

Poster: BSEP, MRP, AND DILI... Just a bad hand at Scrabble?

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Abstract

Cholestatic drug-induced liver injury (DILI) has been associated with the failure to excrete bile acids and as a consequence, associated with the inhibition of the Bile Salt Efflux Pump (BSEP). However recent literature^{1,2} suggests that BSEP is not the only transporter involved and there is a contribution of the Multi-Drug Resistance Protein (specifically MRP4). In our ongoing research towards the prediction of DILI for the European funded HeCaToS project we have produced QSAR models for both of these end points using the literature data and demonstrate superior predictive performance compared to the published models. Unfortunately this did not lead to superior predictive performance in identifying those compounds that caused DILI and our modelling efforts draw into question the strength of the published association between MRP4, BSEP, and DILI.

1. Köck et al. Drug Metab. Dispos. (2014) 42 pp. 665-674

2. Welch et al. Drug Metab. Dispos. (2015) 43 pp. 725-734

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