Drug Transporters that are Pharmacogenetic

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Short Communication

Pharmacogenomics[1] investigates the genetic variability of interindividual DNA sequences of therapeutic targets, drug enzymes, drug carriers, or disease genes, RNA or gene protein translation of drug response genes, and drug safety. As a result, the clinical impact of pharmacogenomics remains an important research topic.

The role of drug transporters in processes regulating the pharmacokinetic properties of drugs such as absorption, distribution, and elimination, as well as cellular pharmacologic resistance by lower intakes or increased efflux is becoming increasingly important in pharmacogenomics for a wide range of therapeutics including oncology.

Transporters, in general, move substrates from intracellular to extracellular (”efflux” transporters) or vice versa (”influx transporters”). There are several efflux transporters [for example, the ATP-binding cassette transporter family (ABCs) and multidrug toxin extrusion proteins (MATEs)] and influx transporters [for example, the organic anion transporters] (OATs and OATPs) Organic cation transporters (OCTs) [2], oligo peptide transporters (PEPTs), and other bidirectional transporters Furthermore, these transporters are frequently arranged in polarized cells to facilitate substrate movement at a single membrane, either basolateral or apical, thereby regulating substrate distribution frequently arranged in polarized cells to facilitate substrate movement at a single membrane, either basolateral or apical, thereby regulating substrate distribution across epithelial barriers. There is a lot of genetic variation. Polymorphisms are commonly found in drug transport, and some of them, particularly single nucleotide polymorphisms, have a significant impact on activity (SNPs). These polymorphisms have clinical implications in drug pharmacokinetics, particularly for medications with a narrow therapeutic index and inter- and intra-patient variation.

The ultimate goal of transporter pharmacogenomics research is to better understand human diseases and approach in utilize nowadays. Pharmacogenetic approaches tailor therapies to patients based on their unique genetic background, and transporters are central to pharmacogenomics research.

ABCB1 [3] is the efflux transporter that has received the most attention. It is found in nearly all human and rodent tissues, with the highest levels of expression on the apical surface of enterocytes, the canalicular plasma membrane of hepatocytes, and the proximal renal tubule. ABCB1 has at least 66 coding SNPs, 24 of which are synonymous and 42 of which are non-synonymous. Two synonymous SNPs and 12 non-synonymous SNPs are linked to altered ABCB1 protein function or expression. 1236C>T, 3435C>T, and 2677G>T/A have all been thoroughly studied.

ABCC2 [3], also known as MRP2, is found in a variety of tissues, including the liver, intestine, kidney, BBB, and placenta, and is found on the apical membrane of epithelial cells. It actively exports anionic drug conjugates as well as a variety of unconjugated substances, making it an important component of drug detoxification. Furthermore, ABCC2 is important in the transport of anticancer drugs In vitro studies, for example, show that ABCC2 is expressed at higher levels in tamoxifen-resistant breast cancer cells, implying that ABCC2 plays a role in transporting tamoxifen active metabolites.

ABCG2 (BCRP, MXR) is highly expressed in the placenta, the central nervous system (CNS; brain and BBB), the liver, the adrenal gland, the testes, and the large and small intestines, where it effluxes substrates across the apical membrane.