How Modifications in Ethnic Diet Can Alter Drug Efficiency in Individuals

While one medical treatment plan may easily resolve the issues of one patient, the same treatment may be ineffective or introduce complications in another. This reality of varying therapeutic effectiveness, reflected in patients, is made true through pharmacogenetics, which is the idea that a person's genetic information can influence the way their body processes drugs. Every person has their own DNA, passed down from parent to offspring, which is like their own unique fingerprint. This unique identity is constructed through variations in DNA. Variations such as these often consist of SNPs, or single-nucleotide polymorphisms, which are defined as variations of single nucleotides in a genome, or CNVs, which are differences in the number of copies of specific DNA segments, encompassing deletions, insertions, or duplications of DNA (He et al., 2011). Both alter enzyme activity, thus helping to determine an individual's unique reaction to specific medications.

Cytochrome P450 Alleles:

Building upon this concept, scientists have made note of genetic variants, such as those in the cytochrome P450 (CYP) family, that play critical roles in the transport and detoxification of xenobiotics. Humans carry 57 functional CYP genes that fit into 18 major families, many critical ones belonging to the CYP2 and CYP3 families (Swen et al., 2023). They code for enzymes that are crucial in metabolizing medicine and are largely polymorphic, meaning they provide insight into adequate patient treatments. Variations in the CYP genes determine the rate at which an individual will digest and absorb medication, a part of the pharmacokinetic cycle consisting of absorption, dilution, metabolism, and excretion. Within this scope, there are four major classifications of metabolism: ultra-rapid, normal, intermediate, and poor (Zhou & Lauschke, 2022). This information can be used by medical professionals to limit adverse drug effects through appropriate adjustment of drug doses.

However, not all populations exhibit the same genetic variants of CYP enzymes. Although these alleles have a high frequency, geographic location has proven to be a factor in their distribution. This factor implies that people from the same population may exhibit patterns in their metabolic rate. Examples were found in a European study of 6,944 patients who underwent genetic testing prior to treatment. The scientists noted that CYP2D6 alleles were found in 44.6% of people, and numerous genes had differing frequencies in varying populations (Swen et al., 2023). From a global lens, another study involving 141,614 people from 12 distinct populations further confirmed

that a gene's minor allele frequency (MAF) is not constant (as seen in Figure 1), suggesting that while a MAF value might apply to a specific population or group of people, it may not apply to others (Zhou & Lauschke, 2022).

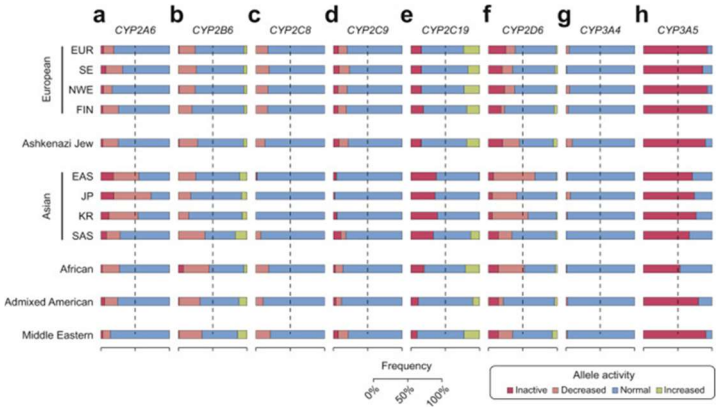

Figure 1. Frequencies of CYP alleles. This graph displays the frequency of inactive, reduced activity, normal, and increased activity alleles in 8 genes from the CYP2 and CYP3 families. Rows represent populations of European (EUR, SE, NWE, FIN), Ashkenazi Jewish, East Asian (EAS, JP, KR), South Asian (SAS), African, Admixed American, and Middle Eastern ancestry, which show additional inter-population variation (Zhou & Lauschke, 2022).

The variation in CYP allele frequency characterized here implies that metabolic differences are biologically rooted and may interact with factors, such as diet. This supports the idea that medical standards of care should be dependent on the patient's ethnic population and background (Zhou & Lauschke, 2022).

Diet:

Specifically, diet is a large defining factor of ethnic populations. While genetics plays a large role in gene expression, diet does also. Frequent consumption of foods native to geographic locations can create patterns in the altered expression of CYP genes (Martinez-Lomeli et al., 2023). Two examples of ingredients that shape gene expression are curcumin and ellagic acid. Curcumin, the bioactive ingredient in turmeric and a prevalent spice in South Asia, is known for its flavor and medicinal properties, such as being antioxidant and anti-inflammatory (Kocaadam & Şanlier, 2017). Similarly, ellagic acid is a bioactive ingredient found in high concentrations in pomegranates, a fruit commonly eaten in Middle Eastern countries, such as Turkey.

RNA Interference:

To understand how these dietary components might influence gene expression, genetic manipulation with the use of RNA interference (RNAi) is pivotal. RNAi is a precise tool that silences specific genes using small RNA molecules that destroy messenger RNA, stopping the creation of proteins. This tool can artificially model populations with inactive genes, more accurately measuring results specific to the location.

Drosophila Melanogaster as a Model:

To model this effectively, Drosophila melanogaster will be used. This species of fruit flies was chosen to represent humans due to their low cost, short lifespan, and ability to be genetically modified (Munnik et al., 2022). However, the most prominent rationale behind using Drosophila is that 178 of 286 human disease genes are conserved in Drosophila, meaning that fly responses can be correlated to human behaviors (Fortini et al., 2000).

Implementation of Pharmacogenetics:

Ultimately, this fly model has the potential to prove the importance of pharmacogenetics as well as kickstart its eventual implementation. Though pharmacogenetic application has already shown a reduction of adverse drug events (Fig. 2), several barriers remain (Swen et al., 2023). First, the cost efficiency has not been determined. A study of 5,288 savings of up to $7,000 in direct medical costs; however, this estimate does not cover the cost of time, gene tests, or insurance (Swen et al., 2023). Furthermore, there has been minimal clinical testing validating pharmacogenetic impact, a lack of standardized guidelines, and a lack of movement towards education of this resource. (Scott, 2011).

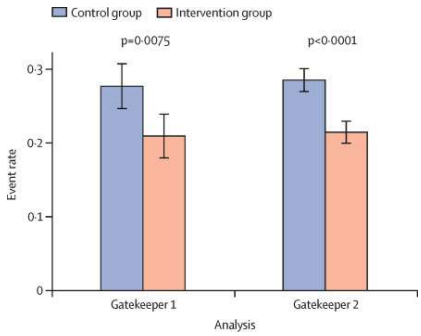

Figure 2. The difference in adverse drug reaction frequencies of 6944 individuals in a study who received pharmacogenetic testing and those who did not. In both trials, the risk of adverse drug reactions was reduced by 30%, signifying a noteworthy reason to employ pharmacogenetics in medical practice (Swen et al., 2023).

Addressing these gaps, this project looks at what could be a root cause of adverse drug effects. It explores why people react to drugs differently, bridging pharmacogenetics and nutrigenetics. Furthermore, it considers shared environmental factors in people, or even countries, providing next steps for pharmacogenetics that are reasonable considering preexisting knowledge and limiting factors.