

**Table S20:** The experimental results of REDIAL-2020, ImageMol\_NonPretrained and ImageMol for anti-SARS-CoV-2 activities estimation. ACC, accuracy; F1, F1 score; SEN, sensitivity; PREC, precision; AUC, area under the receiver operating characteristic curve. ImageMol (3 times) represents the mean  $\pm$  standard deviation of the results of 3 runs with different random seeds.

Datasets	Abbreviation	Methods	Metrics				
			ACC	F1	SEN	PREC	AUC
3CL_enzymatic_activity	3CL	REDIAL-2020	0.712	0.705	0.681	<b>0.731</b>	0.713
		ImageMol NonPretrained	0.621	0.645	0.682	0.612	0.671
		ImageMol	<b>0.731</b>	<b>0.758</b>	<b>0.812</b>	0.710	<b>0.768</b>
		ImageMol (3 times)	0.722 $\pm$ 0.009	0.754 $\pm$ 0.005	0.802 $\pm$ 0.011	0.711 $\pm$ 0.001	0.762 $\pm$ 0.007
ACE2_enzymatic_activity	ACE2	REDIAL-2020	<b>0.755</b>	<b>0.777</b>	<b>0.840</b>	0.724	<b>0.753</b>
		ImageMol NonPretrained	0.633	0.609	0.560	0.667	0.680
		ImageMol	0.728	0.752	0.771	<b>0.733</b>	0.719
		ImageMol (3 times)	0.724 $\pm$ 0.005	0.744 $\pm$ 0.008	0.806 $\pm$ 0.035	0.695 $\pm$ 0.038	0.72 $\pm$ 0.001
Human_fibroblast_toxicity	hCYTOX	REDIAL-2020	0.710	0.713	0.719	0.706	0.710
		ImageMol NonPretrained	0.693	0.679	0.649	<b>0.712</b>	0.686
		ImageMol	<b>0.725</b>	<b>0.739</b>	<b>0.768</b>	<b>0.712</b>	<b>0.753</b>
		ImageMol (3 times)	0.725 $\pm$ 0.004	0.716 $\pm$ 0.013	0.696 $\pm$ 0.044	0.741 $\pm$ 0.022	0.727 $\pm$ 0.009
MERS_Pseudotyped_particle_entry_(Huh7_tox_counterscreen)	MERS-PPE_cs	REDIAL-2020	0.703	0.680	0.629	0.739	0.703
		ImageMol NonPretrained	0.778	0.760	0.704	0.826	0.775
		ImageMol	<b>0.834</b>	<b>0.821</b>	<b>0.761</b>	<b>0.891</b>	<b>0.780</b>
		ImageMol (3 times)	0.823 $\pm$ 0.011	0.820 $\pm$ 0.001	0.771 $\pm$ 0.010	0.876 $\pm$ 0.015	0.771 $\pm$ 0.009
MERS_Pseudotyped_particle_entry	MERS-PPE	REDIAL-2020	0.696	0.698	0.698	0.698	0.696
		ImageMol NonPretrained	0.669	0.692	0.740	0.651	0.709
		ImageMol	<b>0.738</b>	<b>0.750</b>	<b>0.781</b>	<b>0.722</b>	<b>0.784</b>
		ImageMol (3 times)	0.724 $\pm$ 0.014	0.731 $\pm$ 0.019	0.747 $\pm$ 0.034	0.717 $\pm$ 0.005	0.773 $\pm$ 0.011
SARS-CoV_Pseudotyped_particle_entry_(VeroE6_tox_counterscreen)	CoV1-PPE_cs	REDIAL-2020	0.659	0.636	0.583	0.700	0.661
		ImageMol NonPretrained	0.575	0.667	<b>0.833</b>	0.556	0.533
		ImageMol	<b>0.766</b>	<b>0.776</b>	0.792	<b>0.760</b>	<b>0.768</b>
		ImageMol (3 times)	0.768 $\pm$ 0.002	0.775 $\pm$ 0.001	0.778 $\pm$ 0.014	0.773 $\pm$ 0.013	0.775 $\pm$ 0.005
SARS-CoV_Pseudotyped_particle_entry	CoV1-PPE	REDIAL-2020	0.665	0.658	0.643	0.674	0.665
		ImageMol NonPretrained	0.650	0.657	0.667	0.647	0.680
		ImageMol	<b>0.673</b>	<b>0.693</b>	<b>0.735</b>	0.655	<b>0.712</b>
		ImageMol (3 times)	0.681 $\pm$ 0.008	0.682 $\pm$ 0.01	0.686 $\pm$ 0.005	0.684 $\pm$ 0.03	0.703 $\pm$ 0.008
SARS-CoV-2_cytopathic_effect_(CPE)	CPE	REDIAL-2020	0.651	0.643	0.626	0.661	0.651
		ImageMol NonPretrained	0.624	0.627	0.627	0.627	0.639
		ImageMol	<b>0.678</b>	<b>0.696</b>	<b>0.733</b>	<b>0.663</b>	<b>0.658</b>
		ImageMol (3 times)	0.669 $\pm$ 0.01	0.677 $\pm$ 0.019	0.693 $\pm$ 0.04	0.662 $\pm$ 0.001	0.669 $\pm$ 0.011
SARS-CoV-2_cytopathic_effect_(host_tox_counterscreen)	Cytotox	REDIAL-2020	0.688	0.700	0.727	0.675	0.688
		ImageMol NonPretrained	0.683	0.684	0.686	<b>0.682</b>	0.696
		ImageMol	<b>0.694</b>	<b>0.698</b>	<b>0.740</b>	0.661	<b>0.729</b>
		ImageMol (3 times)	0.690 $\pm$ 0.005	0.689 $\pm$ 0.008	0.686 $\pm$ 0.036	0.694 $\pm$ 0.020	0.728 $\pm$ 0.001
Spike-ACE2_protein-protein_interaction_(AlphaLISA)	AlphaLISA	REDIAL-2020	<b>0.790</b>	<b>0.787</b>	0.777	<b>0.798</b>	0.790
		ImageMol NonPretrained	0.735	0.710	0.650	0.784	0.756
		ImageMol	0.758	0.766	<b>0.812</b>	0.724	<b>0.800</b>
		ImageMol (3 times)	0.747 $\pm$ 0.012	0.758 $\pm$ 0.008	0.796 $\pm$ 0.016	0.723 $\pm$ 0.001	0.793 $\pm$ 0.007
Spike-ACE2_protein-protein_interaction_(TruHit_Counterscreen)	TruHit	REDIAL-2020	0.734	0.737	0.746	<b>0.728</b>	0.734
		ImageMol NonPretrained	0.714	0.747	<b>0.841</b>	0.671	0.750
		ImageMol	<b>0.742</b>	<b>0.762</b>	0.825	0.708	<b>0.813</b>
		ImageMol (3 times)	0.750 $\pm$ 0.008	0.758 $\pm$ 0.004	0.782 $\pm$ 0.044	0.738 $\pm$ 0.031	0.806 $\pm$ 0.006