SCREENING OF ENVIRONMENTAL HEAVY METAL INTERACTIONS WITH DRUG TRANSPORTERS

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Background:

Genes of the *SLC22* family encode polyspecific membrane transporters responsible for the delivery of most drugs [1-3]. Heavy metals can impair the function of transporters altering the drug response. The impact of metals can further vary due to the existence of many polymorphisms [2, 4] of the *SLC22* genes that can affect the protein-metal interaction.

Methods and Results:

Using a systematic computational analysis by MIB2 (Metal Ion-Binding site prediction) we have identified metal ion-binding domains in SLC22 proteins and estimated probability score. Few changes have been detected on the polymorphic variants. Impairment of function and hence of drug delivery upon interaction with metals are predicted. Validation of the computational screening has been performed employing the SLC22A4 as a benchmark [5]. The affinity of the transporter for heavy metals released by microplastics has been described in *in vitro* and *ex vivo* systems and compared to the computational screening data with good correspondence of the in silico and wet data.

Conclusions and Significance:

Heavy metals are common environment and food contaminants, vastly released from microplastics. The described data indicates that metals influence the function of the major drug transporters and hence, the delivery of many commonly used drugs. Therapeutic approaches are suggested helping rescue of drug delivery in presence of contaminating heavy metals.

Keywords:

OCT, SLC22, Heavy Metals, Drug, Proteoliposome.

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