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THE HUMAN BIOFLUID RNA ATLAS: EXPANDING THE LIQUID BIOPSY FIELD BEYOND THE BLOOD STREAM

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Liquid biopsies offer a non-invasive alternative to tissue biopsies for both diagnosis and monitoring of treatment response. Over the last decade, extracellular RNAs (exRNAs) circulating in the bloodstream have been identified as potential biomarkers. Apart from plasma and serum, many other human biofluids can be collected and may contain diagnostic, prognostic or theragnostic biomarker potential.

The goal of this study is to unravel the extracellular transcriptome of 22 human biofluids (amniotic fluid, aqueous humor, bile, bronchial lavage fluid, breast milk, cerebrospinal fluid, colostrum, gastric fluid, pancreatic cyst fluid, peritoneal fluid, platelet-free plasma, platelet-poor plasma, platelet-rich plasma, saliva, seminal fluid, serum, sputum, stool, synovial fluid, sweat, tear fluid and urine), each collected from at least two donors. All fluids were centrifuged and frozen within two hours after collection. Total RNA was isolated from the cell-free supernatant and spike-in RNA controls were added to enable absolute quantification of exRNAs. The RNA content was subsequently characterized in all biofluids using established small RNA and mRNA sequencing workflows. Analysis of the small RNA-sequencing data revealed the presence of small RNA species in all biofluids. Highly variable small RNA concentrations (up to 100 000-fold) and marked differences in RNA biotypes among biofluids were observed. Analysis of the mRNA profiles is currently ongoing. By applying computational deconvolution methods, we aim to identify the cell types and tissues that are contributing to the exRNA repertoire in these biofluids. These novel insights may provide a more rational selection of relevant biofluids for biomarker discovery in various human diseases.