1-JS1-4 Joint Symposium

Transporter inhibitors: from target identification and pharmacology to clinical development

Yoshikatsu Kanai[1,2]

[1]Dept. Bio-sys Pharm., Grad. Sch. Med., Osaka Univ., [2]Integ. Front. Res. Med. Sci. Div., OTRI, Osaka Univ.

Transporters on the plasma membrane contribute to determining the distribution of compounds in the intra- and extracellular compartments and eventually their disposition in the body. Thus, the drugs that affect the functions of transporters are expected to alter the distribution of compounds in the body and to ameliorate disrupted homeostasis in pathological conditions. In fact, the drugs targeting transporters, such as antidepressants, diuretics and uricosuric agents, have been used clinically. They were, however, developed before the identification of targets. Now, we have a lot of information on transporters in human genome that can be targets of new drug discovery. For example, anti-diabetic drugs have been successfully developed targeting renal Na^+/glucose cotransporter SGLT2. The molecular identification of SGLT2 contributed to the critical optimization of the compounds. We have identified an amino acid transporter LAT1 expressed in cancer cells with high cancer-specificity. Based on the structure-activity relationship analyses, we have developed its inhibitors which are now in the clinical trials. In the lecture, the issues we have experienced in the process of compound developments, pre-clinical studies and bridging toward clinical trials will be summarized, and the importance of basic and clinical pharmacology collaboration will be discussed in terms of academia drug discovery.