**Figure S1**Data analysis process for identifying and validating somatic mutations in 187 cases of HR-ALL

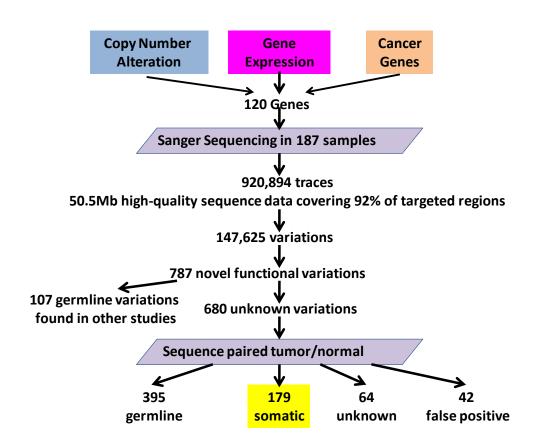
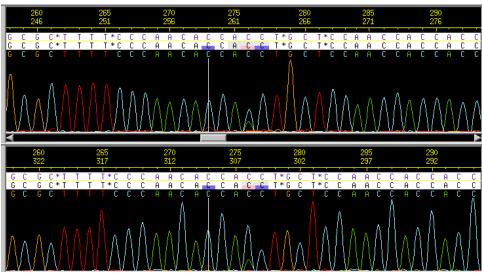


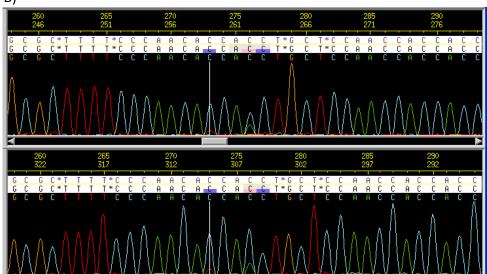
Figure S2. Double-mutants in NRAS and KRAS

A) KRAS G12D and G13D double-mutation in case  $9906\_215.$  B) NRAS G12V and G13D double-mutation in case  $9906\_106$ 

A)



B)



## Figure S3. IKZF1 deletion pattern in R8 (top), R7 (middle) and R6 (bottom)

The blue bars indicate the location of the deletion for each sample. The green vertical bars indicate somatic sequence mutation.



**Figure S4**There was no significant association between the presence or number mutations affecting Ras signaling and outcome in this study.

