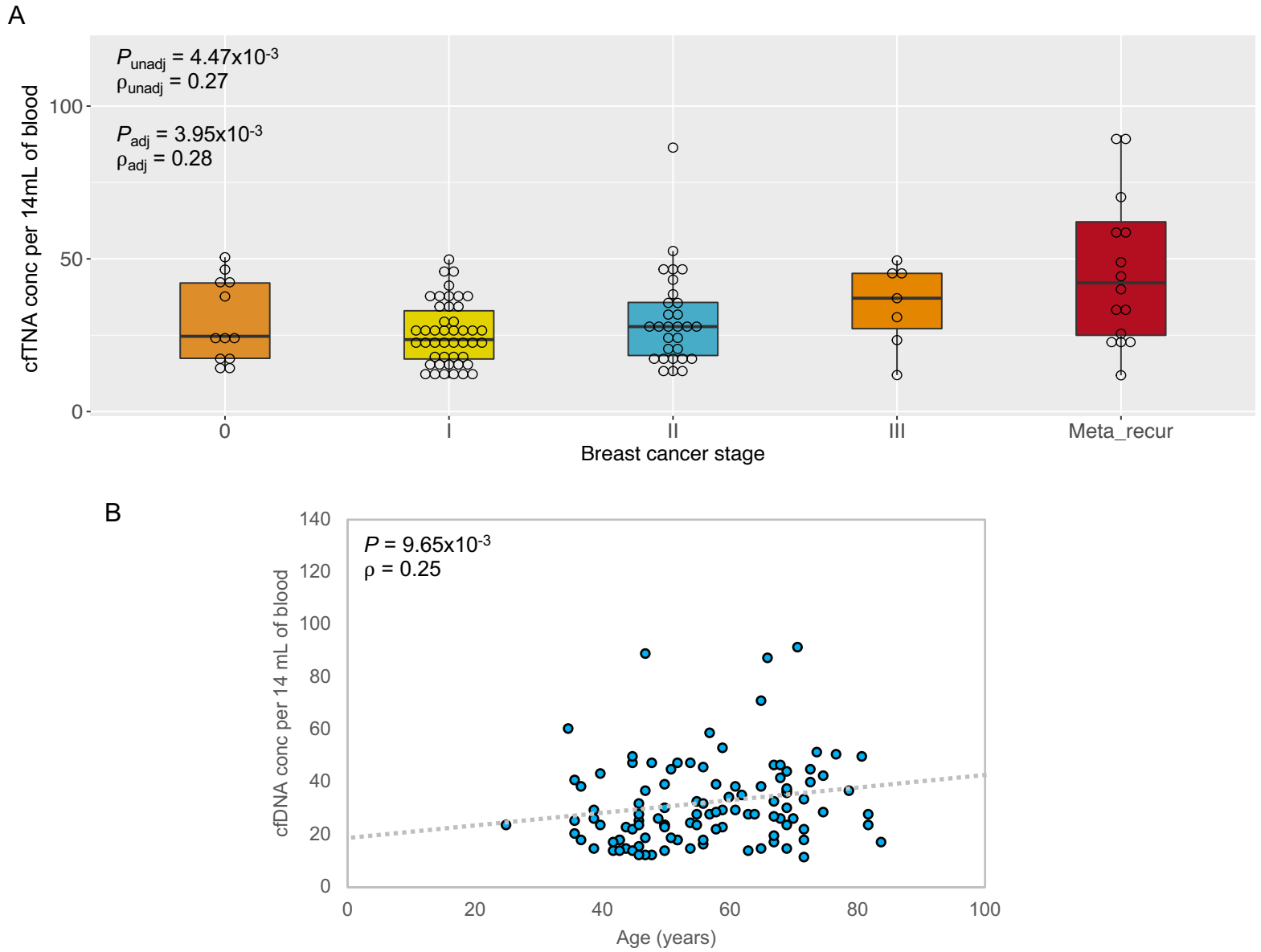


Figure S1. Association of cfTNA concentration with (A) breast cancer disease stage and (B) age. In A, *P*-value and correlation coefficient (ρ) calculated using Spearman's rank correlation test for breast cancer stage and cfTNA concentration (P_{unadj}) and for breast cancer stage and cfTNA concentration adjusted for age of patients (P_{adj}). In B, *P*-value and correlation coefficient (ρ) calculated using Spearman's rank correlation test. The box signifies the interquartile range (IQR) of the cfTNA concentration (ng per 14mL blood). Median is denoted by a horizontal line within the box. The whiskers define the lower and upper adjacent values that are 1.5 x IQR on either side. Distribution of cfTNA concentration is shown by the beeswarm plot.

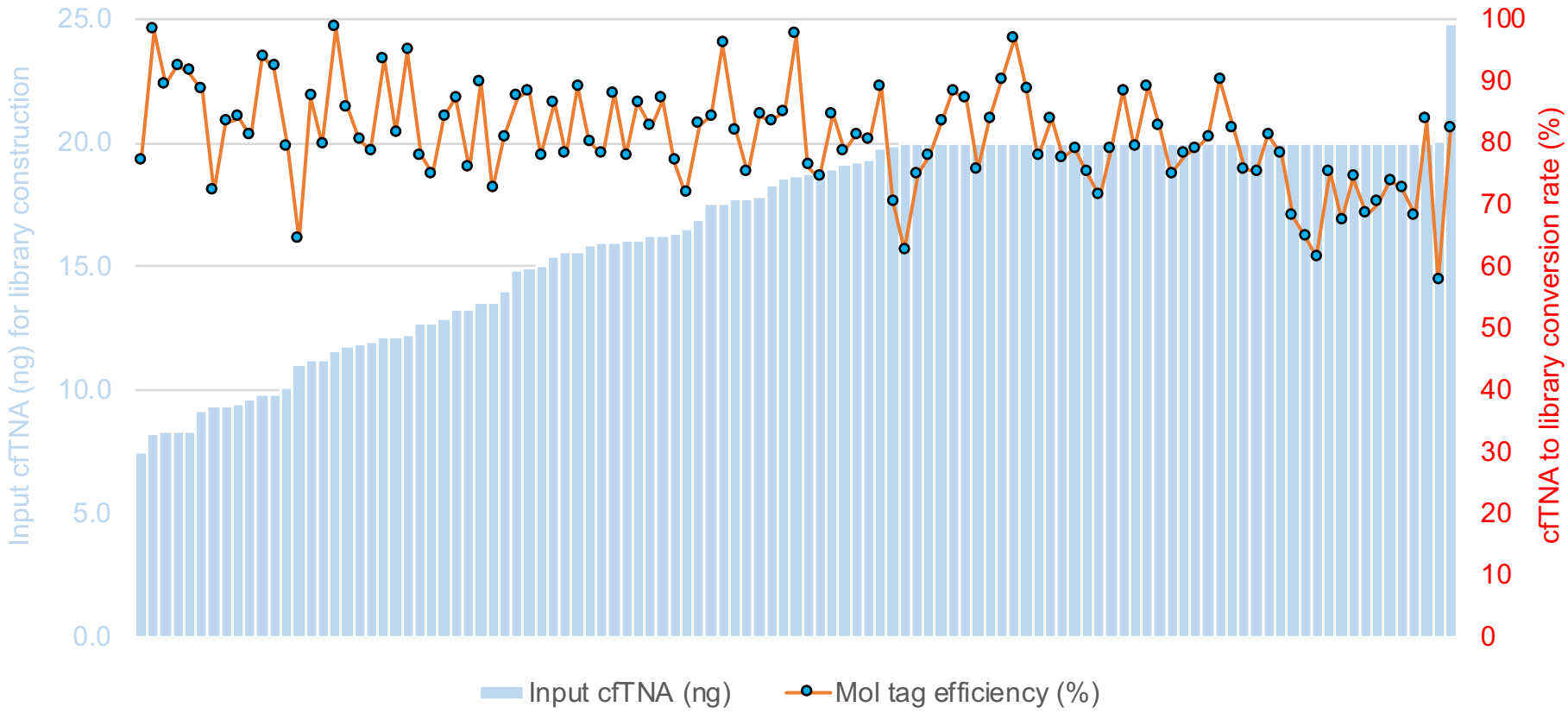
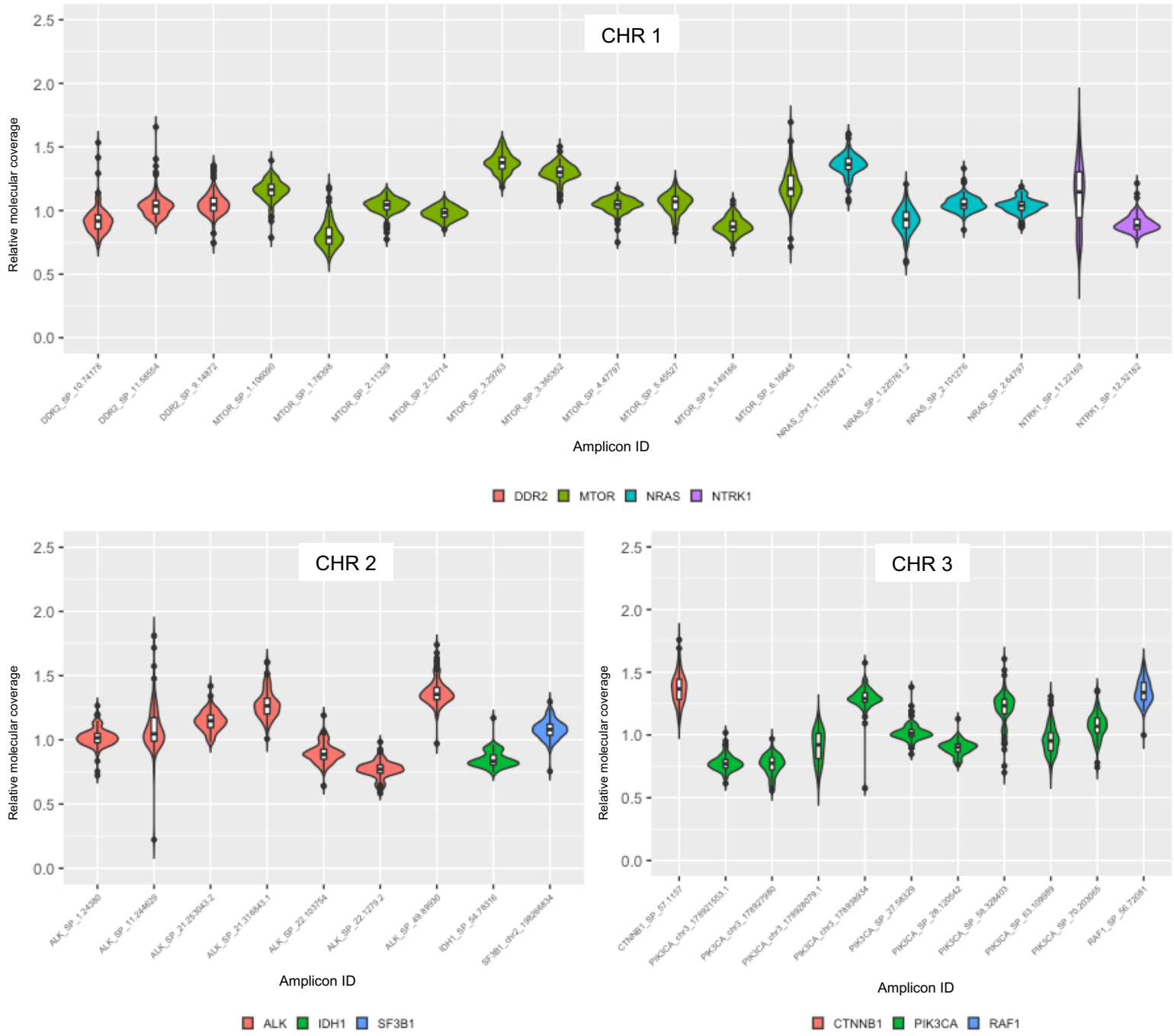


Figure S2. Cell-free total nucleic acid (cfTNA) input and library conversion rate of breast cancer samples. Bar signifies amount of cfTNA input (ng) and line refers to corresponding conversion rate into libraries (%). Each vertical bar or data point represents a single sample. Library conversion rate was calculated using the theoretical assumption that 10 ng of cfTNA would contain ~3000 haploid genome equivalents

Figure S3


CHR 1
Relative molecular coverage
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2.0
1.5
1.0
0.5
0.0
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DDR2_SP_11.56554
DDR2_SP_9.14872
MTOR_SP_1.106090
MTOR_SP_1.75398
MTOR_SP_2.11329
MTOR_SP_2.52714
MTOR_SP_3.29763
MTOR_SP_3.365362
MTOR_SP_4.47797
MTOR_SP_5.40527
MTOR_SP_6.149186
MTOR_SP_6.16645
NRAS_chr1_115256747.1
NRAS_SP_1.225761.2
NRAS_SP_2.101276
NRAS_SP_2.64797
NTRK1_SP_11.22169
NTRK1_SP_12.32182
Amplicon ID
DDR2
MTOR
NRAS
NTRK1
CHR 2
Relative molecular coverage
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2.0
1.5
1.0
0.5
0.0
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ALK_SP_11.244639
ALK_SP_21.253043.2
ALK_SP_21.316843.1
ALK_SP_22.103754
ALK_SP_22.1279.2
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Amplicon ID
ALK
IDH1
SF3B1
CHR 3
Relative molecular coverage
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2.0
1.5
1.0
0.5
0.0
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PIK3CA_chr3_178921553.1
PIK3CA_chr3_178927960
PIK3CA_chr3_178928079.1
PIK3CA_chr3_178936094
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Amplicon ID
CTNNB1
PIK3CA
RAF1

Figure S3 continued …

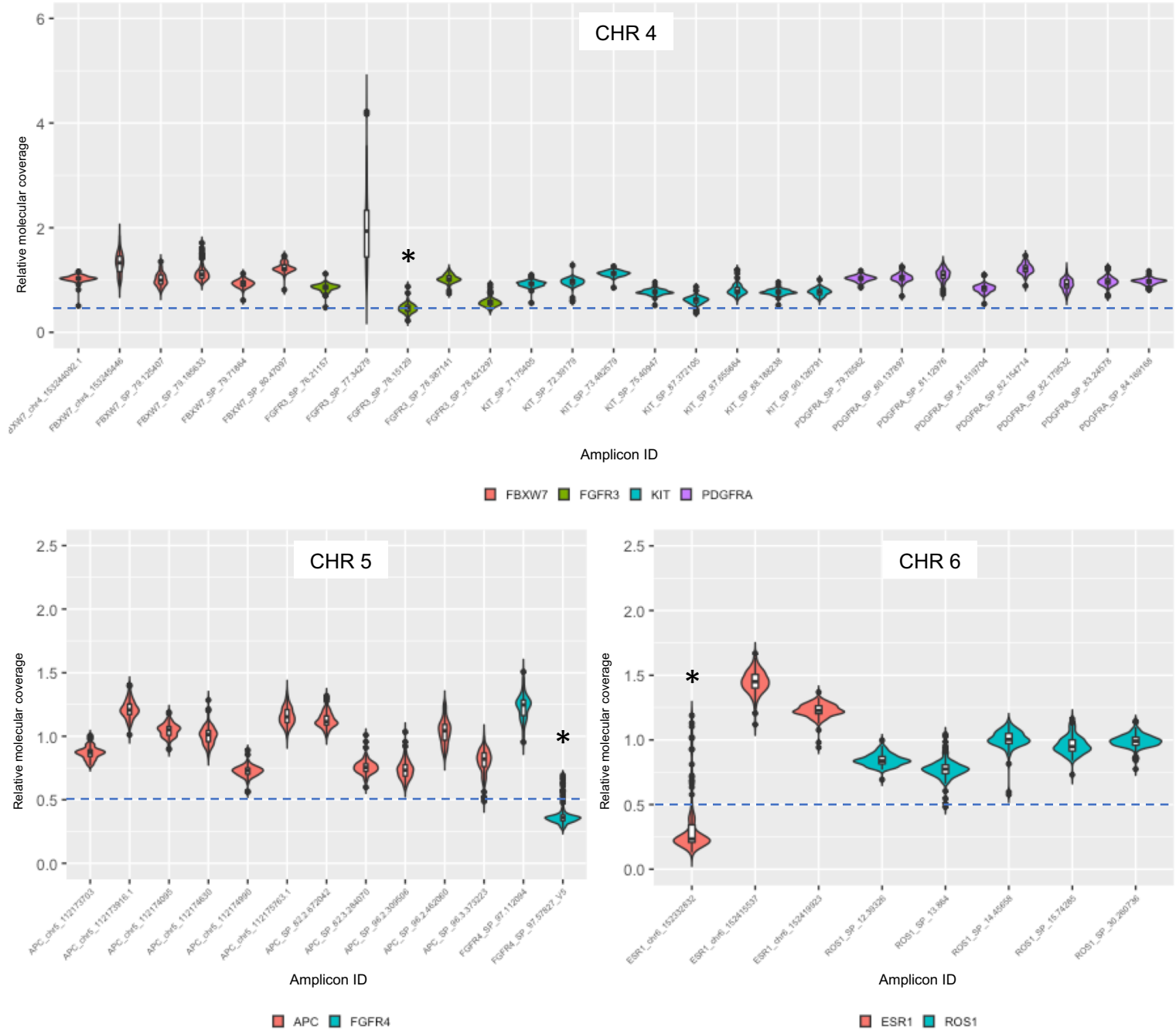
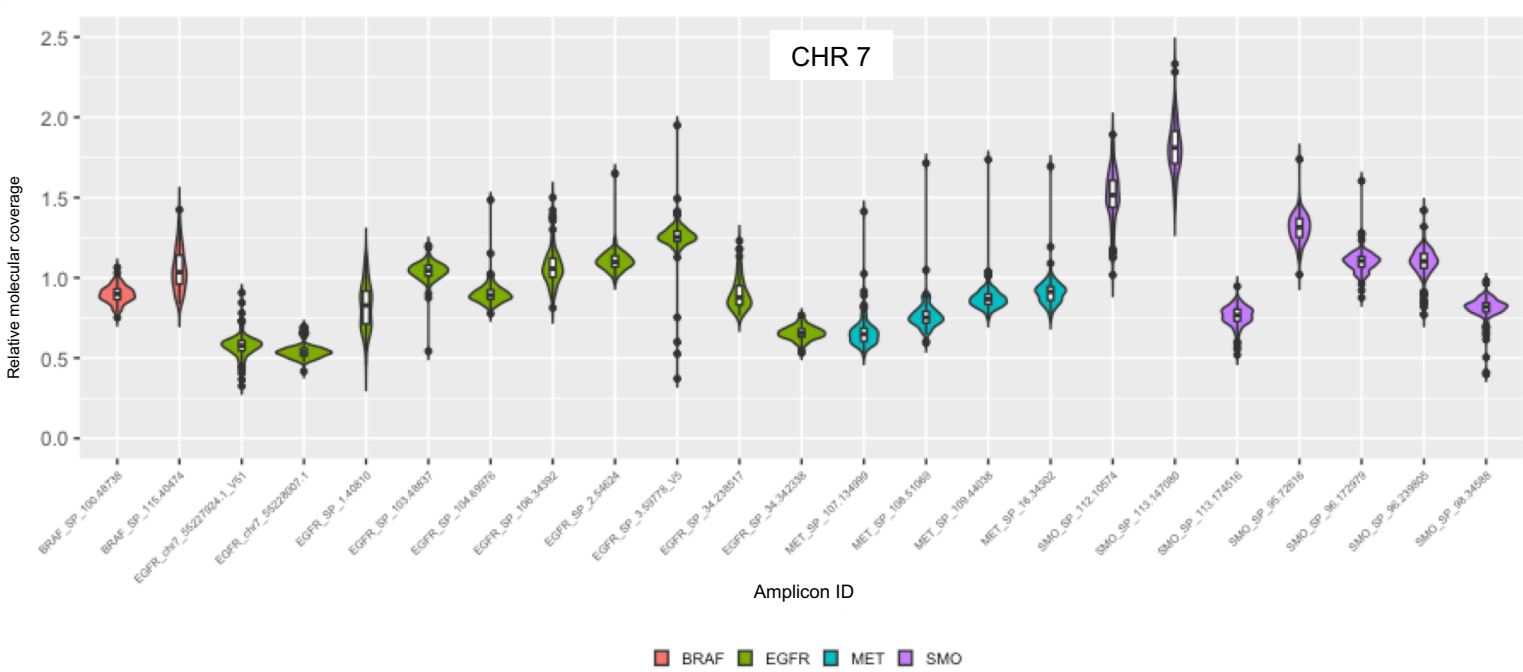


Figure S3 continued …



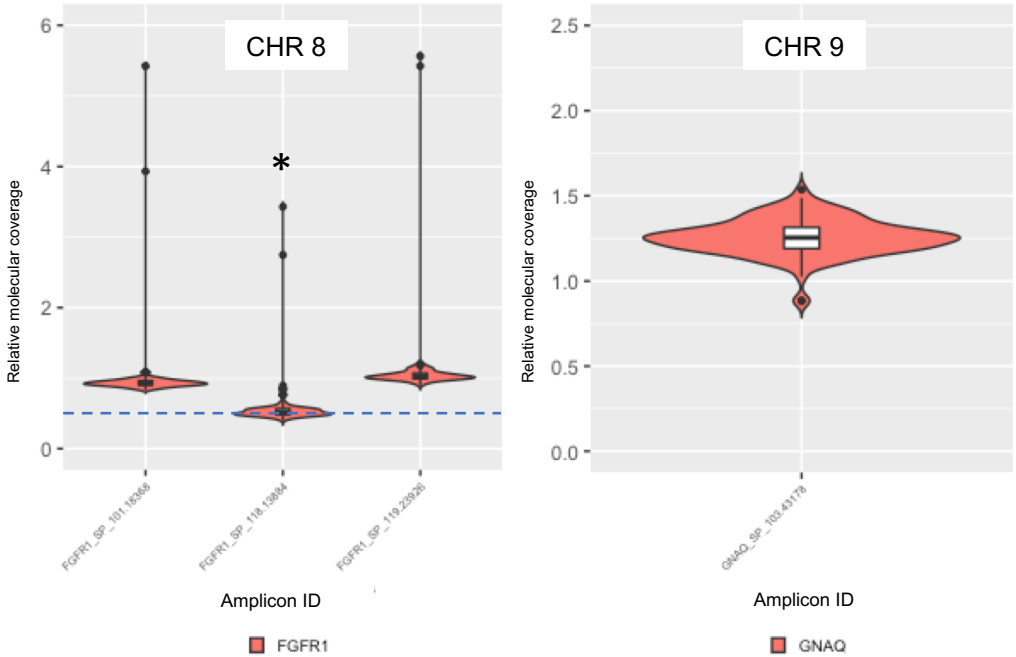


Figure S3 continued …

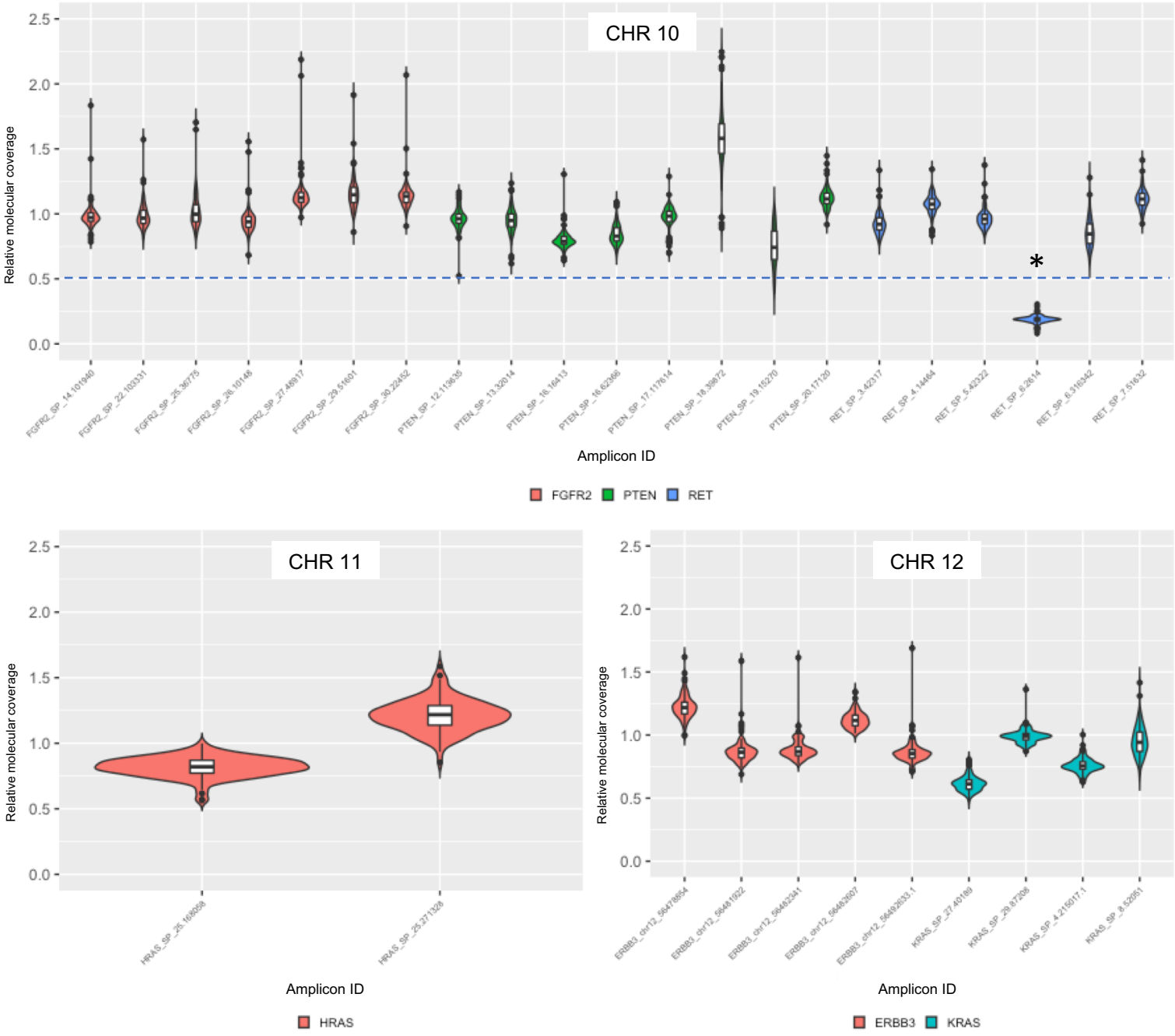
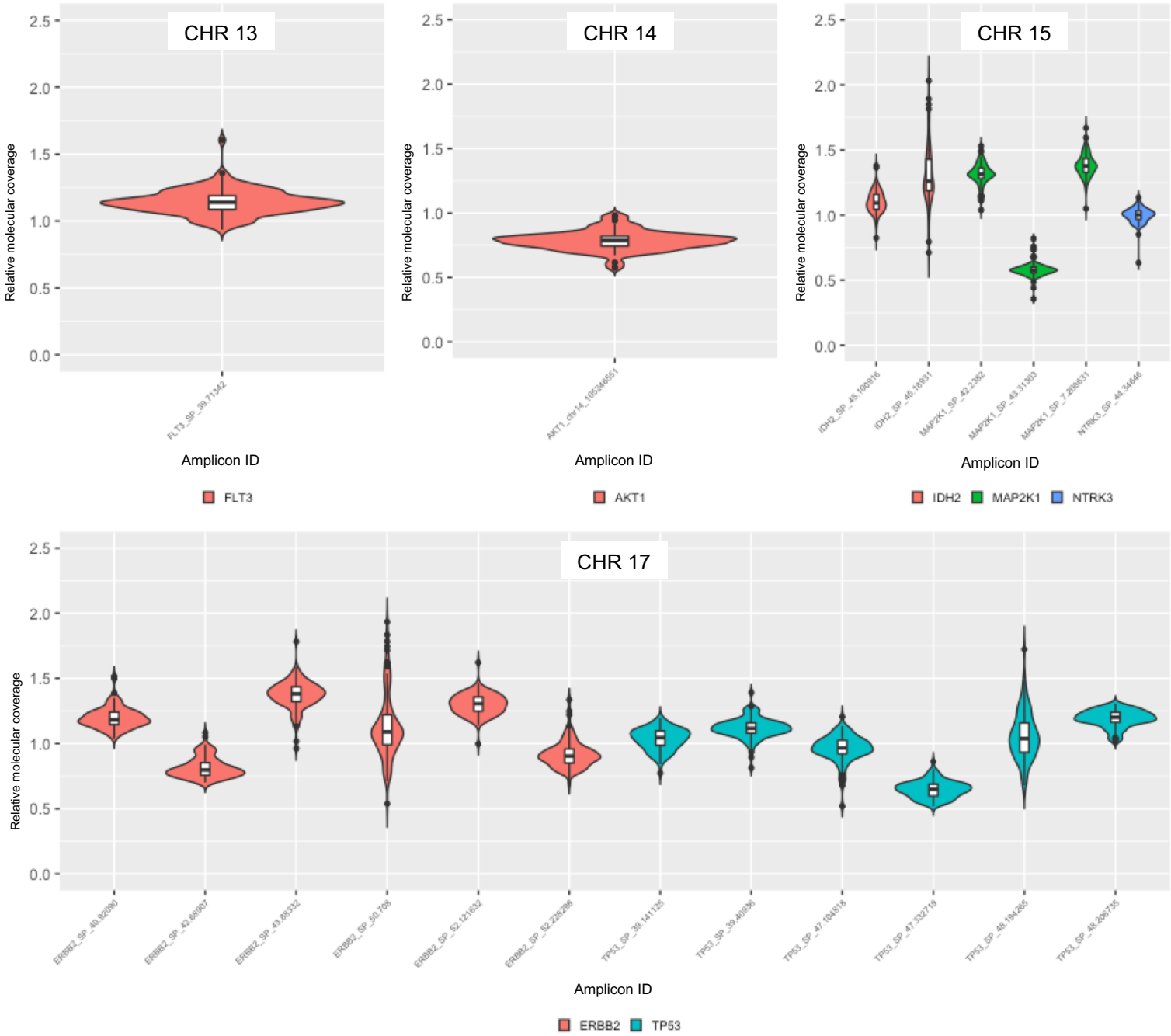


Figure S3 continued …



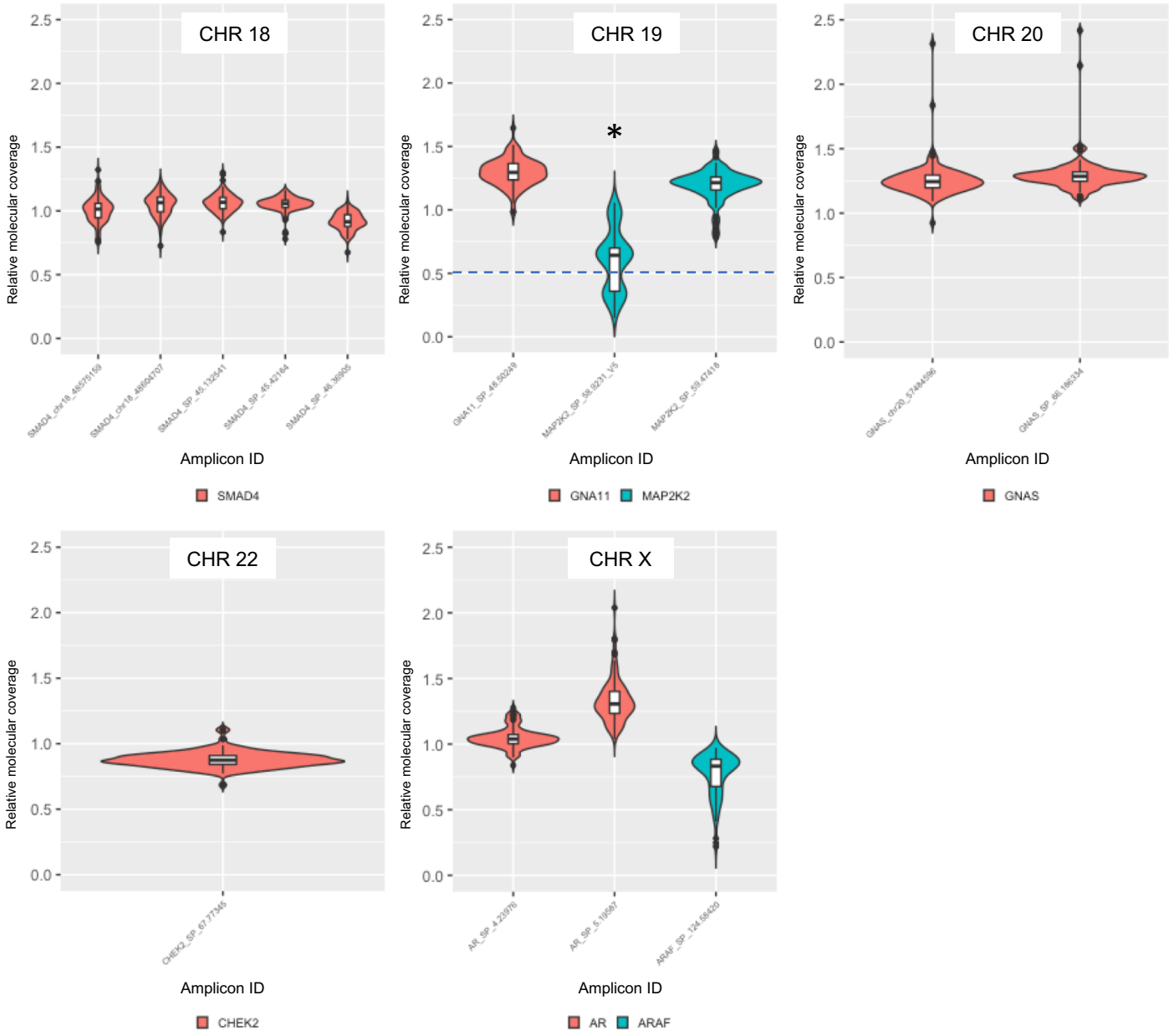


Figure S3. Distribution of the relative consensus coverage of amplicons. The combination violin and box plot demonstrates the distribution of relative molecular coverage (RMC) for all 109 patients per amplicon, grouped by chromosome with colors denoting different genes. The box signifies the interquartile range (IQR) of the RCC. Median is denoted by a horizontal line within the box The whiskers define the lower and upper adjacent values that are 1.5 x IQR on either side. The density distribution in the violin plot demonstrates the distribution of data points. Where amplicons show RMC<0.5 in at least 25% of all patients, a threshold line is drawn, and the amplicon marked with an asterisk. RMC is calculated by normalizing consensus coverage of each individual amplicon against the median consensus coverage of all amplicons within a particular sample.

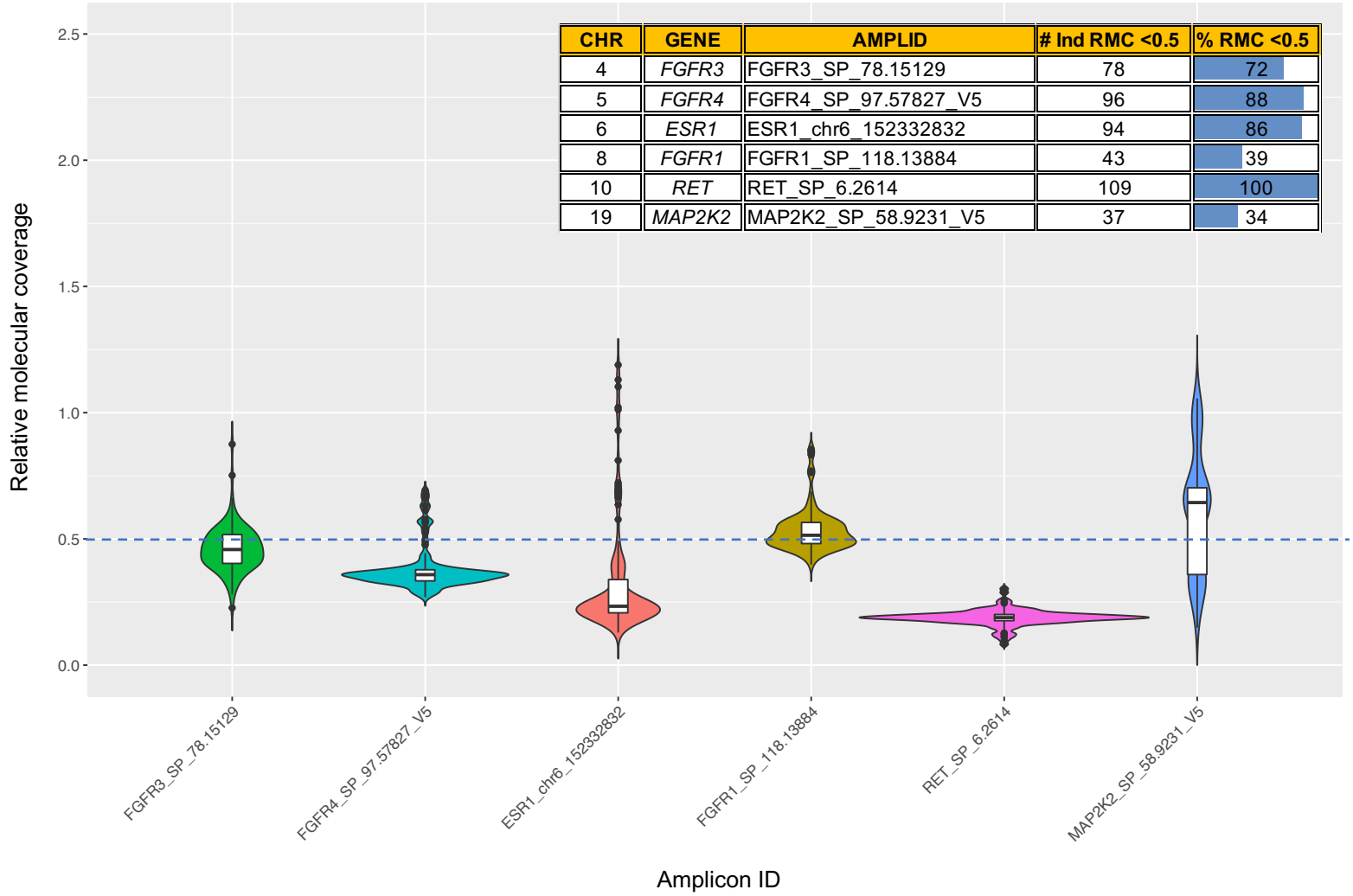


Figure S4. Amplicons showing relative molecular coverage (RMC) of <0.5 in at least 25% of total 109 patients. The violin plot denotes the density distribution of RMC of each patient for a particular amplicon. The box plot denotes the median, IQR and lower/upper adjacent values of the amplicon RMC.

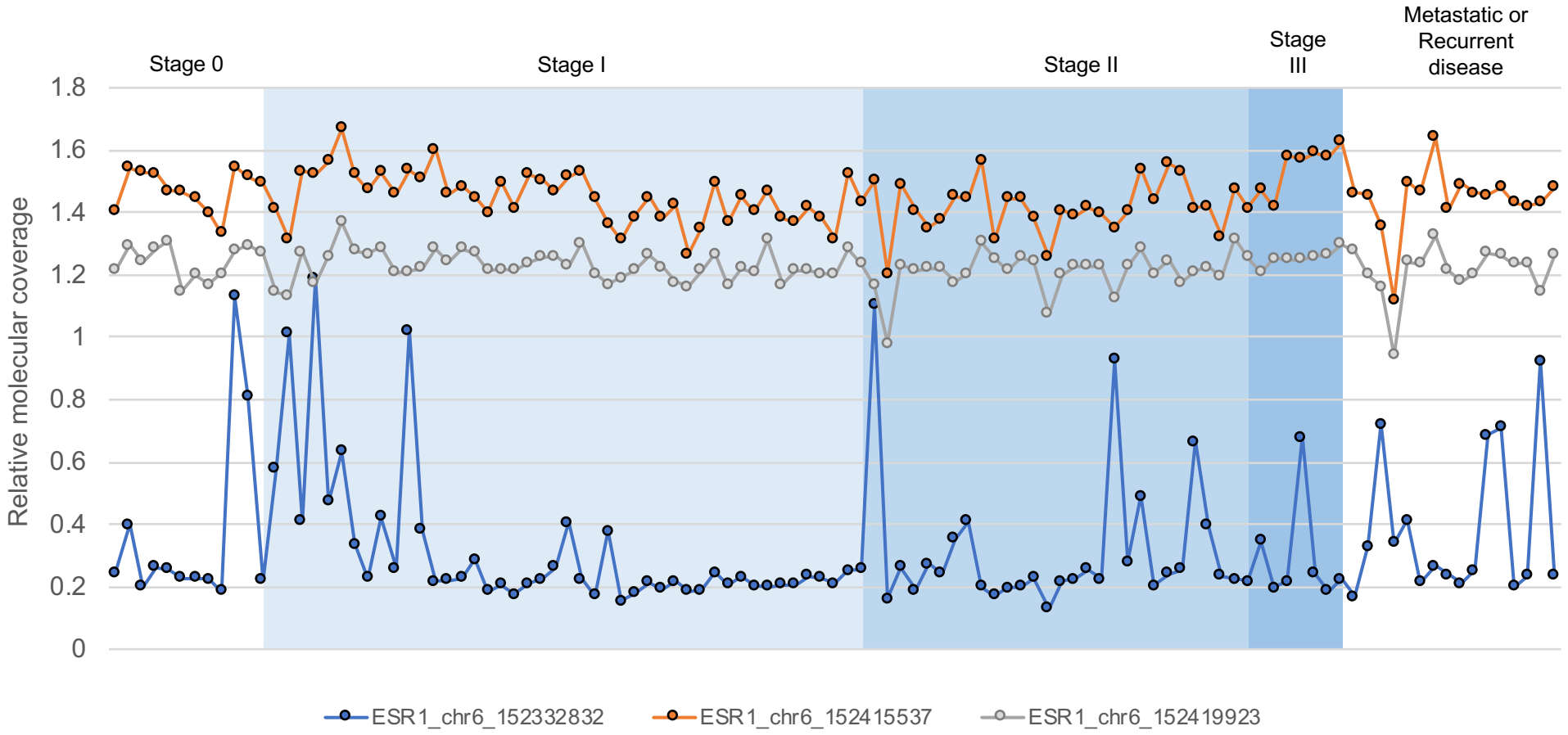
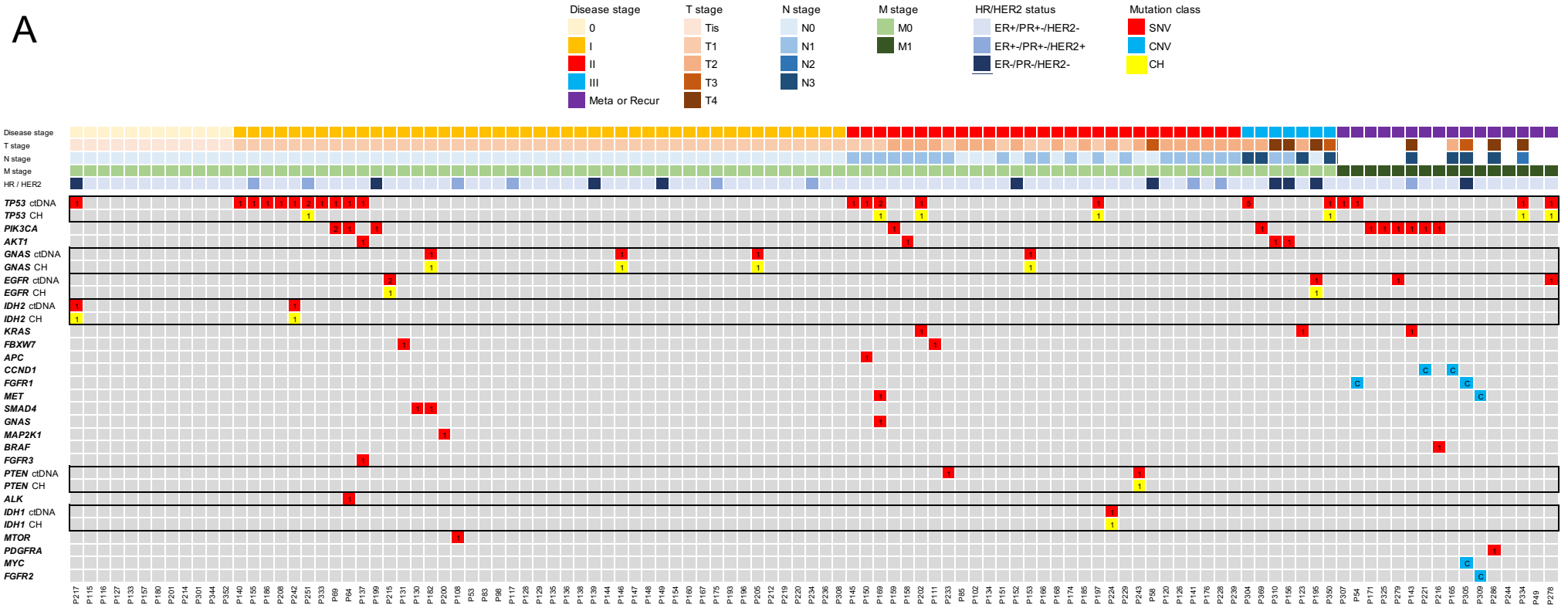


Figure S5. Relative molecular coverage of *ESR1* amplicons. Each line signifies relative consensus coverage of the respective *ESR1* amplicons across all 109 patients: Blue=ESR1_chr6_152332832; Red=ESR1_chr6_152415537; Grey=ESR1_chr6_152419923. Relative consensus coverage calculated by normalizing consensus coverage of each individual amplicon against the median consensus coverage of all amplicons within a particular sample.



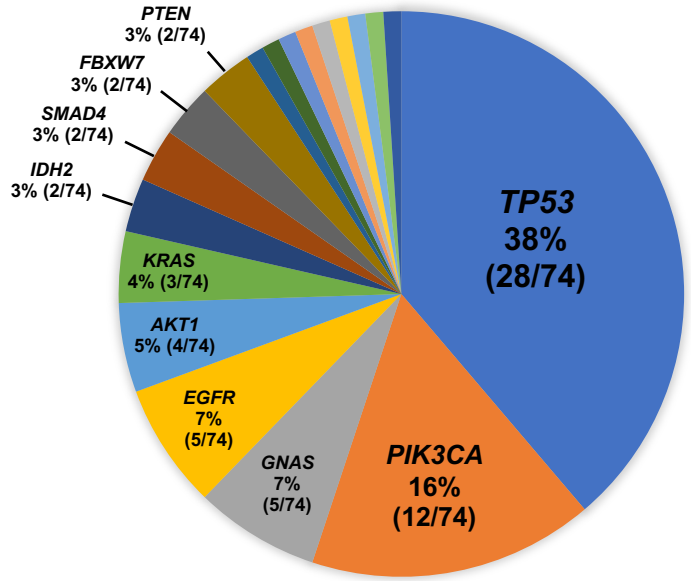


Figure S6. Genomic landscape of ctDNA variants from breast cancer before excluding CH variants. (A) Heatmap showing all ctDNA SNVs and CNVs detected from plasma. The clinical characteristics of patients are represented by the tiles at the top of the heatmap with details stated in the legend. Type of variant (SNV, CNV or CH) is denoted by color in the heatmap while numbers signify the number of SNVs for a gene per patient. SNVs that were detected from both plasma and corresponding WBC sequencing are denoted in yellow. The genes where these CH variants were detected are highlighted with black outside borders. (B) Overall distribution of SNVs calculated as number of SNVs per gene over the total 74 SNVs detected before excluding CH variants.