Regulation of Drug Transport Proteins-From Mechanisms to Clinical Impact: A White Paper on Behalf of the International Transporter Consortium.

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4656044
Author(s) Brouwer, Kim L R; Evers, Raymond; Hayden, Elizabeth; Hu, Shuiying; Li, Cindy Yanfei; Meyer Zu Schwabedissen, Henriette E; Neuhoff, Sibylle; Oswald, Stefan; Piquette-Miller, Micheline; Saran, Chitra; Sjöstedt, Noora; Sprowl, Jason A; Stahl, Simone H; Yue, Wei
Author(s) at UniBasel Meyer zu Schwabedissen, Henriette ;
Year 2022
Title Regulation of Drug Transport Proteins-From Mechanisms to Clinical Impact: A White Paper on Behalf of the International Transporter Consortium.
Journal Clinical pharmacology and therapeutics
Volume 112
Number 3
Pages / **Article-Number** 461-484
Mesh terms Biological Transport; Carrier Proteins, metabolism; Gene Expression Regulation; Humans; Membrane Transport Proteins, genetics, metabolism; Pharmaceutical Preparations; Receptors, Cytoplasmic and Nuclear, genetics
Membrane transport proteins are involved in the absorption, disposition, efficacy, and/or toxicity of many drugs. Numerous mechanisms (e.g., nuclear receptors, epigenetic gene regulation, microRNAs, alternative splicing, post-translational modifications, and trafficking) regulate transport protein levels, localization, and function. Various factors associated with disease, medications, and dietary constituents, for example, may alter the regulation and activity of transport proteins in the intestine, liver, kidneys, brain, lungs, placenta, and other important sites, such as tumor tissue. This white paper reviews key mechanisms and regulatory factors that alter the function of clinically relevant transport proteins involved in drug disposition. Current considerations with in vitro and in vivo models that are used to investigate transporter regulation are discussed, including strengths, limitations, and the inherent challenges in predicting the impact of changes due to regulation of one transporter on compensatory pathways and overall drug disposition. In addition, translation and scaling of in vitro observations to in vivo outcomes are considered. The importance of incorporating altered transporter regulation in modeling and simulation approaches to predict the clinical impact on drug disposition is also discussed. Regulation of transporters is highly complex and, therefore, identification of knowledge gaps will aid in directing future research to expand our understanding of clinically relevant molecular mechanisms of transporter regulation. This information is critical to the development of tools and approaches to improve therapeutic outcomes by predicting more accurately the impact of regulation-mediated changes in transporter function on drug disposition and response.

ISSN/ISBN 1532-6535
Full Text on edoc ;
Digital Object Identifier DOI 10.1002/cpt.2605
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/35390174