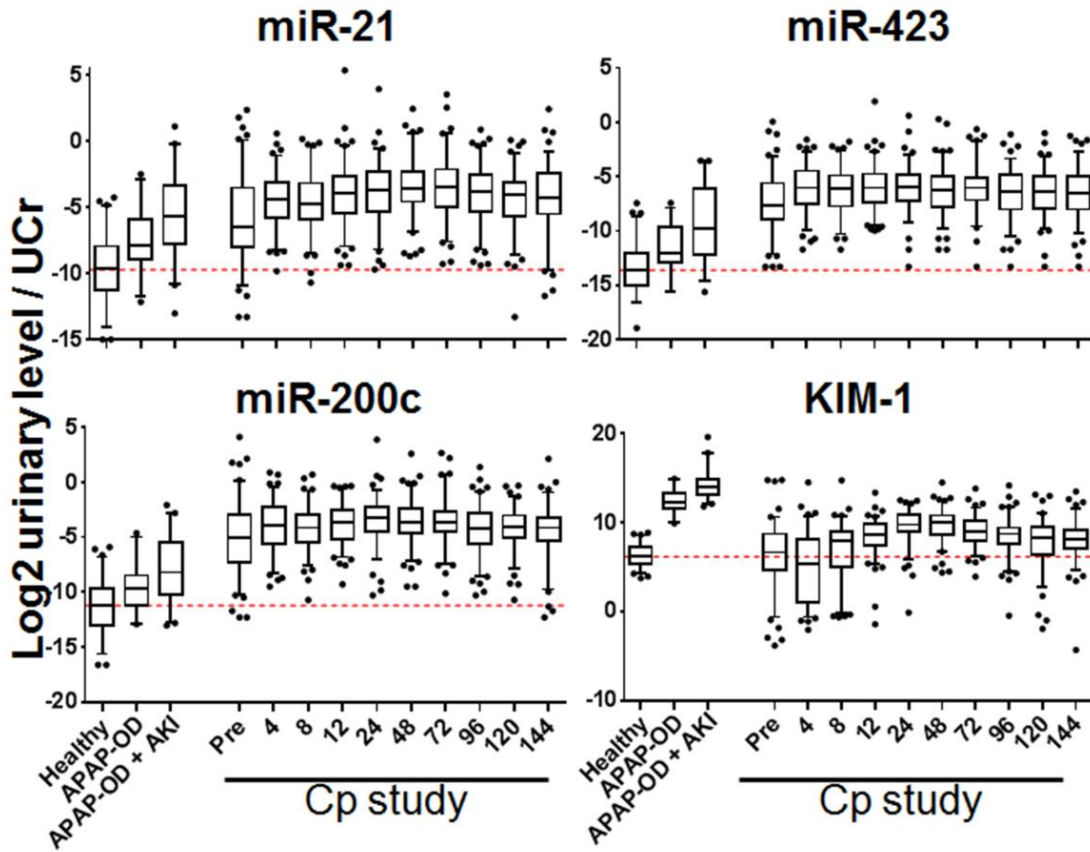


Manuscript: Detection of Drug-induced Acute Kidney Injury in Humans Using Urinary KIM-1, miR-21, -200c and -423

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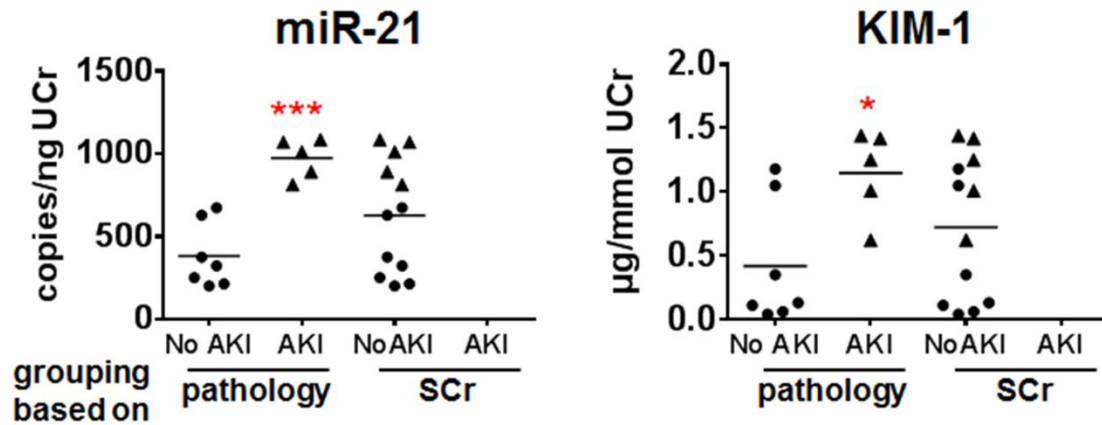
Supplementary material

- 1) Supplementary Figure 1
 - Urinary levels of miR-21, -200c, -423 and KIM-1 from both studies
- 2) Supplementary Figure 2
 - Literature example: inaccuracy of serum creatinine as gold standard
- 3) Supplementary Figure 3
 - Technical controls for qRT-PCR

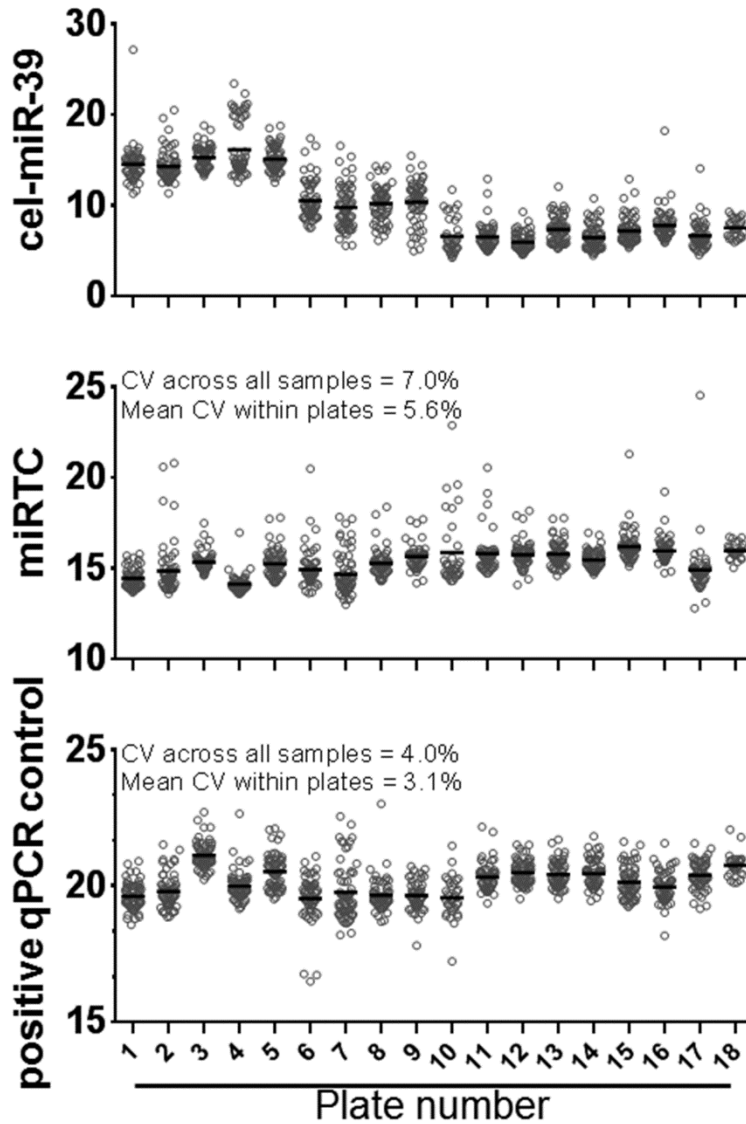


p-values Healthy vs.	APAP-OD patients		Mesothelioma patients									
	w/o AKI	with AKI	Pre Cp	4h after Cp	8h after Cp	12h after Cp	24h after Cp	48h after Cp	72h after Cp	96h after Cp	120h after Cp	144h after Cp
miR-21	0.0008	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
miR-200c	0.0013	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
miR-423	0.0005	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
KIM-1	<0.0001	<0.0001	0.7920	0.0036	0.3294	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Pre Cp vs.												
miR-21	-/-	-/-	-/-	0.0001	0.0018	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0001	0.0001
miR-200c	-/-	-/-	-/-	0.0143	0.0401	0.0006	0.0001	0.0001	0.0003	0.0664	0.0240	0.1627
miR-423	-/-	-/-	-/-	0.0002	0.0019	<0.0001	0.0001	0.0010	0.0001	0.0186	0.0037	0.0186
KIM-1	-/-	-/-	-/-	0.0026	0.5085	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0009	0.0002

Supplementary Figure 1 Urinary levels of miR-21, -200c, -423 and KIM-1 from both studies (APAP overdose and Cp treatment in cancer patients). Data sets were log2 transformed urinary levels presented as box plots (median with 25th and 75th percentiles) with 5th and 95th percentile as whiskers. 1. Red broken line represents the median level of the healthy group. T-test was used for p-value calculation with an adjusted significance cut-off of $p < 0.0006$ (bold).



Supplementary Figure 2 Serum creatinine inaccuracy as gold standard and its potential impact on clinical biomarker evaluation. Example from preclinical studies illustrating how misclassification of AKI based on SCr can affect biomarker profiles. Wistar rats were treated with Cp (1 or 3 mg/kg body weight, i.p.) or vehicle control. After three days miR-21 and KIM-1 were measured in urine. AKI grouping was performed based on corresponding histopathology results (tubular necrosis) or SCr increase compared to vehicle treated rats. Data is extracted from Pavkovic et al., 2014^{21, 22}.



Supplementary Figure 3 Coefficient of variability for technical controls across all samples and plates. Individual Ct values with means are plotted for the three technical controls (cel-miR-39, miRTC and positive qPCR control) for all 18 plates (1033 samples). For evaluation of the inter- and intraplate variation; coefficients of variation (CV%) were calculated for the technical controls and normalizer. Since three different concentrations were accidentally used for spiking of the cel-miR-39, an overall comparison was not performed. For miRTC and the positive qPCR control, the interplate efficiency is represented by the CV% across all samples, and the mean CV% within each plate represents the intraplate efficiency.