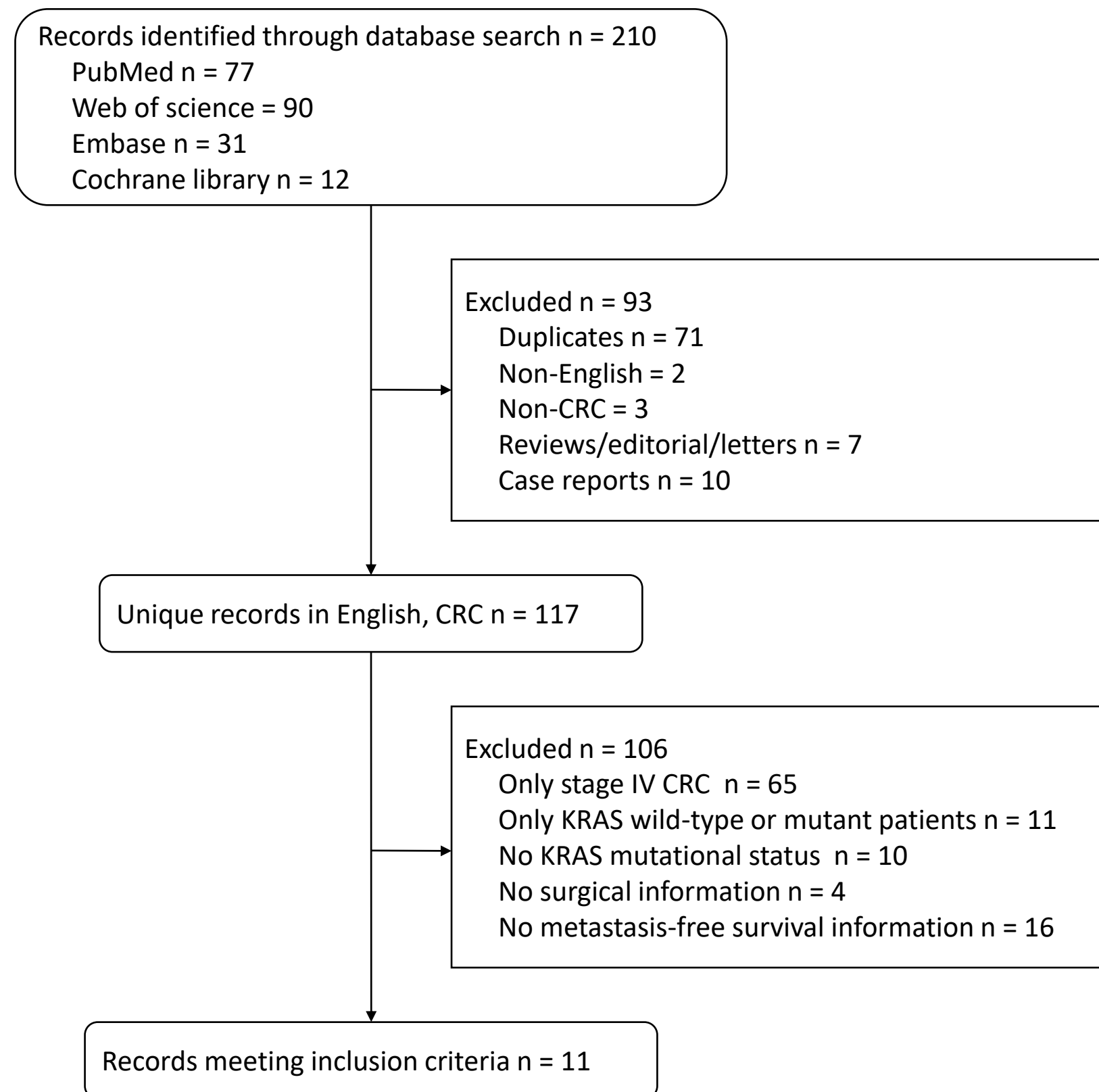
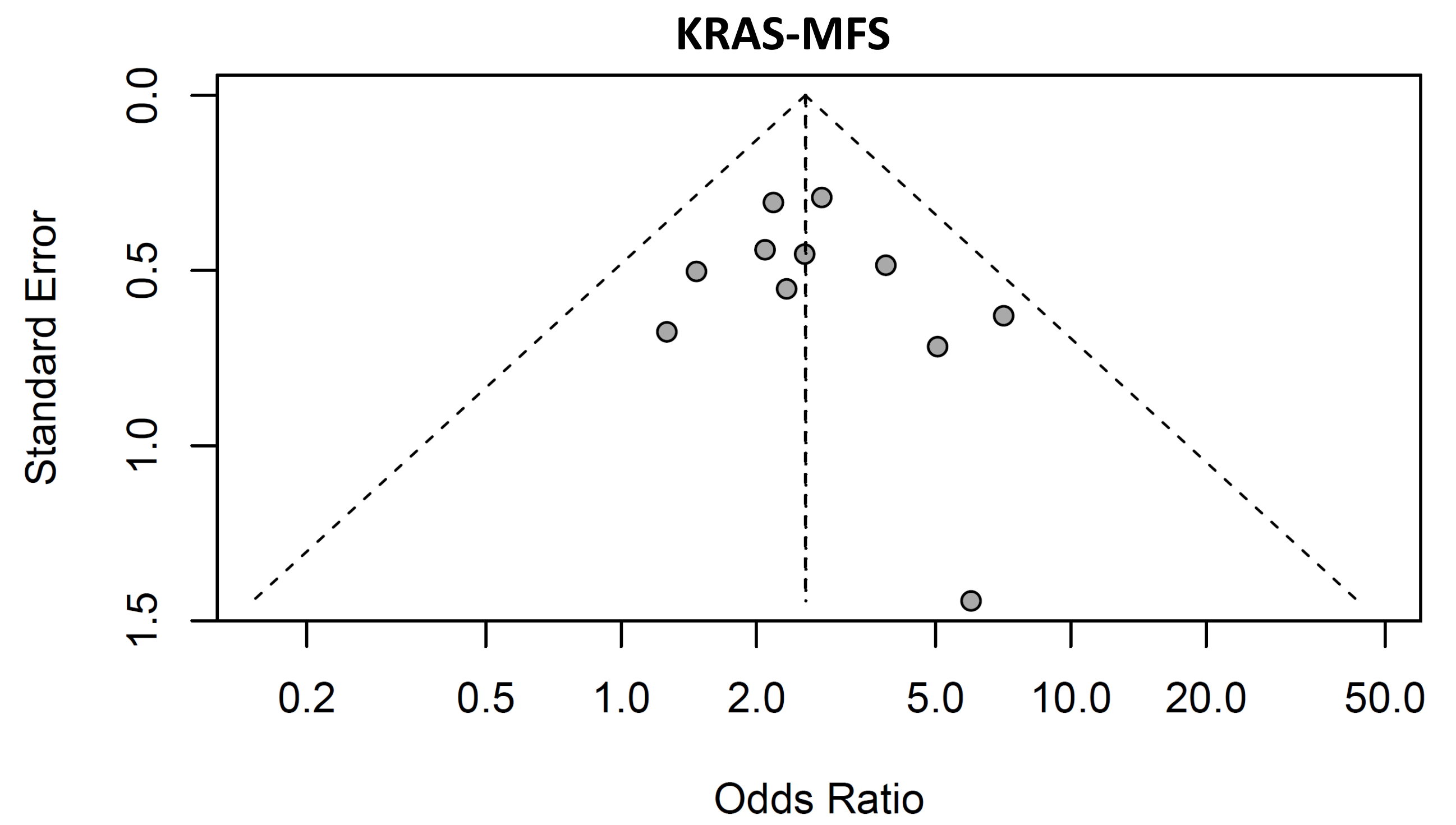


A

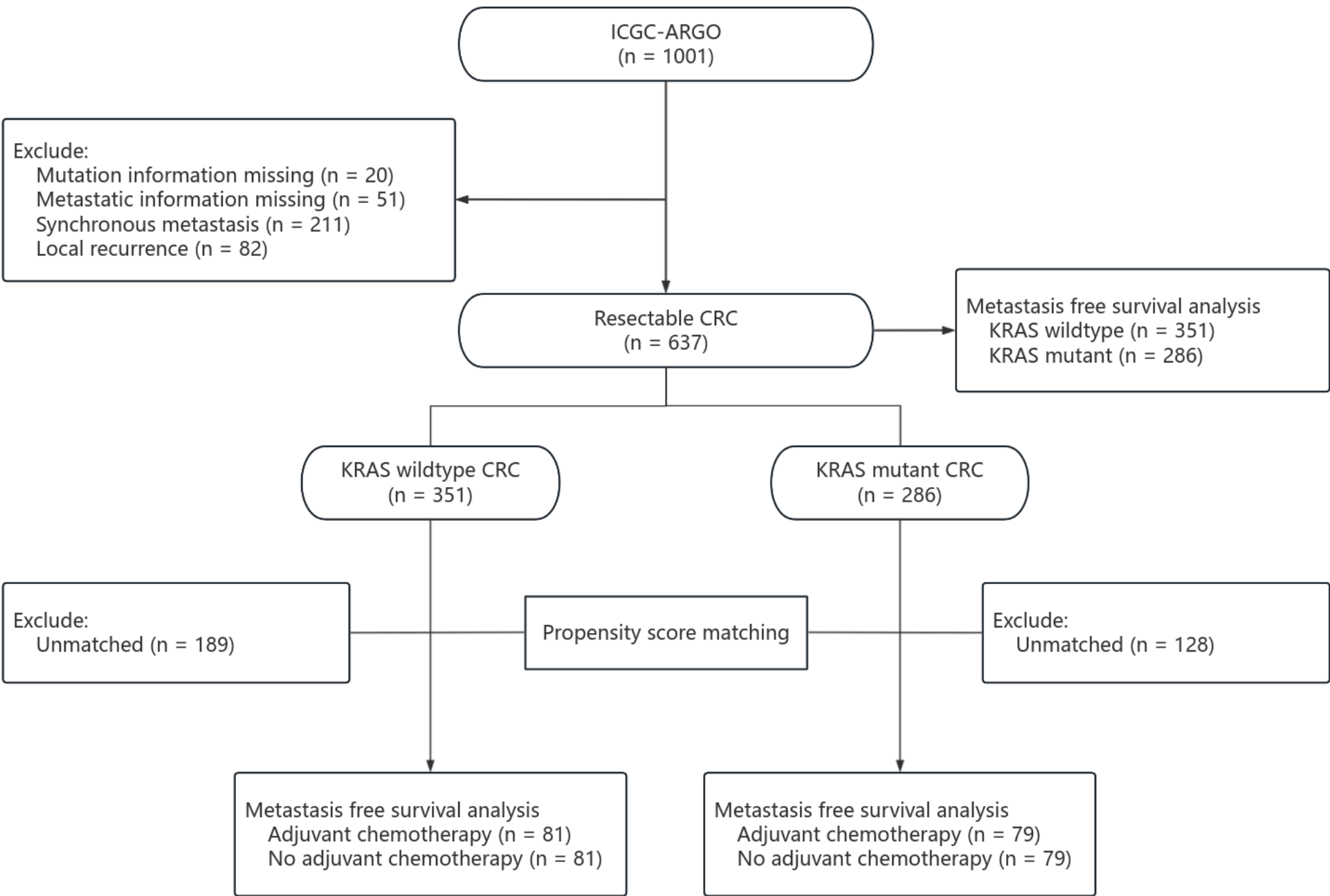


D

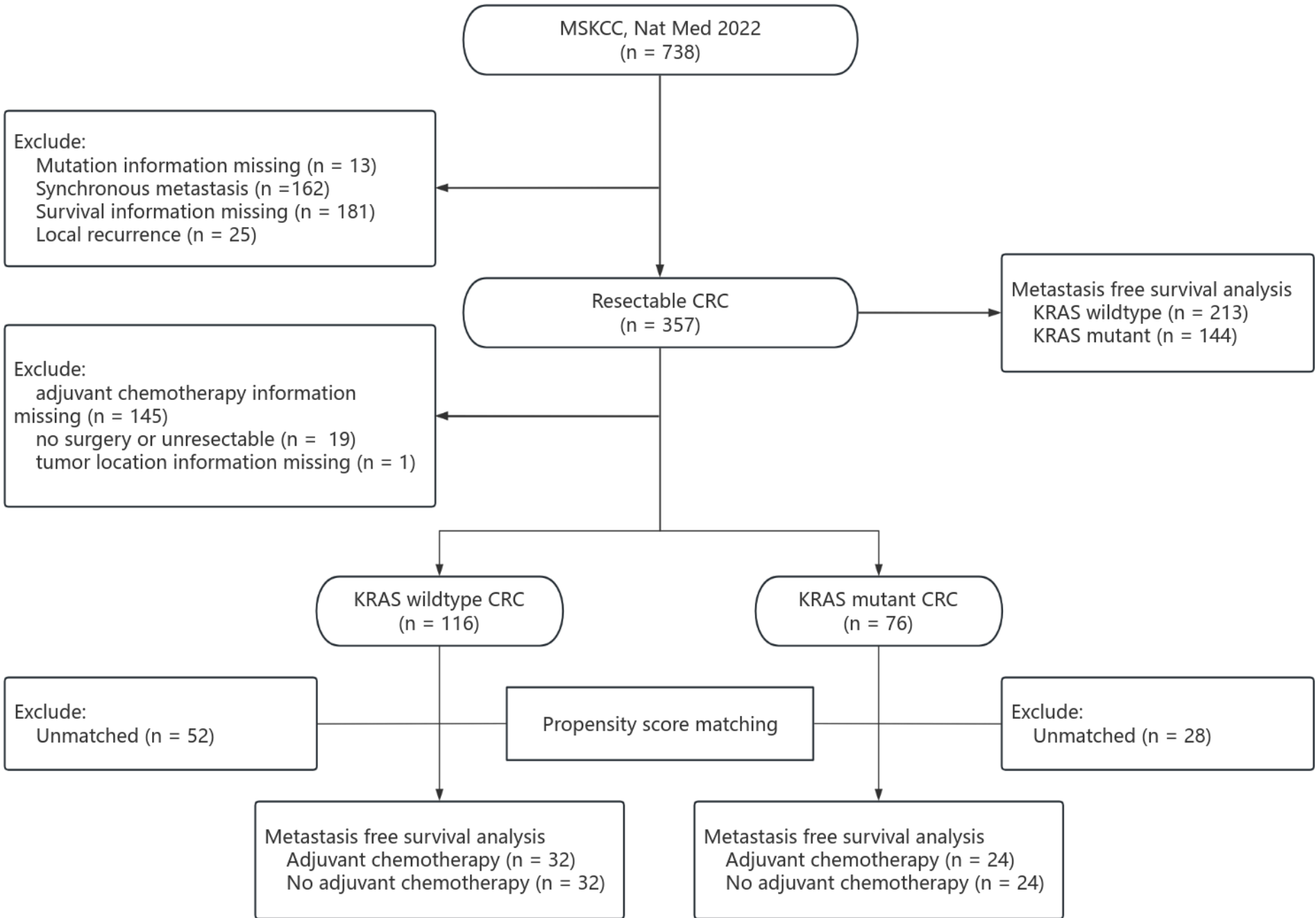


Supplementary figure 1. (A) Study selection flow chart showing the article selection process. The search string was built to identify studies of patients undergoing curative surgery of stage I-III CRC in whom metastasis-free survival was assessed according to KRAS mutation status. **(B)** Funnel plots to inspect for publication bias. CRC, colorectal cancer; MFS, metastasis-free survival.

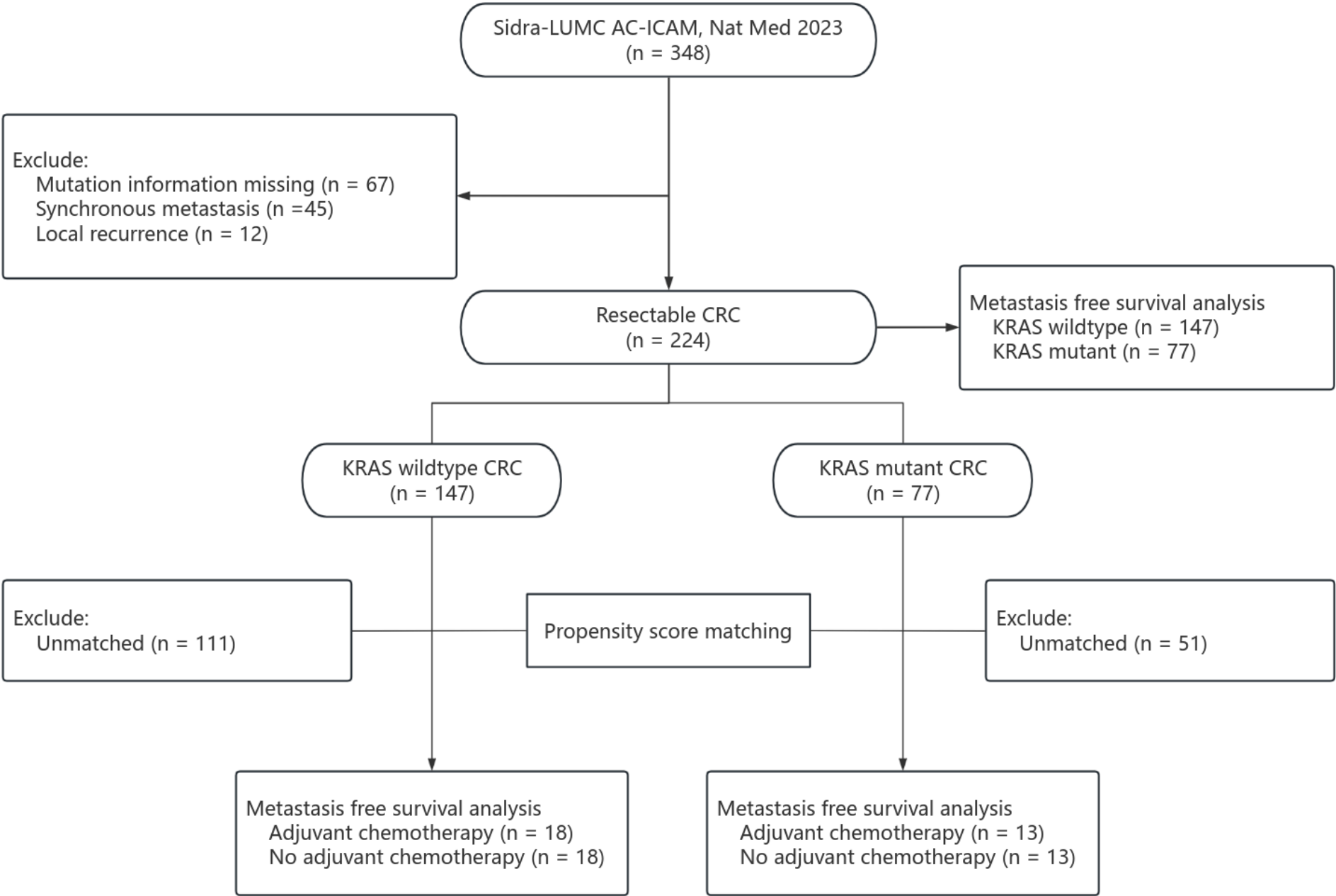
A



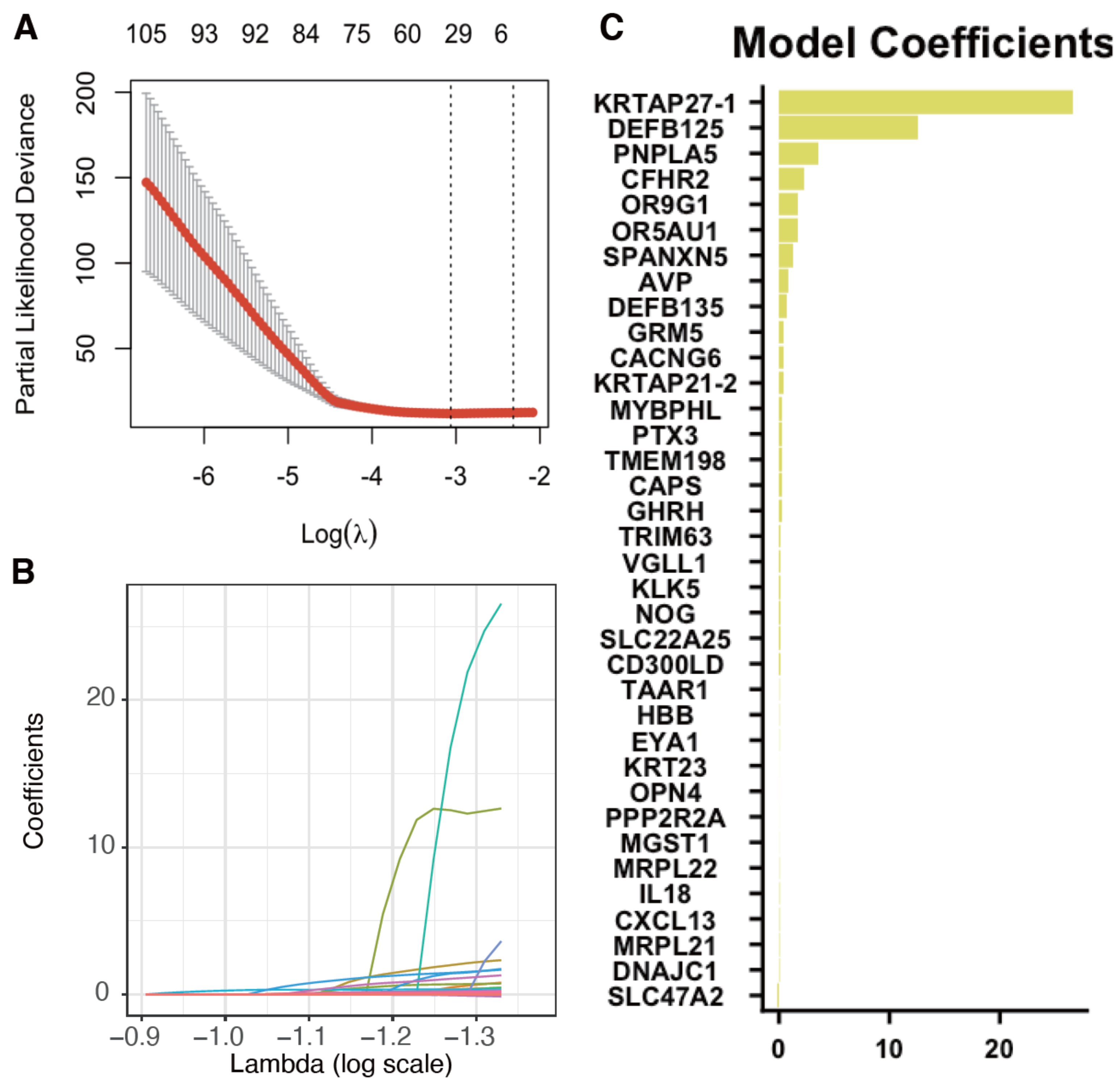
B



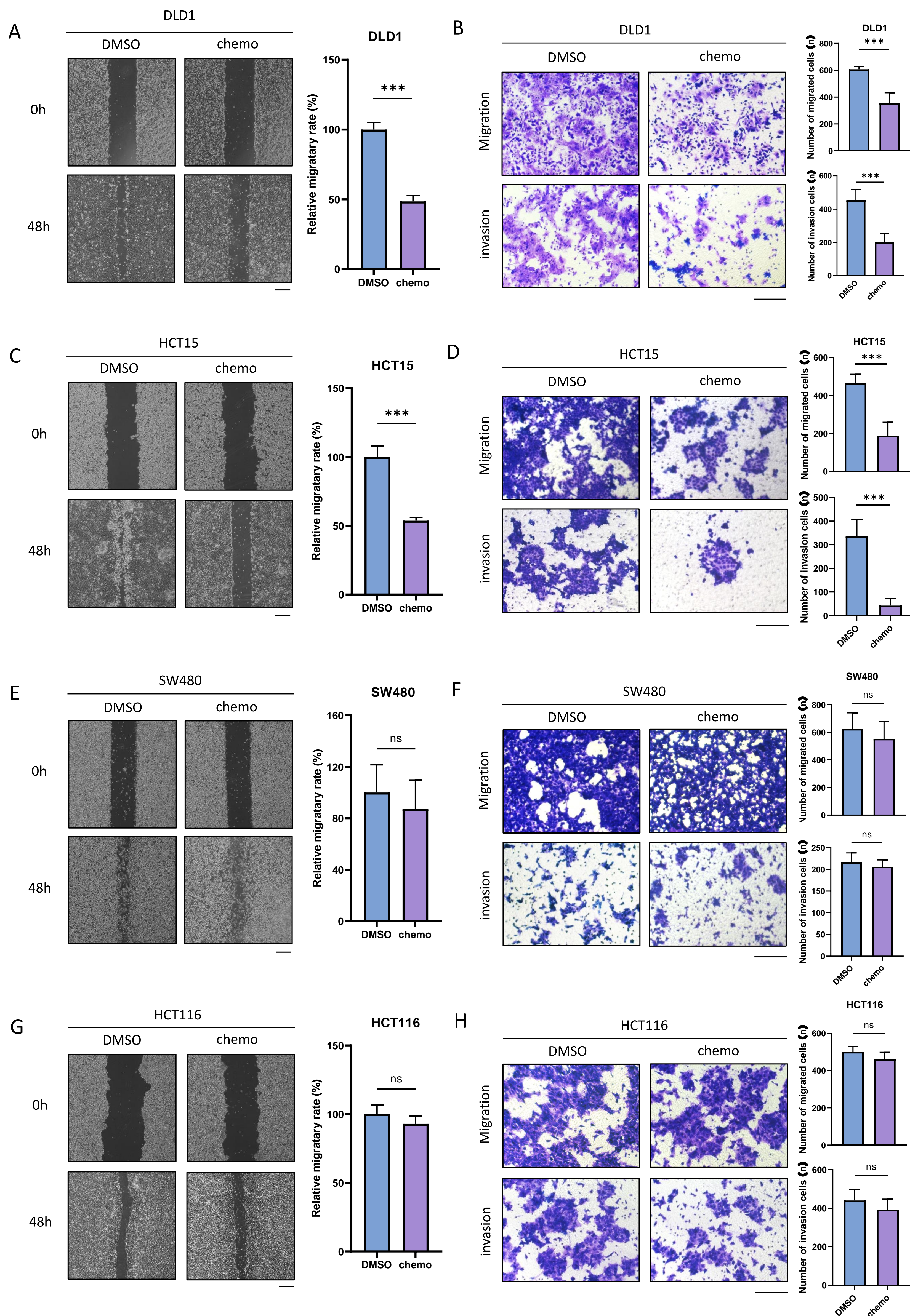
C



Supplementary figure 2. Inclusion and exclusion flowcharts of databases for metastasis-free survival analysis. **(A)** ICGC-ARGO flowchart. **(B)** MSKCC flowchart. **(C)** Sidra-LUMC AC-ICAM flowchart.

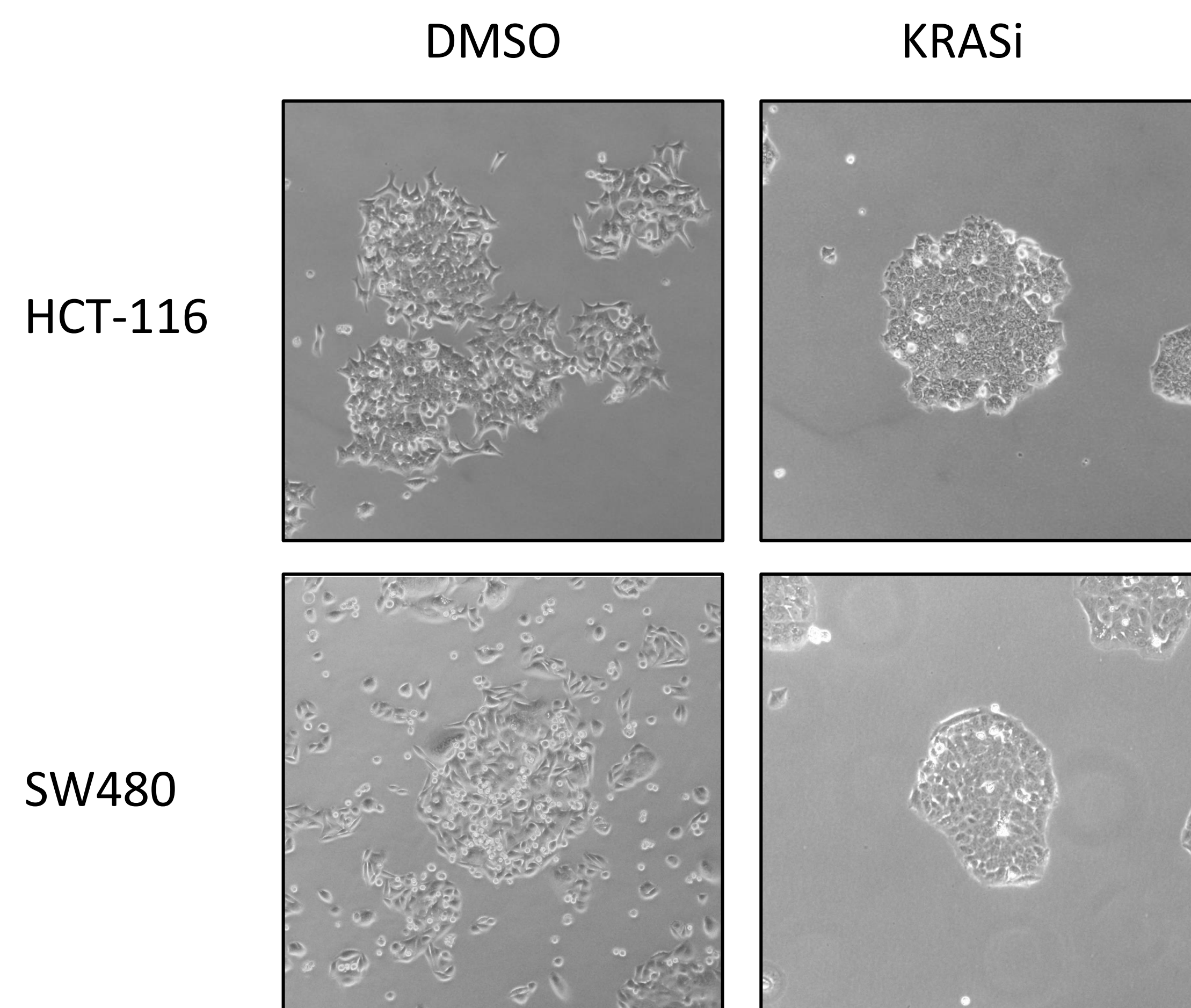


Supplementary figure 3. Establishment of KRAS metachronous metastasis risk prediction model. **(A-B)** Training of the metastasis risk prediction model. **(C)** Gene feature coefficients of the metastasis risk prediction model.

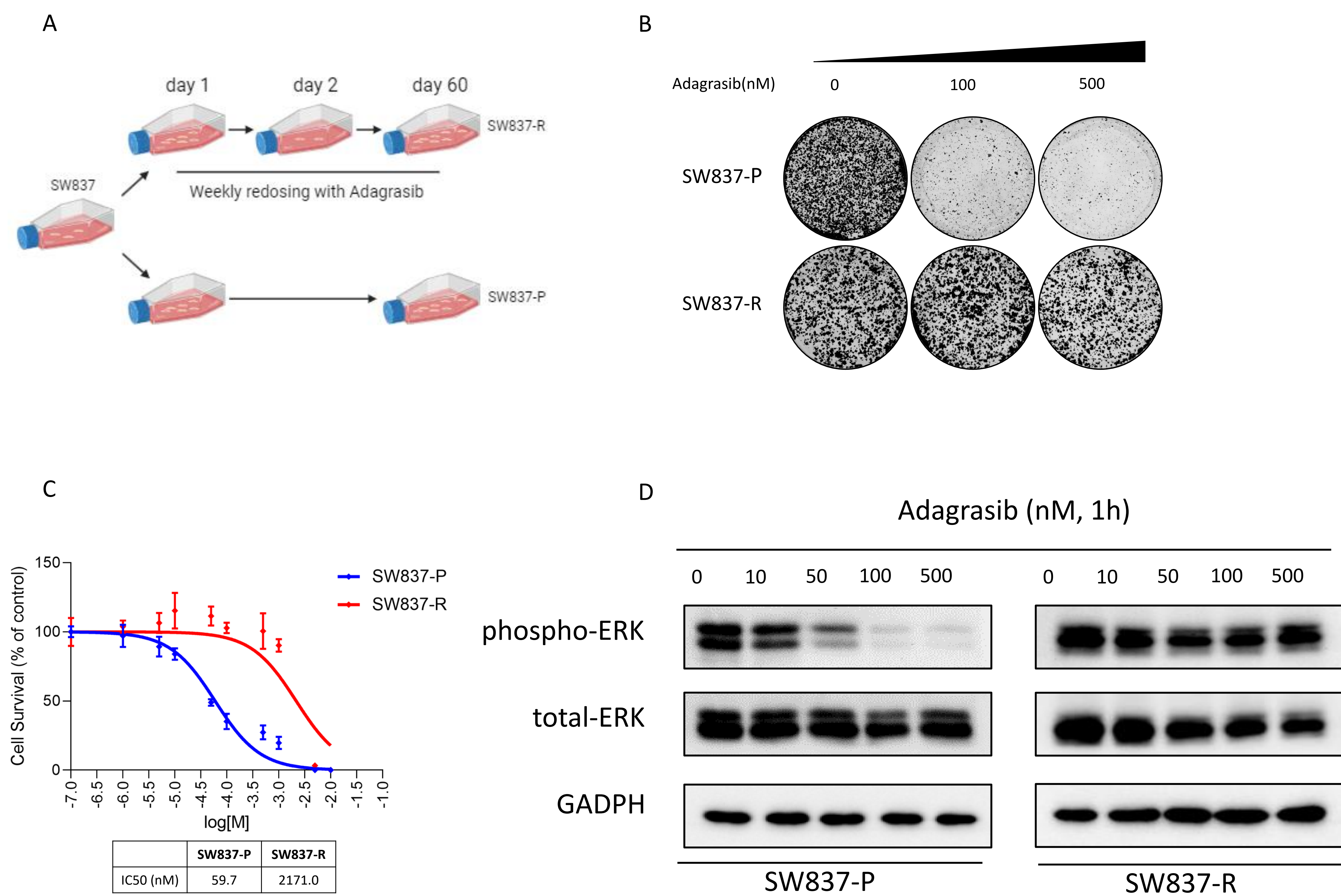


Supplementary figure 4. Inhibitory effect of chemotherapy on colorectal cell lines.

Migratory ability of DLD1 (A), HCT15 (C), SW480 (E) and HCT116 (G) treated with DMSO or chemotherapy was assessed by scratch wound healing assay (scale bar: 200 μ m). The effect of chemotherapy on the migration and invasion in DLD1 (B), HCT15 (D), SW480 (F) and HCT116 cells (H) was examined using Boyden chamber transwell assay (scale bar: 200 μ m). Chemo, chemotherapy (5-fluoracil plus oxaliplatin). *** $P < 0.001$.



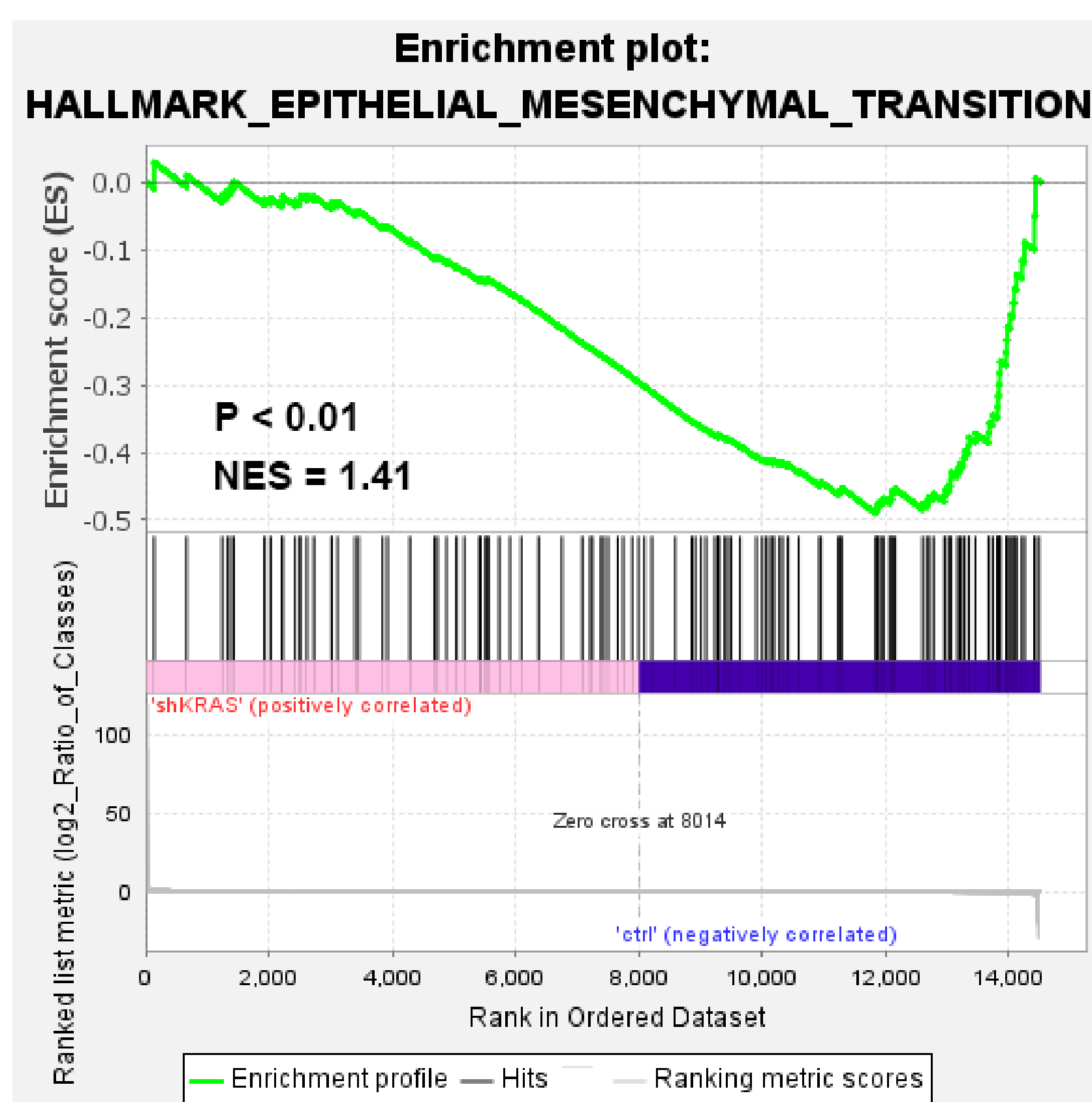
Supplementary figure 5. Morphology alternation induced by KRAS inhibitor in colorectal cancer cell line. KRASi, KRAS inhibitor (BI-2865).



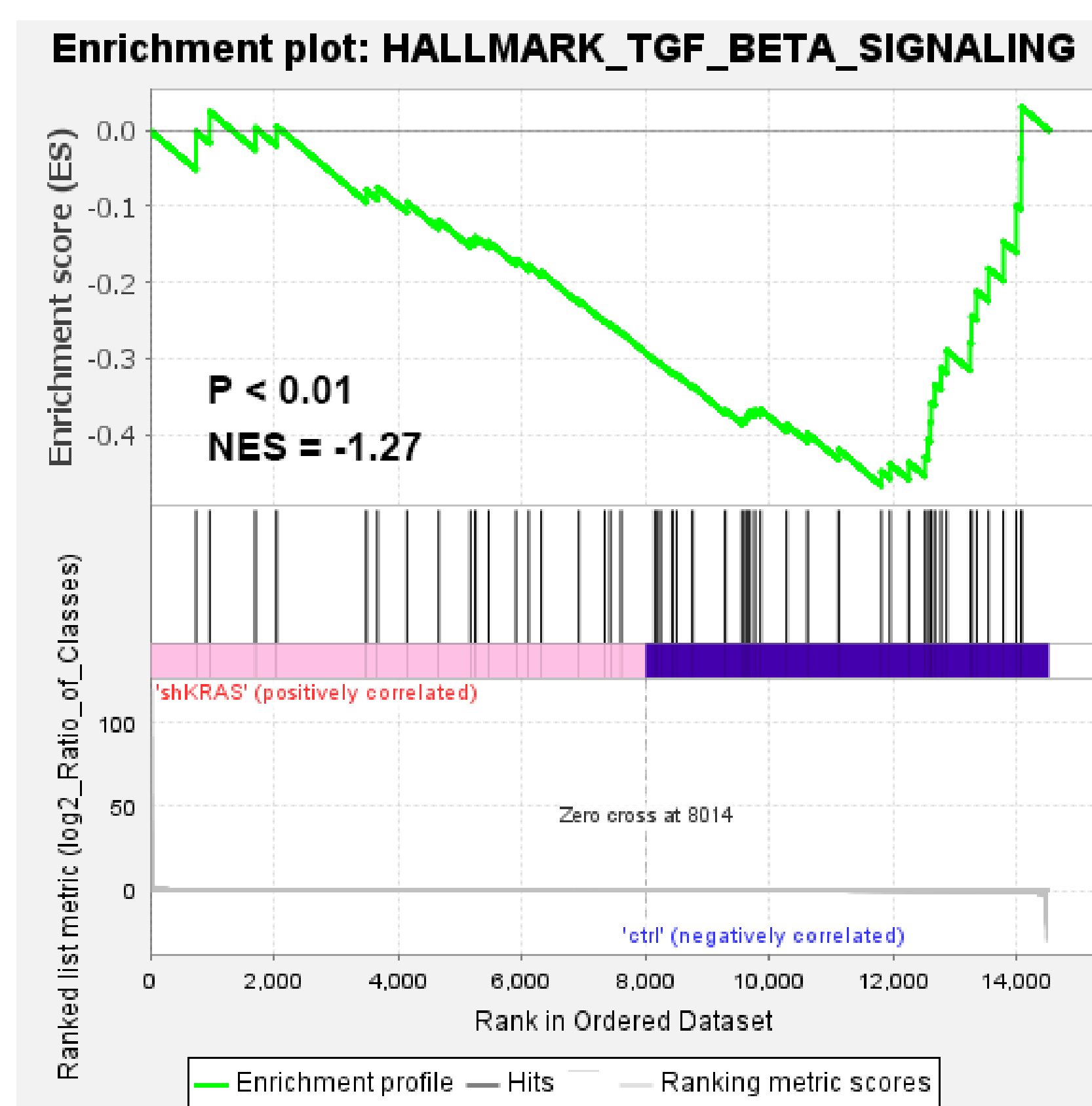
Supplementary figure 6. Induction and validation of Adagrasib acquired resistance in SW837. (A)

Schematic diagram showing long term treatment of adagrasib modeling KRAS^{G12C} mutant CRC cell line SW837. **(B)** Colony formation assay of SW837-P and SW837-R treated with vehicle or adagrasib (100 or 500 nM). **(C)** SW837-P and SW837-R were treated with the indicated concentrations of adagrasib. **(D)** Immunoblot analysis of ERK signaling in SW837-P/R treated with increasing concentrations of adagrasib for 1 hour.

A



B



Supplementary figure 7. GSEA enrichment analysis of GSE116823 dataset. Hallmark pathway analysis enriched by downregulated genes in HCT116 following KRAS knockdown. **(A)** EMT pathway enrichment plot; **(B)** TGF-beta pathway enrichment plot.