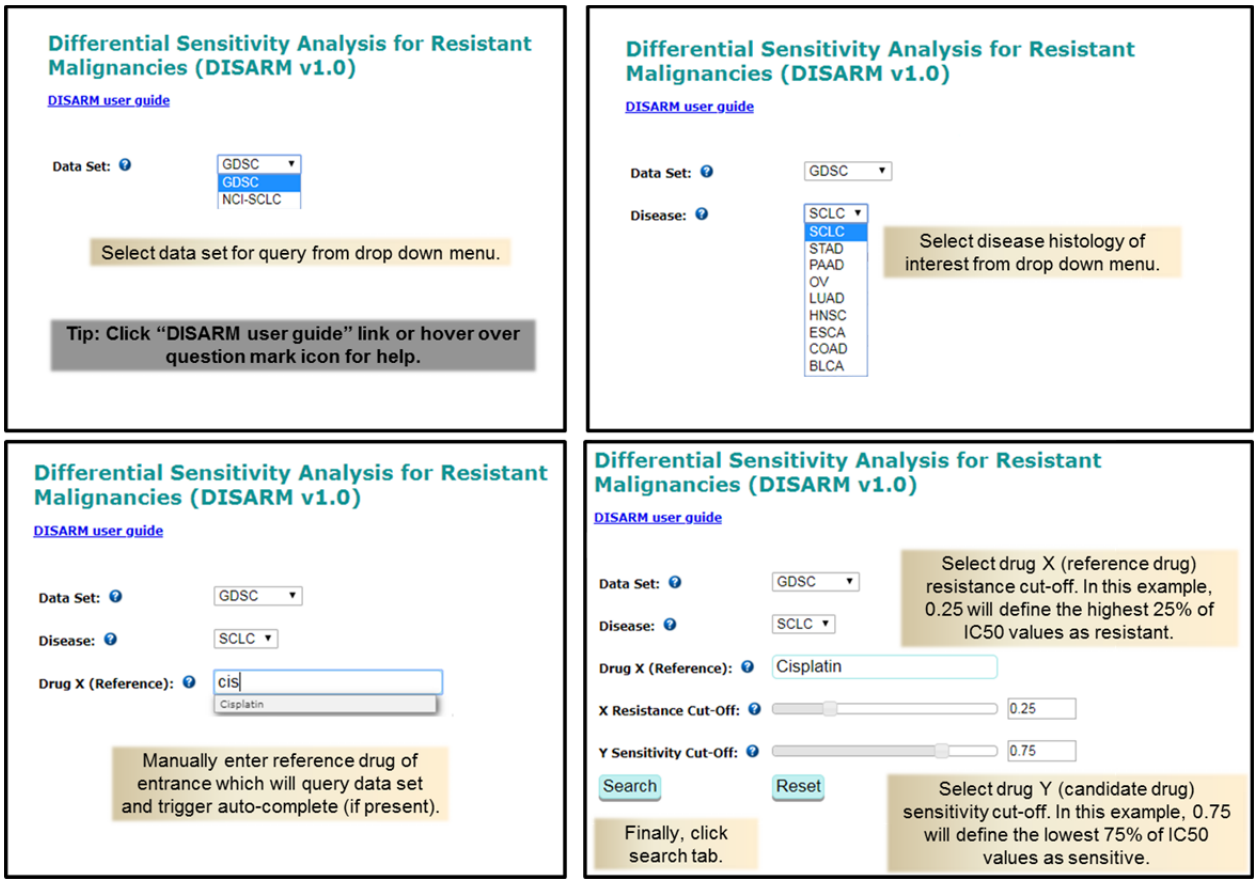
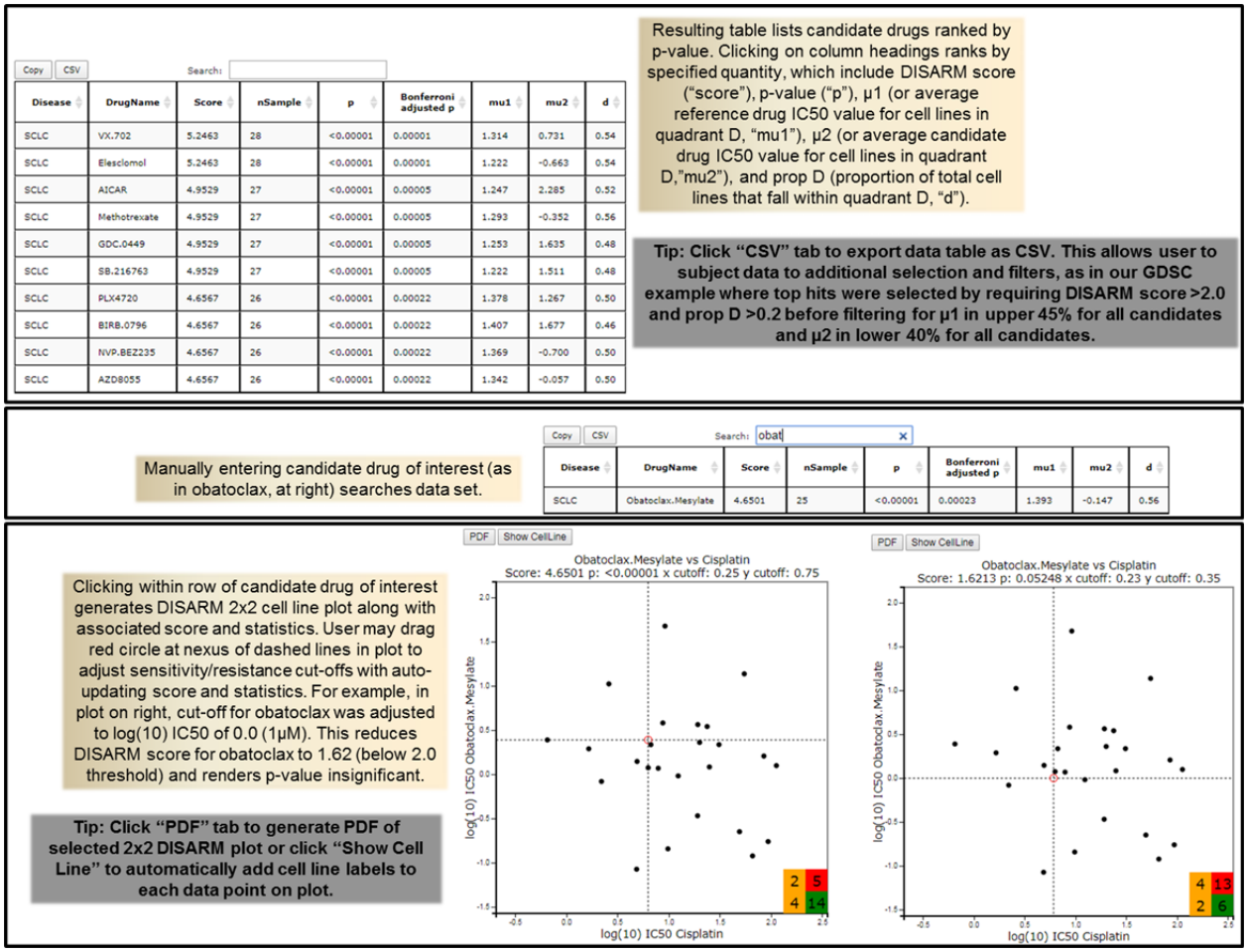
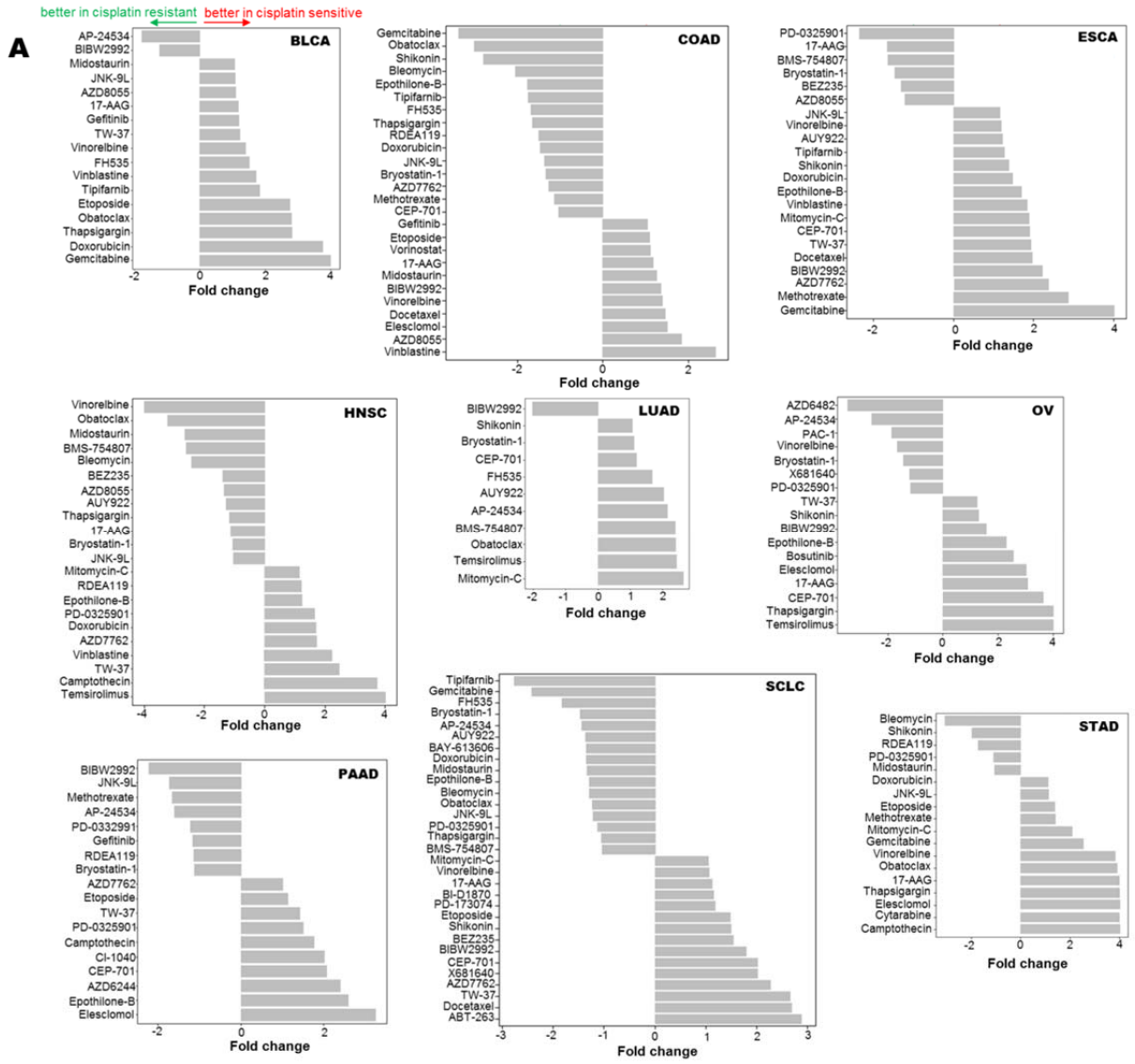
Supplementary Material



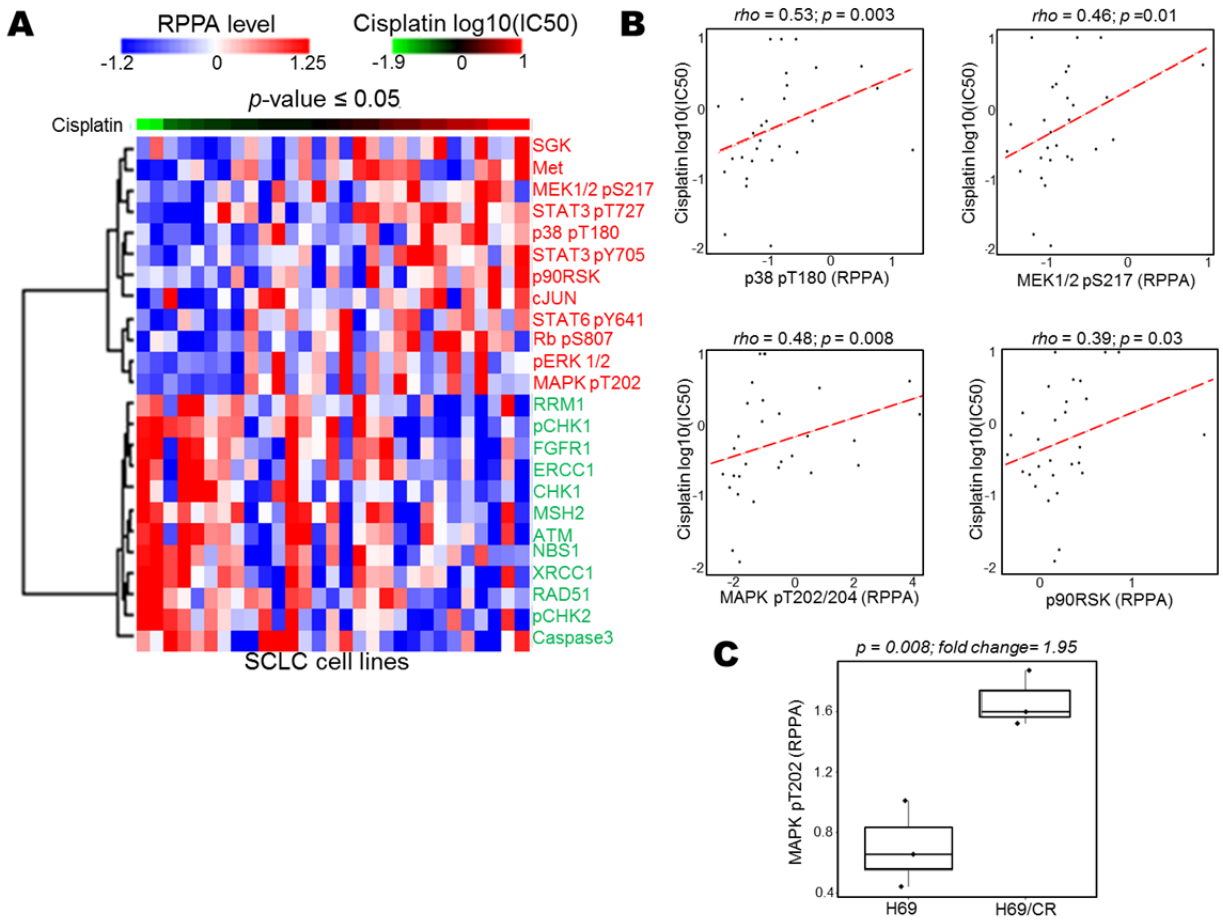
Supplementary Figure S1. Step-by-step user guide for DISARM application – Part 1. The above panels outline the steps required by the user to perform a query in DISARM web application or, similarly, DISARM software package, using the example of cisplatin as reference drug to query GDSC database for DISARM candidate drugs.



Supplementary Figure S2. Step-by-step user guide for DISARM web application – Part 2. The above panels highlight features of DISARM application following initial query, including sortable characteristics, searchable candidate drug list, and interactive DISARM 2x2 plots. The application also allows users to export data as comma-separated value (.csv) file in order to perform additional sorting and filtering as described.

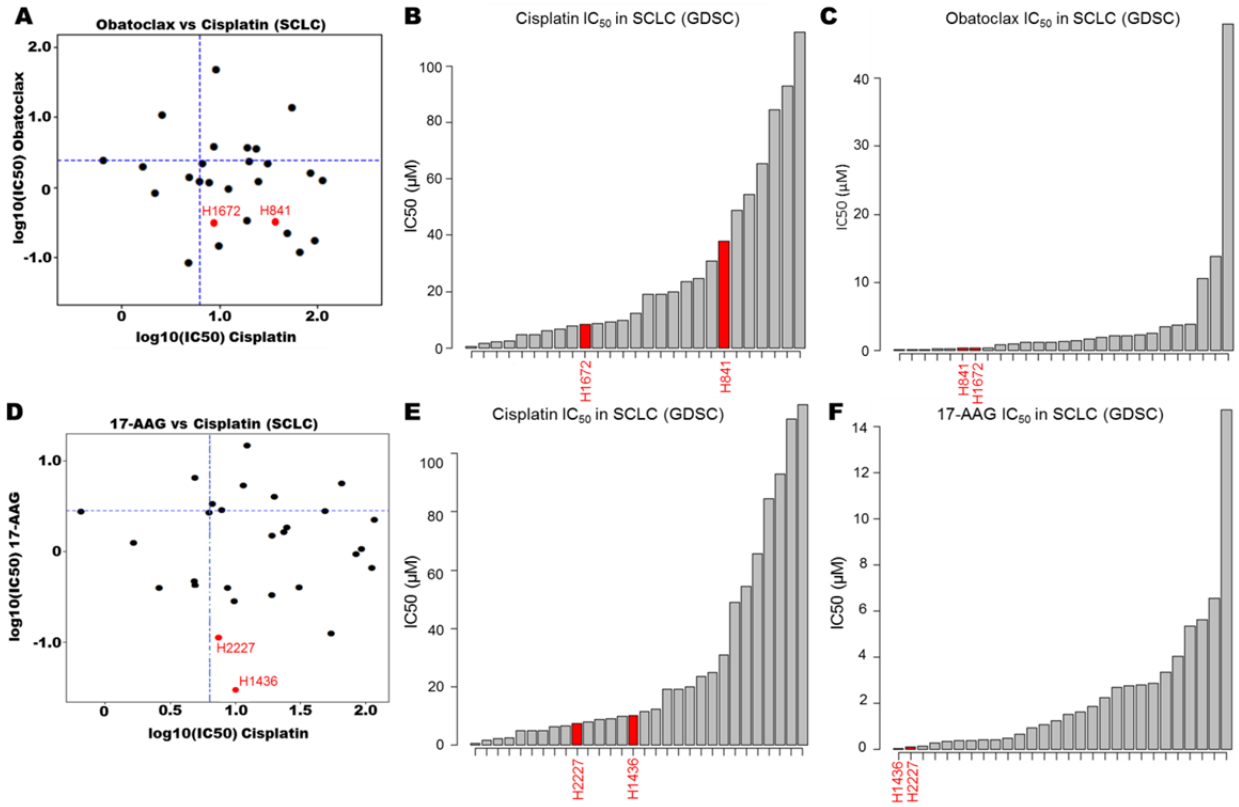


Supplementary Figure S3. Comparison of DISARM-selected candidates from GDSC in cisplatin-sensitive and –resistant models identifies numerous drugs that are more effective in cisplatin-resistant models (A) Bar charts illustrating fold change comparing mean IC_{50} values for specified drugs from GDSC data base in models that are cisplatin-sensitive or cisplatin-resistant on the basis of DISARM categorization. As indicated at top left, those to left of zero trend toward improved IC_{50} values in cisplatin-resistant models.



Supplementary Figure S4. Cisplatin-resistance in SCLC, both *de novo* and acquired, is associated with increased expression of RAF-MEK-ERK (MAPK) pathway, a target predicted by DISARM

(A) Heatmap illustrating proteins whose expression, as quantified by RPPA, is correlated significantly with *de novo* cisplatin response in SCLC cell lines. **(B)** Correlation plots for selected proteins from **(A)** highlighting the abundance of components of the MAPK signaling pathway. **(C)** Box plot showing significant increase in phospho-MAPK expression by RPPA following acquired cisplatin-resistance by prolonged exposure to cisplatin in SCLC cell lines.



Supplementary Figure S5. Cisplatin-resistant SCLC models not previously analyzed by DISARM are sensitive to DISARM candidates. (A,D) Updated DISARM 2x2 plots for cisplatin/obatoclax **(A)** and cisplatin/17-AAG **(D)** illustrating placement of experimentally observed SCLC IC_{50} values in context of GDSC data. **(B-C, E-F)** Bar graphs highlighting our own experimentally calculated IC_{50} values for for cisplatin **(A, D),** obatoclax **(B)**, and 17-AAG **(E)** in cell lines not previously included in the respective GDSC analyses. All IC_{50} values are expressed as µM