Schriftliche Sessionsprüfung

Concepts in Modern Genetics

(WS 06/07)

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Samstag 24.2.2007
HG E7
09:00 - 11:30

Hilfsmittel: keine / Dauer: 150 Minuten

Name, Vorname: _____

Email: _____

Eingeschrieben: ETH UZH

Unterschrift _____

Remarks

- Maximum number of points in total: 24
- Maximum number of points for every question is stated.
- The exam is diveded into 4 parts (I - IV). The answers for the different parts must be **on separate sheets**!
- Please indicate on the question sheet if you don't answer a question.
- Label all **extra sheets with your name, first name and page number / total page number (e.g. 1/12).**
- We accept answers in **English and/or German.**
- **Unreadable and unclear writing** and **drawings** will not be interpreted by the examiners, and will not be considered when assigning points.

Part I

Question 1. Key terms (2 Points):

What are histone modifications? Provide examples (Do not list their functions).

What are SARs? What are their presumed roles?

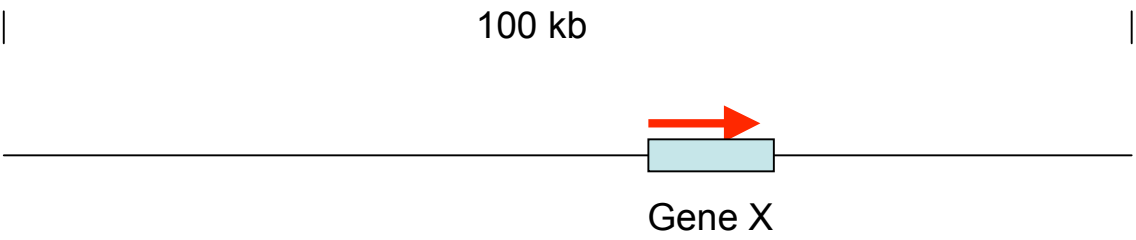
Question 2. Concepts (2 Points):

System: Mice. Observation: a gene X that is transcribed in liver, but not in brain. The DNA sequence of a 100 kb domain surrounding the gene is known (Figure).

Questions:

1. Describe one possible mechanism of transcriptional regulation.

2. Describe and illustrate a chromatin based approach to find putative regulatory regions involved in transcription control within 100 kb.



Question 3. Genomes (2 Points):

Observation: Aging yeast cells (*S. cerevisiae*) accumulate extrachromosomal ribosomal DNA circles (ERCs).

- How are ERCs generated? What mechanisms are involved?
- Why are they maintained extrachromosomally?
- How can ERCs be detected as circular DNAs?

Part II

Question4. (2 point):
The drawing below summarizes the different mating type loci of the haploid wild type strains used here. Some mechanism ensures that the *HMLa* and *HMRalpha* loci are kept silent, and only the *MAT* locus is expressed. Let's imagine that you want to understand the genetic basis underlying this silencing process:

- Design and outline a screen aiming at isolating mutants defective in this process specifically.
- Indicate the phenotypes that you expect silencing mutants (*sil-*) to exhibit.
- How could you distinguish *sil-* mutants from mutants that are defective in the mating signaling pathway downstream of the pheromone receptor?

CHRIII a:

HMLa Centromer MATa HMRalpha .

CHRIII alpha:

HMLa Centromer MATalpha HMRalpha .

Question 5. (4 points):
The screen for silencing deficient mutants has been carried out using a *MATa* strain. One of the mutations, called *sil-B10*, has the following features: when the *sil-B10 MATa* strain is crossed with a *MATalpha gil1-* strain, the following tetrads are obtained.

MATa GIL1 [sil-]	*MATa GIL1 [sil-]*	*MATa GIL1 [sil-]*
MATa GIL1 [sil-]	*MATa gil1 [SIL+]*	*MATa gil1 [sil-]*
MATalpha gil1 [SIL+]	*MATalpha GIL1 [SIL+]*	*MATalpha GIL1 [SIL+]*
MATalpha gil1 [SIL+]	*MATalpha gil1 [SIL+]*	*MATalpha gil1 [SIL+]*
174 tetrades	110 tetrades	8 tetrades
MATa gil1 [SIL+]	*MATa gil1 [sil-]*	*MATa GIL1 [sil-]*
MATa gil1 [SIL+]	*MATa GIL1 [SIL+]*	*MATa GIL1 [SIL+]*
MATalpha GIL1 [SIL+]	*MATalpha GIL1 [SIL+]*	*MATalpha gil1 [SIL+]*
MATalpha GIL1 [SIL+]	*MATalpha gil1 [SIL+]*	*MATalpha gil1 [SIL+]*
4 tetrades	2 tetrades	2 tetrades

The *GIL1* gene is 0.8 cM close to *HMRalpha*. [*sil-*] indicates that the expected phenotype due to loss of silencing is observed, while [*SIL+*] indicates that the cells behave like wild type.

1- What is the location of the different loci relative to each other?
2- Formulate a hypothesis about how the mutation *sil-B10* functions.

IMPORTANT: document clearly and as completely as possible the logic behind your argumentation, not just the final result.

Part III

Question 6. (2 Points)

A gain-of-function mutation in the *C. elegans glp-1* gene causes an overproliferation of the mitotic germ cells in the gonad. A loss-of-function mutation in the *lag-2* gene blocks the proliferation of the mitotic germ cells in the gonad. Describe an experiment that could be used to order the activities of *glp-1* and *lag-2* relative to each other. Discuss the different results you could obtain from this experiment.

Question 7. (2 Points)

Human Cowden syndrome is a genetic disease caused by mutations in the PTEN tumor suppressor gene. Cowden syndrome patients develop multiple benign tumors in the skin, intestine, central nervous system and many other organs. The disease shows a *dominant inheritance* pattern, i.e. one mutant PTEN allele inherited from the mother or father is sufficient to cause the disease symptoms. However, in the tumors that develop in Cowden syndrome patients there is no wild-type PTEN protein detectable.

Why is no PTEN protein made in the Cowden syndrome tumors even if only one mutant allele has been inherited from one of the parents and the other inherited allele was wild-type?

Question 8. (2 Points)

Why is angiogenesis an essential process during tumor development?

What is the advantage of a tumor therapy that inhibits tumor angiogensis rather than tumor cell proliferation?

Part IV

Question 9. (2 Points)

You recovered a loss-of-function mutation in the Drosophila gene X. Homozygosity for this alleles causes lethality at the pupal stage. In situ hybdrization with a probe of this gene reveals that a substantial amount of X transcripts is present in mature oocytes and early embryos. What does this finding suggest and how can it be tested?

Question 10. (2 Points)

As an counselor you have to determine the cause for infertility of a female patient. A first analysis reveals that this woman is karyotypically XY and has an intact SRY. What other possible causes may have led to sex reversal in this patient? How do you test this?

Question 11. (2 Points)

What are the roles of noncoding RNAs in dosage compensation in mammals and in Drosophila?