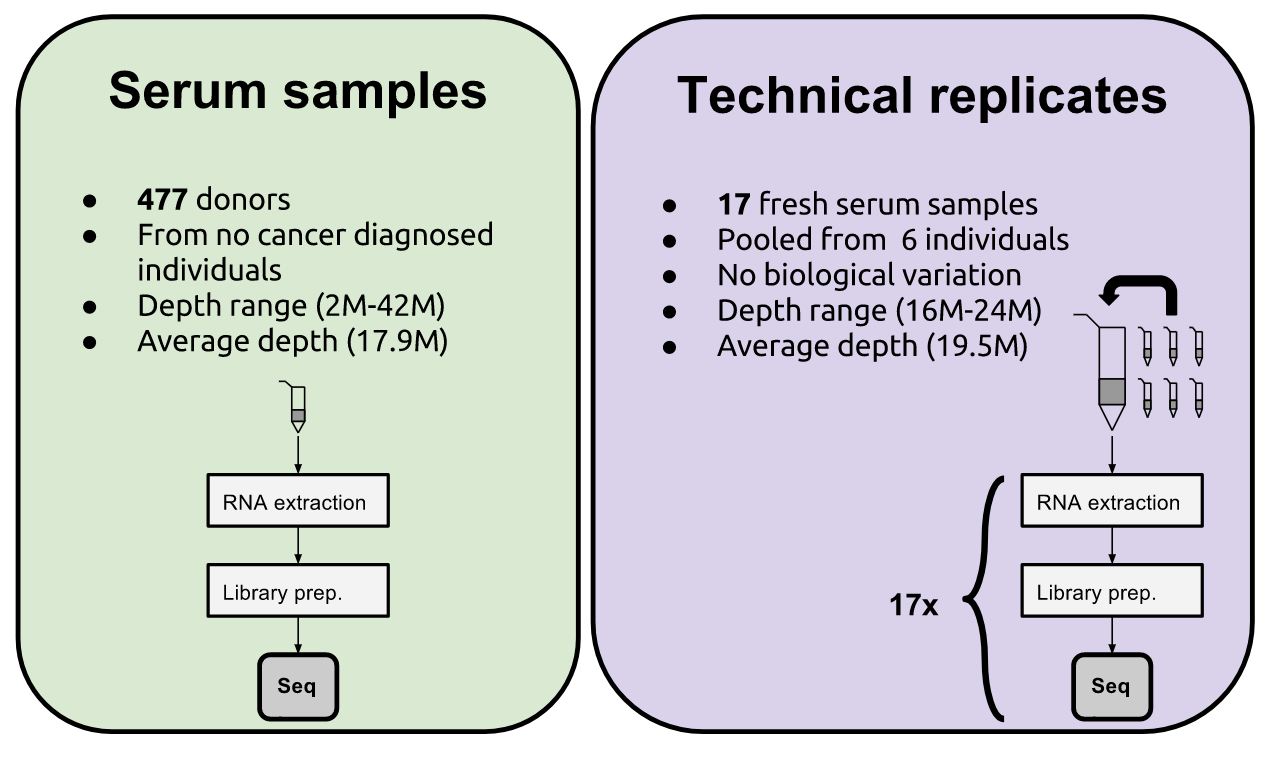
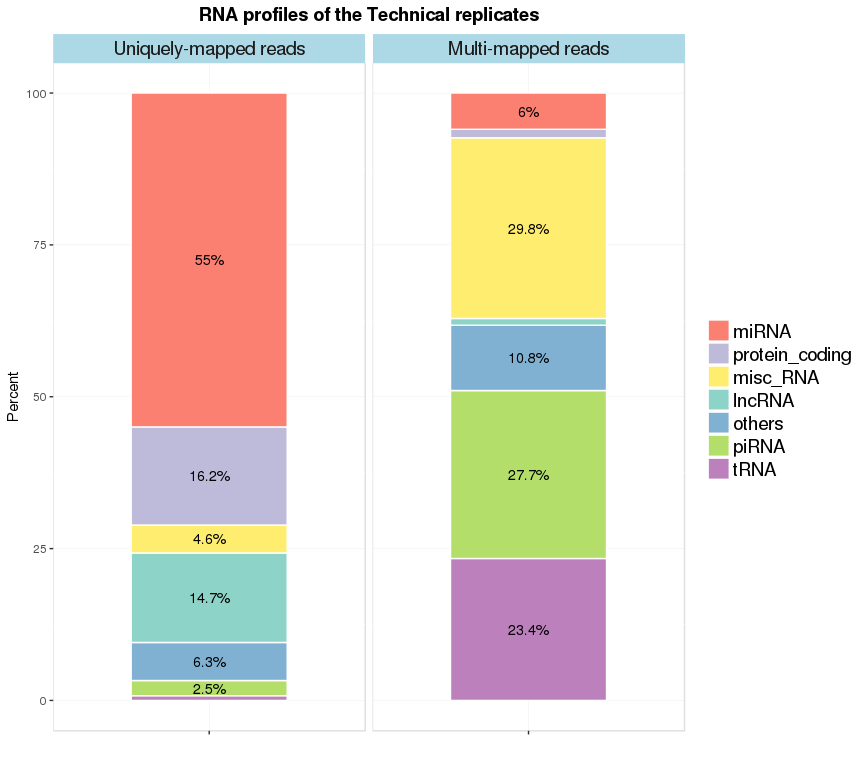
**A comprehensive profile of circulating RNAs in human serum**

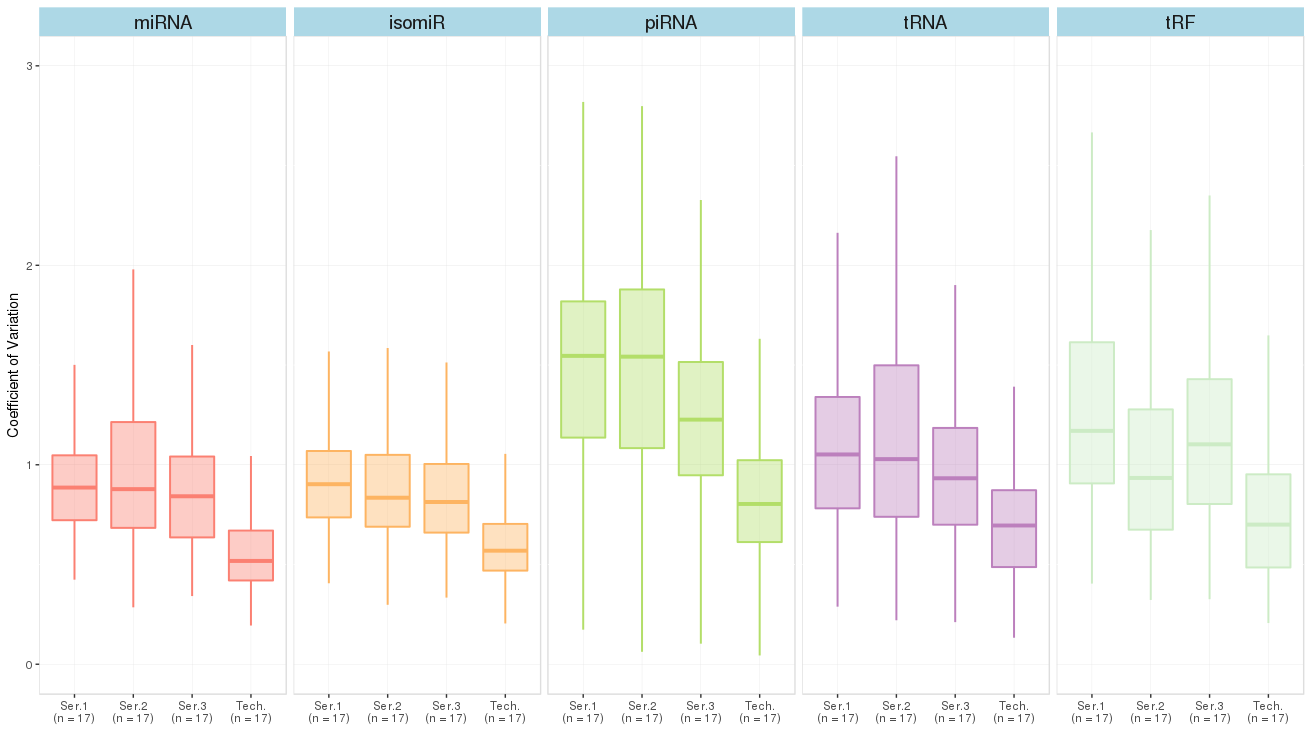
**Supplementary Figures**



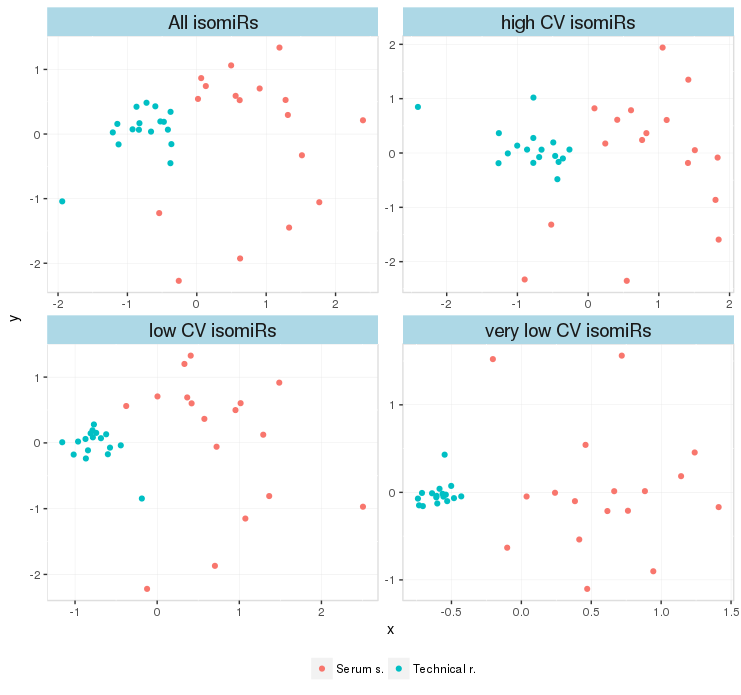
**Supplementary Figure 1.** A summary of the overall design and the sample groups in this study. There are two groups of samples: serum and technical replicates.



**Supplementary Figure 2.** An overall classification of the mapped reads of the technical replicates (n=17). **(A)** This pie-chart, generated using uniquely-mapped reads, shows an abundance of miRNAs followed by protein-coding mRNAs and misc-RNAs. This is quite similar with the Figure 1 of the main manuscript. **(B)** Allowing multi-mapped reads is affecting overall profiles. For multi-mapped reads, misc-RNAs (yellow) are the most abundant RNA type followed by piRNAs (green) and tRNAs (purple). The annotations of GENCODE v26 and piRBase were used to create these plots.



**Supplementary Figure 3.** Another version of the Figure 4 of the main manuscript. Here we randomly sub-sampled the serum samples to compare CV values between identical sized sub-samples of the serum and technical replicates. All the serum sub-samples have larger CV values than their associated technical replicates (Mann-Whitney U test, p < 0.0001). This shows that the circulating RNAs contain biological signal.



**Supplementary Figure 4.** We divided the detected isomiRs into four groups: all the serum and technical replicate isomiRs (n= 1642), isomiRs with low CV (n= 797), isomiRs with very low CV (n=403) and lastly isomiRs with high CV (n= 845) in the technical replicates. A hierarchical clustering of the serum and technical replicates using isomiR expression data shows that both the low CV isomiRs and very low CV isomiRs are successfully clustering because they do not have much internal variation. Furthermore, the very low CV group has 403 isomiRs which are enough for clustering. The high CV isomiRs are not successful because of high technical variation.



**Supplementary Figure 5.** In this figure, the x-axis shows the age of samples (in years) while the y-axis shows the number of sncRNAs identified. Each color represents a different sncRNA type. This analysis summarizes that sample age has a significant effect on overall sncRNA profiles (p < 0.01) but not very strong.