**Supplementary Methods**

Lactate dehydrogenase (LDH) cytotoxic analysis

After another 24 hours, 10μL of sterile, ultrapure water were added to one set of triplicate wells containing Effector and Target Cell Spontaneous LDH. Forty-five minutes before harvesting the supernatant, 10μL of Lysis Buffer (10X) were added to another set of triplicate wells containing Target Cell Maximal LDH Release Control and Volume Correction Control. Next, 50μL of Reaction Mixture were added to another 96-well flat bottom plate to hold the collected 50μL supernatant of each sample medium at room temperature for 30 minutes, protected from light, after the 45-minute incubation. Finally, 50μL of Stop Solution were added to each well of the 96-well plate for stopping the reaction.

PrestoBlue cell viability assay

After collecting half of the supernatant for LDH assay, the original 96-well plates containing cells and the other half were added 10μL of PrestoBlue each well and further incubated (37°C, 5% CO2, 98% humidity) for 0.5 hour.

CyQUANT cell proliferation assay

After finishing LDH and PrestoBlue assay, the 96-well plates containing cells were gently inverted and blotted onto paper towels to remove medium from the wells. The cells in the
microplate were then frozen and stored at -70°C. At the desired time, the plates were thawed at room temperature and 200 µL of the previously prepared CyQUANT GR dye/cell-lysis was added to each sample well. Next, the plates were incubated for 2–5 minutes protected from light.

Post-sequencing RNA-seq data analysis

1) Data quality control: raw data (raw reads) in fastq format were processed with fastp ¹. Clean data (clean reads) for all downstream analyses were obtained after quality control, adapter trimming, quality filtering and per-read quality cutting.

2) Mapping of reads to the reference genome: reference genome and gene model annotation files were downloaded from genome website directly. Paired-end clean reads were aligned to the reference genome using a graph-based alignment program, HISAT2 (v2.1.0) ².

3) Quantification of gene expression level: a read summarization program, featureCounts, was used for counting reads mapped to each gene, and then the FPKM (fragments per kilobase of exon model per million reads mapped) of each gene was calculated (from its length and mapped reads count) for estimating its expression level.

4) Differential expression analysis: differential expression analysis of two conditions/groups (two biological replicates per condition) was performed using DESeq (v1.18.1), which
provides statistical routines for determining differential expression in digital gene expression
data using a model based on the negative binomial distribution. The resulting P-values
were adjusted using the Benjamini and Hochberg’s approach for controlling the false
discovery rate. Genes with log2 fold change > 1 and adjusted P-value <0.05 were assigned as
differentially expressed.

5) GO and KEGG enrichment analysis of differentially expressed genes: GO (gene ontology)
and KEGG (Kyoto Encyclopedia of Genes and Genomes) enrichment analysis and
visualization of differentially expressed genes was implemented with clusterProfiler (v3.0.4)

Validation via quantitative real-time PCR

The sequences of the PCR primers used in the experiment are as follows: GAPDH, forward
5′-GAAGTGGAAGGTCGGAGTC-3′ and reverse 5′-GAAGATGGTGATGGGATTTC-3′;
CYP24A1, forward 5′-AAA CCA GCA GTG AAC CCT GT-3′ and reverse 5′-CAC CAC ACC
ATA CAA CAG TT-3′; Vitamin D receptor, forward 5′-AGC AGC GCA TCA TTG CCA TA-3′
and reverse 5′-CAG CAT GGA GAG CTC GGA CA-3′; CILP, forward 5′-
AGCGGTGTACGGAAACTCG-3′ and reverse 5′-ACGGCACCTCCCCTTTGT-3′; SHE (Src
homology 2 domain-containing transforming protein E), 5′-
CCGGAATTCCAGCGTGCCCTGGAG-3′ and reverse 5′-
CCGGAATTCCGCTCTGGCTGGTTG-3′; THBD, forward 5′-GACCTCTCTATGCGCCAGTGCA-3′ and reverse 5′-CGTCGCGTTCAGTAGC-3′; TDRD10, forward 5′-
CAAGGATTTGCCAGAACCAC-3′ and reverse 5′-GAGCAGCACAAGAAGGAGC-3′;
SULT1C2, forward 5′-GGGGTACC CAGGCAGCTGAGGGCCAGG-3′ and reverse 5′-GGGGCTAGC AGTGTCTCAGGGTTGGGGTC-3′; KRT16, forward 5′-
TGAGATGGAGCAGCAGAG-3′ and reverse 5′-GACGA GGAGGAGGTGAAG-3′.

References