

Introduction to Drug Transporters

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1 INTRODUCTION

The role of transporter proteins in drug and endogenous substance disposition has increasingly gained recognition over the last decade (Mizuno *et al.*, 2003; Beringer and Slaughter, 2005; Anzai, Kanai and Endou, 2006). For example, the role of transporters in biliary excretion was not recognized as late as 1995 and as a result, species differences in biliary excretion were not readily explainable (Lin, 1995). It has now become clear that transporters are responsible both for the uptake and efflux of drugs and other chemicals in various tissues and may be key determinants of the pharmacokinetic characteristics of a drug. Inhibition or induction of different drug transporters in different tissues can lead to clinical drug–drug interactions that may result in adverse effects or lack of efficacy (Bodo *et al.*, 2003; Van Montfoort *et al.*, 2003; Sai, 2005). Inhibition or induction of transporters that are responsible for endogenous substance disposition (e.g. bile acids) can also result in toxicological consequences (Bodo *et al.*, 2003). This review is not intended to be a comprehensive and in-depth review of all transporter-related topics, but rather focus on the role of drug transporters in drug development. There are many excellent reviews on various topics on transporters (Bodo *et al.*, 2003; Mizuno *et al.*, 2003; Van Montfoort *et al.*, 2003; Beringer and Slaughter, 2005; Sai, 2005; Anzai, Kanai and Endou, 2006; Endres *et al.*, 2006; Zhang *et al.*, 2006; Alrefai and Gill, 2007; Lin, 2007; Urquhart, Tirona and Kim, 2007). The purpose of this review is to provide the readers with fundamental knowledge of drug transporters and their roles in drug development relating to drug absorption, distribution, metabolism, excretion and toxicity, clinical drug–drug interactions, and *in vitro/in vivo* methodologies.

2 TRANSPORTER CLASSIFICATION, LOCALIZATION, AND FUNCTIONS

Table 1 is a summary of transporter families and the individual genes expressed. Transporters have been classified as primary, secondary, or tertiary active transporters.