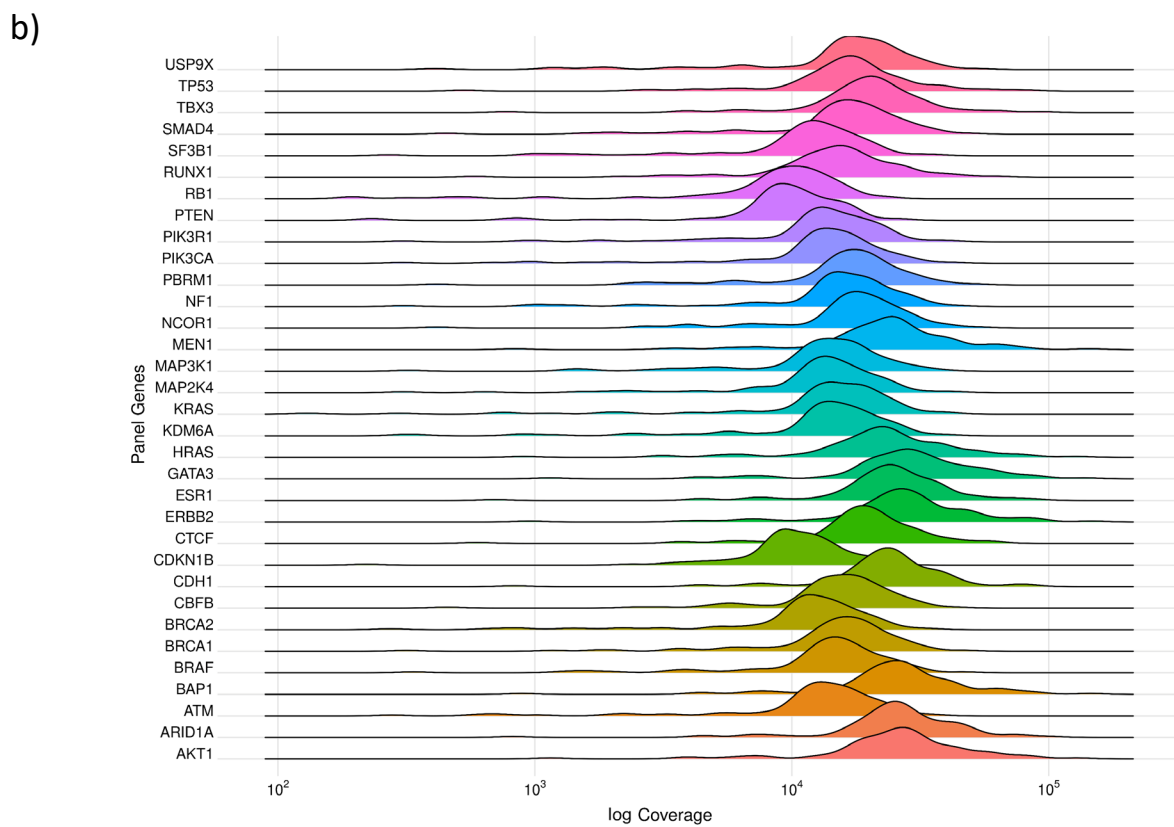
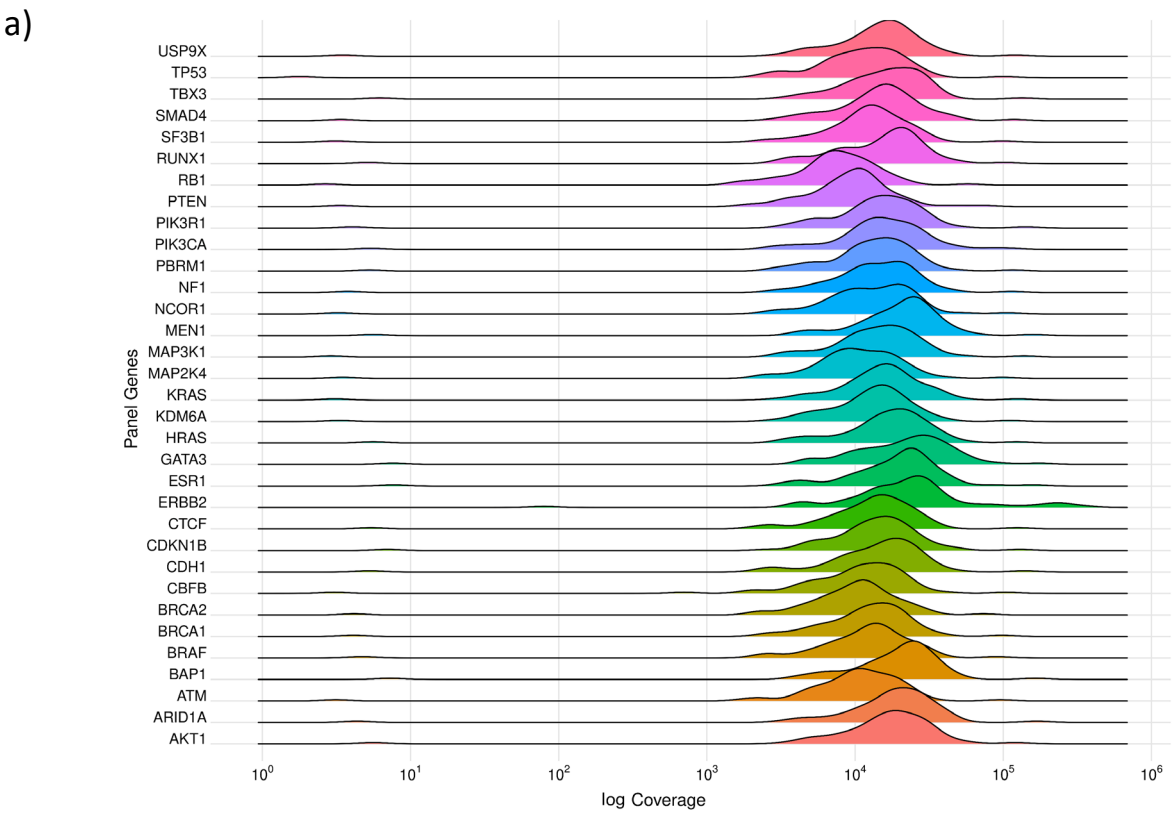
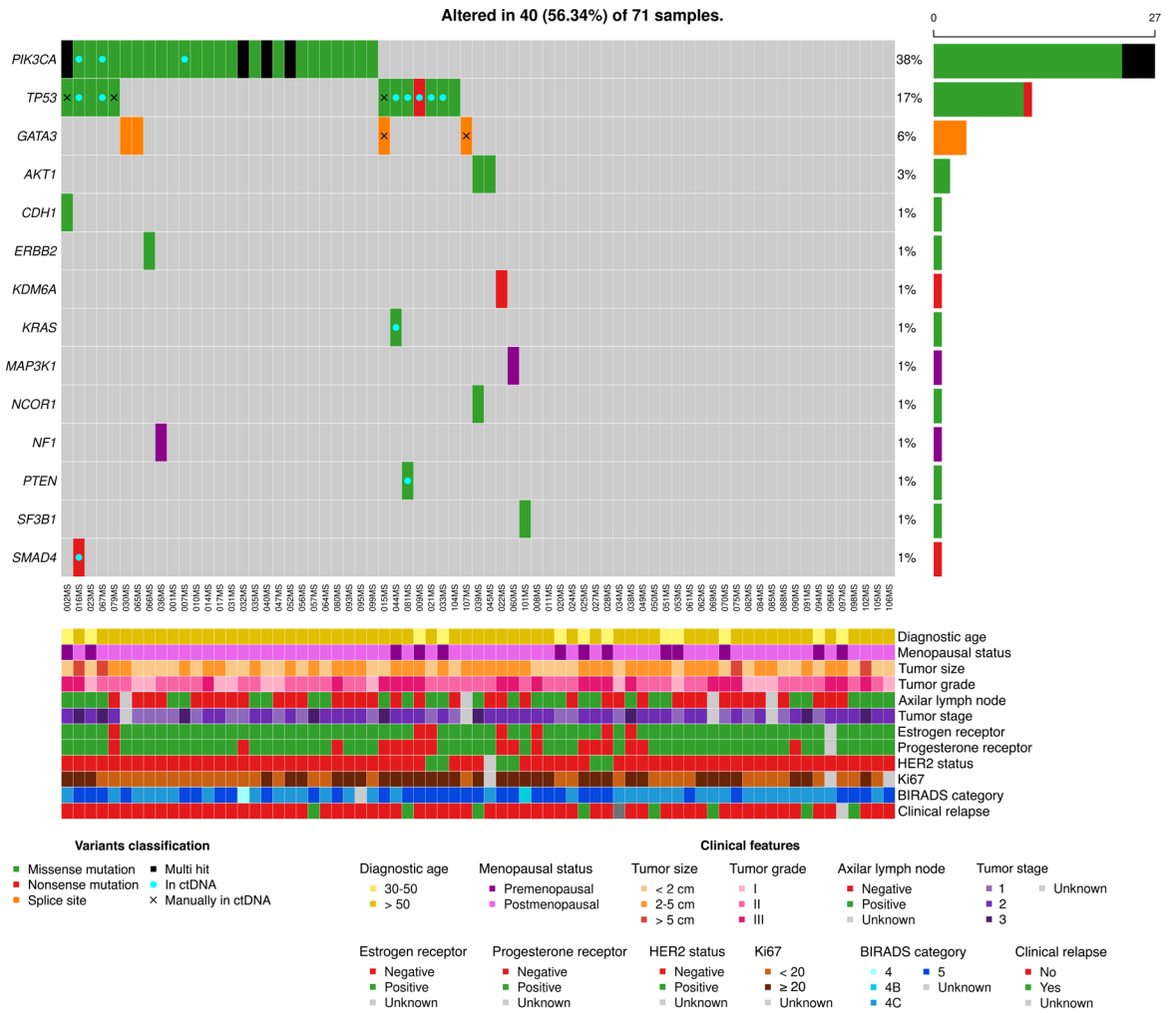


**Figure S1. Median sequencing coverage in tumor and plasma samples before and after bioinformatic processing.**

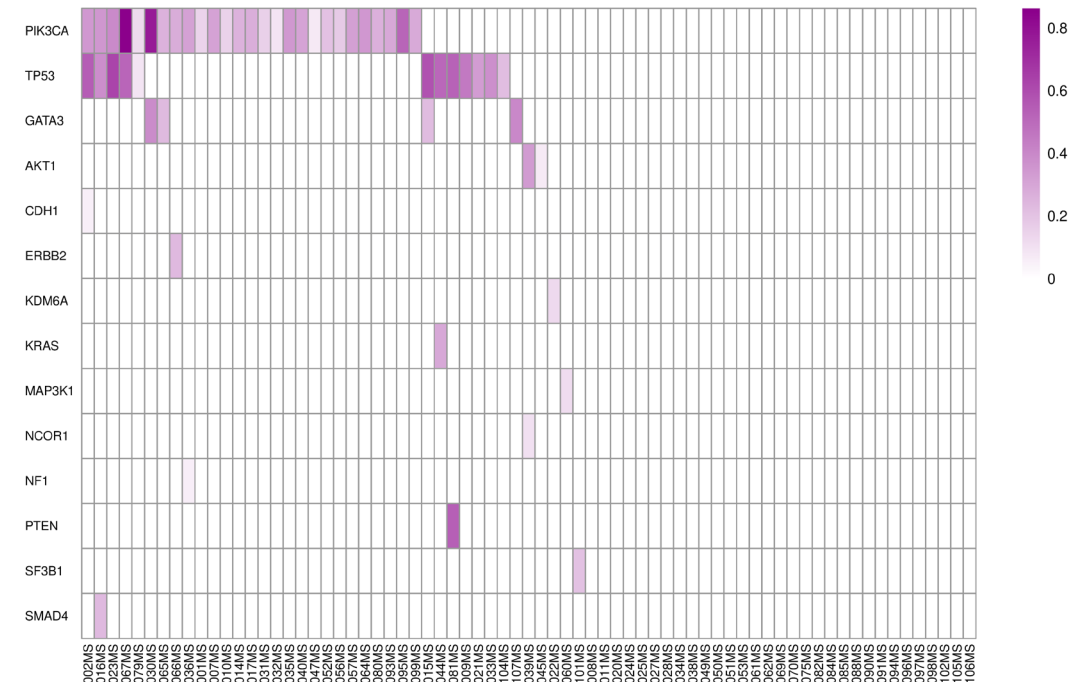


**Figure S2. Sequencing coverage in a) tumor and b) plasma samples for the genes included in the custom panel**

a)

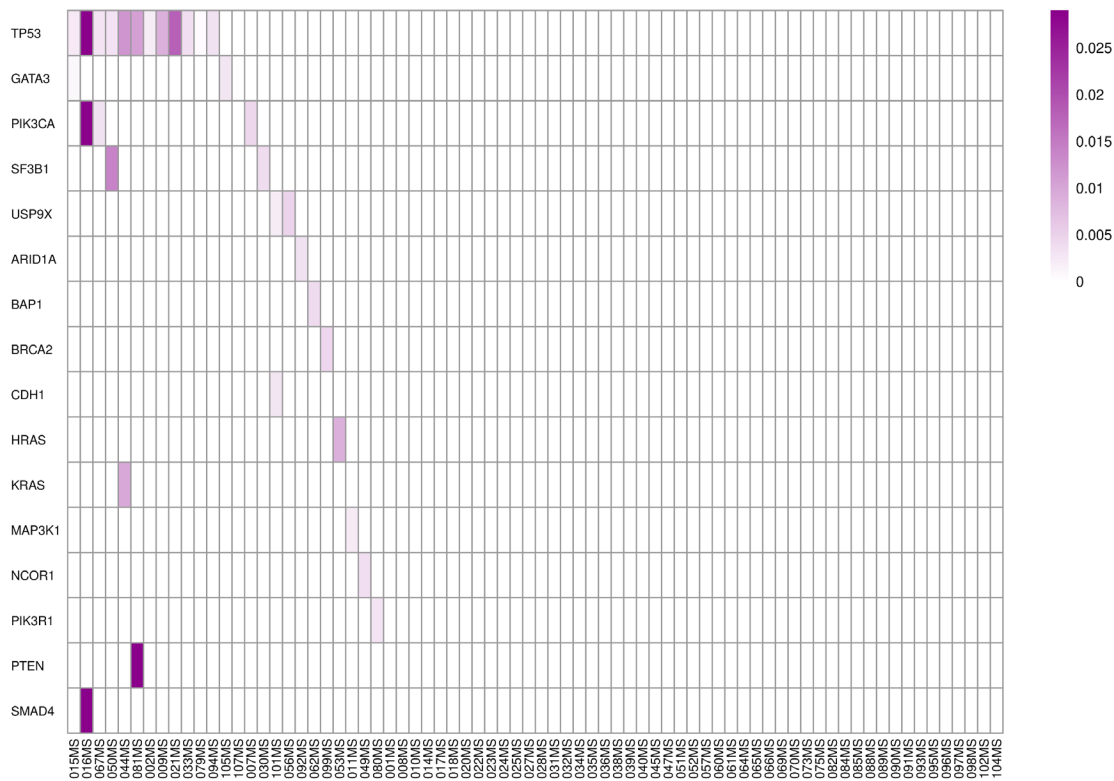


b)



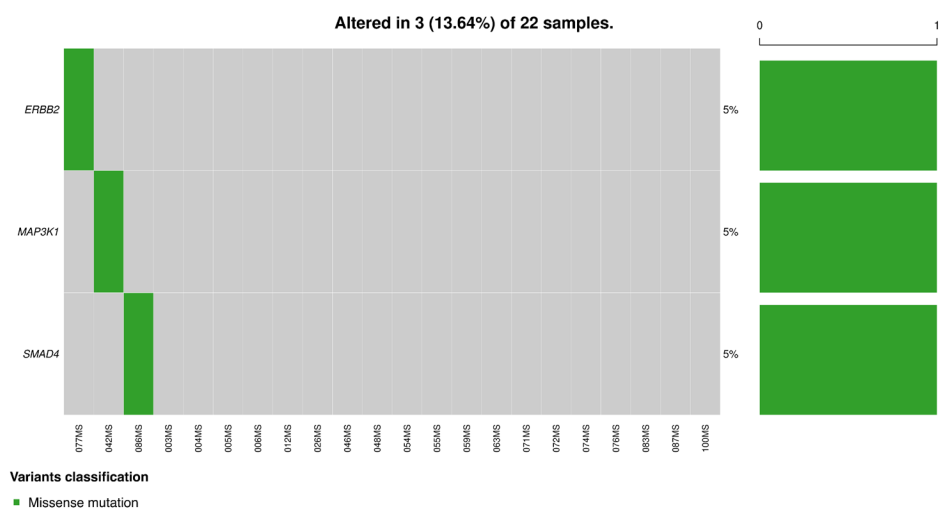
**Figure S3. Mutations identified in the tumor DNA sequencing from the samples included in the study. a)** OncoPrint showing in the *top part* the mutations observed in tumor samples indicating whether they were found in plasma samples. In the *bottom part*, the patients' clinicopathological characteristics are represented. **b)** Variant allele frequencies of the mutations previously shown.

A)

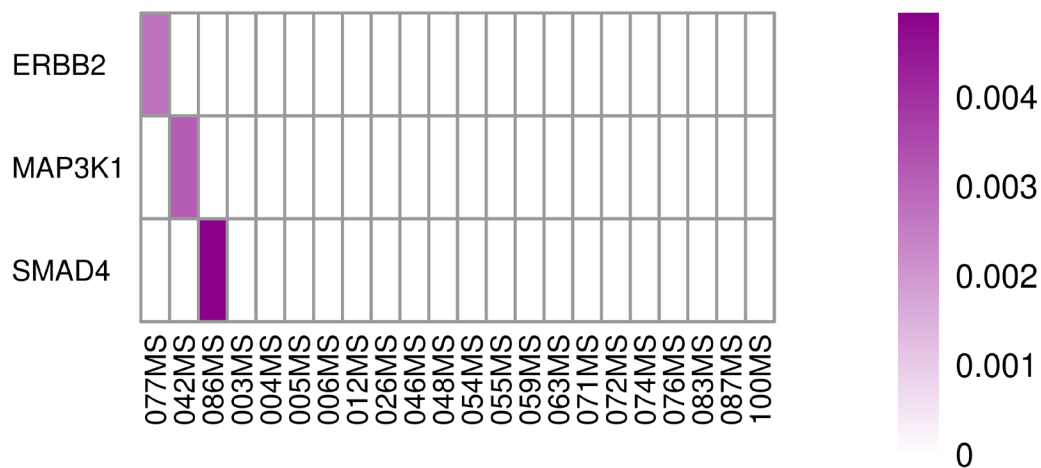


**Figure S4. Variant allele frequencies of the identified plasma mutations.**

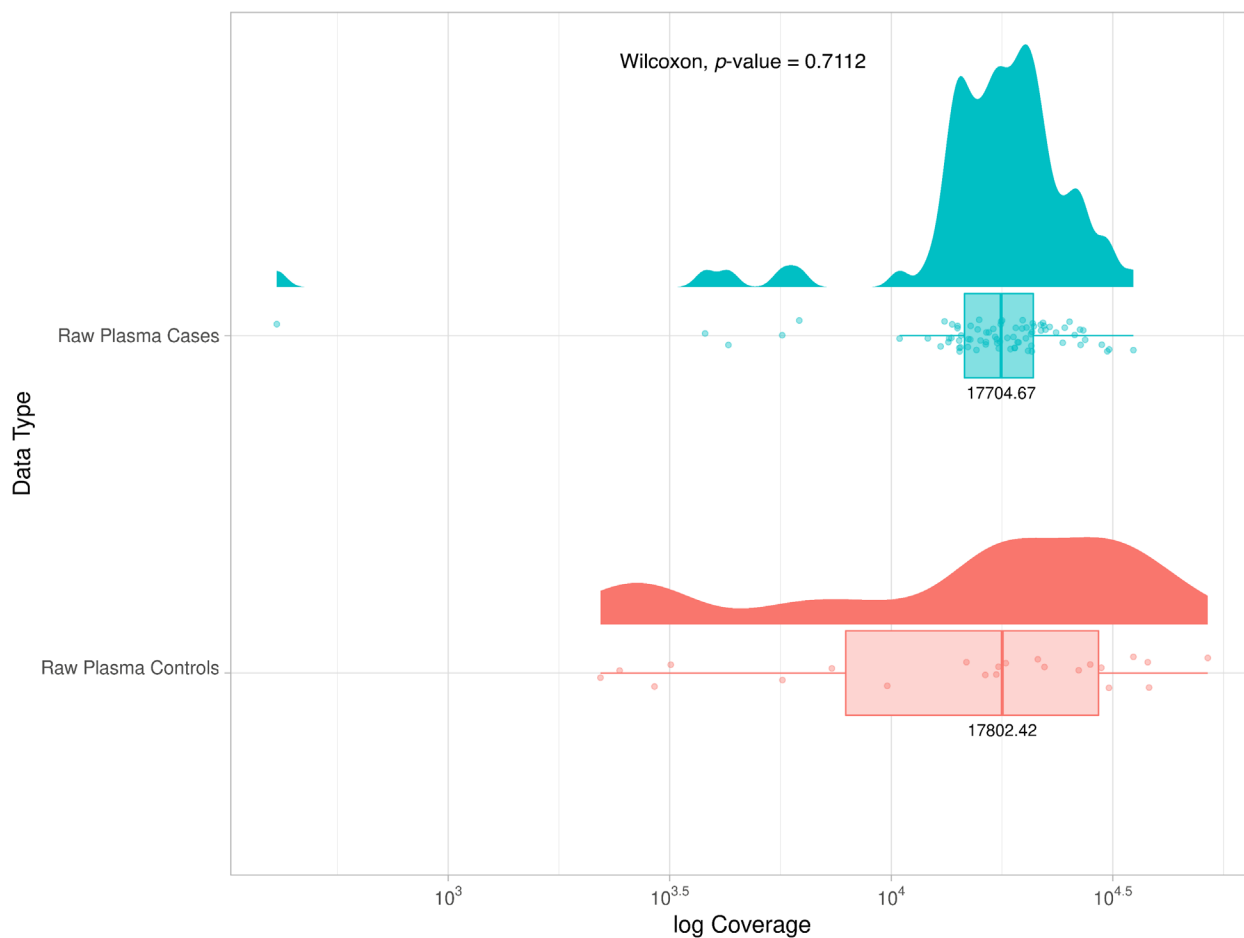
a)



b)

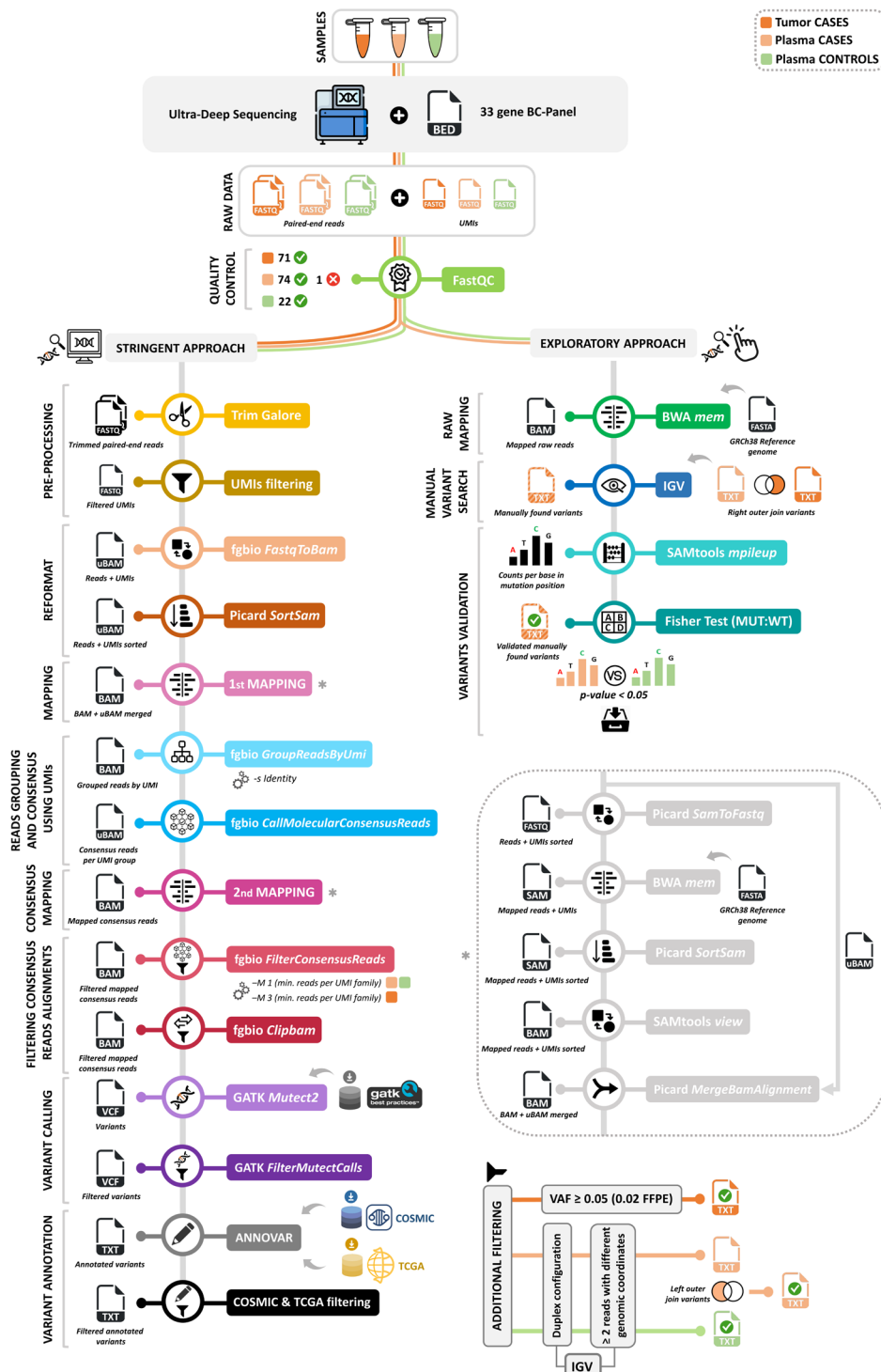


**Figure S5. Mutations identified in the plasma samples from healthy women. a)** Variants observed in the 22 sequenced plasma samples. **b)** Variant allele frequencies of the identified mutations.



**Figure S6. Median sequencing coverage in plasma samples from patients and healthy individuals.** Not statistically significant Wilcoxon  $p$ -value test is shown.

# BC SOMATIC VARIANT DETECTION IN PLASMA



**Figure S7.** Schema representing the employed custom bioinformatic pipeline. Quality control was performed in raw sequencing data and the following steps were conducted: *Stringent approach*. Raw sequencing reads were (1) pre-processed and (2) reformatted for the subsequent (3) mapping step to the reference genome; (4) aligned reads were grouped by UMI and the generated consensus reads were (5) mapped again to the reference genome; (6) consensus reads supported by a minimum number of reads were kept and forward and reverse reads overlapping regions were removed; (7) variant calling using gatk resource bundle data for germline and non-cancer variants was performed followed by (8) variant annotation and selection. Tumor and plasma variants not detected in control samples and supported by more than 2 reads with different genomic coordinates and duplex configuration were identified. *Exploratory approach*. (1) Raw sequencing reads were mapped and (2) variants found called in tumor samples but not in plasma samples were manually checked and (3) assessed performing a Fisher test.