

Supplemental Table 1) Detailed summary of T-ALL patient mutations

Summary of re-sequencing data showing mutation data observed in 36 T-ALL samples.

Supplemental Table 2) In vivo toxicity analysis of (±)-CR-31-B

The multi-panel table provides results of a detailed analysis of the toxic effects of CR treatment in non-tumour bearing c57/B6 mice. a) Body and organ weights; b) Individual haematology; c) Bone marrow and spleen cytology; d) Individual chemistry.

Supplemental Table 3) Genes with changes in Translational Efficiency (TE) and/or rDiff.

a) Genes with decreased Translational Efficiency (TE down); b) Genes with increased Translational Efficiency (TE up); c) Background genes with no change in Translational Efficiency (TE background); d) Complete list of genes that showed a significant change in RF distribution across the length of their transcript (rDiff positive gene set); e) Genes that are both TE down and rDiff positive.

Supplemental Table 4) Sequence motifs and G-quadruplexes.

a-b) Complete lists of TE Down genes that harbour the 12-mer (a) or 9-mer (b) in their 5'UTRs; c-d) Complete lists of rDiff genes that harbour the 12-mer (c) or 9-mer (d) in their 5'UTRs; Prevalence of the TE Down 12-mer motif; e) TE Down genes with one or more predicted G-quadruplex structures; f) rDiff genes with one or more predicted G-quadruplex structures; g-h) Overlap of TE Down 12-mer motif (g) or 9-mer motif (h) with predicted G-quadruplexes. i-j) Overlap of rDiff 12-mer motif (i) or 9-mer motif (j) with predicted G-quadruplexes; k) Nucleotide-level depiction of the overlap between 9-mer motifs and G-quadruplexes. The motif is located at the positions marked X in the sequence. The middle row shows the structure. + represents that it is part of a G-quadruplex, ) ( represents a bond with another nucleotide.

Supplemental Table 5) RNA oligos used for Circular Dichroism (CD) and thermal denaturation analysis.

Note: 12-mers or 9-mers are shown in red.

Supplemental Table 6) T-ALL super-enhancer associated Silvestrol targets.

Overlap of TE down or rDiff genes with reported super-enhancer associated genes in the T-ALL cell lines DND41, JURKAT, or RPMI-840234. '+' indicates presence of one or more 12-mers, 9-mers, or predicted G-quadruplexes in the 5'UTR.