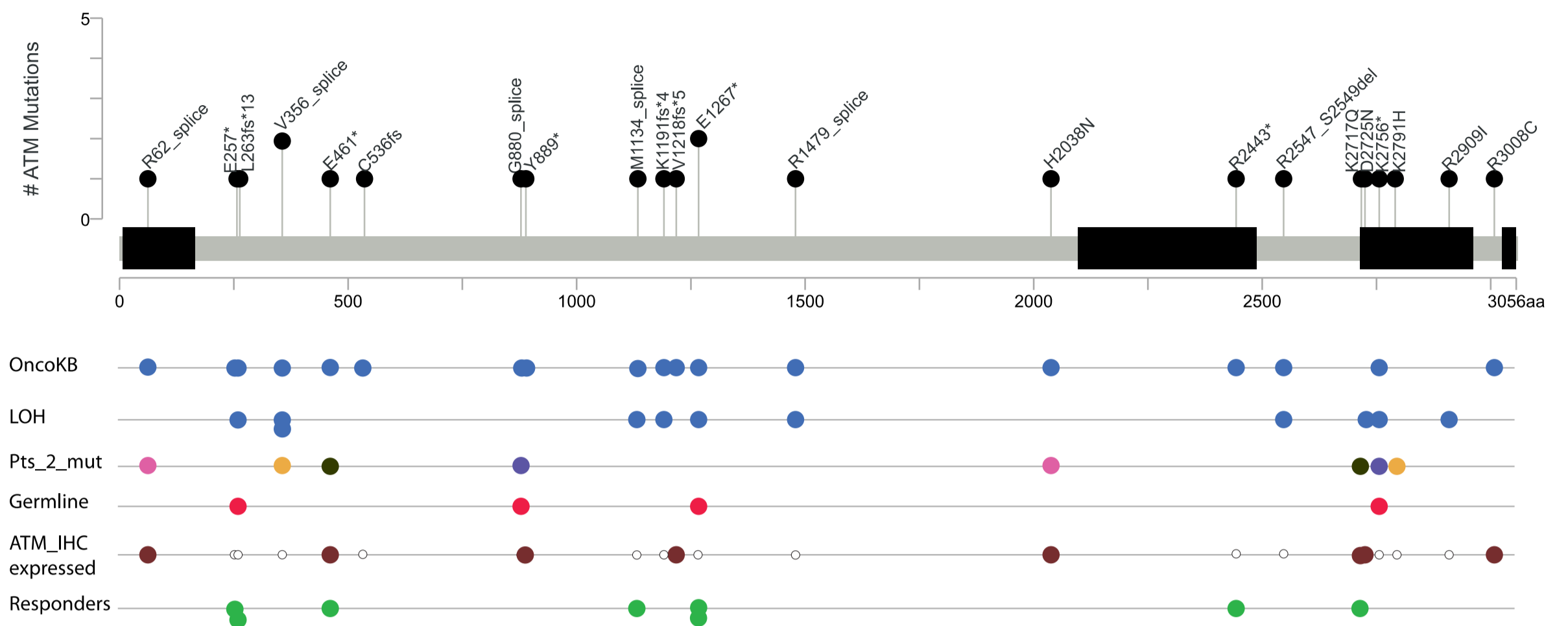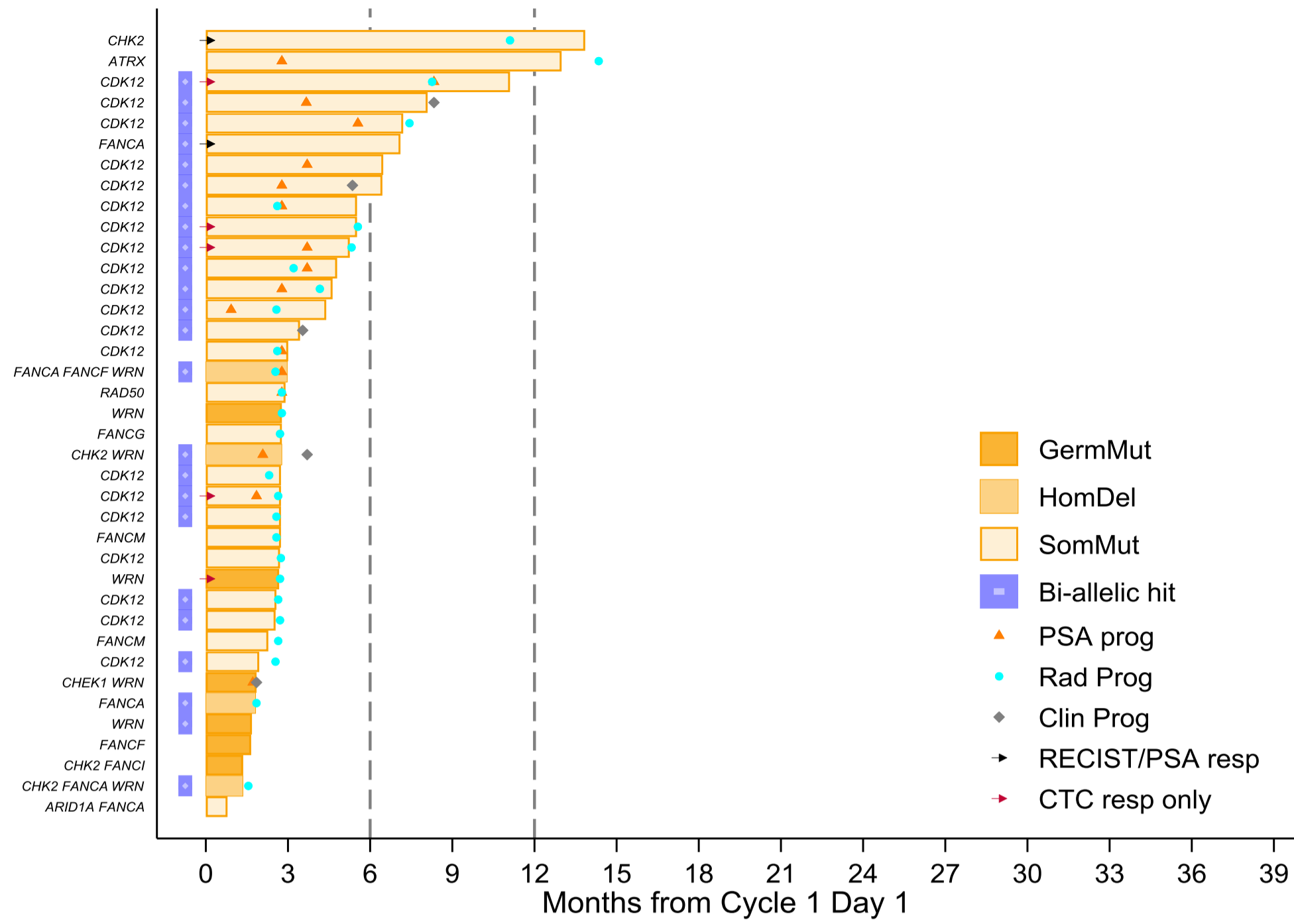**Supplementary Figure 1: rPFS and OS for the 5 DDR gene-subgroups.** Kaplan-Meier curves depicting rPFS and OS for the 5 DDR gene-subgroups.
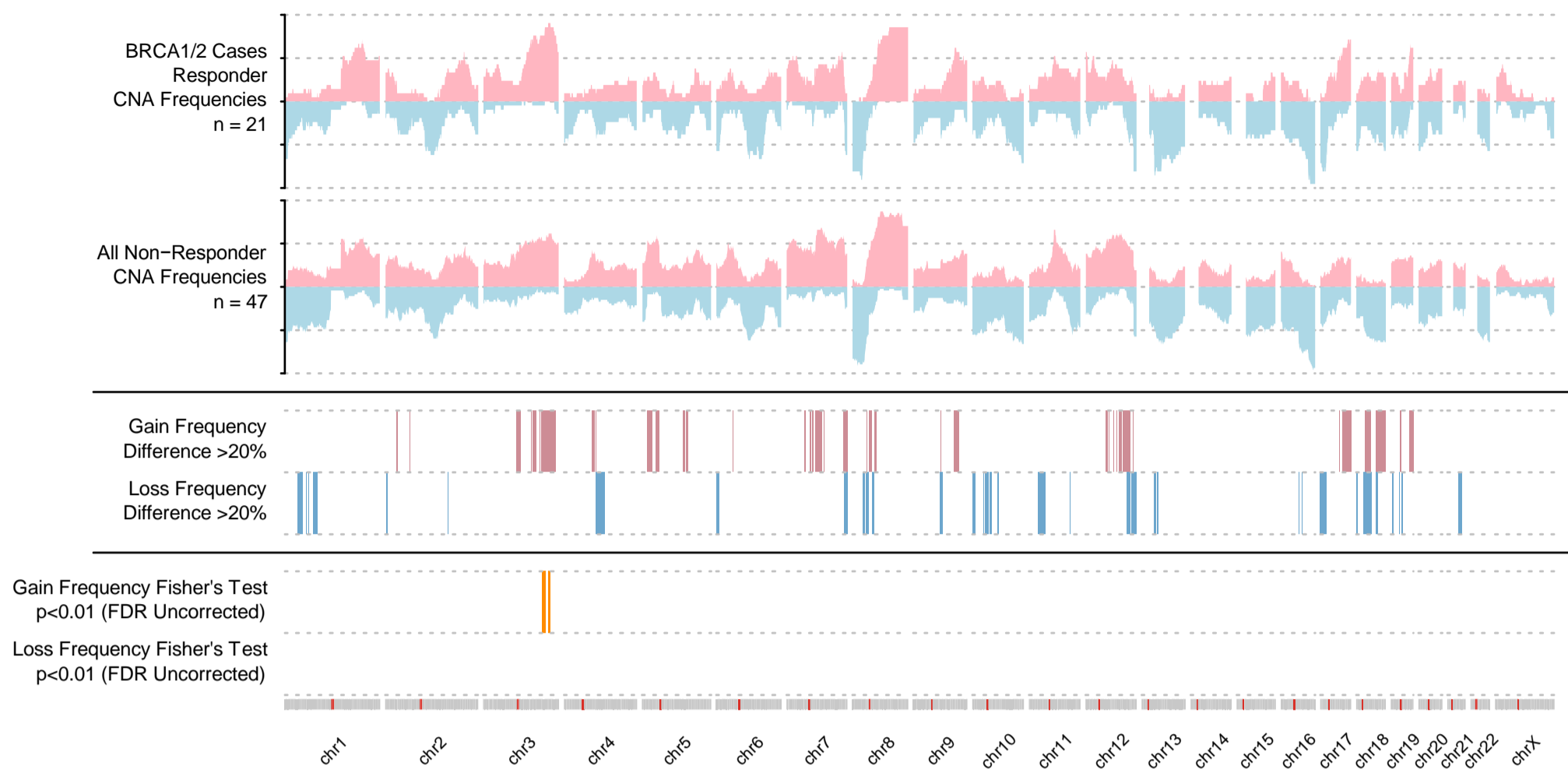
Supplementary Figure 2: ATM alterations lollipop . ATM alterations in the TOPARP-B ATM subgroup showing the related location, origin (germline vs somatic), biallelic hit, expression by IHC and patient response.
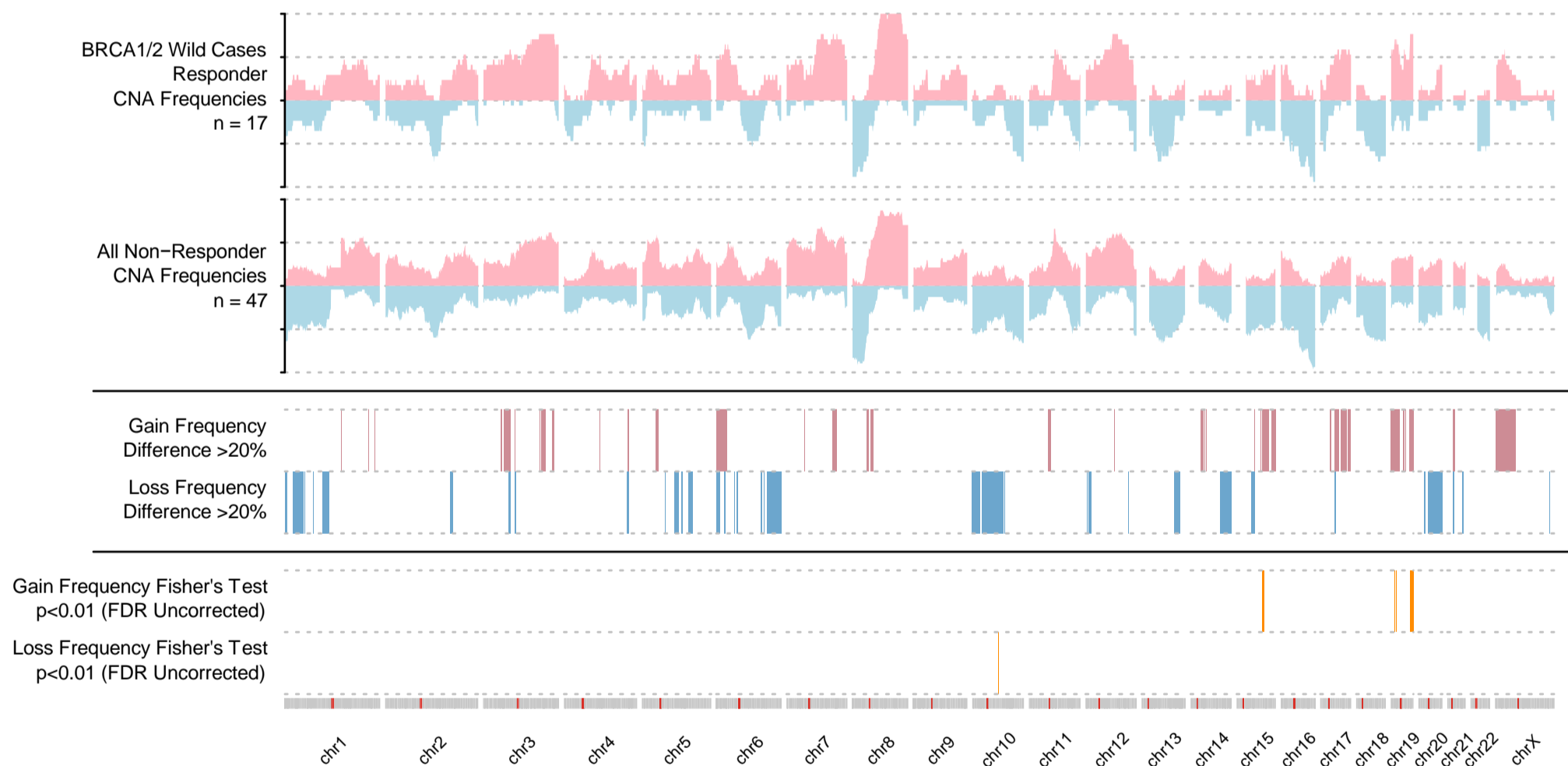
Supplementary Figure 3: Swimmer plots depicting time on treatment per origin/type alterations in CDK12 and Other genes.

Supplementary Figure 4: CNV Frequency plots of the advanced prostate cancers in the TOPARP-B BRCA1/2 and non- BRCA1/2 Responders and All Non-Responders and significant genomic copy number differences between the two groups. **A.** CNV Frequency plots of the advanced prostate cancers in the TOPARP-B BRCA1/2 Responders and All Non-Responders and significant genomic copy number differences between the two groups. B. CNV Frequency plots of the advanced prostate cancers in the TOPARP-B Non-BRCA1/2 Responders and All Non-Responders and significant genomic copy number differences between the two groups.

A
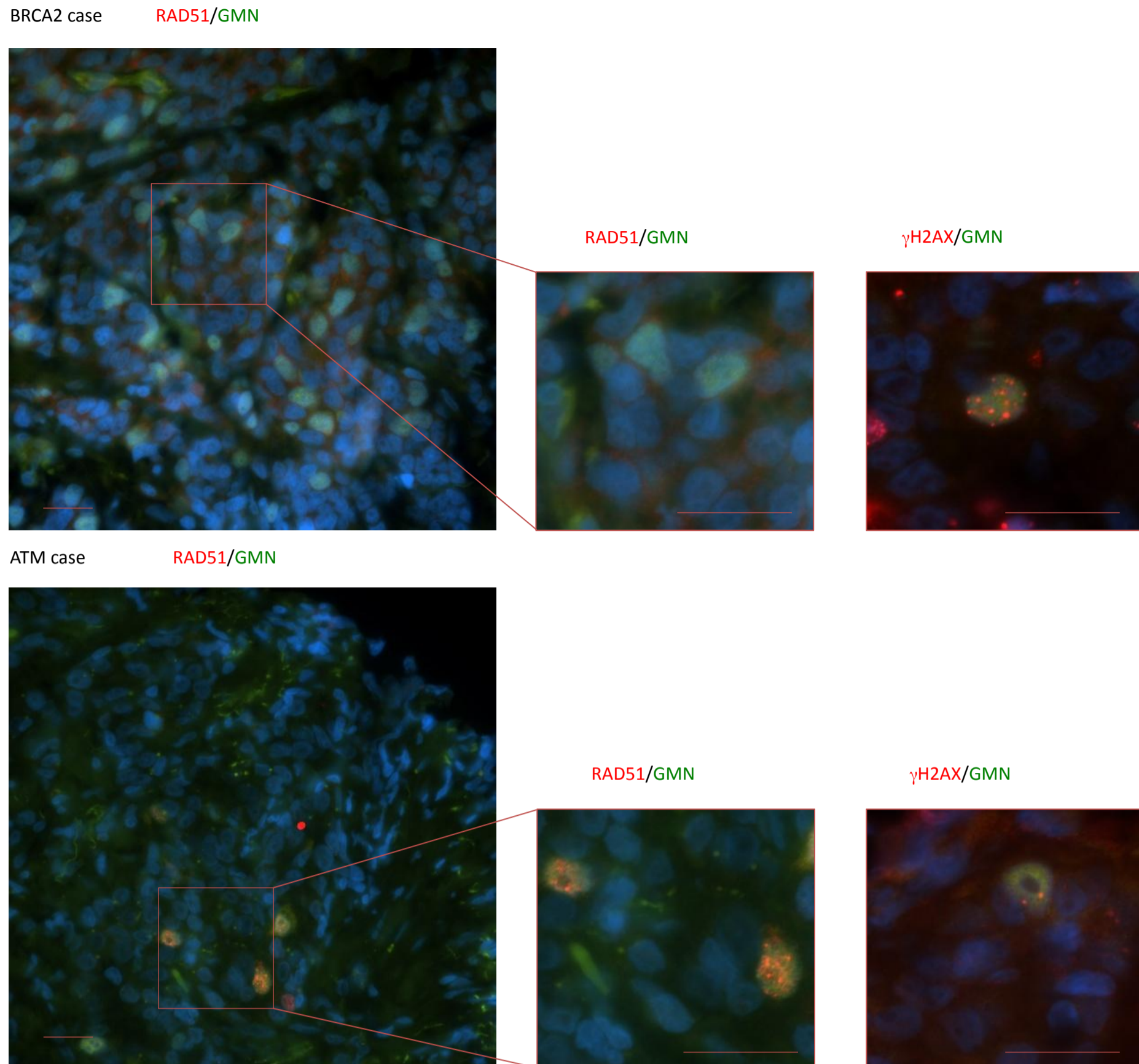
B
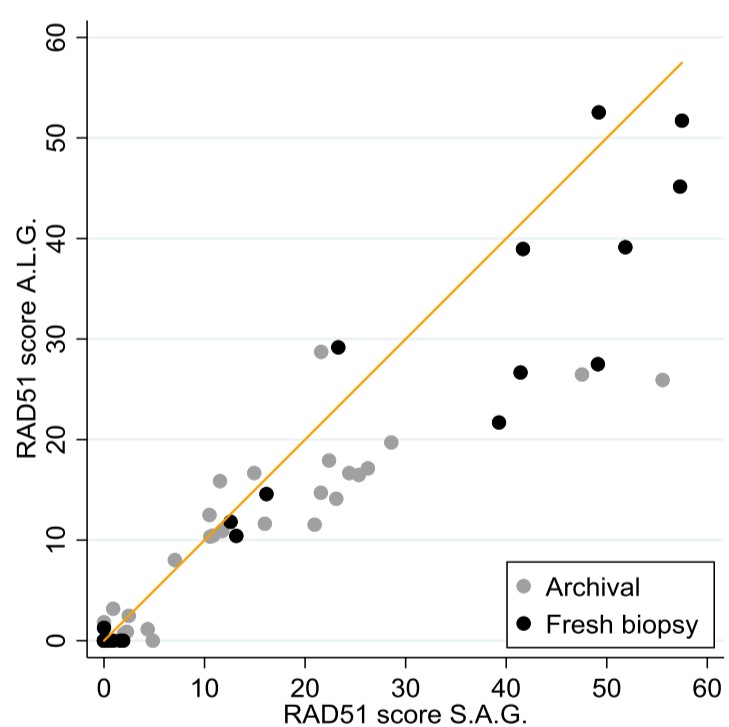
The ICC is 0.878034 (equivalent to Lin's concordance coefficient rho_C).

Supplementary Figure 5: RAD51 Immunofluorescence assay and scatter plot of RAD51 assay inter- observer scoring variability by tissue sample and concordance analysis. **A.** representative images of the RAD51 Immunofluorescence assay. Top: Olaparib responding BRCA2 biallelic patient with a RAD51 low score. Bottom: Non-responding ATM mono-allelic patient with a RAD51 high score. Bar = 20µm **B.** Scatter plot of RAD51 assay inter-observer scoring variability by tissue sample and concordance analysis.