Data (drug information)

- Efficacy of each compound for each cell line
  - ① IC50
  - ② Slope of the dose-response curve for drug
  - ③ Maximum cells killed (percentage) with drug
  - Y Estimated total synergy between drug A and drug B in combination (for training)
- Drug chemical information
  - ⑤ MW - Molecular weight
  - ⑥ HBA - H-bond acceptors
  - ⑦ HBD - H-bond donors
  - ⑧ cLogP - Calculated log P
  - ⑨ Lipinski - Lipinski's rule of 5

Molecular data

	mutation snp			cnv			methylation			expression levels data		
	C1	C2	C3	C1	C2	C3	C1	C2	C3	C1	C2	C3
GENE1												
GENE2												
GENE3												
GENE4												
GENE5												
GENE6												
GENE7												
GENE8												
GENE9												
GENE10												
GENE11												
GENE12												
GENE13												
GENE14												
GENE15												
GENE16												
GENE17												
GENE18												
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GENE20186												

Molecular data

	mutation snp			cnv			methylation			expression levels data		
	C1	C2	C3	C1	C2	C3	C1	C2	C3	C1	C2	C3
GENE1												
GENE2												
GENE3												
GENE4												
GENE5												
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GENE7												
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GENE20186												

Feature selection; select genes to build regression model for drug-combination synergy

Molecular data

	mutation snp			cnv			methylation			expression levels data		
	C1	C2	C3	C1	C2	C3	C1	C2	C3	C1	C2	C3
GENE1												
GENE2												
GENE3												
GENE4												
GENE5												
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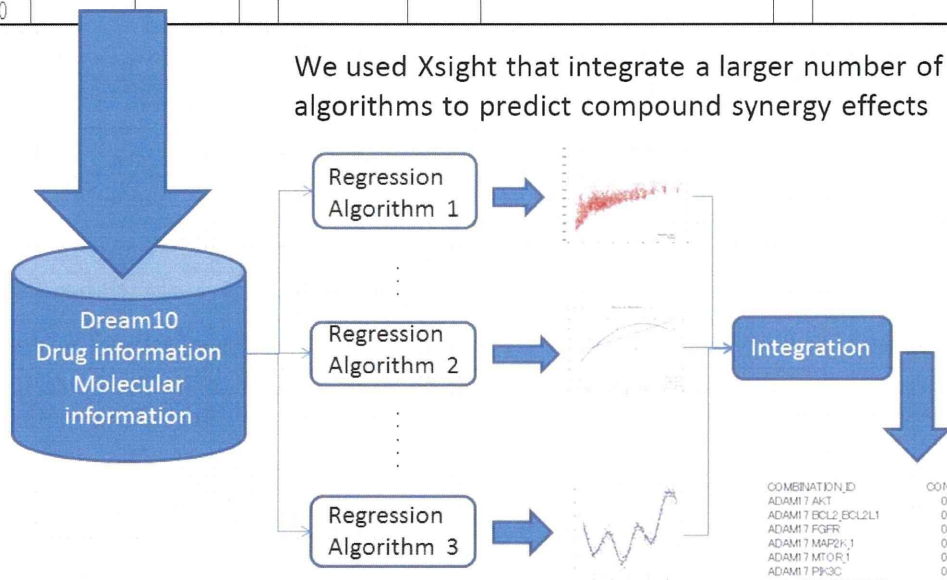
GENE20186												

Based on molecular interaction network, we selected informative genes to infer compound synergy effects.

Training data

Combination		Cell line	Drug information					Molecular information		
Drug A	Drug B	Cell line	IC50 Drug A	IC50 Drug B	···	Lipinski Drug B	Synergy	Mutation(SNPS) Gene 1 in Cell line	···	Expression level Gene 15 in Cell line
D1	D2	C1								
D1	D2	C2								
D2	D3	C10								

We used Xsight that integrate a larger number of algorithms to predict compound synergy effects



Sub challenge 1A round 3 leader board

Q1A

ID	Date	name	team	Global Correlation	Mean Correlation (all)	STE (all)	Mean Correlation (top 30%)	STE (top 30%)	Mean Correlation (top 20%)	STE (top 20%)	Mean Correlation (top 10%)	STE (top 10%)
5601858			FINCHIPS	0.19	0.27	0.73	0.56	0.54	0.56	0.63	0.57	0.59
5608044			FINCHIPS	0.21	0.28	0.72	0.56	0.54	0.56	0.63	0.57	0.59
5608141			Alex_1	0.29	0.31	0.71	0.47	0.53	0.46	0.53	0.53	0.41
5609574			GMM	0.18	0.21	0.72	0.4	0.58	0.46	0.51	0.45	0.55
5609367			Xtract	0.18	0.25	0.73	0.33	0.72	0.45	0.65	0.29	0.77
5605043			OurTeam	0.32	0.33	0.72	0.42	0.64	0.42	0.65	0.21	0.78
5608863			S.E.R.G.E	0.28	0.25	0.73	0.41	0.64	0.4	0.69	0.42	0.73
5609342			Xtract	0.15	0.26	0.73	0.41	0.69	0.4	0.68	0.43	0.69
5609123			BigHero5	0.21	0.16	0.76	0.26	0.66	0.39	0.58	0.45	0.63
5580961			GodzikLab	0.11	0.2	0.73	0.34	0.74	0.38	0.72	0.52	0.64
									0.38	0.59	0.36	0.6
									0.38	0.7	0.62	0.51
									0.37	0.73	0.24	0.8
									0.37	0.69	0.61	0.51
									0.36	0.69	0.15	0.87
									0.36	0.71	0.58	0.53
									0.35	0.74	0.55	0.62
									0.35	0.54	0.55	0.49
									0.34	0.71	0.51	0.61
									0.34	0.6	0.37	0.55
									0.33	0.46	0.12	0.32
									0.33	0.74	0.33	0.8
									0.32	0.67	0.51	0.65
									0.32	0.67	0.34	0.71
5609124			BigHero5	0.22	0.17	0.74	0.29	0.58	0.32	0.6	0.55	0.53

Previous 1-25 of 139 Next

Among 139 submissions, we are in top 5th (and 8th).

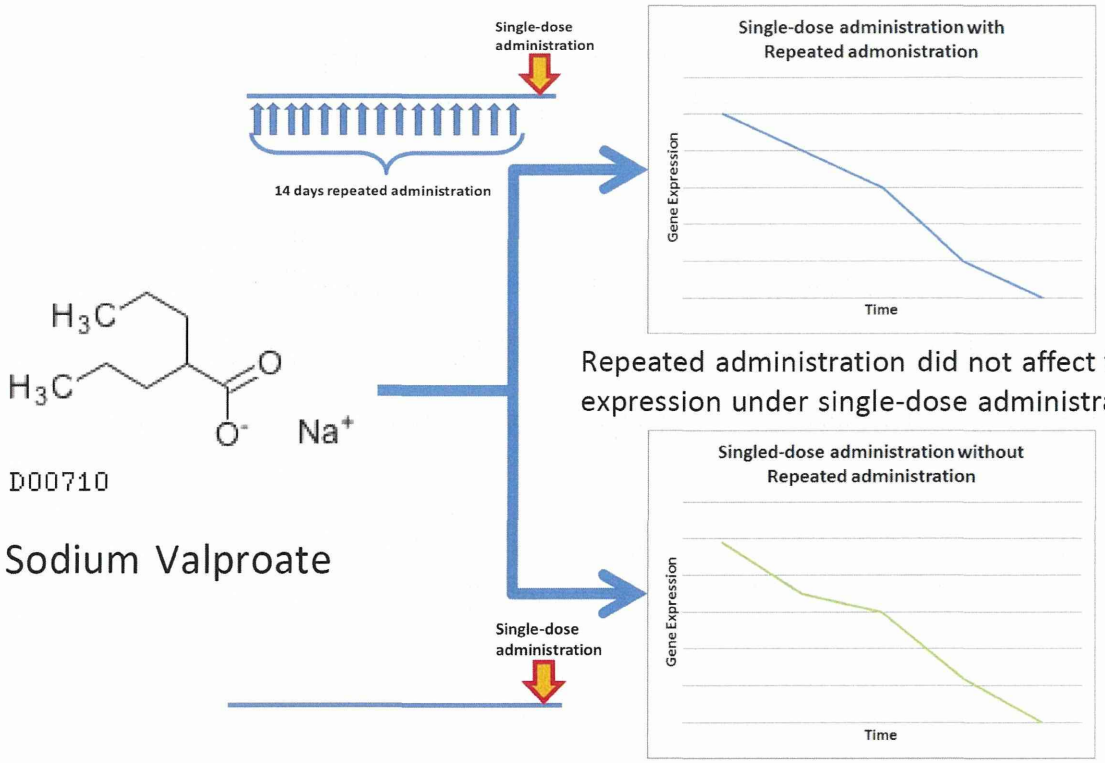
These results demonstrated that our Xsight system successfully infer compound synergy effects from multi-dimensional omics data

Xsight system current status

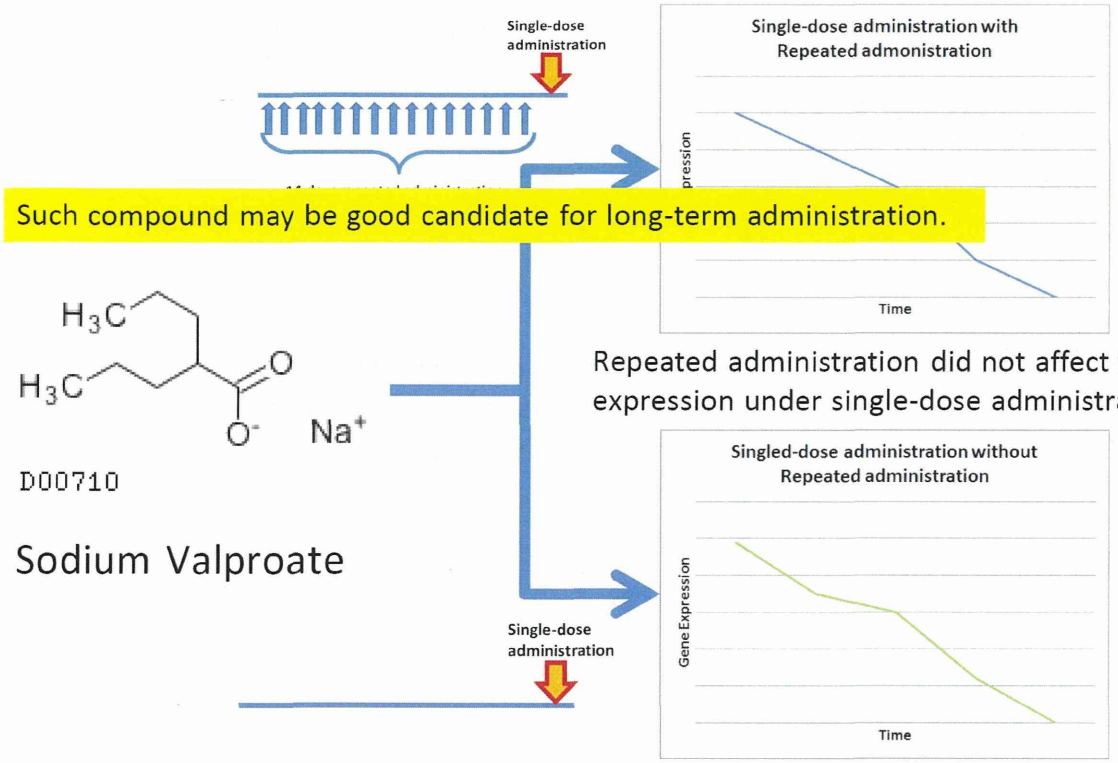
- Xsight system is an ensemble machine-learning based computational system for big data analysis
- Xsight system integrates more than **100** algorithms (e.g., **120** regression methods, **58** binary classifiers, and **51** multiclass classifiers to answer your question.)
- We are now implementing other algorithms (e.g., feature selection methods) on Xsight system.

Application of Xsight system for toxicology

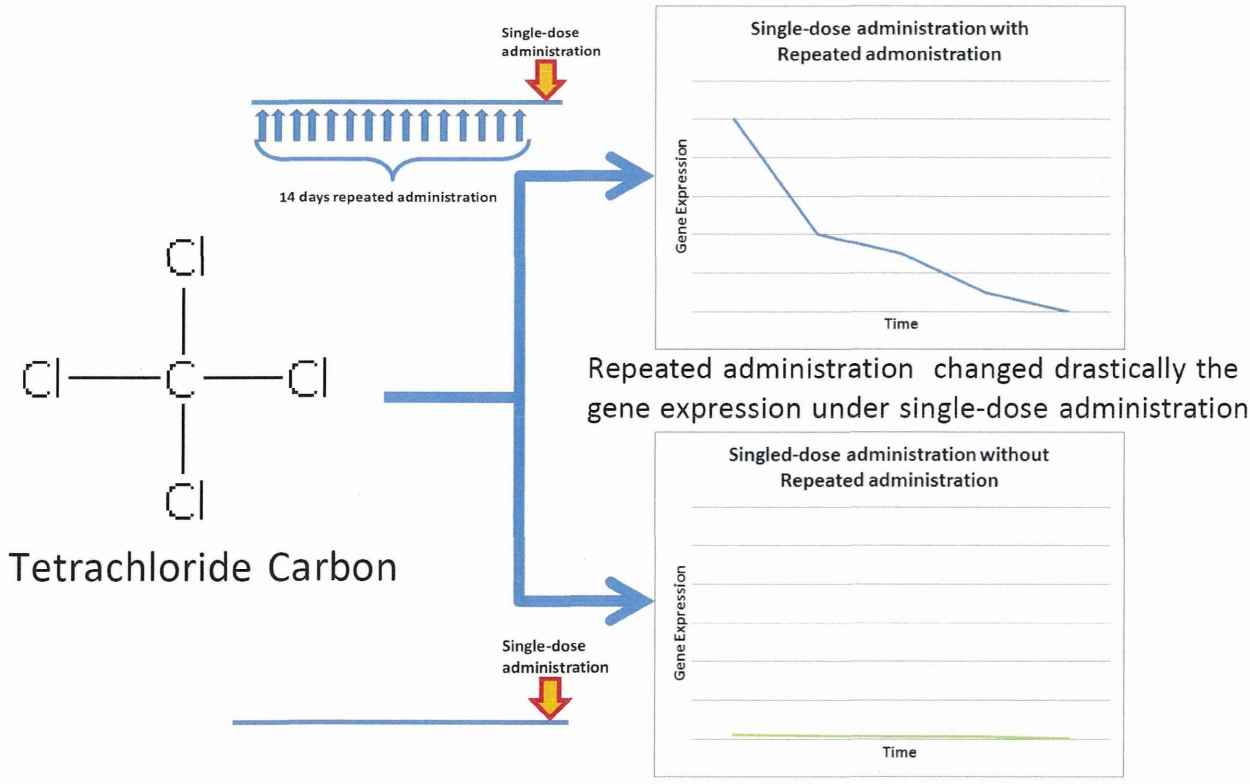
Application of Xsight to predict effect of repeated administration of drug compounds



Application of Xsight to predict effect of repeated administration of drug compounds



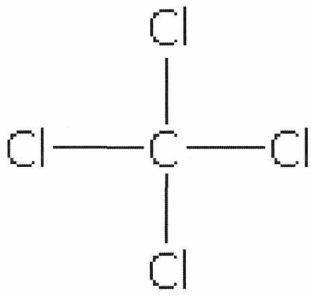
Application of Xsight to predict effect of repeated administration of drug compounds



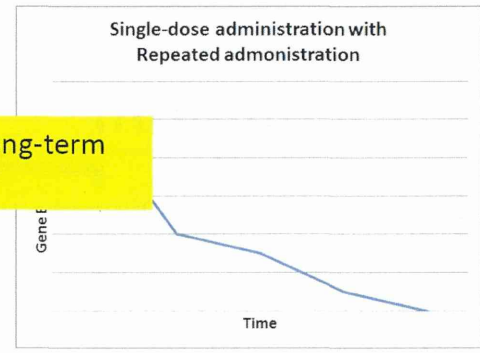
Application of Xsight to predict effect of repeated administration of drug compounds

Single-dose administration

Such compound could not be candidate for long-term administration

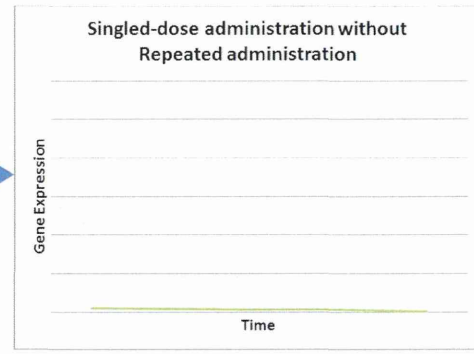


Tetrachloride Carbon



Repeated administration changed drastically the gene expression under single-dose administration

Single-dose administration

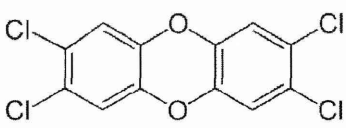


Application of Xsight to predict effect of repeated administration of drug compounds

Based on high-dimentional toxicology data (parcellome, expression data of repetitive administration, chemincal structure),

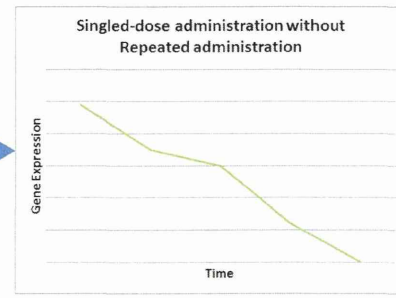
Percellome Project

Data of repetitive administration of several compounds

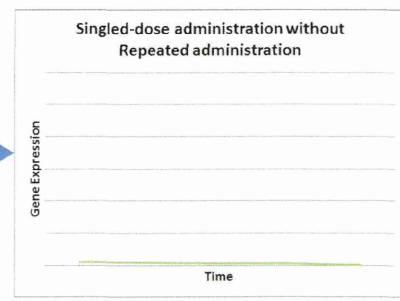


Chemical features of target compound

Xsight

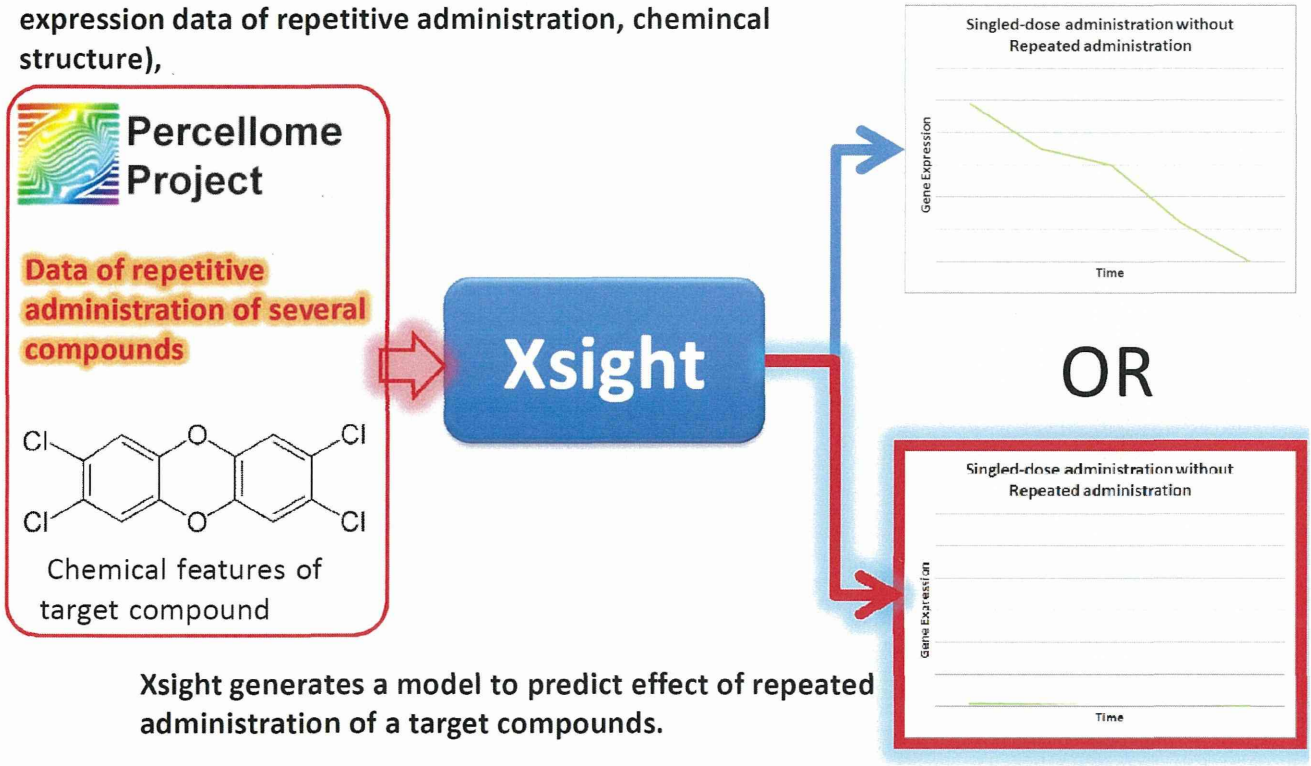


OR



Application of Xsight to predict effect of repeated administration of drug compounds

Based on high-dimentional toxicology data (parcellome, expression data of repetitive administration, chemincal structure),



Xsight generates a model to predict effect of repeated administration of a target compounds.

- We developed an ensemble learning system, Xsight, that integrates more than 100 machine learning algorithms.
- We applied Xsight for multi-omics data, DREAM10 data, to test predictive performance of Xsight.
- We are planning to apply Xsight system to predict effects of repeated administration of a compound.

別添５

Ⅲ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻名	ページ	出版年
Juliandi B, Tanemura K, Igarashi K, Tominaga T, Furukawa Y, Otsuka M, Moriyama N, Ikegami D, Abematsu M, Sanosaka T, Tsujimura K, Narita M, Kanno J, Nakashima K.	Reduced Adult Hippocampal Neurogenesis and Cognitive Impairments following Prenatal Treatment of the Antiepileptic Drug Valproic Acid.	Stem Cell Reports	5(6)	996 - 1009	2015
Hieu T Nim, Milena B Furtado, Mauro W Costa, Nadia A Rosenthal, Hiroaki Kitano and Sarah E Boyd.	VISIONET: intuitive visualisation of overlapping transcription factor networks, with applications in cardiogenic gene discovery.	BMC Bioinformatics	16	141	2015
北野宏明	システム・トキシコロジーの展開.	QIGEN eyes	12	7 - 9	2015
北野宏明	システム・トキシコロジーの展開(第2回).	QIGEN eyes	13	7 - 9	2015
Tiago J. S. Lopes, Jason E. Shoemaker, Yukiko Matsuoka, Yoshihiro Kawaoka, Hiroaki Kitano.	Identifying problematic drugs based on the characteristics of their targets.	frontiers in Pharmacology	6	186	2015