Uptake Transporters of the SLC21, SLC22A, and SLC15A Families in Anticancer Therapy - Modulators of Cellular Entry or Pharmacokinetics?

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Solute carrier transporters comprise a large family of uptake transporters involved in the transmembrane transport of a wide array of endogenous substrates such as hormones, nutrients, and metabolites as well as of clinically important drugs. Several cancer therapeutics, ranging from chemotherapeutics such as topoisomerase inhibitors, DNA-intercalating drugs, and microtubule binders to targeted therapeutics such as tyrosine kinase inhibitors are substrates of solute carrier (SLC) transporters. Given that SLC transporters are expressed both in organs pivotal to drug absorption,
distribution, metabolism, and elimination and in tumors, these transporters constitute determinants of cellular drug accumulation influencing intracellular drug concentration required for efficacy of the cancer treatment in tumor cells. In this review, we explore the current understanding of members of three SLC families, namely SLC21 (organic anion transporting polypeptides, OATPs), SLC22A (organic cation transporters, OCTs; organic cation/carnitine transporters, OCTNs; and organic anion transporters OATs), and SLC15A (peptide transporters, PEPTs) in the etiology of cancer, in transport of chemotherapeutic drugs, and their influence on ecacy or toxicity of pharmacotherapy. We further explore the idea to exploit the function of SLC transporters to enhance cancer cell accumulation of chemotherapeutics, which would be expected to reduce toxic side eects in healthy tissue and to improve efficacy.

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