Contribution of intestinal transporters to drug absorption: Strategy for drug discovery

Takuo Ogihara
(Faculty of Pharmacy, Takasaki University of Health and Welfare)

It has the function to take the nutrients into the inside of the body efficiently and the function to prevent the xenobiotic drugs from going into it, and influx and efflux transporters play a part of the role on the intestinal epithelial cell, respectively. For example, peptide transporter 1 (PEPT1) has been found to be one of the most versatile influx transporters with great substrate range for di- or tripeptide and peptide mimic compounds. This observation has been exploited successfully as a mechanism for improving oral bioavailability of several drugs. However, some of them are thought lucky examples of going well consequentially, and there are a lot of cases with a not clear how influx transporters contribute to the oral absorption of drugs.

In addition, the troublesome one is participation of efflux transporter, for example, P-glycoprotein (P-gp). Several researchers have suggested that the influence of P-gp on intestinal absorption of drugs is relatively limited, since the absorption of various P-gp substrates after oral administration are excellent in humans. However, this is thought to be a conclusion from the result of examining the medicine that has already been in the market. Moreover, in order to explain the absorption profile of drugs, the case where the participation of efflux transporter cannot be disregarded is found especially in the first stage of drug discovery in recent years. It introduces some of these cases in this lecture, and the technique of the evaluation method, the problem, and the solution will be considered.