Genetic methods of linkage analysis

Linkage is one of the exceptions to Mendelian Laws. Individual loci are arranged linearly on chromosomes and each chromosome forms a linkage group. Genes on it are more likely to be inherited together. Genetic linkage can be *complete* (no recombination occurs), or *incomplete*, when recombination can occur with a probability that we can express using the recombination fraction. Linkage is used in genetics in mapping or diagnostics. The bond strength is expressed using the unit ``centimorgan.

Genetic mapping

We can use linkage to find out where a certain gene A is located. If it is near marker B, fewer recombinants than non-recombinants are produced, or no recombinants are produced (the ratio of AaBb x aabb backcrossing is not 1:1:1:1). The exact position must then be determined by positional cloning.

- ***Three point mapping:*** We have locus A, B and C. We know the position of loci A and C. We want to find B. If B is between A and C, then recombination between A and B occurs with probability x, recombination between B and C occurs with probability y. The probability of double recombination (ie between A and B and between B and C) is considerably lower and is equal to the product of the probabilities x and y. We therefore determine the correct order of loci A, B and C with the help of double recombinants, of which there must be the least number.
  - In reality, there are even slightly fewer double recombinants than the calculation would indicate. This explains the phenomenon called ***interference***. Interference means that the occurrence of one crossing-over negatively affects the occurrence of another crossing over right next to it.
    - ***Interference coefficient*** gives the percentage of expected recombinations inhibited and is calculated as *i = 1 - (observed proportion of double recombinants/expected probability of double recombination)*
    - ***Coefficient of coincidence*** expresses the percentage of double recombinations produced out of all expected ones. We can calculate it as *coc = (observed proportion of double recombinants/expected probability of double recombination)*

Indirect DNA diagnostics

By using a marker that is linked to the mutation causing the given disease, we can analyze the probability of transmission of the defective allele without the need to analyze the mutated gene itself. This can be used, for example, if we know the gene responsible for the disease, but do not know the exact mutation. Multiple different mutations may also be responsible for a given disease.

For this diagnosis, we need to examine several family members, at least two of whom must be sick. The disadvantage is that each family may have a different marker allele associated with the disease. The family also does not have to be informative for the analysis, we only have to evaluate the result using Mendel's laws of inheritance. The probability that recombination occurs reduces the accuracy of the result (for example, if the binding strength is 2cM, then the certainty of the examination is 98%). 100% certainty of the result is when using an intragenous probe.

Linkage disequilibrium

Some alleles occur more often in connection with certain diseases, although they are not related to them. For example, Bechterev's disease (*ankylosing spondylitis*) is often linked to **MHC-B27**. It is probably caused by the similarity between the pathogen and this antigen, so that the organism then defends itself less against it. Adrenogenital syndrome, on the other hand, is linked to MHC-B47. This AR syndrome is caused by a **21-hydroxylase defect** located in the MHC III gene group classes. Thus, the locus for 21-hydroxylase and for MHC-B47 are both on the *short arm of chromosome 6*, at a distance of 2 to 3 cM. The probability of recombination is therefore small. The founder effect probably plays a role in the occurrence of this linkage disequilibrium.

Links

Related articles

- Gene linkage
- Genetic methods of association analysis

External links

- Genetická kartografie (Aktuální genetika) (http://biol.lf1.cuni.cz/ucebnice/geneticka_kartografie.htm)

Used literature

- OTOVÁ, Berta. *Lékařská biologie a genetika, 1.díl.* 1. edition. Karolinum, 2008. 123 pp. vol. 1. ISBN 978-80-

246-1594-3.