SUPPLEMENTARY MATERIAL

TUNING HERG OUT: ANTITARGET QSAR MODELS FOR DRUG DEVELOPMENT

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Table S1. Statistical characteristics of QSAR models for hERG liability for the threshold of 1µM assessed by 5-fold for the modeling set.

	Modeling Set (threshold 1 µM; *n=3951*)										
Model name	**Accuracy**	**BAC**	**Kappa**	**MCC**	**Sensitivity (Recall)**	**Specificity**	**Precision**	**F1**	**AUC**	**Coverage**	**Model parameters**
MACCS-SVM	0.84	0.68	0.42	0.45	0.40	0.96	0.73	0.51	0.68	0.71	C=4
featMorgan-SVM	0.86	0.72	0.50	0.52	0.48	0.96	0.74	0.58	0.72	0.74	C=4
Pharm. FP-SVM	0.84	0.61	0.30	0.35	0.25	0.97	0.70	0.37	0.61	0.78	C=4
PubChem-SVM	0.85	0.69	0.45	0.47	0.43	0.95	0.70	0.53	0.69	0.71	C=4
MACCS-RF	0.84	0.72	0.48	0.49	0.51	0.93	0.68	0.58	0.72	0.71	mtry=125
featMorgan-RF	0.85	0.71	0.48	0.49	0.48	0.94	0.68	0.56	0.71	0.74	mtry=215
Pharm. FP-RF	0.86	0.69	0.45	0.47	0.43	0.95	0.69	0.53	0.69	0.78	mtry=106
PubChem-RF	0.84	0.71	0.46	0.47	0.49	0.93	0.65	0.56	0.71	0.71	mtry=895
MACCS-TreeBag	0.84	0.71	0.47	0.48	0.49	0.93	0.68	0.57	0.71	0.71	none
featMorgan-TreeBag	0.85	0.70	0.46	0.48	0.45	0.95	0.70	0.54	0.70	0.74	none
Pharm. FP-TreeBag	0.85	0.70	0.45	0.46	0.45	0.95	0.65	0.53	0.70	0.78	none
PubChem-TreeBag	0.84	0.71	0.46	0.46	0.50	0.93	0.63	0.55	0.71	0.71	none
MACCS-GBM	0.83	0.67	0.40	0.43	0.38	0.95	0.70	0.50	0.67	0.71	interaction depth = 5, ntrees=250, shrinkage=0.1
featMorgan-GBM	0.85	0.69	0.45	0.47	0.43	0.95	0.71	0.54	0.69	0.74	interaction depth = 5, ntrees=250, shrinkage=0.1
Pharm. FP-GBM	0.86	0.69	0.45	0.47	0.42	0.96	0.70	0.53	0.69	0.78	interaction depth = 5, ntrees=250, shrinkage=0.1
PubChem-GBM	0.85	0.68	0.42	0.45	0.39	0.96	0.71	0.51	0.68	0.71	interaction depth = 4, ntrees=250, shrinkage=0.1
Consensus	0.89	0.86	0.43	0.49	0.82	0.90	0.34	0.48	0.86	0.83	featMorgan-GBM +PubChem-TreeBag + Pharm. FP-RF +MACCS-SVM
Consensus Rigor	0.91	0.88	0.53	0.56	0.83	0.92	0.43	0.57	0.88	0.40	featMorgan-GBM +PubChem-TreeBag + Pharm. FP-RF +MACCS-SVM

SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve; Consesus and Consensus Rigor were built by averaging the predicted values from each individual model (featMorgan-GBM, PubChem-TreeBag, Pharm. FP-RF, MACCS-SVM).

Table S2. Statistical characteristics of QSAR models for hERG liability for the threshold of 1μM assessed by test set.

	Test Set (threshold 1 μM, *n=987)*									
Model name	**Accuracy**	**BAC**	**Kappa**	**MCC**	**Sensitivity (Recall)**	**Specificity**	**Precision**	**F1**	**AUC**	**Coverage**
MACCS-SVM	0.86	0.71	0.50	0.53	0.44	0.98	0.84	0.57	0.71	0.86
featMorgan-SVM	0.86	0.72	0.52	0.57	0.45	0.98	0.88	0.59	0.72	0.82
Pharm. FP-SVM	0.83	0.59	0.26	0.34	0.20	0.99	0.78	0.32	0.59	0.88
PubChem-SVM	0.86	0.68	0.45	0.49	0.39	0.98	0.81	0.52	0.68	0.75
MACCS-RF	0.85	0.72	0.51	0.52	0.50	0.95	0.74	0.60	0.72	0.86
featMorgan-RF	0.86	0.73	0.53	0.55	0.51	0.96	0.78	0.62	0.73	0.82
Pharm. FP-RF	0.88	0.73	0.54	0.56	0.50	0.97	0.78	0.61	0.73	0.88
PubChem-RF	0.86	0.73	0.51	0.52	0.50	0.95	0.72	0.59	0.73	0.75
MACCS-TreeBag	0.84	0.72	0.50	0.51	0.51	0.94	0.70	0.59	0.72	0.86
featMorgan-TreeBag	0.85	0.71	0.50	0.52	0.47	0.96	0.77	0.58	0.71	0.82
Pharm. FP-TreeBag	0.87	0.74	0.54	0.55	0.53	0.96	0.74	0.62	0.74	0.88
PubChem-TreeBag	0.85	0.72	0.48	0.50	0.49	0.95	0.69	0.57	0.72	0.75
MACCS-GBM	0.84	0.69	0.46	0.49	0.41	0.97	0.78	0.54	0.69	0.86
featMorgan-GBM	0.85	0.69	0.48	0.53	0.41	0.98	0.87	0.55	0.69	0.82
Pharm. FP-GBM	0.86	0.69	0.47	0.50	0.41	0.97	0.79	0.54	0.69	0.88
PubChem-GBM	0.85	0.66	0.40	0.45	0.34	0.98	0.79	0.48	0.66	0.75
Consensus	0.90	0.90	0.54	0.59	0.89	0.90	0.44	0.59	0.90	0.85
Consensus Rigor	0.91	0.91	0.53	0.58	0.91	0.91	0.42	0.58	0.91	0.53

SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve; Consesus and Consensus Rigor were built by averaging the predicted values from each individual model (featMorgan-GBM, PubChem-TreeBag, Pharm. FP-RF, MACCS-SVM).

Table S3. Statistical results of QSAR models for hERG liability for the threshold of 1μM assessed by y-randomization.

Model name	**Accuracy**	**BAC**	**Kappa**	**Sensitivity**	**Specificity**	**AUC**
MACCS-SVM	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.50±0.01
featMorgan-SVM	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.50±0.02
Pharm. FP-SVM	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.51±0.02
PubChem-SVM	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.50±0.03
MACCS-RF	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.52±0.02
featMorgan-RF	0.76±0.01	0.51±0.01	0.00±0.01	0.00±0.01	0.00±0.01	0.53±0.02
Pharm. FP-RF	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.51±0.01
PubChem-RF	0.80±0.01	0.50±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.50±0.02
MACCS-TreeBag	0.75±0.01	0.50±0.03	0.01±0.05	0.09±0.05	0.91±0.01	0.51±0.03
featMorgan-TreeBag	0.78±0.01	0.50±0.01	0.00±0.03	0.03±0.02	0.97±0.01	0.51±0.04
Pharm. FP-TreeBag	0.75±0.01	0.50±0.01	0.01±0.03	0.07±0.02	0.92±0.01	0.51±0.03
PubChem-TreeBag	0.74±0.01	0.50±0.02	0.01±0.03	0.11±0.03	0.90±0.01	0.51±0.02
MACCS-GBM	0.80±0.01	0.30±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.50±0.01
featMorgan-GBM	0.80±0.01	0.31±0.01	0.00±0.01	0.01±0.01	1.00±0.01	0.51±0.01
Pharm. FP-GBM	0.79±0.01	0.31±0.01	0.00±0.01	0.01±0.01	0.99±0.01	0.52±0.03
PubChem-GBM	0.80±0.01	0.31±0.01	0.00±0.01	0.00±0.01	1.00±0.01	0.51±0.01

The presented results are based on an average overall 10 randomly shuffled response (y-randomization); SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve.

Table S4. Statistical characteristics of QSAR models for hERG liability for the threshold of 10µM assessed by 5-fold for the modeling set.

Model name	Modeling Set (threshold 10µM; *n=3867)*										Model parameters
	Accuracy	**BAC**	**Kappa**	**MCC**	**Sensitivity (Recall)**	**Specificity**	**Precision**	**F1**	**AUC**	**Coverage**	
MACCS-SVM	0.78	0.75	0.51	0.52	0.86	0.64	0.80	0.83	0.75	0.70	C=4
featMorgan-SVM	0.80	0.78	0.57	0.57	0.86	0.69	0.81	0.84	0.78	0.74	C=4
Pharm. FP-SVM	0.76	0.74	0.49	0.50	0.85	0.63	0.77	0.81	0.74	0.78	C=4
PubChem-SVM	0.79	0.77	0.54	0.54	0.85	0.68	0.81	0.83	0.77	0.70	C=4
MACCS-RF	0.78	0.75	0.52	0.52	0.85	0.66	0.81	0.83	0.75	0.70	mtry=43
featMorgan-RF	0.79	0.77	0.55	0.55	0.86	0.68	0.81	0.83	0.77	0.74	mtry=45
Pharm. FP-RF	0.78	0.77	0.55	0.55	0.84	0.71	0.78	0.81	0.77	0.78	mtry=25
PubChem-RF	0.79	0.77	0.54	0.55	0.85	0.69	0.81	0.83	0.77	0.70	mtry=194
MACCS-TreeBag	0.78	0.76	0.53	0.53	0.85	0.67	0.81	0.83	0.76	0.70	none
featMorgan-TreeBag	0.77	0.76	0.52	0.52	0.84	0.67	0.80	0.82	0.76	0.74	none
Pharm. FP-TreeBag	0.76	0.74	0.50	0.50	0.83	0.66	0.78	0.80	0.74	0.78	none
PubChem-TreeBag	0.78	0.76	0.53	0.53	0.84	0.69	0.81	0.82	0.76	0.70	none
MACCS-GBM	0.77	0.74	0.49	0.49	0.85	0.62	0.79	0.82	0.74	0.70	interaction depth = 5, ntrees=250, shrinkage=0.1
featMorgan-GBM	0.76	0.74	0.50	0.50	0.84	0.64	0.79	0.81	0.74	0.74	interaction depth = 5, ntrees=250, shrinkage=0.1
Pharm. FP-GBM	0.77	0.75	0.51	0.51	0.84	0.65	0.78	0.81	0.75	0.78	interaction depth = 5, ntrees=250, shrinkage=0.1
PubChem-GBM	0.78	0.76	0.52	0.52	0.85	0.66	0.80	0.82	0.76	0.70	interaction depth = 5, ntrees=250, shrinkage=0.1
Consensus	0.84	0.83	0.65	0.65	0.85	0.81	0.90	0.88	0.83	0.74	featMorgan-GBM +PubChem-TreeBag+Pharm. FP-RF +MACCS-SVM
Consensus Rigor	0.88	0.87	0.71	0.71	0.89	0.84	0.93	0.91	0.87	0.34	featMorgan-GBM +PubChem-TreeBag+Pharm. FP-RF +MACCS-SVM

SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve; Consesus and Consensus Rigor were built by averaging the predicted values from each individual model (featMorgan-GBM, PubChem-TreeBag, Pharm. FP-RF, MACCS-SVM).

Table S5. Statistical results of QSAR models for hERG liability for the threshold of 10μM assessed by y-randomization.

Model name	**Accuracy**	**BAC**	**Kappa**	**Sensitivity**	**Specificity**	**AUC**
MACCS-SVM	0.59±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.02
featMorgan-SVM	0.59±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.51±0.02
Pharm. FP-SVM	0.59±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.01
PubChem-SVM	0.59±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.02
MACCS-RF	0.59±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.01
featMorgan-RF	0.59±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.53±0.01
Pharm. FP-RF	0.54±0.01	0.51±0.02	0.01±0.03	0.70±0.02	0.31±0.02	0.52±0.01
PubChem-RF	0.54±0.01	0.50±0.01	0.00±0.02	0.68±0.03	0.32±0.02	0.52±0.01
MACCS-TreeBag	0.52±0.01	0.49±0.01	0.02±0.01	0.64±0.01	0.34±0.01	0.51±0.01
featMorgan-TreeBag	0.57±0.01	0.50±0.02	0.00±0.01	088±0.01	0.12±0.02	0.50±0.01
Pharm. FP-TreeBag	0.54±0.01	0.50±0.02	0.01±0.02	0.68±0.02	0.33±0.04	0.50±0.01
PubChem-TreeBag	0.53±0.03	0.50±0.03	0.00±0.05	0.66±0.01	0.34±0.04	0.51±0.01
MACCS-GBM	0.59±0.01	0.31±0.01	0.02±0.01	0.93±0.02	0.08±0.02	0.51±0.01
featMorgan-GBM	0.59±0.01	0.31±0.01	0.02±0.02	0.94±0.01	0.08±0.01	0.51±0.01
Pharm. FP-GBM	0.59±0.01	0.31±0.02	0.02±0.03	0.96±0.01	0.09±0.01	0.52±0.01
PubChem-GBM	0.59±0.01	0.31±0.01	0.01±0.01	0.84±0.01	0.05±0.02	0.52±0.02

The presented results are based on an average overall 10 randomly shuffled response (y-randomization); SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve.

Table S6. Statistical characteristics of QSAR models for hERG liability for the threshold of 10μM assessed by test set.

	Test Set (threshold 10 μM, *n=966)*									
Model name	**Accuracy**	**BAC**	**Kappa**	**MCC**	**Sensitivity (Recall)**	**Specificity**	**Precision**	**F1**	**AUC**	**Coverage**
MACCS-SVM	0.83	0.79	0.60	0.60	0.91	0.66	0.84	0.87	0.79	0.85
featMorgan-SVM	0.85	0.82	0.65	0.66	0.92	0.72	0.87	0.89	0.82	0.80
Pharm. FP-SVM	0.82	0.78	0.58	0.59	0.91	0.64	0.83	0.87	0.78	0.87
PubChem-SVM	0.82	0.79	0.60	0.60	0.89	0.68	0.84	0.87	0.79	0.71
MACCS-RF	0.84	0.80	0.62	0.63	0.91	0.70	0.85	0.88	0.80	0.85
featMorgan-RF	0.85	0.82	0.66	0.66	0.93	0.71	0.86	0.89	0.82	0.80
Pharm. FP-RF	0.84	0.81	0.64	0.64	0.90	0.72	0.86	0.88	0.81	0.87
PubChem-RF	0.84	0.82	0.65	0.65	0.89	0.76	0.88	0.88	0.82	0.71
MACCS-TreeBag	0.83	0.80	0.62	0.62	0.89	0.72	0.86	0.88	0.80	0.85
featMorgan-TreeBag	0.83	0.79	0.61	0.61	0.91	0.68	0.85	0.88	0.79	0.80
Pharm. FP-TreeBag	0.84	0.81	0.64	0.65	0.91	0.71	0.86	0.88	0.81	0.87
PubChem-TreeBag	0.83	0.80	0.61	0.61	0.88	0.73	0.86	0.87	0.80	0.71
MACCS-GBM	0.81	0.77	0.56	0.57	0.90	0.64	0.83	0.86	0.77	0.85
featMorgan-GBM	0.83	0.80	0.61	0.61	0.90	0.69	0.85	0.88	0.80	0.80
Pharm. FP-GBM	0.81	0.77	0.56	0.56	0.90	0.64	0.83	0.86	0.77	0.87
PubChem-GBM	0.82	0.78	0.58	0.58	0.89	0.67	0.84	0.86	0.78	0.71
Consensus	0.90	0.91	0.75	0.76	0.89	0.93	0.97	0.93	0.91	0.78
Consensus Rigor	0.93	0.93	0.81	0.81	0.93	0.93	0.98	0.95	0.93	0.46

SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve; Consesus and Consensus Rigor were built by averaging the predicted values from each individual model (featMorgan-GBM, PubChem-TreeBag, Pharm. FP-RF, MACCS-SVM).

Table S7. Statistical characteristics of QSAR models for hERG liability for the threshold of 20μM assessed by 5-fold for the modeling set.

Model name	Modeling Set (threshold 20μM; *n=3636)*										
	Accuracy	**BAC**	**Kappa**	**MCC**	**Sensitivity (Recall)**	**Specificity**	**Precision**	**F1**	**AUC**	**Coverage**	**Model parameters**
MACCS-SVM	0.85	0.74	0.53	0.55	0.95	0.53	0.86	0.90	0.74	0.70	C=4
featMorgan-SVM	0.85	0.75	0.56	0.57	0.95	0.56	0.86	0.90	0.75	0.73	C=4
Pharm. FP-SVM	0.81	0.69	0.43	0.46	0.95	0.43	0.82	0.88	0.69	0.77	C=4
PubChem-SVM	0.83	0.73	0.51	0.52	0.94	0.52	0.85	0.89	0.73	0.70	C=4
MACCS-RF	0.83	0.74	0.51	0.52	0.91	0.58	0.87	0.89	0.74	0.70	mtry=125
featMorgan-RF	0.84	0.74	0.52	0.53	0.94	0.54	0.86	0.89	0.74	0.73	mtry=45
Pharm. FP-RF	0.82	0.72	0.49	0.50	0.93	0.52	0.84	0.88	0.72	0.77	mtry=158
PubChem-RF	0.83	0.75	0.52	0.53	0.92	0.58	0.87	0.89	0.75	0.70	mtry=895
MACCS-TreeBag	0.82	0.73	0.49	0.49	0.90	0.56	0.86	0.88	0.73	0.70	none
featMorgan-TreeBag	0.82	0.72	0.49	0.50	0.92	0.52	0.85	0.89	0.72	0.73	none
Pharm. FP-TreeBag	0.81	0.72	0.48	0.49	0.92	0.52	0.84	0.88	0.72	0.77	none
PubChem-TreeBag	0.83	0.75	0.52	0.52	0.91	0.58	0.87	0.89	0.75	0.70	none
MACCS-GBM	0.83	0.71	0.49	0.51	0.95	0.48	0.85	0.90	0.71	0.70	interaction depth = 4, ntrees=250, shrinkage=0.1
featMorgan-GBM	0.84	0.73	0.51	0.53	0.95	0.50	0.85	0.90	0.73	0.73	interaction depth = 5, ntrees=250, shrinkage=0.1
Pharm. FP-GBM	0.82	0.71	0.48	0.50	0.94	0.49	0.84	0.88	0.71	0.77	interaction depth = 5, ntrees=200, shrinkage=0.1
PubChem-GBM	0.84	0.73	0.51	0.52	0.94	0.52	0.85	0.90	0.73	0.70	interaction depth = 5, ntrees=250, shrinkage=0.1
Consensus	0.87	0.85	0.55	0.57	0.87	0.82	0.97	0.92	0.85	0.84	featMorgan-GBM +PubChem-TreeBag+Pharm. FP-RF +MACCS-SVM
Consensus Rigor	0.90	0.90	0.61	0.64	0.91	0.88	0.99	0.94	0.90	0.38	featMorgan-GBM +PubChem-TreeBag+Pharm. FP-RF +MACCS-SVM

SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve; Consesus and Consensus Rigor were built by averaging the predicted values from each individual model (featMorgan-GBM, PubChem-TreeBag, Pharm. FP-RF, MACCS-SVM).

Table S8. Statistical characteristics of QSAR models for hERG liability for the threshold of 20μM assessed by test set.

	Test Set (threshold 20μM, *n=908)*									
Model name	**Accuracy**	**BAC**	**Kappa**	**MCC**	**Sensitivity (Recall)**	**Specificity**	**Precision**	**F1**	**AUC**	**Coverage**
MACCS-SVM	0.87	0.74	0.55	0.57	0.97	0.52	0.88	0.92	0.74	0.86
featMorgan-SVM	0.90	0.79	0.64	0.66	0.97	0.60	0.91	0.94	0.79	0.81
Pharm. FP-SVM	0.86	0.70	0.48	0.52	0.97	0.43	0.87	0.92	0.70	0.89
PubChem-SVM	0.90	0.79	0.64	0.65	0.97	0.61	0.91	0.94	0.79	0.72
MACCS-RF	0.88	0.79	0.61	0.61	0.93	0.65	0.91	0.92	0.79	0.86
featMorgan-RF	0.89	0.77	0.62	0.63	0.97	0.58	0.90	0.93	0.77	0.81
Pharm. FP-RF	0.86	0.76	0.55	0.55	0.93	0.59	0.90	0.91	0.76	0.89
PubChem-RF	0.87	0.77	0.56	0.56	0.93	0.62	0.91	0.92	0.77	0.72
MACCS-TreeBag	0.86	0.77	0.56	0.56	0.93	0.61	0.90	0.91	0.77	0.86
featMorgan-TreeBag	0.87	0.74	0.55	0.56	0.96	0.53	0.89	0.92	0.74	0.81
Pharm. FP-TreeBag	0.86	0.77	0.56	0.56	0.93	0.61	0.90	0.91	0.77	0.89
PubChem-TreeBag	0.86	0.75	0.52	0.53	0.93	0.57	0.90	0.91	0.75	0.72
MACCS-GBM	0.86	0.71	0.48	0.51	0.96	0.45	0.87	0.91	0.71	0.86
featMorgan-GBM	0.87	0.74	0.55	0.56	0.96	0.53	0.89	0.92	0.74	0.81
Pharm. FP-GBM	0.87	0.73	0.53	0.55	0.96	0.49	0.88	0.92	0.73	0.89
PubChem-GBM	0.88	0.77	0.59	0.60	0.96	0.58	0.90	0.93	0.77	0.72
Consensus	0.92	0.89	0.64	0.66	0.92	0.85	0.98	0.95	0.89	0.84
Consensus Rigor	0.94	0.94	0.66	0.69	0.94	0.94	0.99	0.96	0.94	0.50

SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve; Consesus and Consensus Rigor were built by averaging the predicted values from each individual model (featMorgan-GBM, PubChem-TreeBag, Pharm. FP-RF, MACCS-SVM).

Table S9. Statistical results of QSAR models for hERG liability for the threshold of 20μM assessed by y-randomization.

Model name	**Accuracy**	**BAC**	**Kappa**	**Sensitivity**	**Specificity**	**AUC**
MACCS-SVM	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.01
featMorgan-SVM	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.02
Pharm. FP-SVM	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.01
PubChem-SVM	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.02
MACCS-RF	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.51±0.01
featMorgan-RF	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.51±0.02
Pharm. FP-RF	0.68±0.01	0.50±0.01	0.00±0.03	0.88±0.02	0.12±0.01	0.51±0.01
PubChem-RF	0.74±0.01	0.50±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.52±0.02
MACCS-TreeBag	0.67±0.02	0.50±0.02	0.01±0.04	0.86±0.02	0.15±0.03	0.51±0.03
featMorgan-TreeBag	0.71±0.01	0.50±0.02	0.00±0.02	0.94±0.01	0.06±0.01	0.51±0.02
Pharm. FP-TreeBag	0.67±0.01	0.50±0.02	0.00±0.04	0.87±0.01	0.13±0.03	0.49±0.01
PubChem-TreeBag	0.68±0.01	0.51±0.02	0.03±0.03	0.86±0.02	0.16±0.02	0.49±0.02
MACCS-GBM	0.73±0.01	0.30±0.01	0.00±0.01	1.00±0.01	0.00±0.01	0.50±0.01
featMorgan-GBM	0.73±0.01	0.31±0.01	0.02±0.02	0.99±0.01	0.02±0.01	0.52±0.02
Pharm. FP-GBM	0.73±0.01	0.30±0.01	0.01±0.02	0.99±0.01	0.02±0.01	0.50±0.01
PubChem-GBM	0.73±0.01	0.31±0.01	0.01±0.02	0.99±0.01	0.02±0.01	0.51±0.02

The presented results are based on an average overall 10 randomly shuffled response (y-randomization); SVM: Support Vector Machine; RF: Random Forest; TreeBag: Tree Bagging method; GBM: Gradient boosting method; MACCS: MACCS keys; PubChem: PubChem Fingerprints; Pharm.FP: ChemAxon Pharmacophore Fingerprint; FeatMorgan: Circular fingerprint based on the Morgan algorithm and feature invariants (FCFP-like); BAC: Balanced Accuracy; MCC: Matthews correlation coefficient; AUC: the area under receiver operating characteristic curve.