Drug metabolism comes with many consequences. Before we can appreciate those consequences, we need to cover the oxidative liver enzymes – the cytochrome P-450 (CYP) enzyme superfamily.

The CYP superfamily in humans 57 different enzymes. Each CYP enzyme is classified through a code that includes a number (gene family), a letter (subfamily), and another number (the gene number). Specific examples include CYP26C1 and CYP4F12. These enzymes are involved in a number of processes in the body. The most relevant enzymes for drug metabolism are 3A4, 3A5, 1A2, 2C9, 2C19, and 2D6. This set of CYP enzymes metabolizes the majority of drugs. Since so few enzymes carry the burden of drug metabolism, the proper function of these enzymes is essential for the predictable behavior of drugs. Important factors to consider include both inhibition of one or more of these enzymes and genetic factors.

Drugs are often substrates for the various CYP enzymes, but they can also serve as inhibitors of these enzymes. A drug that inhibits a CYP enzyme has the potential to slow the metabolism of another drug. For example, a patient is taking Drug A. Drug A is metabolized primarily by CYP1A2. The patient later begins taking Drug B, which is an inhibitor of CYP1A2. With Drug B in the patient's system, the action of CYP1A2 will be diminished. Hepatic clearance, $CL_H$, for Drug A will decrease. As clearance for Drug A decreases, $AUC$ and $C_p$ of Drug A increases. It may be possible that the standard dosing regimen of Drug A will exceed the drug's therapeutic window.

$$AUC = \frac{D_0}{CL}$$

The effect of one drug upon another is called a drug interaction, drug-drug interaction, or DDI. Drug interactions pose potential safety concerns and are disclosed in the prescribing information of drugs.

Because drugs that inhibit CYP enzymes can have such a dramatic impact on the behavior of other drugs, the ability of a molecule to inhibit CYP enzymes is studied very early in drug discovery – at the lead discovery stage. Hits are studied for their properties as inhibitors before being promoted to lead status.

In a similar manner, genetic factors can also play a key role in drug metabolism. Some CYP enzymes show high variability among different populations. CYP2C9 is an example of a CYP enzyme that shows genetic variability. Around 10% of the population has a less active form of CYP2C9. If those people with a less active form of CYP2C9 take a drug that is metabolized primarily by 2C9, then they must follow a lower dosage regimen or else risk have excessive levels of drug in their systems.

Early in lead discovery, lead candidates can be screened for which forms of CYP are responsible for metabolism a given molecule. Hits that are exclusively metabolized by CYP forms that carry high genetic variability are less likely to be promoted as leads.