

Supplementary Information

Table S5. Balancing strategy selection for MN in vitro. The best values are in bold.

Balancing strategy	Descriptors +RF			MACCS+RF		
	AUC	Specificity	Sensitivity	AUC	Specificity	Sensitivity
SMOTE	0.771	0.64	0.813	0.746	0.553	0.784
Class weighting	0.746	0.651	0.718	0.731	0.528	0.783

Table S6. Balancing strategy selection for MN in vitro. The best values are in bold.

Balancing strategy	Descriptors +RF			MACCS+RF		
	AUC	Specificity	Sensitivity	AUC	Specificity	Sensitivity
SMOTE	0.715	0.8	0.541	0.679	0.752	0.466
Class weighting	0.725	0.747	0.59	0.68	0.744	0.512

Table S7. Descriptors list determined using Genetic Algorithm, after removing highly intercorrelated ($R^2 > 0.9$) and constant

MN in vitro	MN in vivo
MaxEStateIndex	PEOE_VSA6'
PEOE_VSA4	'SlogP_VSA3'
SMR_VSA10	'SlogP_VSA6'
SMR_VSA2	'EState_VSA8'
SMR_VSA4	NHOHCount
SlogP_VSA10	fr_Ar_COO
SlogP_VSA12	fr_Ar_NH
NumAliphaticRings	fr_NH0
fr_Ar_N	fr_SH
fr_Ndealkylation2	fr_amide
fr_SH	fr_aniline
fr_bicyclic	fr_benzene
fr_ester	fr_epoxide
fr_lactone	fr_hdrzine
fr_phenol_noOrthoHbond	fr_isocyan
fr_sulfone	fr_morpholine
fr_unbrch_alkane	fr_nitro
	fr_phenol_noOrthoHbond
	fr_sulfide
	fr_term_acetylene

Table S8. Fingerprint/algorithm selection for MN in vitro dataset. AUC/ Specificity/Sensitivity is indicated. The best values are in bold.

Fingerprint	RF	SVM	XGB
Maccs	0.745/0.553/0.784	0.727/0.525/0.769	0.742/0.583/0.773
Daylight	0.702/0.460/0.839	0.695/0.499/0.769	0.710/0.518/0.794
ECPF2 (512)	0.734/0.572/0.768	0.726/0.507/0.812	0.718/0.619/0.695
ECPF2 (1024)	0.727/0.558/0.753	0.721/0.493/0.815	0.728/0.644/0.693
ECPF2 (2048)	0.732/0.591/0.763	0.727/0.493/0.813	0.743/0.622/0.708
ECPF4 (512)	0.698/0.431/0.818	0.693/0.413/0.820	0.689/0.553/0.716
ECPF4 (1024)	0.720/0.482/0.799	0.698/0.435/0.825	0.719/0.611/0.724
ECPF4 (2048)	0.717/0.514/0.776	0.699/0.439/0.815	0.737/0.640/0.714
ECPF6 (512)	0.679/0.363/0.855	0.673/0.381/0.825	0.706/0.546/0.752
ECPF6 (1024)	0.699/0.414/0.823	0.681/0.403/0.825	0.707/0.590/0.718
ECPF6 (2048)	0.709/0.474/0.792	0.676/0.403/0.714	0.727/0.644/0.708
Toxprint	0.717/0.575/0.753	0.710/0.518/0.773	0.718/0.597/0.732

Table S9. Fingerprint/algorithm selection for mouse MN in vivo dataset. AUC/ Specificity/Sensitivity is indicated. The best values are in bold.

Fingerprint	RF	SVM	XGB
Maccs	0.694/0.771/0.489	0.664/0.726/0.509	0.70/0.744/0.512
Daylight	0.676/0.808/0.398	0.663/0.723/0.474	0.684/0.783/0.483
ECPF2 (512)	0.684/0.746/0.503	0.666/0.791/0.421	0.674/0.663/0.598
ECPF2 (1024)	0.679/0.732/0.512	0.666/0.796/0.416	0.662/0.658/0.604
ECPF2 (2048)	0.68/0.723/0.523	0.669/0.791/0.436	0.66/0.648/0.599
ECPF4 (512)	0.662/0.811/0.366	0.647/0.8/0.36	0.668/0.723/0.526
ECPF4 (1024)	0.667/0.775/0.439	0.658/0.809/0.381	0.658/0.666/0.579
ECPF4 (2048)	0.681/0.736/0.508	0.647/0.799/0.349	0.687/0.653/0.631
ECPF6 (512)	0.665/0.832/0.314	0.643/0.804/0.308	0.673/0.755/0.494
ECPF6 (1024)	0.667/0.799/0.364	0.65/0.819/0.308	0.671/0.708/0.532
ECPF6 (2048)	0.663/0.752/0.448	0.638/0.805/0.294	0.674/0.674/0.585
Toxprint	0.690/0.695/0.561	0.687/0.735/0.537	0.70/0.689/0.607