

# Glossary

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### Allelic heterogeneity

If a number of different mutations occur in the same gene and produce a disorder, that gene is said to manifest allelic heterogeneity. This term is often used when a number of different alleles cause similar or different phenotypes in the human population (ie. sickle cell anemia can be caused by various mutations in the alpha-globin gene).

### Desmosomal components

Desmosomal components are the protein constituents that comprise the desmosome, a symmetrical, disc shaped, cadherin-based intercellular junction that also links intracellularly to the intermediate filament cytoskeleton. Desmosomes function to provide mechanical stability as well as signal transduction pathways between cells including epithelia and cardiac muscle. The  $\text{Ca}^{2+}$ -dependent cadherins, desmoglein and desmocollin interact via their N-terminal regions, providing the sites for intercellular contact between desmosomes on adjacent/neighbouring cells. The cytoplasmic domains of desmoglein and desmocollin bind to intracellular proteins including plakoglobin and desmoplakin. Plakoglobin may serve as a molecular linker, as it also interacts with the N-terminal domain of desmoplakin, the C-terminal domain of which interacts with intermediate filaments of the cytoskeleton. Plakophilin proteins interact with the desmosomal components described. Recent research interest has focused on specific protein isoforms of the desmosome including desmoglein-2, desmocollin-2, and plakophilin-2, as mutations in the genes encoding these proteins underlie arrhythmogenic right ventricular cardiomyopathy.

Mutations in plakophilin-2 appear to be the most prevalent.

### Penetrance

Penetrance is the percentage of individuals with a specific genotype that exhibit the associated phenotype. As an example, if 40% of all individuals who possess the "hazel eye" allele actually have hazel eyes, then the "hazel eye" allele has a 40% penetrance.

### Phenocopy

A phenocopy is an individual whose phenotype (biochemical or physical characteristic/ characteristics) under a specific environmental condition is identical to that of another individual where the phenotype is determined by genotype (allelic composition).

### Variable expressivity

Variable expressivity takes place when a phenotype is expressed at various degrees amongst individuals who have the same genotype. For example, individuals who possess the same allele for the gene involved in a quantitative trait like height might have a large variance (ie. one individual might be 6 foot 9, while the other is 6 foot 4). This can make it difficult to predict a phenotype solely based on genotype alone. Age and environmental factors are some modifiers that can often influence the expression of a phenotype that is subject to variable expressivity.