

Genetics 201 – Final Exam Solutions

1ai. 1 informative chromosome/mouse
Supplied by F1 parent

1bi. BC classes 2 and 3 contain recombinant chromosomes
(Myopic, 4/4 and wild-type, 2/4)

1bii. Theta = 0.1
Total # informative chromosomes = 200
NR = 170, R = 30

$$\text{LOD} = R\log\theta + \text{NR}\log(1-\theta) + (R+\text{NR})\log 2$$

$$\text{LOD} = 30\log(0.1) + 170\log(0.9) + 200\log 2$$

$$\text{LOD} = -30 + (-7.78) + 60.21$$

$$\text{LOD} = 22.43$$

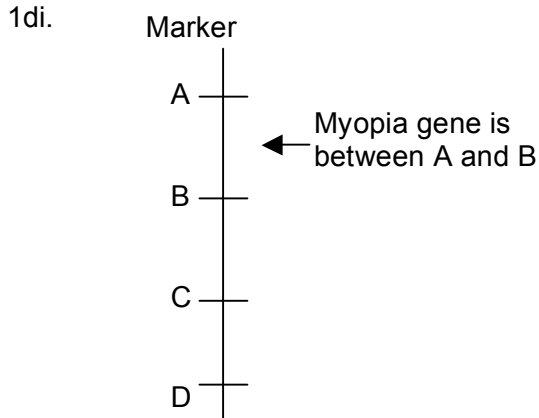
1biii. Yes, this is a significant LOD score because it is > 3.3 .

1ci. X linked recessive: No; individual II-2 (she is affected, but her father (I-1) is not).

1cii. X linked dominant: No, individual IV-1 (he is affected, mom (III-3) is not)
OR, III-2 is affected, but his daughter (IV-3) is not

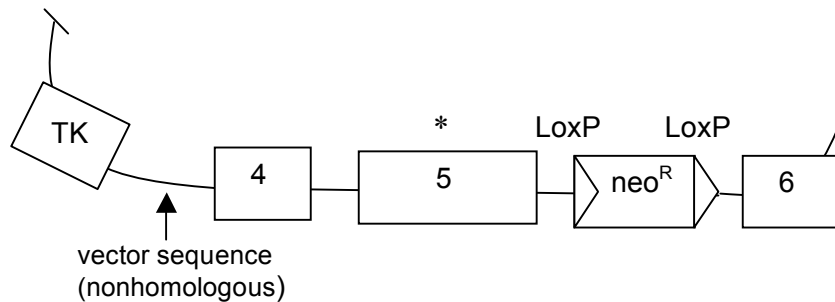
1ciii. Autosomal dominant: Yes.

1civ. Mitochondrial inheritance: No; individuals IV-1,2 are affected but mom is not)
OR, IV-3 is unaffected, but siblings IV-1 and IV-2 are affected



1dii. You would only be able to state that myopia gene mapped north of marker B. It could also be located north of marker A, since you have eliminated a breakpoint critical in defining the region.

1ei. Vector should contain exon 5 (with point mutation) and flanking sequence, such as exons 4 and 6. Vector should also contain neo sequence flanked by loxP sites inserted into nearby intron, and thymidine kinase gene outside homologous sequence.

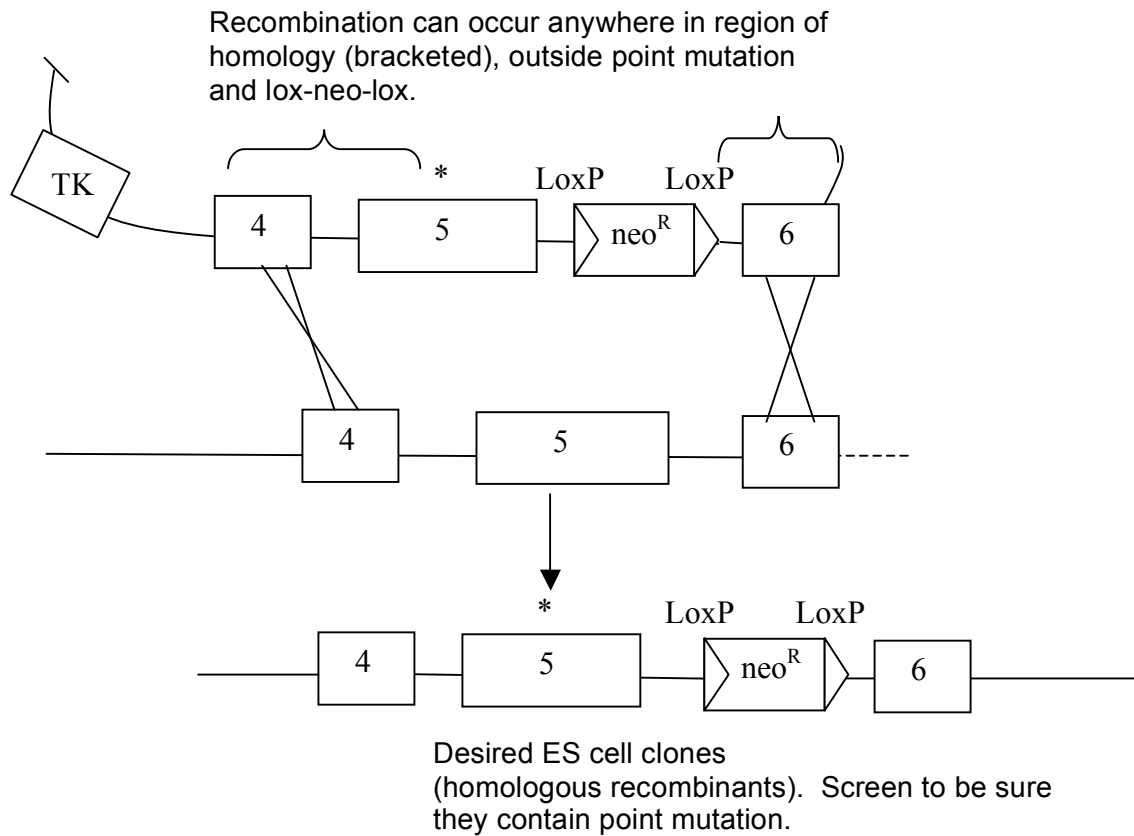


1eii. Experimental steps:

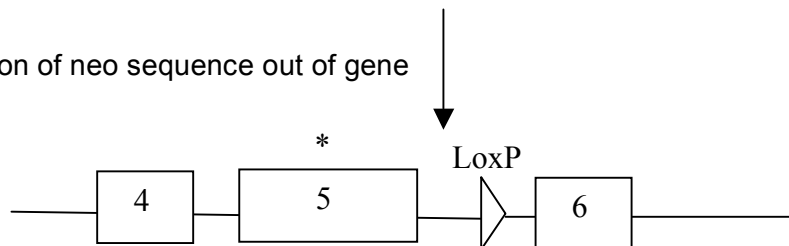
1. Electroporate the construct into WT ES cells (derived from 129 strain). Select with neomycin (G418) and gancyclovir to obtain ES cell clones that are neo^R TK^S.
2. Screen ES cell clones that survive selection using PCR and/or Southern blots, to confirm that they contain homologous recombinants.
3. Transform ES cell clones with Cre-expressing plasmid. Screen with PCR and/or Southern to identify cells that have excised neo gene.
4. Inject ES cells into C57Bl/6 (“black”) blastocysts; reimplant injected blastocysts into foster mother.
5. Screen pups for coat color to identify chimeric animals. Patches of agouti indicate contribution from 129 ES cells.
6. Breed chimeric mice to get +/- pups which carry exon 5 mutation in their germline (identified by agouti coat and genotyping).

1eiii. There are 2 important recombination events.

1. Homologous recombination of targeting vector into ES cells:



2. Cre-mediated recombination of neo sequence out of gene



1f. Group 2's data is more convincing. They performed fewer tests, so they only need to demonstrate a p value threshold of $.05/20 = .0025$ to demonstrate a significant association. By this threshold, two of the three SNPs shown have significant association.

Group 1 evaluated 100,000 SNPs, so must use a P value of $.05/100,000 = 5 \times 10^{-7}$. By this threshold, none of the SNPs presented show significant evidence for an association with the myopia phenotype.

2ai. Chromosome V.

2aii. Absence of Age Dpy progeny in F2 indicates that they are on the same chromosome.

Presence of Age Unc progeny in F2 indicates that they are not on the same chromosome. (Technically, *age-1* and *unc-5* could be very apart on same chromosome, and recombination could produce Age Unc progeny. However, the Dpy data rules this out).

2b.

age-101 —| *age-103* —| *age-102* —| *age-100* —| long life

2c. You would perform a complementation test and look at the phenotype of the cross progeny. The *dpy* mutation must be in the hermaphrodite parent so that you can distinguish self from cross progeny.

P: *age-101 dpy-33* hermaphrodites X *rt526* males



F1: Look only at cross progeny (nonDpy) and score them for their life span

If cross progeny have short life span, then *age-101* and *rt526* fail to complement one another, and may be mutations in the same gene.

If cross progeny have normal life span, then *age-101* and *rt526* complement one another, and may be mutations in two different genes.

(Possible exceptions: intragenic complementation and unlinked noncomplementation; not required for correct answer).

2di. AB

2dii. P₁

2diii. P₂

2div. Required in musculature

3a. EMS

P: $+/+$ multiple males X $Tb/ TM3 Sb$ multiple virgin females

↓
 $+/ Tb$ and $+/ TM3 Sb$ - save Sb males

Take single F1 $+/ TM3 Sb$ males X 3-5 $Tb/ TM3 Sb$ virgin females

↓
F2 genotype: $+/ TM3 Sb$ $+/Tb$ $Tb/ TM3 Sb$ $TM3 Sb/ TM3 Sb$
Phenotype: Sb Tb $Tb Sb$ $Dead$

Intercross Sb sibs to get F3:

$+/ TM3 Sb$ X $+/ TM3 Sb$
↓
F3 genotype: $+/ +$ $+/TM3 Sb$ $TM3 Sb/ TM3 Sb$
Phenotype: $screen$ Sb $Dead$

Screen non Sb F3 flies for flight defect.

3bi. Compare $fli-1 /fli-1$ vs. $fli-1/del$

Predicted results for null: same phenotype in both strains.

3bii. Compare $Fli-4/+$ to $Fli-4/Del$. If $Fli-4/Del$ has less severe phenotype, may be hypermorphic.

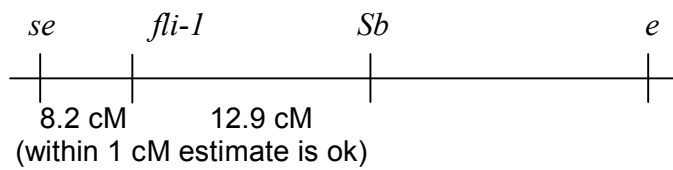
OR, compare $Fli-4/+$ to $Dp/+$ to see if they are similar

OR, compare $Fli-4/+$ to $Fli-4/Dp$ to see if phenotype is more severe in second strain.

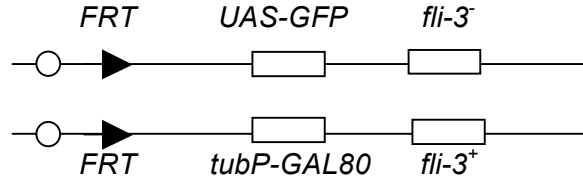
3ci.

F2 phenotypic class	Number	# crossovers
fli	665	parental
se Sb e	671	parental
wild type	9	2
fli se SB e	8	2
Sb e	68	1
fli se	60	1
fli Sb e	102	1
se	108	1
e	0	3
fli se Sb	1	3
fli e	126	1
se Sb	134	1
fli Sb	14	2
se e	16	2
fli se e	10	2
Sb	8	2
Total F2 flies	2000	

3cii and 3ciii.



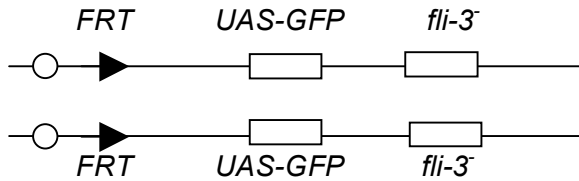
3di.



Note: Order of *UAS-GFP* and *fli-3* is not important, as long as *FRT* is between markers and centromere. Same applies to order of *tubP-GAL80* and *fli-3*. Both chromosomes may carry *UAS-GFP*, but only one may carry *tubP-GAL80*.

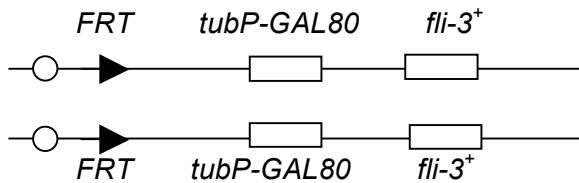
Alternative answer: CEN-GFP-FRT-*fli-3*⁺-GAL80
CEN-GFP-FRT-*fli-3*⁻

3dii. Cell type 1:



fli-3 ^{-/-} genotype; GFP⁺

Cell type 2:



fli-3 ^{+/+} genotype; GFP⁻

3diii. Look at phenotype of GFP⁺ neurons (*fli-3*⁻). If GFP expression correlates with abnormal short phenotype, then phenotype is cell-autonomous. If not, then phenotype is non-cell-autonomous.