Editorial

The problem of multidrug resistance has gained increasing importance in the fields of tumour therapy and treatment of bacterial and fungal infections. One of the major mechanisms responsible for development of multiple drug resistance is overexpression of drug efflux pumps. These membrane bound, ATP driven transport proteins efflux a wide variety of natural product toxins and chemotherapeutic drugs out of cells and give rise to decreased intracellular accumulation of these compounds. Thus, inhibition of efflux pumps is a versatile approach for overcoming multiple drug resistance, and several compounds are in clinical phase III studies. The main target is P-glycoprotein, which is responsible for MDR in tumour cells, and transport systems in *S. aureus*, *P. aerugiosa* and *E. coli*. Due to the fact, that 3D-structures of the proteins at atomic resolution were not available, drug development was performed solely on basis of ligand based design. However, electron microscopy studies as well as X-ray structures of three bacterial efflux pumps may open the door to target based drug design in the near future.

The hot topic issue will deal with the topic of drug efflux pumps from different perspectives. The article of Klopman and Zhu present new methodologies for estimating lipophilicity and their impact on prediction of membrane transport properties of drugs. Seelig and Gatlik-Landwojtowicz highlight the biophysical characterisation of inhibitors of efflux pumps and their membrane and protein interactions. An overview on the approaches used for lead identification and optimisation for inhibitors of P-glycoprotein is given by Pleban and Ecker. Peer *et al*. focus in their article on recent progress in identifying substrate binding domains of P-glycoprotein by means of photoaffinity labeling. Analogous multidrug transport systems in lactic acid bacteria are dealt by Mazurkiewicz *et al.* Last but not least Fischer *et al*. give an overview on the clinical relevance of efflux transporter. These articles will demonstrate, that, although much progress has been made in the development of EPIs, we are far away from understanding the basic principle of drug recognition and transport mechanism of this class of pumps. These issues will continue to be one of the major tasks in the field of modulation of drug resistance!

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