

Supplemental Data

Cationic Compounds with SARS-CoV-2 Antiviral Activity and their Interaction with OCT/MATE Secretory Transporters

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Table S1. Bayesian machine learning model details and statistics

title	targetName	numActives	numCompounds	model.ROC	model.F1	model.kappa	model.MCC	domainCompat
MATE1 inhibition: ASP transport (Wittwer2013)	Multidrug And Toxin Extrusion Protein 1 (SLC47A1)	80	827	0.689	0.2783	0.1523	0.1961	0.3253
MATE1 inhibition: Cimetidine transport (Martínez-Guerrero)	Multidrug And Toxin Extrusion Protein 1 (SLC47A1)	101	395	0.5502	0.4047	0.0699	0.0907	0.3195
MATE1 inhibition: MPP transport (Martínez-Guerrero)	Multidrug And Toxin Extrusion Protein 1 (SLC47A1)	132	395	0.5692	0.4516	0.1535	0.1541	0.3195
MATE1 inhibition: Metformin transport (Martínez-Guerrero)	Multidrug And Toxin Extrusion Protein 1 (SLC47A1)	114	395	0.5676	0.4138	0.1314	0.1338	0.3195
MATE1 inhibition: NBD-MTMA transport (Martínez-Guerrero)	Multidrug And Toxin Extrusion Protein 1 (SLC47A1)	127	395	0.5457	0.4309	0.0814	0.0852	0.3195
OCT2 inhibition: ASP transport	Organic Cation Transporter 2 (SLC22A2)	92	400	0.7493	0.5161	0.3417	0.3492	0.3144
OCT2 inhibition: ASP transport (Kido2011)	Organic Cation Transporter 2 (SLC22A2)	243	907	0.7911	0.6266	0.4914	0.4915	0.3313
OCT2 inhibition: ASP transport - Sandoval + Kido	Organic Cation Transporter 2 (SLC22A2)	262	1056	0.7904	0.5881	0.4097	0.4312	0.3411
OCT2 inhibition: ASP/Consensus transport - Sandoval + Kido	Organic Cation Transporter 2 (SLC22A2)	236	1075	0.7947	0.5673	0.4225	0.4303	0.3406
OCT2 inhibition: Cimetidine transport	Organic Cation Transporter 2 (SLC22A2)	80	400	0.7823	0.5114	0.3452	0.3701	0.3144
OCT2 inhibition: Consensus transport	Organic Cation Transporter 2 (SLC22A2)	83	480	0.7926	0.4577	0.282	0.3377	0.3127
OCT2 inhibition: MPP transport	Organic Cation Transporter 2 (SLC22A2)	43	480	0.7728	0.3179	0.2072	0.2726	0.3127
OCT2 inhibition: Metformin transport	Organic Cation Transporter 2 (SLC22A2)	86	480	0.8213	0.5088	0.3456	0.4054	0.3127
OCT2 inhibition: NBD-MTMA transport	Organic Cation Transporter 2 (SLC22A2)	91	480	0.8244	0.5153	0.343	0.4013	0.3127
OCT2 inhibition: TEA transport	Organic Cation Transporter 2 (SLC22A2)	72	480	0.7866	0.4392	0.2854	0.343	0.3127

Table S2. Bayesian machine learning model predictions and model domain values (the larger this value the more overlap in molecule features with the model training set).

Model	Chloroquine	Hydroxychloroquine	Quinacrine	Tilorone	Pyronaridine	Cetylpyridinium	Miramistin
MegaTrans/mate1/wittwer	0.412	0.452	0.411	0.395	0.555	0.745	0.651
MegaTrans/mate1/wittwer_Domain	0.700	0.697	0.708	0.786	0.584	1.000	0.875
MegaTrans/mate1/wright/cimet	0.523	0.604	0.477	0.571	0.491	0.626	0.465
MegaTrans/mate1/wright/cimet_Domain	0.600	0.606	0.597	0.714	0.558	0.500	0.679
MegaTrans/mate1/wright/met	0.458	0.500	0.452	0.420	0.482	0.461	0.356
MegaTrans/mate1/wright/met_Domain	0.600	0.606	0.597	0.714	0.558	0.500	0.679
MegaTrans/mate1/wright/mpp	0.474	0.518	0.478	0.416	0.498	0.449	0.361
MegaTrans/mate1/wright/mpp_Domain	0.600	0.606	0.597	0.714	0.558	0.500	0.679
MegaTrans/mate1/wright/nbd	0.475	0.513	0.461	0.451	0.503	0.465	0.377
MegaTrans/mate1/wright/nbd_Domain	0.600	0.606	0.597	0.714	0.558	0.500	0.679
MegaTrans/oct2/asp/training_testing	0.583	0.622	0.651	0.448	0.580	0.477	0.425
MegaTrans/oct2/asp/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679
MegaTrans/oct2/asp/sandoval_v_kido	0.649	0.653	0.701	0.555	0.597	0.481	0.595
MegaTrans/oct2/asp/sandoval_v_kido_Domain	0.700	0.697	0.708	0.810	0.584	1.000	0.875
MegaTrans/oct2/asp/kido	0.602	0.613	0.621	0.519	0.560	0.453	0.550
MegaTrans/oct2/asp/kido_Domain	0.700	0.697	0.708	0.786	0.584	1.000	0.875
MegaTrans/oct2/consensus/sandoval_v_kido	0.614	0.606	0.639	0.515	0.564	0.468	0.599
MegaTrans/oct2/consensus/sandoval_v_kido_Domain	0.700	0.697	0.708	0.810	0.584	1.000	0.875
MegaTrans/oct2/cimet/training_testing	0.745	0.740	0.833	0.546	0.594	0.479	0.491
MegaTrans/oct2/cimet/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679
MegaTrans/oct2/consensus/training_testing	0.639	0.660	0.657	0.502	0.616	0.545	0.583

MegaTrans/oct2/consensus/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679
MegaTrans/oct2/met/training_testing	0.665	0.660	0.715	0.507	0.604	0.547	0.553
MegaTrans/oct2/met/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679
MegaTrans/oct2/mpp/training_testing	0.509	0.467	0.427	0.426	0.581	0.517	0.600
MegaTrans/oct2/mpp/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679
MegaTrans/oct2/nbd/training_testing	0.740	0.699	0.751	0.589	0.647	0.552	0.580
MegaTrans/oct2/nbd/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679
MegaTrans/oct2/tea/training_testing	0.555	0.479	0.616	0.487	0.617	0.526	0.580
MegaTrans/oct2/tea/training_testing_Domain	0.600	0.606	0.639	0.762	0.558	0.567	0.679

Table S3. Tanimoto similarity coefficients for MATE1 substrates using MDL keys in Discovery Studio (Biovia).

	atenolol	metformin	cimetidine	MPP	NBD-MTMA
atenolol	1	0.228	0.313	0.125	0.278
metformin		1	0.385	0.205	0.288
cimetidine			1	0.182	0.392
MPP				1	0.258
NBD-MTMA					1