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Acute alcohol consumption has a significant impact on microRNA expression in the serum of healthy adults and has potential to confound toxicity biomarker development

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Introduction: Cell-free circulating microRNAs represent a reservoir for biomarker discovery. Promising candidates have been identified that may have clinical utility in pharmacology and toxicology.(1) In the Western world, recreational alcohol use is common in most societies. However, the effect of alcohol consumption on the expression of biomarkers is rarely studied. The objective of this study was to comprehensively profile the change in human circulating microRNA induced by acute recreational use of alcohol among healthy young adults in a pragmatic 'real world' setting.

Methods: South East Scotland Research Ethics Committee approved the study and informed consent was obtained from all subjects. Blood was collected from healthy volunteers (N=16) before and after unsupervised recreational consumption of alcohol (ethanol) at a student party. Routine biochemistry and haematology measurements were performed. Ethanol ingestion was quantified by measurement of its serum concentration. The change in the small RNA fraction of serum - which accompanied recreational alcohol use - was quantified using an RNA Sequencing protocol that incorporated unique molecular index assignment of the cDNA, which was sequenced on a NextSeq 500 platform.

Results: Blood ethanol concentration was undetectable at study entry in all subjects (<10mg/dL). After attending the party, the median concentration was 78mg/dL [IQR: 69-103. Min-max 20-173] - an ethanol median concentration below the English drink drive limit. There were no clinically significant changes in routine biochemistry and haematology. RNA sequencing demonstrated statistically significant changes [P value <0.05, fold change 2 or more] in 360 microRNA species [a quarter of total microRNAs identified; median fold increase 2.6 [IQR:2.1-2.5. Max: 3.7]]. 74 microRNAs were consistently increased in 14 subjects after alcohol consumption.

Discussion: In comparison with standard haematological and biochemical clinical tests, the microRNA composition of human serum is more dynamic. Environmental factors can have a significant impact over a relatively short time period and alcohol consumption should be considered when developing a microRNA for clinical use. Within its context of use the fold change of a microRNA biomarker must be large enough to allow accurate patient stratification without the risk of false positive results being produced by modest alcohol consumption.

References:

1. Vliegenthart AD *et al.* (2015) Sci Rep. **5:**15501.