studies in cultured BCECs suggests that several members of the MRP family (MRP1,4,5,6) are found in the BBB.

Recent evidence has also demonstrated expression of OAT, OCT, and OCTN transport families in the CNS. Established substrates for these transporters including acyclovir (OAT1), methotrexate (OAT1), quinidine (OCT2) are known to be actively transported out of the brain (38). Therefore, it is likely that these transport families play a role in CNS efflux. Further characterization of these transporters and their function is eminent.

8. IMPACT OF MEMBRANE TRANSPORTERS ON OTHER ORGANS AND TISSUES

A major focus of this chapter was the role of membrane transport on organs involved in absorption, metabolism, and excretion of medications. Not unexpectedly, the expression and characterization of membrane transporters in other tissues of the body are actively being pursued. For example, understanding the role of efflux transporters in the placenta will allow for the development of treatment strategies for pregnant women that minimize the risk of harm to the fetus. Likewise, understanding the role of mammary gland transporters on drug excretion into breast milk is important from a clinical and toxicological perspective. The impact of membrane transport on placenta and mammary drug transfer has been the subject of recent review articles (169,170). The impact of membrane transporters on these tissues, as well as others (e.g., testes, eyes), will undoubtedly be realized in the near future.

9. IMPLICATIONS FOR PRECLINICAL DRUG DEVELOPMENT

The objective of this chapter was to provide an overview of the various transport systems that contribute to drug disposition in vivo. In this context, a number of transport systems such as the bile-acid transporters were not emphasized, although they may prove to be useful routes for drug delivery. As membrane transport is a rapidly evolving area of study, detailed characterization of these and other transporters will be achieved in the near future.

Assessment of membrane transport and the role of transporters on pharmacokinetics and drug activity have significantly impacted preclinical drug development and will continue to affect the drug development paradigm in the future. Specific implications of membrane transport for preclinical drug development are provided in what follows.