

## Recombination and Pedigrees

### A. Chromosomes and Recombination

1. What is the physical basis of the genetic phenomenon of gene recombination?
2. Why is the recombination frequency between two genes correlated with the physical distance between the two genes?
3. Recombination can occur anywhere along the length of the chromosome. However, we have been relying on the fact that genes are inherited as discrete units. How do we reconcile these two things? (Hint: think about what usually is the difference between two alleles of the same gene.)
4. Why is the highest possible recombination frequency 50%?

### B. Pedigrees

In 1901 a physician in London named Archibald Garrod had some new patients with an unusual condition: when their urine came into contact with air it turned black.

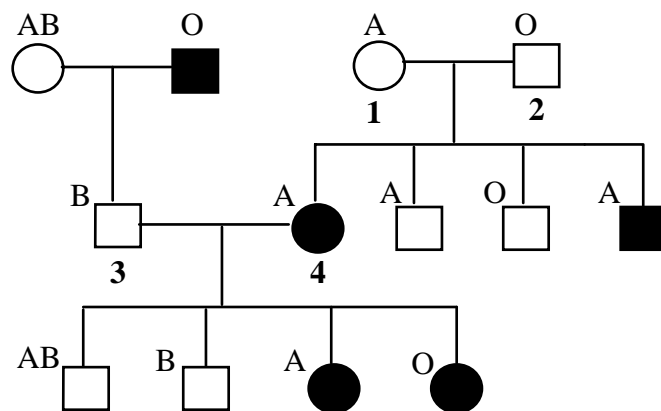
1. What is the wild-type phenotype?
2. What is the assay?
3. Who are the mutants?

Fascinated, Garrod decided to study the disease more.

4. How could he go about determining whether the disease shows dominant, recessive, or codominant inheritance?
  
5. What is your prediction for mode of inheritance of this disease? Why?
  
6. The fact that Garrod saw a number of cases was in fact due to high degree of first cousin marriages in the community where he worked. Such consanguineous matings are often very useful in identifying the modes of inheritance of rare traits. Why is that?
  
7. What, if anything, could he do to study the inheritance pattern experimentally in the lab?

As it turned out, the gene for Alkaptonuria (ALK) is on human chromosome 9 and is linked to the gene encoding the ABO blood group, with a recombination frequency of 11% between the loci.

A pedigree of a family with the disease is shown below, with affected individuals indicated in black. In addition, the blood type of family members is given.



The two alleles at the ALK locus will be denoted  $ALK^+$  and  $ALK^-$ .

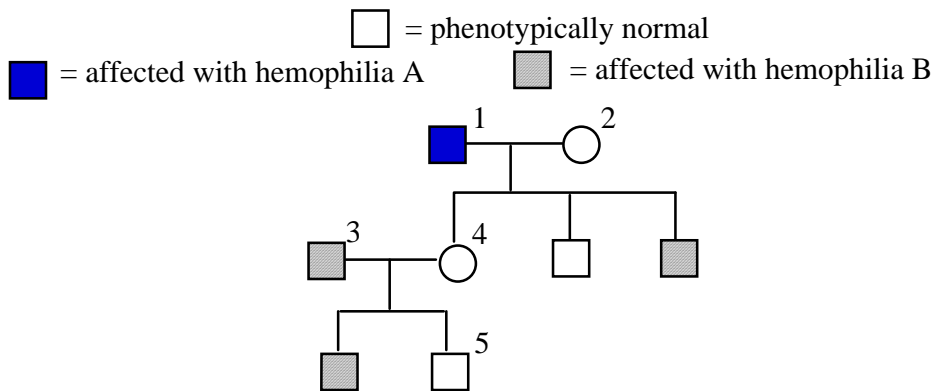
8. The three alleles at the ABO blood group locus will be denoted  $I^A$ ,  $I^B$  (which are co-dominant) and  $I^O$  (which is recessive to  $I^A$  and  $I^B$ ).
  - i) What is the genotype of individual 1 at the ALK and ABO loci?

ii) What is the genotype of individual 2 at the ALK and ABO loci?

iii) What is the genotype of individual 3 at the ALK and ABO loci? Which alleles of each gene are carried on the chromosome he inherited from his father and which alleles are carried on the chromosome he inherited from his mother?

iv) Individuals 3 and 4 are expecting their fifth child. A physician draws a prenatal blood sample and determines that the child has blood type B. Is it likely that the child will have alkaptonuria? Explain your answer.

9. Consider the pedigree below showing the inheritance of two X-linked diseases, hemophilia A and hemophilia B. Hemophilia A is due to a lack of one clotting factor, and hemophilia B is due to a lack of a different clotting factor. These two clotting factors are encoded by two different genes, located at different positions on the X chromosome. Note that no individual shown in this pedigree is affected with both hemophilia A and hemophilia B.



i) Write the genotypes for the following individuals at both the hemophilia A and hemophilia B disease loci. Clearly define your genotype symbols.

| <u>Individual</u> | <u>Genotype</u> |
|-------------------|-----------------|
| 1                 |                 |
| 2                 |                 |
| 3                 |                 |
| 4                 |                 |
| 5                 |                 |

ii) How do you account for individual 5 not being affected with either hemophilia A or hemophilia B?