UNIVERSITETET I OSLO

Det matematisk-naturvitenskapelige fakultet

Exam in:
MBV4320 Eukaryotic transcription factors
– structures, function, regulation
Day of exam:. Tuesday May 24 th 2005
Exam hours: 09.00 – 12.00
This examination paper consists of 2 pages.
Appendices: None
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 what language (Norwegian or English) you prefer to answer.
For all questions, try to provide brief and concise answers.

I

RNA polymerase II (RNAPII) is the key enzyme in the process of transcription. Describe briefly its overall structural design and mention some key regions in the enzyme including the three main channels and their function. The largest subunit of RNAPII contains a particular repeat-structure. Describe briefly its composition, modification and function including how it changes during the transcription cycle.

II

RNAPII cooperates with general transcription factors (GTFs) to form a functional pre-initiation complex (PIC). Describe how the GTF called TFIIB operates during PIC assembly. In particular, point out how TFIIB interacts with promoter DNA, with other GTFs and with RNAPII and try to provide a functional explanation for the interactions where relevant.

III

Explain briefly the function of the elongation factor TFIIS and how its action helps the RNAPII during specific steps in the elongation process?

IV

The packing of genes into chromatin reduces their accessibility for the transcriptional apparatus. Therefore processes have evolved that increase the accessibility of genes before they are transcribed. While one set of mechanisms involves post-translational modification of histone tails, another process consumes ATP to increase accessibility without changing histone tails. Explain some key elements in the latter process, mentioning proteins involved and basic ideas on how selective opening of chromatin is achieved.

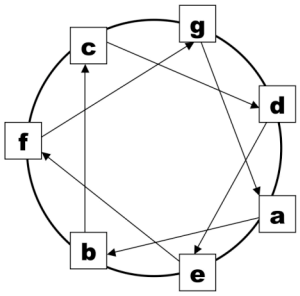
V

Transcription factors in the leucine zipper family operate as dimers. Explain briefly the determinants/principles for dimer formation in this family. Below is shown the sequence (one letter codes) of the leucine zippers of human c-Fos and c-Jun with abcd etc indicating their position relative to a helical wheel representation (see illustration). Apply the dimerisation principles to explain which of the three possible dimers, Fos-Jun, Fos-Fos or Jun-Jun, are most easily formed and which are less favourable.

```
Helical Wheel pos abcdefgabcdefgabcdefgabcdefgabcdefgabc
Fos       TDTLQAETDQLEDEKSALQTEIANLLKEKEKLEFILAA
Jun       IARLEEKVKTLKAQNSELASTANMLREQVAQLKQKVMN

Fos       TDTLQAETDQLEDEKSALQTEIANLLKEKEKLEFILAA
Fos       TDTLQAETDQLEDEKSALQTEIANLLKEKEKLEFILAA

Jun       IARLEEKVKTLKAQNSELASTANMLREQVAQLKQKVMN
Jun       IARLEEKVKTLKAQNSELASTANMLREQVAQLKQKVMN
```



VI

Myc is a member of the related basic-helix-loop-helix-zipper family of transcription factors, where also dimerisation partners are important for understanding function. Describe 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.

VII

The Rb (retinoblastoma) protein is a transcriptional repressor operating as an important link between the cell cycle and key transcriptional processes. Explain some key elements in how this link operates, particularly how the repressor function of Rb is modulated through the cell cycle including both upstream and downstream events (only a brief summary with main points).

UNIVERSITETET I OSLO

Det matematisk-naturvitenskapelige fakultet

Exam in **MBV4230 Eukaryotic transcription factors**
Day of exam: **Wednesday 26.05.2004**
Exam hours: **13 - 16**
This examination paper consists of 3 pages.
Appendices:
Permitted materials:

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 what language (Norwegian or English) you prefer to answer.

I

When studying eukaryotic transcription, one encounters a long list of abbreviations. Below is a selection of twelve of these. Write out the full names that these abbreviations refer to.

1. TBP
2. CTD
3. HAT
4. STAT
5. HMT
6. NR
7. N-CoR
8. CPSF
9. IKK
10. POU
11. FACT
12. ARC

II

Transcription activators are grouped into families, usually based on the structure of their DNA-binding domains (DBDs). Below is a list of 10 names of transcription factors as well as 5 families. Place each factor into the correct family:

The transcription factors to classify:

1. TFIIIA
2. Myc
3. RXR
4. E2F1
5. GAL4
6. PPARγ
7. p50/p65
8. c-Jun/c-Fos
9. CREB
10. ER (estrogen receptor)

The families:

A. Helix-loop-helix (bHLH) proteins
B. Zinc finger proteins
C. Rel family
D. Nuclear receptor
E. Leucine zipper (bZIP)

For simplicity you may answer by a list of the form 3C, 8B etc (examples are not correct combinations).

III

One of the GTFs (general transcription factors) has enzymatic activities – which GTF and what type of enzymatic activity?

TAFs are subunits of the TFIID complex. The largest subunit called $TAF_{II}250$ has been found to harbour several distinct enzymatic activities. List these activities.

IV

The "Histone code hypothesis" has become a key to understand how the transcriptional apparatus interacts with chromatin. Describe briefly key elements in this hypothesis, including how code patterns are generated and how they are read (decoded).

V

Several components in or associated with a pre-initiation complex (PIC) become subject to ubiquitylation during the process of transcriptional activation. List some transcriptional targets of this modification and select one example where you explain in more detail its presumed mechanism of action.

VI

ATP is one of the substrates during RNA synthesis by RNA polymerase II, but other ATP-dependent processes linked to transcription initiation also consume ATP. List two examples of the latter and state very briefly what kind of process is taking place here when ATP is consumed.

VII

Several types of signalling (warning signs of DNA damage, oncogenic activation etc) may lead to activation of p53. Limiting your focus to the p53 protein itself, what kind of changes are taking place when p53 is undergoing activation. During this process the interaction of p53 with another key protein is modulated. What is this protein and how is the interaction modulated as a result of signalling?

VIII

Describe briefly the key elements of signalling pathways involving IKK and NF-κB.

IX

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 vitamin D into one that is responsive to thyroid hormone using only a simple mutation?