Dramatic differences in RNA purification kit performance in the extracellular RNA quality control study – important considerations for liquid biopsies

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In search of easily accessible biomarkers, extracellular RNAs (exRNAs) have emerged as potential candidates. Unfortunately, exRNA quantification is influenced by many pre-analytical variables whose impact is still unknown. A comprehensive quality control study for blood-based liquid biopsies, evaluating these pre-analytical variables in a controlled and systematic manner, is currently lacking. Therefore, we initiated the exRNA quality control (exRNAQC) study to systematically evaluate the effect of the type of blood collection tube (n=10), time between blood draw and plasma preparation (n=3), centrifugation speed during plasma preparation (n=5), input volume and RNA purification method (n=8). The impact of these factors is assessed by unbiased transcriptome exRNA profiling of all microRNAs and messenger RNAs from healthy donors' plasma using established RNA-sequencing workflows. In the first phase of our study, we already observed differences in RNA purification kit performance in terms of reproducibility, yield and transcriptome complexity. We are currently analyzing the blood collection tube exRNA profiles. Once all pre-analytical variables are evaluated separately, we will integrate our findings into a full factorial experiment and plan dedicated follow-up experiments to validate our results. Using this systematic approach, we aim to develop quality control metrics and guidelines for the study of exRNA in order to facilitate further progress in the field.