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Comprehensive microRNA profiling in acetaminophen toxicity identifies novel circulating biomarkers for human liver and kidney injury

The objective of the study was to identify microRNA (miRNA) biomarkers of drug-induced liver and kidney injury by profiling the circulating miRNome in patients with acetaminophen overdose.

Plasma miRNAs were quantified in age- and sex-matched acetaminophen overdose patients with (N=27) and without (N=27) organ injury (APAP-TOX and APAP-no TOX, respectively). Classifier miRNAs were tested in a separate test cohort (N=81). miRNA specificity was determined in non-acetaminophen liver injury and murine toxicity models. Sensitivity, in comparison with the current biomarker ALT, was tested by stratification of patients at hospital presentation (N=67). From 1809 miRNAs, 75 were 3-fold or more increased and 46 were 3-fold or more decreased with APAP-TOX. A 16 miRNA classifier model accurately diagnosed APAP-TOX in the test cohort. The miRNAs with the largest fold increase (miR-122-5p, miR-885-5p and miR-151a-3p) and highest ranked miRNA from the classifier model (miR-382-5p) accurately reported non-acetaminophen liver injury and were unaffected by kidney injury. A panel of novel miRNAs were associated with kidney dysfunction. miR-122-5p was more sensitive than ALT for the diagnosis of liver injury at hospital presentation, especially when combined with miR-483-3p.

Profiling of acetaminophen toxicity identified **multiple miRNAs that** report acute liver injury and potential biomarkers of drug-induced kidney injury.