Supplementary Information

3D-QSAR, design, docking and *in silico* ADME studies of indole-glyoxylamides and indolyl oxoacetamides as potential pancreatic lipase inhibitors

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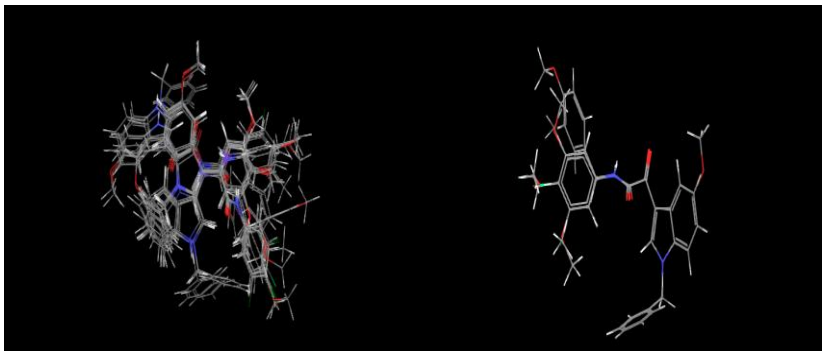

(a) (b)

Fig. S1 — (a) Before and (b) after alignment representation of the ligands

Table S1 — Predicted activities of training and test set along with prediction error

Test set compounds: 3, 4*, 5*, 9*, 12*, 17*, 21*, 23*, 27**

No. of ligand	IC50 (μ M)	pIC_{50}	Predicted Activity 1	Predicted Activity 2	Predicted Activity 3	Predicted Activity 4	Prediction error 1	Prediction error 2	Prediction error 3	Prediction error 4
			PLS 1	PLS 2	PLS 3	PLS 4	PLS 1	PLS 2	PLS 3	PLS 4
1	27.49	4.560	4.453	4.432	4.455	4.446	-0.107743	-0.12783	-0.105414	-0.114045
2	26.13	4.582	4.465	4.464	4.514	4.548	-0.117514	-0.118518	-0.0680164	-0.0347809
3*	26.07	4.583	4.500	4.533	4.623	4.670	-0.0836683	-0.0503553	0.0398168	0.0870579
4*	23.72	4.624	4.554	4.626	4.665	4.706	-0.0700533	0.0013196	0.0410065	0.0818652
5*	17.39	4.759	4.633	4.749	5.007	4.889	-0.126234	-0.0105295	0.248087	0.129854
6	17.28	4.762	4.723	4.925	4.860	4.849	-0.0391621	0.163424	0.098107	0.0874871
7	43.36	4.362	4.430	4.388	4.353	4.334	0.0675677	0.0258398	-0.0090364	-0.0279333
8	44.27	4.353	4.420	4.364	4.276	4.243	0.0661501	0.110879	-0.0775485	-0.110446
9*	47.62	4.322	4.452	4.427	4.409	4.385	0.129942	0.104859	0.0873774	0.0634414
10	18.24	4.738	4.889	4.771	4.770	4.772	0.150025	0.0323664	0.0313286	0.0337877
11	12.9	4.889	4.901	4.802	4.829	4.874	0.0118543	-0.086721	-0.0596739	0.0153482
12*	10.62	4.973	4.936	4.871	4.938	4.996	-0.0377671	-0.102025	-0.0353075	0.0230239
13	10.86	4.964	4.990	4.964	4.980	5.032	0.0265796	0.0003813	0.0166139	0.0685629
14	5.83	5.234	5.069	5.087	5.322	5.215	-0.164947	-0.146814	0.0883478	-0.0187941
15	4.92	5.308	5.159	5.264	5.175	5.175	-0.148823	-0.0438077	-0.132579	-0.132109
16	25.76	4.589	4.866	4.727	4.668	4.660	0.277342	0.138043	0.0797124	0.0719057
17*	26.72	4.573	4.855	4.703	4.591	4.569	0.282795	0.130161	0.018075	-0.0037362
18	24.18	4.616	4.888	4.765	4.724	4.711	0.271526	0.148873	0.107937	0.0950909
19	18.260	4.738	4.529	4.593	4.699	4.739	-0.20892	-0.145043	-0.0395007	0.0007134
20	18.120	4.741	4.584	4.686	4.741	4.775	-0.157621	-0.0556848	-0.0006273	0.0332044

21*	17.930	4.746	4.662	4.809	5.083	4.957	-0.0835641	0.0627033	0.33669	0.211431
22	16.380	4.785	4.752	4.985	4.935	4.918	-0.0330032	0.200147	0.1503	0.132553
23*	34.620	4.460	4.449	4.424	4.351	4.311	-0.0112437	-0.0357425	-0.109008	-0.148932
24	37.830	4.422	4.481	4.487	4.484	4.453	0.0593773	0.0648583	0.062747	0.0317841
25	9.140	5.039	4.965	4.931	5.013	5.065	-0.0735567	-0.107251	-0.0251631	0.0261413
26	6.280	5.202	5.020	5.024	5.056	5.101	-0.181902	-0.177537	0.145934	-0.101012
27*	5.120	5.290	5.098	5.147	5.398	5.283	-0.191957	-0.14326	0.107272	-0.0068968
28	4.530	5.343	5.188	5.324	5.250	5.244	-0.155301	-0.0197225	-0.931236	-0.0996801
29	23.210	4.634	4.885	4.763	4.666	4.637	0.251022	0.128952	0.0322319	0.0033981
30	19.480	4.710	4.917	4.825	4.799	4.779	0.207048	0.114958	0.0893918	0.0695193

Table S2 — Predicted activities of training and test set along with prediction error *Test set compounds: 3*, 4*, 5*, 9*, 12*, 17*, 21*, 23*, 27**										
No. of ligand	IC50 (μ M)	p IC50	Predicted Activity 1	Predicted Activity 2	Predicted Activity 3	Predicted Activity 4	Prediction error 1	Prediction error 2	Prediction error 3	Prediction error 4
			PLS 1	PLS 2	PLS 3	PLS 4	PLS 1	PLS 2	PLS 3	PLS 4
1	27.49	4.560	4.450	4,433	4.431	4.402	-0.110463	-0.127088	-0.12968	-0.158362
2	26.13	4.582	4.437	4.425	4.462	4.499	-0.145133	-0.157346	-0.120684	-0.0834657
3*	26.07	4.583	4.475	4.498	4.594	4.677	-0.108824	-0.0857596	0.0104191	0.093256
4*	23.72	4.624	4.565	4.633	4.677	4.738	-0.0596137	0.0081584	0.0524949	0.113332
5*	17.39	4.759	4.651	4.770	5.045	4.904	-0.108151	0.0105527	0.285913	0.144341
6	17.28	4.762	4.738	4.909	4.857	4.847	-0.0238256	0.14753	0.0952913	0.0846415
7	43.36	4.362	4.430	4.406	4.398	4.387	0.067943	0.0437662	0.0358025	0.024389
8	44.27	4.353	4.430	4.398	4.333	4.284	0.07675	0.0447961	-0.0201422	-0.0696613
9*	47.62	4.322	4.446	4.425	4.416	4.382	0.123788	0.103696	0.094242	0.0605274
10	18.24	4.738	4.876	4.766	4.740	4.725	0.137545	0.070355	0.0015846	-0.013393
11	12.9	4.889	4.863	4.757	4.771	4.822	-0.025525	-0.131622	-0.117819	-0.066897
12*	10.62	4.973	4.901	4.830	4.903	5.000	-0.0726823	-0.143503	-0.0701828	0.0263579
13	10.86	4.964	4.991	4.965	4.986	5.061	0.0272593	0.0011468	0.0226247	0.0971648
14	5.83	5.234	5.077	5.102	5.355	5.227	-0.156624	-0.131805	0.120697	-0.0071713
15	4.92	5.308	5.164	5.242	5.167	5.170	-0.143246	-0.0657754	-0.140873	-0.137814
16	25.76	4.589	4.857	4.738	4.708	4.710	0.267957	0.149896	0.119074	0.121364
17*	26.72	4.573	4.856	4.730	4.643	4.607	0.283635	0.157796	0.0699993	0.0341841
18	24.18	4.616	4.872	4.758	4.725	4.705	0.255613	0.141636	0.109324	0.0893127
19	18.260	4.738	4.517	4.573	4.668	4.737	-0.221423	-0.164663	-0.0697562	0.0005330
20	18.120	4.741	4.607	4.708	4.751	4.799	0.134529	-0.0330616	0.0100034	0.0572269
21*	17.930	4.746	4.693	4.845	5.120	4.964	-	0.09957	0.373659	0.218473

							0.0528291			
22	16.380	4.785	4.780	4.985	4.932	4.907	-0.0050141	0.200037	0.146526	0.12263
23*	34.620	4.460	4.472	4.474	4.408	4.345	0.0120088	0.0137502	-0.0524597	-0.115593
24	37.830	4.422	4.488	4.501	4.490	4.443	0.0658761	0.079479	0.068754	0.0214255
25	9.140	5.039	4.943	4.906	4.978	5.061	-0.0958193	-0.132945	-0.0608962	0.0220308
26	6.280	5.202	5.033	5.041	5.061	5.122	-0.16857	-0.160987	-0.14078	-0.0798532
27*	5.120	5.290	5.119	5.178	5.429	5.288	-0.17092	-0.112467	0.138763	-0.0027
28	4.530	5.343	5.206	5.318	5.241	5.231	-0.137072	-0.0259058	-0.102275	-0.112834
29	23.210	4.634	4.898	4.806	4.717	4.668	0.264515	0.172372	0.083302	0.0338739
30	19.480	4.710	4.914	4.833	4.800	4.766	0.203786	0.123505	0.0899212	0.0562965

Table S3 — Physically relevant descriptors and ADME Predictions of QSAR model (I)												
Molecule	#stars	CNS	mol-MW	SASA	FOSA	FISA	PISA	WPSA	Volume	DonorHB	Acceptor HB	AC. DN^.5/SA
1	0	0	264.283	519.242	0	110.588	408.654	0	864.552	0.25	2.75	0.0026481
2	0	0	278.31	550.662	87.79	110.588	352.285	0	923.396	0.25	2.75	0.002497
3	0	0	292.337	574.346	150.966	110.588	312.792	0	972.385	0.25	2.75	0.002394
4	0	-1	294.309	551.198	90.151	110.588	350.459	0	932.374	0.25	3.5	0.0031749
5	0	-1	308.336	579.418	128.945	114.701	335.772	0	992.767	0.25	3.5	0.0030203
6	0	-1	354.362	619.352	258.834	103.353	257.165	0	1082.117	0.25	5	0.0040365
7	1	0	343.179	548.53	0	110.466	360.861	77.204	918.004	0.25	2.75	0.0025067
8	1	0	333.173	564.254	0	110.564	323.71	129.98	950.112	0.25	2.75	0.0024368
9	1	0	282.273	528.275	0	110.518	370.961	46.795	880.716	0.25	2.75	0.0026028
10	1	0	354.407	657.055	37.721	78.346	540.988	0	1148.493	0.25	3.75	0.0028536
11	2	0	368.434	687.074	125.511	80.991	480.571	0	1206.678	0.25	3.75	0.002729
12	2	0	382.461	718.969	185.413	77.881	455.674	0	1263.984	0.25	3.75	0.0026079
13	1	0	384.434	689.011	127.872	78.346	482.793	0	1216.315	0.25	4.5	0.0032656
14	0	0	398.46	621.195	151.627	80.555	389.013	0	1199.349	0.25	4.5	0.0036221
15	0	-1	444.486	747.41	283.857	75.57	387.983	0	1369.098	0.25	6	0.0040139
16	2	0	433.303	686.363	37.721	78.189	493.248	77.204	1201.958	0.25	3.75	0.0027318
17	2	0	423.298	705.182	37.806	82.256	455.139	129.98	1236.612	0.25	3.75	0.0026589
18	1	0	372.398	666.1	37.721	78.261	503.322	46.795	1164.663	0.25	3.75	0.0028149

19	0	-1	322.363	606.09	240.224	109.931	255.935	0	1040.274	0.25	3.5	0.0028874
20	0	-1	324.335	582.942	179.409	109.931	293.602	0	1000.263	0.25	4.25	0.0036453
21	0	-1	338.362	599.284	222.765	109.609	266.909	0	1050.194	0.25	4.25	0.0035459
22	0	-1	384.388	651.097	348.092	102.696	200.308	0	1150.006	0.25	5.75	0.0044156
23	0	0	363.199	595.998	89.259	109.906	266.853	129.98	1018.001	0.25	3.5	0.0029363
24	0	0	312.3	560.019	89.259	109.861	314.105	46.795	948.605	0.25	3.5	0.0031249
25	1	0	412.487	742.501	277.946	80.334	384.222	0	1323.555	0.25	4.5	0.0030303
26	0	-1	414.46	719.353	217.131	80.334	421.889	0	1283.544	0.25	5.25	0.0036491
27	1	-1	428.487	761.69	253.068	83.351	425.271	0	1351.116	0.25	5.25	0.0034463
28	0	-1	474.512	784.585	376.706	73.586	334.293	0	1439.036	0.25	6.75	0.0043016
29	1	0	453.324	737.169	127.065	81.621	398.503	129.98	1304.423	0.25	4.5	0.0030522
30	0	0	402.424	688.749	124.598	76.678	440.678	46.795	1234.058	0.25	4.5	0.0032668

#stars: ADME compliance score, CNS: Central nervous system, mol-MW: molecular weight, SASA: Solvent accessible surface area, FOSA: Hydrophobic components of SASA, FISA: Hydrophilic components of SASA, PISA: Pi-carbon and attached hydrogen components of SASA, WPSA: Van der Waals surface area of polar -N and -O atoms, Donor HB: Estimated number of hydrogen bonds donated by solute to water molecules, Acceptor HB: Estimated number of hydrogen bonds accepted by the solute from water molecules, AC. DN^.5/SA: Index of cohesive interactions in solids.

Table S4 — Physically relevant descriptors and ADME Predictions of QSAR model (II)												
Molecule	glob	QPpolrz	QPlogPoct	QPlogPw	QPlogPo/w	QPlogHERG	QPPCaco	QPlogBB	QPPMDCK	QPlogKp	#metab	QPlogKhsa
1	0.845259	30.422	12.676	6.914	3.352	-5.985	885.51	-0.649	433.783	-1.83	1	0.333
2	0.832795	32.238	13.171	6.606	3.663	-5.918	885.51	-0.68	433.783	-2.029	1	0.498
3	0.826451	33.822	13.659	6.394	3.932	-5.832	885.51	-0.697	433.783	-2.168	2	0.635
4	0.837371	31.938	13.42	7.113	3.384	-5.835	885.51	-0.729	433.783	-1.939	1	0.31
5	0.830624	33.573	13.99	6.888	3.726	-5.874	809.458	-0.846	393.658	-1.971	2	0.436
6	0.823019	35.756	15.138	7.629	3.61	-5.622	1037.05	-0.815	514.55	-1.942	3	0.296
7	0.832775	32.104	13.512	6.685	3.934	-5.959	887.877	-0.49	1151.986	-1.996	0	0.483
8	0.828338	33.035	14.039	6.49	4.297	-5.853	885.983	-0.373	2236.429	-2.129	0	0.573
9	0.841129	30.709	12.93	6.695	3.59	-5.872	886.868	-0.544	784.038	-1.962	0	0.378
10	0.807202	41.765	16.622	8.47	5.104	-7.232	1790.383	-0.539	928.442	-0.578	2	0.814
11	0.797791	43.516	17.149	8.149	5.39	-7.096	1689.892	-0.586	872.245	-0.839	2	0.978
12	0.78635	45.572	17.704	8.036	5.75	-7.162	1808.636	-0.578	938.677	-0.87	3	1.139
13	0.799778	43.281	17.366	8.669	5.132	-7.074	1790.383	-0.615	928.442	-0.687	2	0.786
14	0.878822	41.064	17.408	7.663	4.912	-5.348	1706.082	-0.554	881.281	-0.962	3	0.71
15	0.797803	47.206	19.375	9.182	5.339	-6.654	1902.256	-0.71	991.304	-0.777	4	0.776
16	0.796534	43.448	17.458	8.242	5.688	-7.177	1796.514	-0.37	2467.634	-0.743	1	0.964
17	0.790108	44.471	18.05	8.074	6.039	-7.099	1643.857	-0.297	4362.201	-0.952	1	1.062
18	0.803698	42.052	16.876	8.251	5.343	-7.109	1793.714	-0.431	1678.698	-0.709	1	0.86

19	0.819206	35.354	14.404	6.598	3.969	-5.678	898.312	-0.77	440.565	-2.26	3	0.611
20	0.829754	33.47	14.164	7.316	3.421	-5.687	898.311	-0.802	440.565	-2.031	2	0.285
21	0.833769	34.571	14.57	6.951	3.713	-5.495	904.635	-0.849	443.918	-2.023	3	0.383
22	0.815304	37.287	15.883	7.833	3.642	-5.476	1052.043	-0.888	522.596	-2.034	4	0.266
23	0.821144	34.566	14.784	6.693	4.335	-5.699	898.791	-0.445	2271.397	-2.221	1	0.548
24	0.833718	32.24	13.674	6.898	3.629	-5.721	899.689	-0.616	796.297	-2.054	1	0.355
25	0.785168	46.631	18.382	8.141	5.692	-6.841	1714.324	-0.667	885.884	-1.07	4	1.087
26	0.794018	44.748	18.142	8.86	5.137	-6.877	1714.324	-0.708	885.884	-0.842	3	0.755
27	0.775976	46.842	18.707	8.785	5.552	-7.185	1605.015	-0.841	824.99	-0.789	4	0.9
28	0.785669	48.85	20.069	9.411	5.394	-6.594	1986.476	-0.774	1038.826	-0.834	5	0.748
29	0.783207	46.002	18.79	8.28	6.072	-6.94	1666.807	-0.366	4428.065	-1.044	2	1.032
30	0.807844	43.589	17.758	8.387	5.388	-6.743	1856.791	-0.467	1742.596	-0.804	2	0.837

glob: Globularity descriptor, QPpolrz: Predicted polarizability in cubic angstroms, QPlogPoct: Predicted octanol/gas partition coefficient, QPlogPw: Predicted water/gas partition coefficient, QPlogHERG:Precited IC50 value for blockage of HERG K^+ channels, QPPCaco: Predicted apparent Caco-2 cell permeability in nm/sec, QPlogBB: Predicted brain/blood partition coefficient, QPPMDCK: Predicted apparent MDCK (Madin-Darby canine kidney) cell permeability in nm/sec, QPlogK_p: Predicted skin permeability, #metab: Number of likely metabolic reactions, QPlogKhsa: Prediction of binding to human serum albumin.

Table S5 — Physically relevant descriptors and ADME Predictions of QSAR model (III)						
Molecule	Human Oral Absorption	Percent Human Oral Absorption	PSA	Rule of Five	Rule of Three	Jm
1	3	100	72.758	0	0	0.199
2	3	100	72.758	0	0	0.035
3	3	100	72.758	0	0	0.01
4	3	100	81.231	0	0	0.136
5	3	100	83.47	0	0	0.058
6	3	100	95.91	0	0	0.088
7	3	100	72.707	0	0	0.023
8	3	100	72.768	0	0	0.005
9	3	100	72.738	0	0	0.067
10	3	100	60.65	1	1	0.079
11	1	100	60.65	1	1	0.012
12	1	100	60.406	1	1	0.003
13	3	100	69.123	1	1	0.054
14	3	100	70.655	0	0	0.766
15	1	100	83.559	1	1	0.043
16	1	100	60.6	1	1	0.009
17	1	100	60.58	1	1	0.001
18	1	100	60.631	1	1	0.026
19	3	100	81.208	0	0	0.007
20	3	100	89.681	0	0	0.098
21	3	100	91.083	0	0	0.076
22	3	100	104.36	0	0	0.064
23	3	100	81.219	0	1	0.004
24	3	100	81.189	0	0	0.048
25	1	100	69.101	1	1	0.002
26	1	100	77.574	1	1	0.036
27	1	100	79.92	1	1	0.01
28	1	100	91.775	1	1	0.027
29	1	100	69.021	1	1	0.001
30	1	100	69.392	1	1	0.027

Human Oral Absorption: Predictive human oral absorption 1,2, or 3 (Low, medium, high), Percent Human Oral Absorption: Predicted human oral absorption on 0 to 100% scale, PSA: van der Waals of polar nitrogen and oxygen atoms, Rule of five: Number of violations of Lipinski's rule of five, Rule of three: Number of violations of Jorgensen's rule of three, Jm: Predicted maximum transdermal transport rate.