Schriftliche Sessionsprüfung

Concepts in Modern Genetics

(WS 06/07)

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Montag 19.2.2007
Y34 J01
13:00 - 15:30

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. 3/12).**
- 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 variants? Name two examples and their functional role.
- What are locus control regions, how do they work? Schematically illustrate with one example.

Question 2. Concepts (2 Points):

Brehm et al (1998) reported:

System: Human cells. Title: "Retinoblastoma protein recruits histone deacetylase to repress transcription." Abstract: The retinoblastoma protein (Rb) silences specific genes that are active in the S phase of the cell cycle and which are regulated by E2F transcription factors.

Question: How might that work?

- Discuss and illustrate in a drawing one hypothetical mechanism for Rb mediated repression.
- Describe a method how to test your hypothesis starting with human cells.

Question 3. Genomes (2 Points):

Describe briefly and illustrate the generation of a new gene by exon shuffling. Name one mechanism and the elements that are involved.

Part II

Question 4. (2 Points)
Diploid and haploid yeast cells behave differently with respect to their ability to mate, respond to pheromones or undergo meiosis. With the help of drawings, explain what is the genetic basis for these differences.

Question 5. (4 Points)
A screen for mating type switching deficient mutants has been carried out. One of the mutations, called *swi-A3*, has the following features:

1 - The *swi-A3 trp1 MATa* strain is crossed with a wild type (*SWI+ TRP1+ MATalpha*), the diploid is sporulated and the spores are dissected. In each tetrad, two spores are deficient for mating type switch, and two spores are proficient. The tetrads obtained were as follows:

trp1 swi- MATa	*trp1 swi- MATa*	*trp1 swi- MATa*
trp1 swi- MATa	*TRP1 swi- MATa*	*trp1 SWI+ MATa*
TRP1 SWI+ MATalpha	*trp1 SWI+ MATalpha*	*TRP1 swi- MATalpha*
TRP1 SWI+ MATalpha	*TRP1 SWI+ MATalpha*	*TRP1 SWI+ MATalpha*
42 tetrads	112 tetrads	1 tetrad

trp1 SWI+ MATalpha
trp1 SWI+ MATalpha
TRP1 swi- MATa
TRP1 swi- MATa

45 tetrads

What can you learn from this?

2 - In order to test whether the mutation is dominant or recessive, a *MATalpha* tester strain was constructed, in which the *MAT* locus is flanked with Lox recombinant sites, both being in the same orientation. This strain is then crossed with a *MATa, swi-A3* mutant strain carrying a plasmid allowing expression of the Cre recombinase in response to the presence of galactose. After crossing, the diploids are grown in a galactose containing medium. Upon Cre induction, all these diploid cells are now found to respond to alpha pheromone and to mate with *MATalpha* cells, but not with *MATa* cells. They are also defective for sporulation. These phenotypes are stable over many generations.

- What is the purpose of this tester strain?
- How do you interpret the results?
- Combining all the data above, can you make a hypothesis about the nature of the *swi-A3* mutation?

Part III

Question 6. (2 Points)

A reduction-of-function mutation in the *C. elegans daf-2* gene **increases** the average life-span of the animals by about 50%. A loss-of-function mutation in the *daf-16* gene **decreases** the average life span by about 40%.

Describe an experiment that could be used to order the activities of *daf-2* and *daf-16* relative to each other. Discuss the different results you could obtain from this experiment.

Question 7. (2 Points)

From a cross of *Drosophila* flies where both males and females are heterozygous for a mutation in the Cappucino gene (capu/+), you obtain 25% homozygous capu mutant animals (capu/capu) that develop normally and become adult flies. When you mate the homozygous capu/capu females with wild-type males, 100% of their offspring dies during embryogenesis.

What is the genotype of the offspring? Why do they die as embryos?

Question 8. (2 Points)

What is a linkage map? How can you generate a linkage map and what is it used for?

Part IV

Question 9. (2 Points)

The mutation *a* is a rezessive embyronic lethal in Drosophila. Studies with a temperature-sensitive mutation in the same gene uncovered an additional late function of this gene in female meiosis. The mouse homologue of this gene was found to cause embryonic lethality when knocked out by homologous recombination. Design an experiment to test whether this gene is also needed for proper female meiosis in adult mice.

Question 10. (2 Points)

Gene targeting by homologous recombination in the mouse and in Drosophila. In which aspects does this method differ in the two systems?

Question 11. (2 Points)

In one of your Drosophila lines a spontanous mutation occured that, when homozygous, causes masculinization of XX individuals. You therefore name this gene *masculinizer* (*mas*). The mutant XX animals produce the male variant of DSX. How would you go about determining the position of this new gene in the pathway with respect to the primary signal, *Sxl* and *tra*.