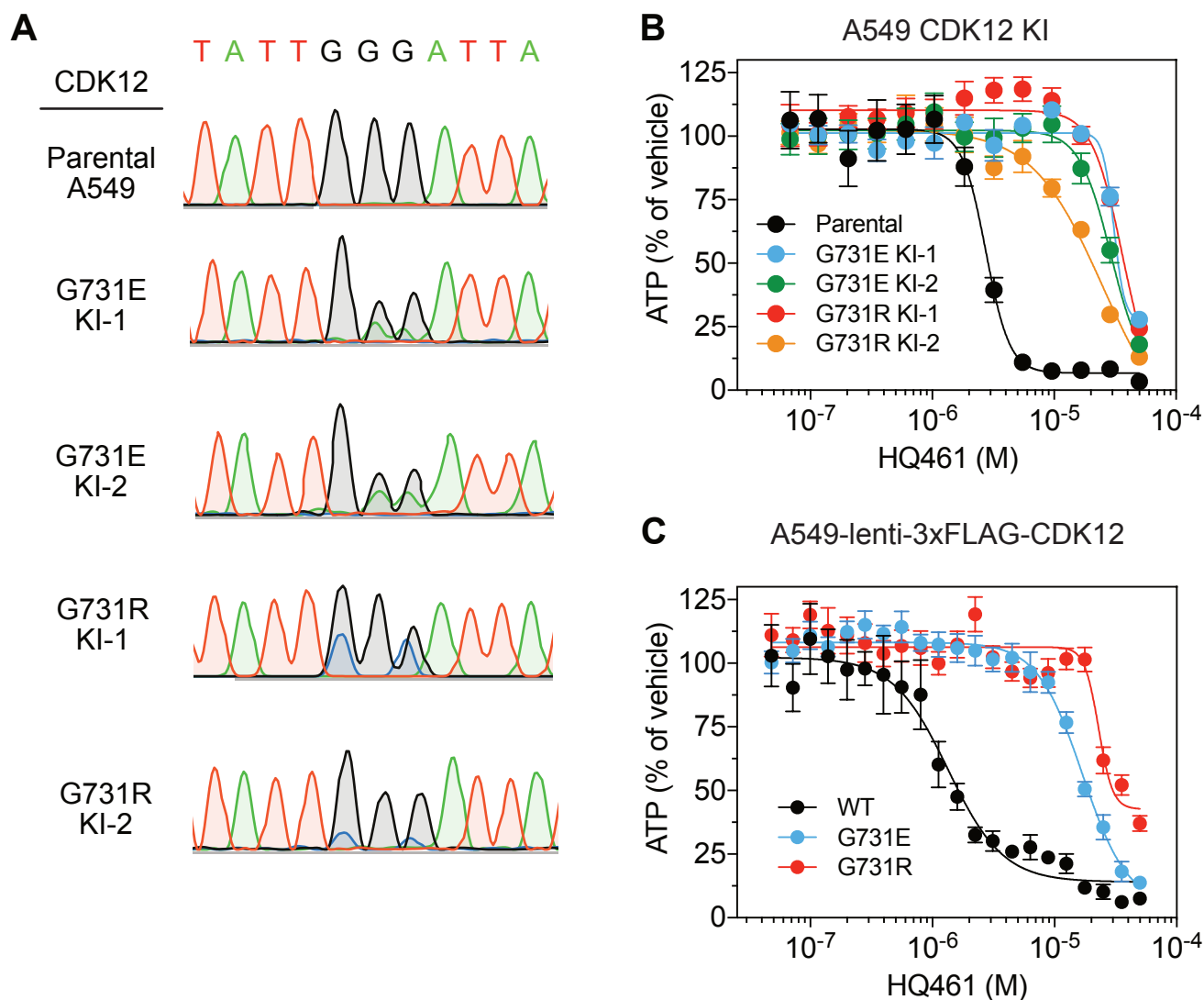


## Figure 2—figure supplement 1



**Figure 2—figure supplement 1. The *CDK12* G731E and G731R mutations confer HQ461 resistance.**

(A) Sanger sequencing verification of GGG to GAA and GGG to CGC mutations introduced by CRISPR-Cas9 mediated homology dependent repair in A549 cells.

(B) Measurement of the HQ461  $IC_{50}$  on the viability of CDK12 G731E or G731R knock-in A549 cells ( $IC_{50}$  ranging from 25.2  $\mu$ M to 36.5  $\mu$ M). Error bars represent SEM from three biological replicates.

(C) Measurement of the HQ461  $IC_{50}$  on the viability of A549 cells stably expressing wild-type ( $IC_{50}$ =1.3  $\mu$ M, 95% CI: 1.1  $\mu$ M-1.7  $\mu$ M) or G731E/R mutant CDK12 (G731E  $IC_{50}$ =16.9  $\mu$ M, 95% CI: 14.2  $\mu$ M-20.2  $\mu$ M; G731R  $IC_{50}$ =22.9  $\mu$ M, 95% CI: 19.7  $\mu$ M-26.8  $\mu$ M). Error bars represent SEM from three biological replicates.