodimers to direct repeats	I. Prostaglandine, vitamine D, thyroid hormone
E. STAT	5. …has two distinct domains. The N-terminal is responsible for specific DNA contact, while the C-terminal is necessary for dimerisation and unspecific DNA contact.	J. Cortisol, testosterone, estradiol

Part II: Normal questions

A

Myc is a member of the family of basic-helix-loop-helix-zipper transcription factors. Describe briefly the DNA-binding domain of the active dimer that Myc forms with its dimerization partner. Describe then briefly the Myc-network of interacting partners including how Myc-responsive genes either may be activated or repressed depending on the presence of various members in this network.

B

Nuclear receptors have in common that they are ligand-responsive factors.

1. Describe basic features of the ligand binding domain found in this family and explain how it changes conformation and interactions with other proteins upon binding of ligand.
2. The DNA-binding domains of nuclear receptors and of GATA-factors share some features despite clear differences. Describe briefly similarities and differences between these two classes of DNA-binding domains.
3. RXR acts as a partner for nuclear receptors such as Vitamin D receptor (VDR), thyroid hormone receptor (TR) and PPAR. These dimers bind to related cis-elements in responsive promoters. Explain how discrimination between responsive elements for these factors is obtained? How is it possible to change a promoter responsive to thyroid hormone into one that is responsive to vitamin D using only a simple mutation?