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LifeSciences

## Important Genotyping Information to Consider When Designing Experiments

Designing a thoughtful and well-planned experiment can be a challenge. The overall aim is to lessen the experimental process variability to maximize the detection of the biological variability. Analyzing biological variability is a stalwart focus of personalized medicine. This experimental aspect plays a huge role in designing the best therapeutic approaches for individual patients.

But how does one incorporate diversity and ethnicity into an experiment? One way is to select primary cells based on their genetic variation. It is well known that not every individual responds to a therapeutic drug in the same way. The basis is that an individual's genetic variation can dictate how well a particular drug gets to the target tissue or cell and how well it is absorbed, metabolized, distributed, and excreted.

**What information is important to consider in an experimental design?**

Several types of genetic variation information (genotyping data) are usually analyzed to infer the individual's response to a therapy (phenotype). This information may include:

1. the genotyping result
2. the rs number – a unique identifier for the particular variation, which can directly link the investigator to the National Center for Biotechnology Information (NCBI)'s Single Nucleotide Polymorphism (SNP) database
3. the allele frequency and reference allele matched to the individual donor's ethnicity
4. the common or specific gene name
5. the most updated reference to the DNA reference sequence and type of variation using the Human Genome Variation Society (HGVS) nomenclature

**How is genotyping data referred to?**

The genotyping result is the individual's own genetic variation information. It will be the same for all cells, tissues, and organs within that individual, although there are rare exceptions. Several nomenclature systems have come into existence to try to describe these genetic variations. One is the star "*" nomenclature, which has been commonly used throughout the scientific literature. An example is CYP1A2*1C, a variation in the cytochrome P450 1A2 family. This nomenclature has changed over time and, more recently, designates haplotypes — genetic variations that are linked or working together. Another system is the HGVS nomenclature. An example is c.35G>T, which refers to a G to T transition within the DNA code at base pair 35. This nomenclature also has changed over time due to more of the human DNA sequence being analyzed and solidified. Finally, the last nomenclature is the rs number. It is an unique identifier of a genetic variation and is directly linked to NCBI's national database for SNPs.

**How does an investigator use this genetic variation information?**

Using the most unique nomenclature, the rs number, an investigator can then examine the genotyping result with respect to the allele frequency and reference allele that matches the individual's ethnicity. The ethnicity of an individual is important in considering these two pieces of information because the reference allele can change with ethnic background, and this change will determine which allele frequency to take into consideration. For example,

individuals with European Caucasian descent have the “A” allele of the transporter gene SLCO1B1 rs2306283 variation as their reference allele, while individuals of African descent have the “G” allele as their reference allele. For individuals of African descent, the most frequent allele is G and designates a “flip” from what is considered “normal.” This “flip” will need to be taken into consideration in interpreting the activity of the SLCO1B1 transporter.

For each lot of LifeNet Health LifeSciences’ primary human hepatocytes, comprehensive medical and social history, histological and serological assessments, and now comprehensive genotyping information are offered. A total of 112 genotypes for the most polymorphic cytochrome P450s, Phase II enzymes, and transporters are analyzed using state-of-the-art, next generation sequencing technology. This genotyping information allows a comprehensive picture of the variant while leaving the interpretation to the expert investigator.

Authored by Mary Jane Cunningham, Ph.D.
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