Toxicology. DOI: 10.1021/tx700079z.

Pharmacogenomics and Personalized Medications

A key area of personalized medicine, whereby our medical professionals as a “one size fits all” medication, is being mainstream across the globe. The focus on making personalized treatment plans are tailored to us as individuals, more accurately targeting the needs of the patient, and its clinical impact.

Over recent years, the medical community has placed increasing emphasis on personalized fields, such as pharmacology, whereby our medical professionals can recommend effective medications.

Increasingly, the role of pharmacogenetics is being evaluated in determining the relative risk of side effects in patients, and the best medication for a given patient. Pharmacogenetics is the study of genetic polymorphisms that affect response to medications.

Drug targets are often proteins. Genetic polymorphisms can therefore alter the encoded protein to which the drug would typically bind and impact the drug’s mode of action and efficacy.

Let’s look at how genetic polymorphisms can impact different stages of this process…

Distribution, metabolism and excretion (ADME) – but one that is specific to that drug.

Genetic polymorphisms

A genetic polymorphism is an inherited difference in DNA sequence. It occurs when, within a species, one or more nucleotide variations exist. Single nucleotide polymorphisms (SNPs) are the most common type of genetic polymorphism.

Each SNP represents a difference in a nucleotide; for example, an SNP may replace the nucleotide cytosine with thymine.

There are three main types of genetic polymorphisms:

- Functional driver mutations
- Non-functional mutations
- Non-functional mutations

Distinguishing between these types of mutations is crucial to understanding their potential impact.

Implementing next generation sequencing is enabling the quantification of the economic impact and cost-effectiveness of pharmacogenomic profiling.

Quantifying the economic impact and cost-effectiveness of pharmacogenomic profiling is crucial to its success.

To explore the role of the entire human genome and epigenetics in determining an individual’s drug response, researchers study the genetic variations that exist.

One example of a genetic polymorphism is the 5-HT transporter (5-HTT) gene (SCLC6A4) which has a common length polymorphism that causes a partial deletion of a tandem repeat sequence.

Pharmacogenomics − an example

Pharmacogenomics is the study of genetic factors that influence an individual’s response to medications.

For example, in the case of codeine, a commonly prescribed opioid analgesic, the metabolism of codeine to its active metabolite, morphine, is highly variable across the population.

The FDA drug label for codeine states that even at labeled dosages, patients may experience life-threatening or fatal respiratory depression.

To treat such patients, an absolute reduction in codeine dosage may be required.

Table 1: Pharmacogenetics of codeine metabolism

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Pharmacogenomics − an example with codeine

Let’s consider the case of codeine. Codeine is a pro-drug that is metabolized by the cytochrome P450 enzymes CYP2D6 and codeine.

CYP2D6 is a polymorphic enzyme, meaning there are multiple forms of the enzyme with different levels of activity. These forms are classified into one of four phenotypes:

- Extensive metabolizer (normal activity)
- Intermediate metabolizer (reduced activity)
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The metabolism of up to 25% of codeine is contributed by CYP2D6, with other isoenzymes, such as CYP2C19, also involved.

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