Supplementary material (MATLAB codes and simulation results) for *"Intratumor Heterogeneity Alters Most Effective Drugs in Designed Combinations"*
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This supplementary package contains three folders: ./matlab/, ./simulations/, and ./analyses/

MATLAB classes/datasets (./matlab/)
./matlab/lib: contains all classes for performing Monte Carlo sampling and optimizing drug combinations;
          MATLAB codes in the other two folders create instances of class for simulations and analyses
./matlab/datasets: contains D21H30.m and D21H30.mat, the dataset with 21 drugs and 30 subpopulations (shRNAs).

IMPORTANT NOTE: CPLEX libraries are required to solve the optimization problems – to derive optimal drug combinations. CPLEX libraries for MATLAB need to be placed inside a ./matlab/cplex folder (or on path). The libraries are not included in this supplementary package due to license restrictions.

Simulations (./simulations/)
All simulations were run on a computing cluster. Jobs were written in shell scripts (.sh files).

Simulation (folder name)	Description (brief summary of input parameter values for each simulation run)
N10000	Monte Carlo simulation 10,000 heterogeneous tumor populations Symmetric toxicity Drug optimized based on all subpopulations

N10000_subpopOnly1.2
   Contains two simulations:
   N10000_subpopOnly1
   N10000_subpopOnly2
	Tumor populations given (from simulation results in *N10000*)
	   N10000 results were first processed to remove any weak Pareto optimal
	   solutions (see *anlyz.N10000 postsim_process* in ./analyses/ folder)
	10,000 heterogeneous tumor populations
	Symmetric toxicitydrug optimized based on only predominant (subpopOnly1) or
	   second largest (subpopOnly2) subpopulation

N10000_sametox0	Monte Carlo simulation 10,000 heterogeneous tumor populations Asymmetric toxicity Drug optimized based on all subpopulations

bcN1
   Contains multiple simulations that are
   subsequently combined
	Monte Carlo simulation with first two largest subpopulations fixed (see methods in
	   paper for details)
	13,050 heterogeneous tumor populations
	Symmetric toxicity
	Drug optimized based on all subpopulations

bcN1_subpopOnly1.2
   Contains two simulations:
   bcN1_subpopOnly1
   bcN1_subpopOnly2
	Tumor populations given (from simulation results in *bcN1*)
	   bcN1 results were combined and processed to remove any weak Pareto optimal
	   solutions (see *anlyz.bcN1 postsim_process* in ./analyses/ folder)
	13,050 heterogeneous tumor populations
	Symmetric toxicity
	Drug optimized based on only predominant (subpopOnly1) or second largest
	   (subpopOnly2) subpopulation

rho_selection
   Contains multiple simulations
   (different rho values; modified
   manually in OptimizationModels.m;
   see comments in code)
	Tumor population given (single homogeneous shATM population)
	1 homogeneous tumor population
	Symmetric toxicity
	Drug optimized based on all subpopulations (i.e. in this case just the one)
	Maximum toxicity constraint value set to generate all solutions along Pareto frontier

noToxMaxConstraint
   Contains four simulations (modified
   manually in code; see comments in
   code)
	Tumor population given
	1 homogeneous tumor population
	Symmetric toxicity
	Drug optimized based on all subpopulations
	Maximum toxicity constraint value set to generate all solutions along Pareto frontier

Analyses (./analyses/)

Simulation results (from above, saved as .mat files) were copied into ./analyses/ as working copies for analyses.

Simulation results	Working copy in
N10000, *N10000_ subpopOnly1*, *N10000_ subpopOnly2*, *N10000_ sametox0*	./analyses/output/
bcN1, *bcN1_subpopOnly1*, *bcN1_subpopOnly2*	./analyses/outputs_bc/
rho_selection	./analyses/anlyz.rho_selection/
noToxMaxConstraint	./analyses/anlyz.noToxMaxConstraint/

Some MATLAB codes in ./analyses/ may require varying the parameter values manually to generate all figures (e.g. in specifying which regimen to analyze). These were commented accordingly in codes.

Analysis (folder name)	Description	Used to generate figure…
anlyz.dataset	Generates summary figures (heatmaps/clustergrams) of datasets	Fig. S1, Fig. 7A
anlyz.rho_selection	Analyzes *rho_selection* results	Fig. S3
anlyz.noToxMaxConstraint	Analyzes *noToxMaxConstraint* results	Fig. 2, Fig. S4
anlyz.N10000 postsim_process	Removes weak Pareto optimal solutions from *N10000* results Newly generated results (.mat) copied to ./analyses/outputs	N/A
anlyz.N10000_sametox0	Analyzes *N10000_sametox0* simulation results	Fig. S14, Fig. S15, Fig. 7B, 7C
anlyz.N10000_sametox1	Performs general statistical and sensitivity analyses on *N10000* results	Fig. 3, Fig. 6, Fig. S8
anlyz.N10000_sametox1_subpopOnly1	Performs general statistical and sensitivity analyses on *N10000_subpopOnly1* results	Fig. 4, Fig. S9
anlyz.N10000_sametox1 vs_subpopOnly1	Compares *N10000* and *N10000_subpopOnly1* results	Fig. 5
anlyz.N10000_sametox1 vs_subpopOnly1.2	Compares *N10000* and (*N10000_subpopOnly1* & *N10000_subpopOnly2*) results	Fig S10
anlyz.N10000_sametox1 partial_corr	Matthews correlation and partial spearman correlation analysis of *N10000* and *N10000_subpopOnly1* results	Fig. S5, Fig. S6, Fig. S7
anlyz.N10000_sametox1 drug_distribution	Analyzes *N10000* versus *N10000_subpopOnly1*; *N10000* versus *N10000_subpopOnly1* and *N10000_subpopOnly2* results, decomposed based on predominant and second largest subpopulation proportions	Fig. S11, Fig. S12
anlyz.bcN1 postsim_process	Combines *bcN1* simulation results Removes weak Pareto optimal solutions from combined *bcN1* results Newly generated results (.mat) copied to ./analyses/outputs_bc/	N/A
anlyz.bcN1 drug_distribution	Analyzes *bcN1* versus *bcN1_subpopOnly1*; *bcN1* versus *bcN1_subpopOnly1* and *bcN1_subpopOnly2* results, decomposed based on predominant and second largest subpopulation proportions	Fig. S13