

Penetrance and Expressivity

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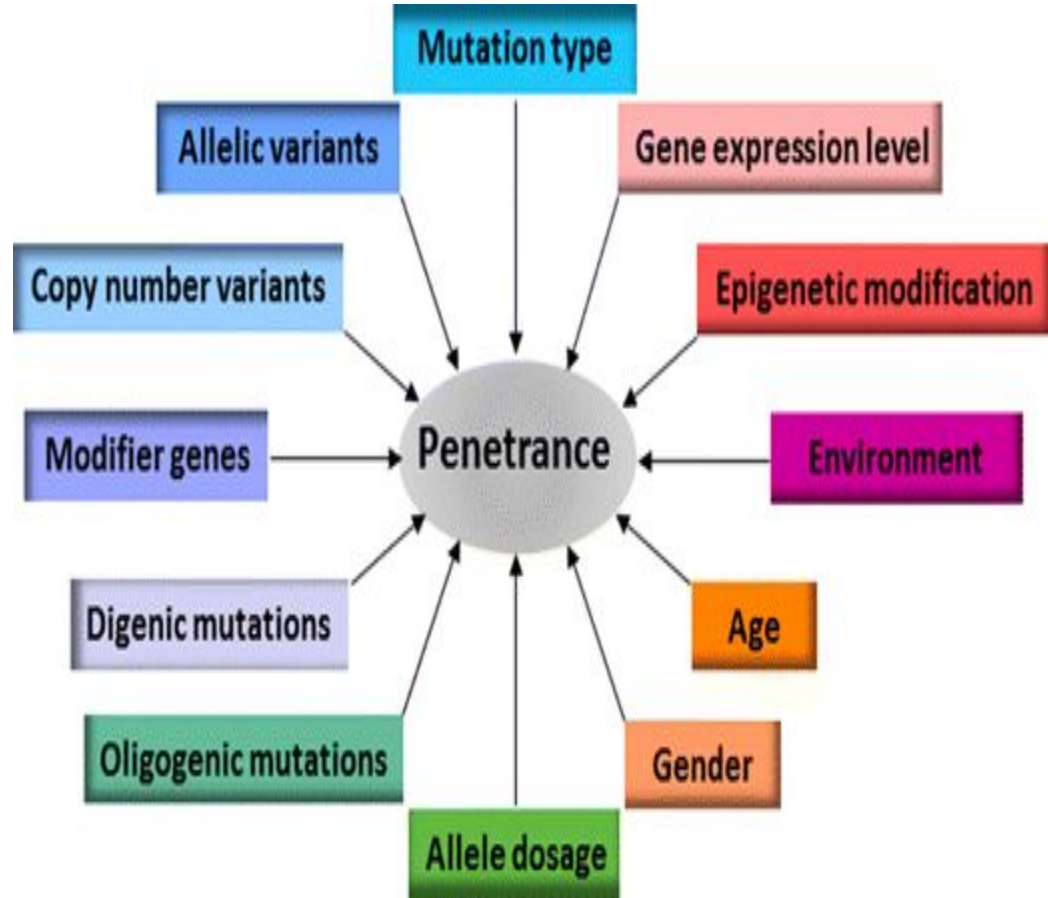
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Significance

- ❖ When studying the relationships between genotype and phenotype, it is important to examine the statistical occurrence of phenotypes in a group of known genotypes. In other words, given a group of known genotypes for one trait, how many identical genotypes show the related phenotype?
- ❖ The terms *penetrance* and *expressivity* quantify the modification of gene expression by varying environment and genetic background; they measure respectively the percentage of cases in which the gene is expressed and the level of expression.
- ❖ For example, say everyone in population W carries the same allele combinations for a certain trait, yet only 85% of the population actually shows the phenotype expected from those allele combinations. The proportion of genotypes that actually show expected phenotypes is called penetrance. Thus, in the preceding example, the penetrance is 85%. This value is calculated from looking at populations whose genotypes we know.
- ❖ Studies of penetrance help us predict how likely it is that a trait will be evident in those who carry the underlying alleles.

Penetrance

- ❖ Penetrance is defined as the percentage of individuals with a given genotype who exhibit the phenotype associated with that genotype.
- ❖ An organism may have a particular genotype but may not express the corresponding phenotype, because of modifiers, epistatic genes, or suppressors in the rest of the genome or because of a modifying effect of the environment.
- ❖ Alternatively, absence of a gene function may intrinsically have very subtle effects that are difficult to measure in a laboratory situation.

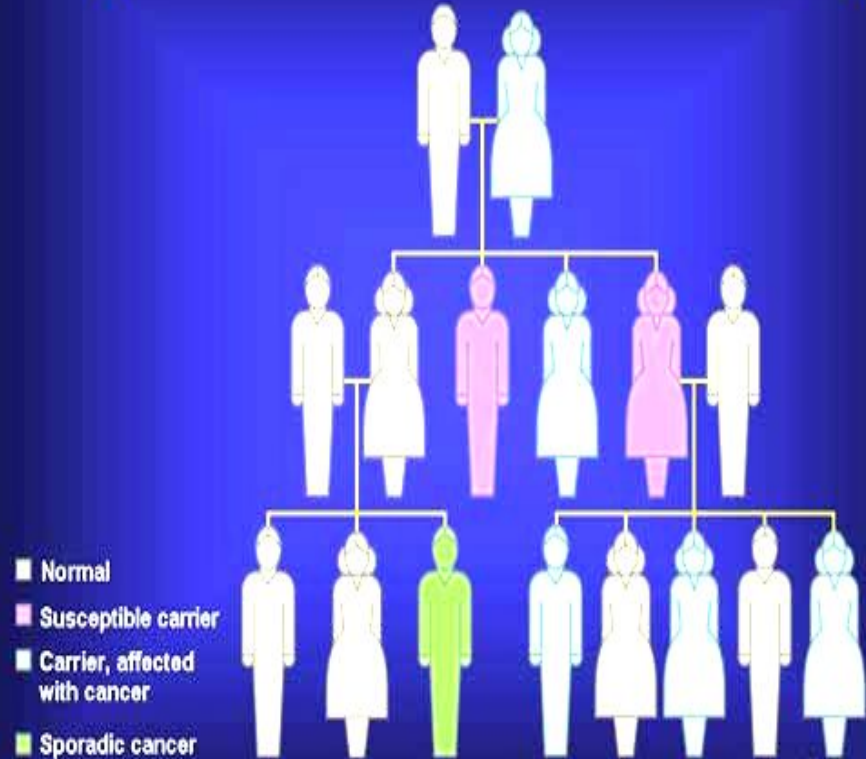


Incomplete Penetrance

★ If the genotype is present but the phenotype is not observable, the trait shows incomplete penetrance. Basically, anything that shows less than 100% penetrance is an example of incomplete penetrance as for BRCA I cancer gene.

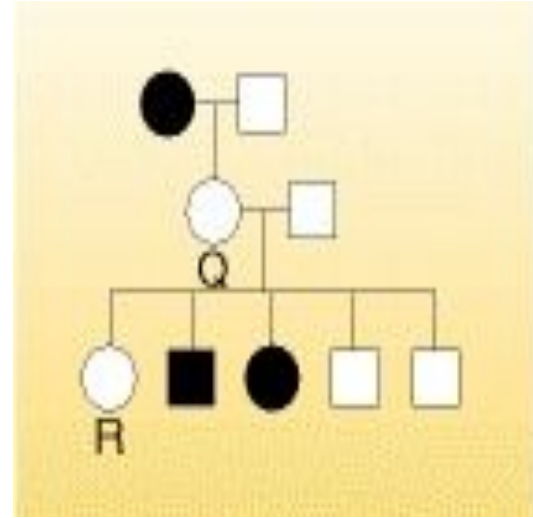
★ Thus, the penetrance of a trait is a statistically calculated value based on the appearance of a phenotype among known genotypes, incomplete penetrance is simply a qualitative description about a group of known genotypes.

Cancer Susceptibility: Incomplete Penetrance and Phenocopies



Lack of Penetrance- Pedigree Analysis

- Individual Q must have the allele (because it was passed on to her progeny), but it was not expressed in her phenotype. An individual such as R cannot be sure that her genotype lacks the allele.
- Any kind of genetic analysis, such as human pedigree analysis and predictions in genetic counseling, becomes more difficult because of the phenomena of incomplete penetrance and variable expressivity.
- For example, if a disease-causing allele is not fully penetrant (as is often the case), it is difficult to give a clean genetic bill of health to any individual in a disease pedigree (for example, individual R in Figure).
- On the other hand, pedigree analysis can sometimes identify individuals who do not express but almost certainly do have a disease genotype (for example, individual Q in Figure).



Expressivity and Examples

- ❑ Individuals with the same genotype can also show different degrees of the same phenotype.
- ❑ Expressivity is the degree to which trait expression differs among individuals.
- ❑ Unlike penetrance, expressivity describes individual variability, not statistical variability among a population of genotypes.
- ❑ Example 1- The features of Marfan syndrome vary widely; some people have only mild symptoms, such as being tall and thin with long, slender fingers, whereas others experience life-threatening complications involving the heart and blood vessels.
- ❑ Although the features of Marfan syndrome are highly variable, all people with this disorder have a dominant mutation in the gene coding for fibrillin 1, *FBN1*.
- ❑ It turns out that the position of the mutation in the *FBN1* gene is correlated with the severity of the Marfan phenotype
- ❑ A mutation in one *FBN1* position is prevalent in families with severe symptoms, whereas a mutation in another position is prevalent in families with less severe symptoms.

Expressivity and Examples (contd.)

- ★ Example 2- Occurrence of extra toes, or polydactyly, in cats.
- ★ The presence of extra toes on a cat's paw is a phenotype that emerges in groups of cats who have interbred for generations. such as "Hemingway's cats". The polydactyly phenotype shows "good penetrance, but **variable expression**" because the gene always causes extra toes on the paw, but the number of extra toes varies widely from cat to cat (Danforth, 1947).
- ★ Through his breeding studies, Danforth found that although a dominant allele underlies the cause of polydactyly, the degree of polydactyly depends on the condition of adjacent layered tissues in the developing limb; that is, the expression of genes in tissues surrounding tissue that will become the toe determines the degree of polydactyly..



Penetrance and Expressivity- Hypothetical Example

#Hypothetical character - “pigment intensity.”

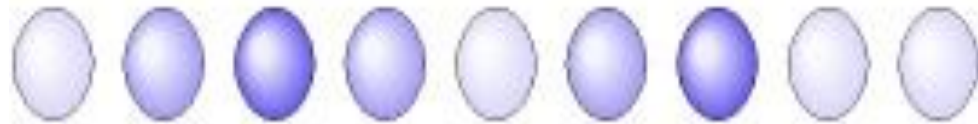
In each row, all individuals have the same allele—say, *P*—giving them the same “potential to produce pigment.”

However, effects deriving from the rest of the genome and from the environment may suppress or modify pigment production in an individual.

Phenotypic expression
(each oval represents an individual)



Variable penetrance



Variable expressivity



Variable penetrance and expressivity

PENETRANCE VERSUS EXPRESSIVITY

Penetrance is the percentage of individuals of a given genotype, exhibiting the phenotype associated with that particular genotype

Explains how often the gene is expressed

Quantitative measurement

Explains whether the disease shows up

Describes the expression of a single gene

Incomplete penetrance makes genetic analysis more difficult

Example: expression of BRCA1 and BRCA2 genes develop cancers in some individuals but not in others

Expressivity is the extent of a given genotype, expressing at the phenotypic level

Explains the extent of gene expression

Qualitative measurement

Explains how a disease shows up

Describes the expression of a group of characters or a syndrome

Variable expressivity makes genetic analysis more difficult

Example: characteristics of Marfan syndrome widely vary among individuals

Thank you