Drug-induced liver injury (DILI) can cause hepatic failure and result in drug withdrawal from the market. Preclinical prediction of DILI risk is very challenging and safety assessments based on animals inadequately forecast human DILI risk. In contrast, human-derived in vitro cell culture-based models could improve DILI risk prediction accuracy. Here, we developed and validated a method to assess DILI risk associated with various compounds. Fifty-four marketed and withdrawn drugs classified as DILI risks of "most concern", "less concern", and "no concern" based on Liver Toxicity Knowledge Base were tested using a combination of four assays addressing mitochondrial injury, intrahepatic lipid accumulation, inhibition of biliary network, and bile acid-dependent toxicity. Using these in vitro testings, an algorithm with the highest available DILI risk prediction power was built by artificial neural network (ANN) analysis. The optimal combination of assays (or descriptors in general) may not yet be achieved, but the strategy we employed here may be one of the strategies to predict DILI risk whose precise pathogenesis is unknown.
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