4.4: Types of Mutations

Mutations (changes in a gene sequence) can result in mutant alleles that no longer produce the same level or type of active product as the wild-type allele. Any mutant allele can be classified into one of five types: (1) amorph, (2) hypomorph, (3) hypermorph, (4) neomorph, and (5) antimorph.

- **Amorph** alleles are complete loss-of-function. They make no active product – zero function. The absence of function can be due to a lack of transcription (gene regulation mutation) or due to the production of a malfunctioning (protein coding mutation) product. These are also sometimes referred to as a Null allele.

- **Hypomorph** alleles are only a partial loss-of-function. They make an incompletely functioning product. This could occur via reduced transcription or via the production of a product that lacks complete activity. These alleles are sometimes referred to as **Leaky** mutations, because they provide some function, but not complete function.

Both amorphs and hypomorphs tend to be recessive to wild type because the wild type allele is usually able to supply sufficient product to produce a wild type phenotype (called haplo-sufficient - see Chapter 6). If the mutant allele is not haplo-sufficient, then it will be dominant to the wild type.

While the first two classes involve a **loss-of-function**, the next two involve a **gain-of-function** – quantity or quality. Gain-of-function alleles are almost always dominant to the wild type allele.

- **Hypermorph** alleles produce more of the same, active product. This can occur via increased transcription or by changing the product to make it more efficient/effective at its function.

- **Neomorph** alleles produce an active product with a new, different function, something that the wild type allele doesn’t do. It can be either new expression (new tissue or time) or a mutation in the product to create a new function (additional substrate or new binding site), not present in the wild type product.

**Antimorph** alleles are relatively rare, and have an activity that is dominant and opposite to the wild-type function. These alleles usually have no normal function of their own and they interfere with the function from the wild type allele. Thus, when an antimorph allele is heterozygous with wild type, the wild type allele function is reduced.
level there are many ways this can happen, the simplest model to explain antimorph effect is that the product acts as a dimer (or any multimer) and one mutant subunit poisons the whole complex. Antimorphs are also known as dominant negative mutations.

**Identifying Muller's Morphs** - All mutations can be sorted into one of the five morphs base on how they behave when heterozygous with other alleles – deletion alleles (zero function), wild type alleles (normal function), and duplication alleles (double normal function).