Preface

Membrane transporters can have a significant impact on the absorption, distribution, metabolism and excretion (ADME) of a drug. For example, transporters can influence drug disposition by being a barrier to exposure or the rate-determining step in the uptake and/or excretion for a drug. The recognition of the influence of transporters on drug disposition has dramatically increased drug transport-related research activities within the pharmaceutical sciences. These activities include identifying and cloning the major drug transporter genes, determining the impact of genetic polymorphisms on plasma pharmacokinetics, elucidating the mechanisms regulating gene and protein expression, examining the structure–activity relationship of transporter substrates, and developing assays to support drug discovery and development.

The identification of membrane transporters that influence the disposition and safety of drugs is a relatively new challenge for drug discovery and development programs, with integration of data from drug metabolism and transporters studies becoming more important in the characterization of a drug’s ADME properties. This special theme issue of European Journal of Pharmaceutical Sciences (EJPS) on “Drug transporters: integration in understanding ADME” highlights through a series of mini-reviews, reviews and original articles current thinking and approaches to integrate a drug’s ADME properties with the importance of transporters in overall drug disposition. The mini-reviews on the “Power of the pump” (Ambudkar et al.) and “siRNA: getting the message out” (Lee and Sinko) briefly summarize two of the most active areas in drug transport research; how ABC transporters bind and transport substrates, and how the new technology of siRNA can selectively be used to knockdown drug transporter genes in vitro and in vivo. The contributed review articles provide detailed reviews on the role of transporters in drug disposition and drug interactions (Shitara et al; Endres et al.), interplay between hepatic transporters and phase II drug metabolizing enzymes (Zamek-Gliszczynski et al.), regulation of drug transporter genes (Kato and Tsuji), and computational modeling of transporter drug binding sites (Chang and Swaan). These reviews were selected to provide a broad overview of the major drug transporter research areas. The issue concludes with a selection of original research papers that highlight some of the most current transporter-based research. These articles include work on recently identified transporters (e.g., MRP5 by Pratt et al. and HPHT1 by Bhattacharyya et al.), validated P-glycoprotein inhibition assays to support clinical development (Kunta and Krogd) and functional characterization of OAT4 in placental cells (Zhou et al.).

We hope that this theme issue provides the readership of EJPS a glimpse into the rapidly expanding area of drug transporter research, and further encourages new researchers to join the ongoing research efforts in this exciting area. Integrating ADME properties with mechanistic drug transporters studies will provide a better understanding of the role these proteins play in drug disposition. Further, this information will be useful in guiding clinical drug interaction studies and improving tomorrow’s medicines.

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