

Supplementary Information

Supplementary Table 1. Basic statistics of six benchmark datasets.

Dataset	Type	#Drugs	#Targets	#Total DTP	#Known DTP	#Sample
Activation	MoA	1,426	281	400,706	1913	21,043
Inhibition	MoA	14,049	1,088	15,285,312	21055	231,605
Yamanishi_08	DTI	791	989	782,299	5,127	56,397
Hetionet	DTI	1,384	5,763	7,975,992	49,942	549,362
Davis	DTA	68	442	30,056	30,056	30,056
KIBA	DTA	2,111	229	483,419	118,254	118,254

Supplementary Table 2. Evaluation performance on two DTI datasets in three scenarios.

Datasets	Metrics	Scenario	CPI-GNN	MPNN-CNN	TransformerCPI	KGE-NFM	DTIAM
Yamanishi_08	AUPR	Warm start	0.431	0.816	0.802	0.817	0.931
		Drug cold start	0.167	0.408	0.41	0.341	0.568
		Target cold start	0.38	0.602	0.646	0.761	0.865
	AUROC	Warm start	0.821	0.952	0.953	0.948	0.982
		Drug cold start	0.629	0.797	0.767	0.779	0.867
		Target cold start	0.8	0.856	0.87	0.923	0.953
Hetionet	AUPR	Warm start	0.441	0.734	-	0.789	0.808
		Drug cold start	0.219	0.453	-	0.391	0.529
		Target cold start	0.433	0.47	-	0.651	0.614
	AUROC	Warm start	0.81	0.956	-	0.968	0.972
		Drug cold start	0.685	0.831	-	0.803	0.865
		Target cold start	0.81	0.858	-	0.936	0.927

Note: Bold numbers represent the best performance.

Supplementary Table 3. Evaluation performance on two DTA datasets in three scenarios.

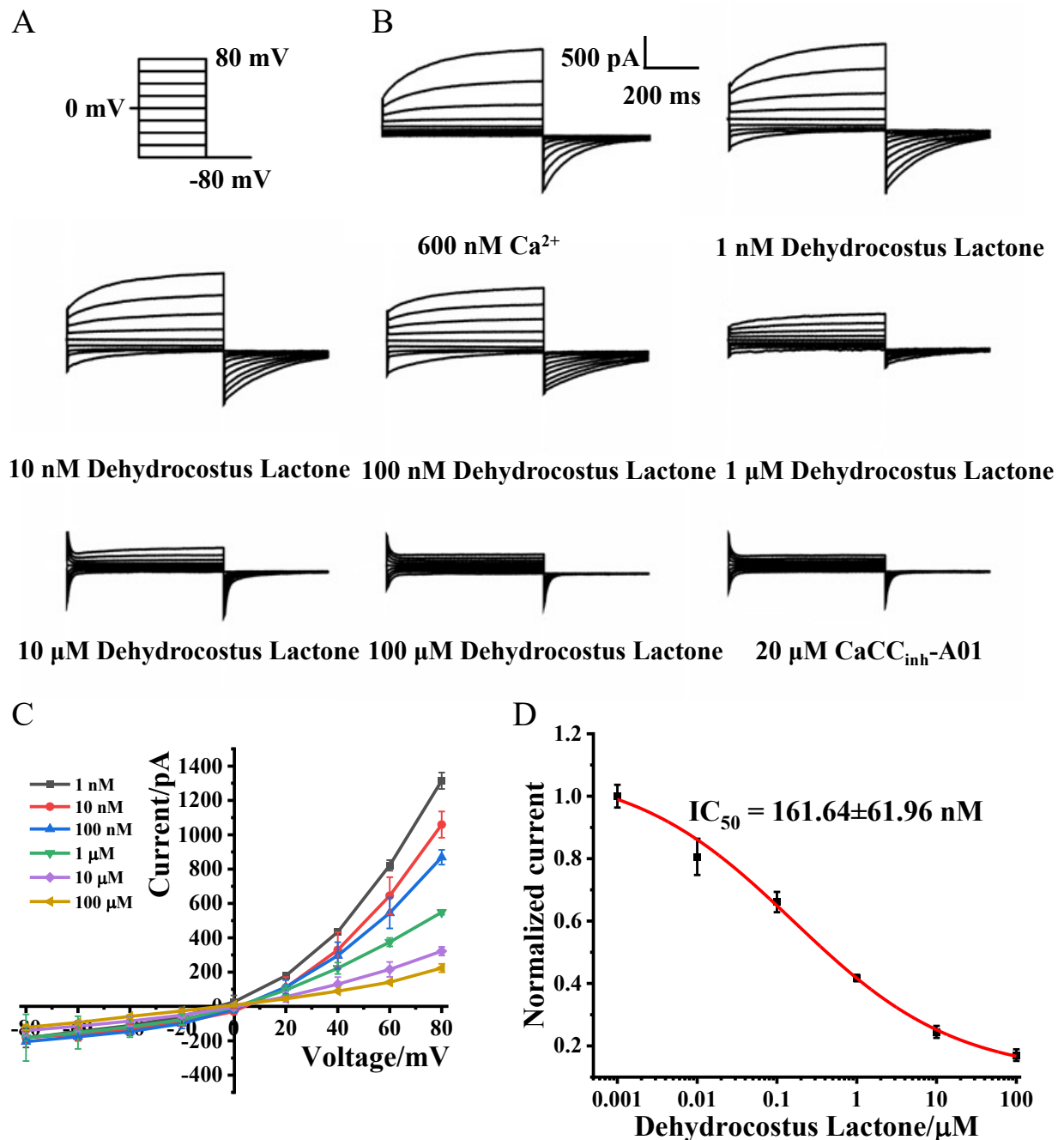
Datasets	Metrics	Scenario	DeepDTA	MONN	BACPI	GraphDTA	DTIAM
Davis	MSE	Warm start	0.325	0.28	0.284	0.25	0.212
		Drug cold start	0.686	0.821	0.671	0.628	0.598
		Target cold start	0.436	0.364	0.458	0.482	0.308
	Pearson correlation	Warm start	0.775	0.812	0.806	0.829	0.858
		Drug cold start	0.423	0.393	0.459	0.496	0.5
		Target cold start	0.681	0.742	0.659	0.661	0.786
	CI	Warm start	0.858	0.868	0.861	0.879	0.904
		Drug cold start	0.684	0.666	0.72	0.711	0.727
		Target cold start	0.818	0.833	0.791	0.777	0.865
KIBA	MSE	Warm start	0.229	0.187	0.172	0.171	0.162
		Drug cold start	0.427	0.436	0.404	0.371	0.334
		Target cold start	0.37	0.332	0.382	0.473	0.311
	Pearson correlation	Warm start	0.824	0.857	0.87	0.87	0.88
		Drug cold start	0.637	0.643	0.666	0.696	0.73
		Target cold start	0.694	0.728	0.675	0.59	0.749
	CI	Warm start	0.836	0.852	0.861	0.873	0.877
		Drug cold start	0.747	0.744	0.744	0.776	0.794
		Target cold start	0.74	0.754	0.727	0.699	0.765

Note: Bold numbers represent the best performance.

Supplementary Table 4. Evaluation performance on two MoA datasets in three scenarios.

Datasets	Scenario	AI-DTI		DTIAM	
		AUPR	AUROC	AUPR	AUC
Activation	Warm start	0.583	0.888	0.744	0.936
	Drug cold start	0.550	0.879	0.729	0.937
	Target cold start	0.219	0.652	0.487	0.85
Inhibition	Warm start	0.840	0.952	0.884	0.97
	Drug cold start	0.830	0.948	0.863	0.964
	Target cold start	0.215	0.605	0.555	0.846

Note: Bold numbers represent the best performance.



Supplementary Figure 1. Dehydrocostus lactone inhibits TMEM16A current on LA795 cell with high endogenous expression of TMEM16A in a concentration-dependent manner. (A) Voltage stimulation waveform scheme. (B) Representative TMEM16A current is activated by 600 nM Ca^{2+} and inhibited by different concentrations of dehydrocostus lactone ($n=3$), with 20 μM $\text{CaCC}_{\text{inh}}\text{-A01}$ as the inhibitor positive control. (C) I-V curve of TMEM16A inhibited by various concentrations of dehydrocostus lactone ($n=3$), with three independent biological replicates performed for each group. Data are presented as mean values $\pm$ SD. (D) Dose-response curve of TMEM16A currents at +80 mV incubated with indicated concentrations

of dehydrocostus lactone (n=3), with three independent biological replicates performed for each group. The IC₅₀ of dehydrocostus lactone on TMEM16A channels was 161.64±61.96 nM. Data are presented as mean values ± SD.