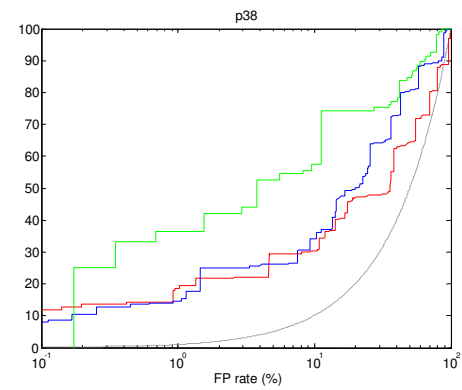
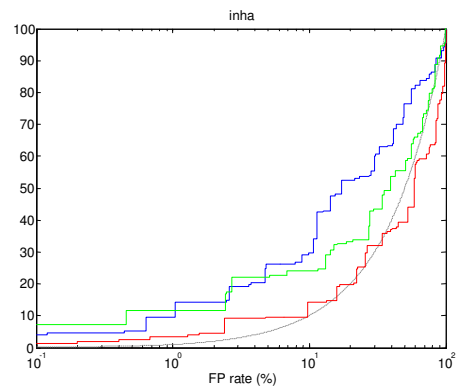
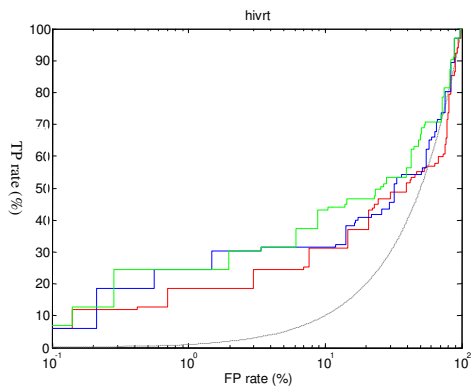
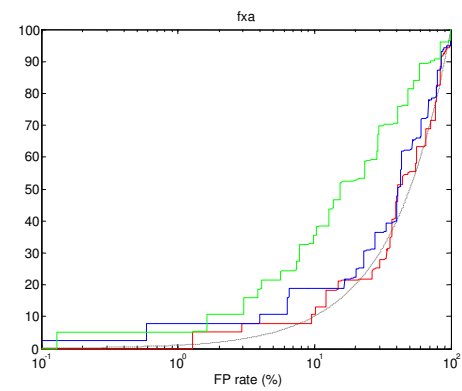
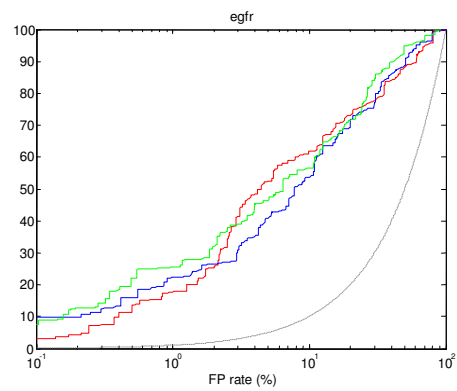
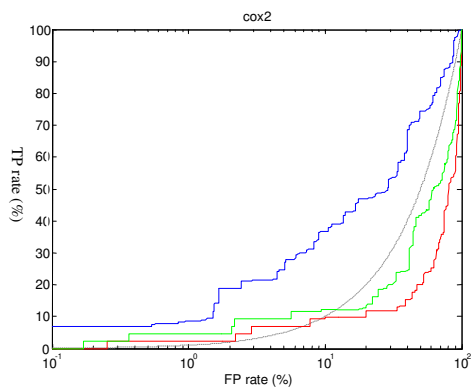
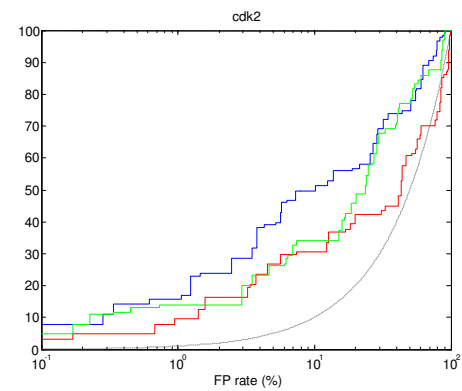
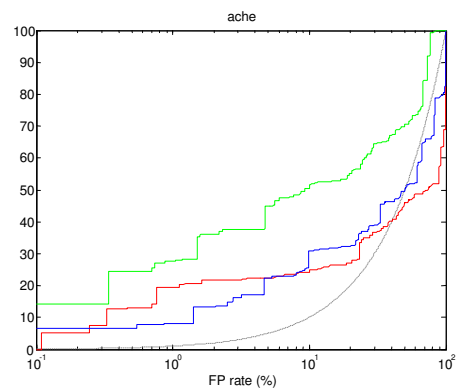
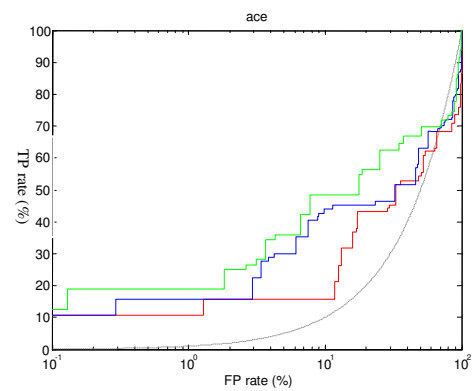


Figure S1. The distribution of poses generated from re-docking cognate ligand against its respective target. The left plot shows the pose distribution based on z-score values of MedusaScore (x-axis) vs. RMSD values (y-axis). The middle plot shows the pose distribution based on the distance to the native pose (x-axis) vs. RMSD (y-axis). The right plot highlights the poses used for constructing filter. The data points are colored corresponding to their z-score values of MedusaScore (the smaller z-score values, the better the MedusaScore)



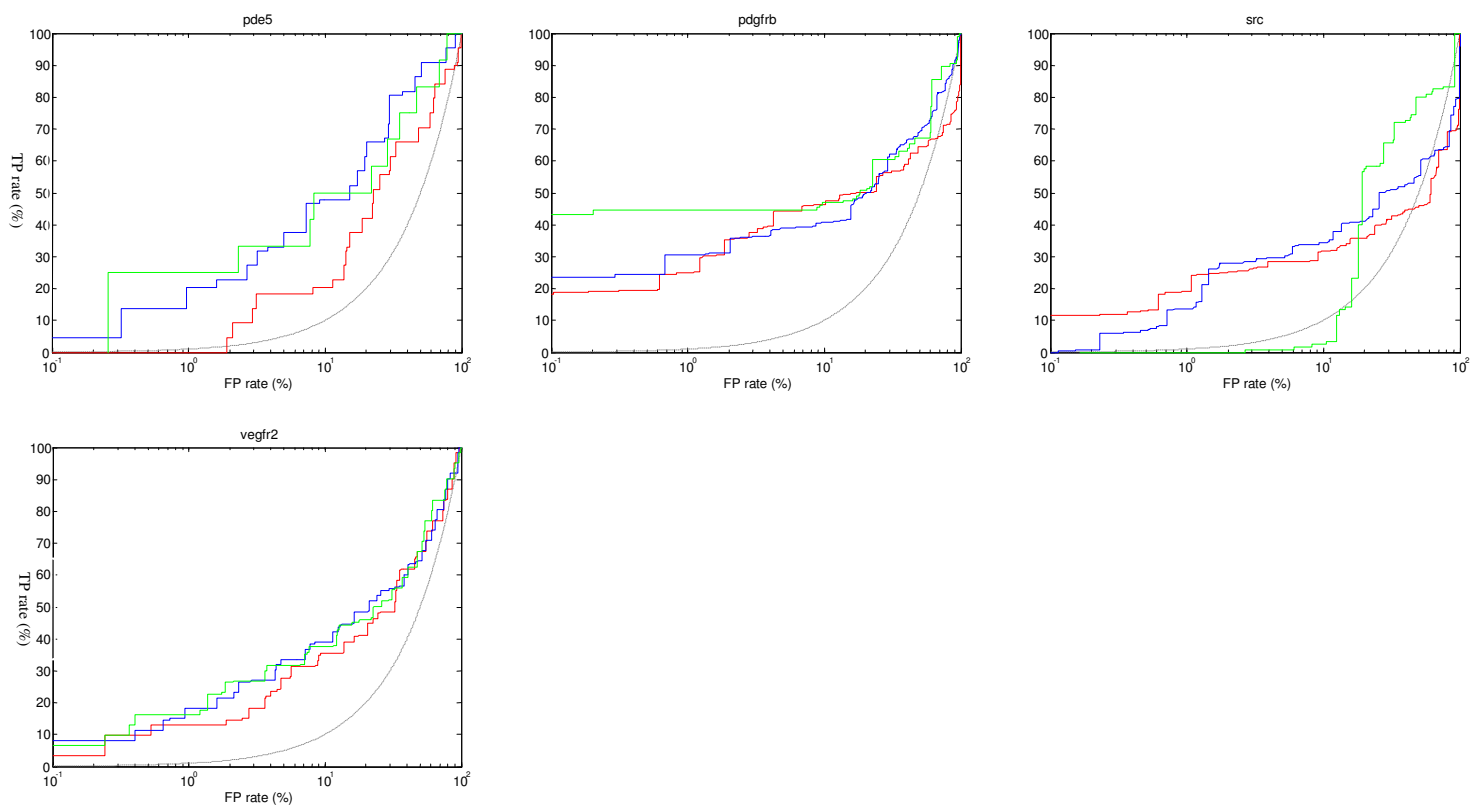


Figure S2. The awROC curves of VS experiments for the 13 DUD data sets. For each target, the true positive (FP) rate is plotted against the logarithmic false positive (FP) rate. Gray dot dash lines correspond to the random VS performance, red lines are from MedusaScore, blue lines are from the MedusaScore +DistScore approach, and green lines are from the MedusaScore + pose filter approach

Table S1. awROCE enrichment at 0.5% of structure-based scoring functions and the combined scoring approach

target	XSCORE::HMSCORE	Fred::ChemScore	Fred::PLP	Fred::Chemgauss3	MedusaScore	MedusaScore + filter
ace	32.78 ± 8.06	25.45 ± 7.70	43.00 ± 9.06	28.11 ± 9.13	21.65 ± 5.53	36.95 ± 8.26
ache	28.48 ± 6.55	0.00 ± 0.00	0.00 ± 0.00	1.12 ± 0.48	24.38 ± 6.74	44.97 ± 10.16
cdk2	8.51 ± 4.13	27.71 ± 7.42	42.88 ± 6.83	27.90 ± 9.02	11.04 ± 3.19	26.73 ± 4.85
cox2	5.89 ± 1.19	0.00 ± 0.00	4.45 ± 2.10	12.07 ± 2.49	4.16 ± 2.07	8.29 ± 2.87
egfr	8.21 ± 1.98	18.38 ± 3.19	5.63 ± 1.70	12.80 ± 2.91	23.59 ± 4.27	41.61 ± 4.49
fxa	8.18 ± 5.71	14.52 ± 4.79	6.70 ± 4.99	4.86 ± 4.04	0.00 ± 0.00	9.69 ± 4.87
hivrt	23.77 ± 7.62	11.33 ± 5.73	0.01 ± 0.39	15.66 ± 5.91	23.92 ± 8.00	46.03 ± 9.60
inha	8.79 ± 1.29	17.79 ± 5.89	15.70 ± 4.28	17.23 ± 4.25	5.92 ± 1.35	21.66 ± 6.24
p38	0.00 ± 0.15	12.75 ± 6.45	13.03 ± 6.46	13.12 ± 6.39	28.69 ± 7.32	66.95 ± 17.33
pde5	0.00 ± 0.00	1.11 ± 3.36	0.06 ± 0.84	9.59 ± 5.05	0.00 ± 0.00	59.08 ± 13.50
pdgfrb	29.65 ± 5.32	15.16 ± 4.12	16.58 ± 4.07	16.26 ± 6.02	37.18 ± 6.51	86.46 ± 11.56
src	0.50 ± 0.42	25.97 ± 7.23	0.00 ± 0.00	5.62 ± 1.26	24.77 ± 6.29	0.00 ± 0.00
vegfr2	7.85 ± 4.38	34.53 ± 6.75	6.18 ± 3.11	14.18 ± 5.57	19.97 ± 5.94	30.00 ± 6.66

Table S2. awROCE enrichment at 1% of structure-based scoring functions and the combined scoring approach

target	XSCORE::HMSCORE	Fred::ChemScore	Fred::PLP	Fred::Chemgauss3	MedusaScore	MedusaScore + filter
ace	23.71 ± 4.24	15.47 ± 4.77	24.56 ± 4.15	21.33 ± 4.50	10.91 ± 2.86	18.44 ± 4.13
ache	14.64 ± 3.31	0.00 ± 0.00	0.02 ± 0.08	1.37 ± 0.38	18.37 ± 3.91	26.22 ± 4.95
cdk2	8.99 ± 2.42	20.90 ± 4.84	26.56 ± 4.03	20.13 ± 4.57	9.47 ± 2.06	14.36 ± 2.33
cox2	9.67 ± 1.85	0.83 ± 0.51	2.79 ± 1.07	8.79 ± 1.64	2.08 ± 1.03	4.14 ± 1.44
egfr	6.46 ± 1.34	19.48 ± 2.33	4.75 ± 1.34	10.37 ± 1.78	17.22 ± 1.99	25.69 ± 2.13
fxa	4.86 ± 2.42	11.26 ± 2.73	15.20 ± 3.76	13.82 ± 4.35	0.15 ± 0.95	4.85 ± 2.44
hivrt	11.94 ± 3.90	9.12 ± 3.49	4.13 ± 3.35	18.13 ± 5.15	17.39 ± 4.45	22.88 ± 4.77
inha	9.28 ± 2.15	16.46 ± 3.17	7.96 ± 2.15	10.33 ± 2.39	3.73 ± 0.63	11.26 ± 2.91
p38	6.28 ± 3.31	6.52 ± 3.22	6.51 ± 3.23	6.56 ± 3.19	18.46 ± 4.71	35.65 ± 8.41
pde5	0.00 ± 0.00	4.80 ± 2.39	4.23 ± 2.43	7.24 ± 2.86	0.00 ± 0.00	26.49 ± 6.07
pdgfrb	14.82 ± 2.66	16.93 ± 3.20	12.28 ± 2.73	11.59 ± 2.74	23.49 ± 3.46	43.18 ± 5.77
src	0.53 ± 0.21	21.37 ± 4.10	0.52 ± 0.31	7.27 ± 1.98	18.46 ± 3.93	0.00 ± 0.00
vegfr2	6.47 ± 2.38	17.25 ± 3.37	3.09 ± 1.55	13.22 ± 3.34	12.30 ± 2.89	15.39 ± 3.23

Table S3. awROCE enrichment at 2% of structure-based scoring functions and the combined scoring approach

target	XSCORE::HMSCORE	Fred::ChemScore	Fred::PLP	Fred::Chemgauss3	MedusaScore	MedusaScore + filter
ace	15.47 ± 3.01	12.00 ± 2.54	12.72 ± 2.05	14.39 ± 2.60	7.84 ± 1.78	11.53 ± 2.56
ache	7.72 ± 1.60	0.77 ± 0.38	0.82 ± 0.60	0.94 ± 0.23	10.47 ± 1.89	17.16 ± 2.60
cdk2	7.71 ± 1.57	15.60 ± 1.91	14.42 ± 1.88	14.97 ± 1.76	8.30 ± 1.33	7.18 ± 1.16
cox2	7.34 ± 1.21	2.07 ± 0.59	3.10 ± 0.79	8.23 ± 1.10	1.04 ± 0.52	2.07 ± 0.72
egfr	4.92 ± 0.79	13.08 ± 1.39	4.63 ± 0.78	8.18 ± 0.98	12.46 ± 1.22	15.78 ± 1.25
fxa	2.45 ± 1.22	10.63 ± 1.99	10.46 ± 1.99	7.72 ± 1.73	2.40 ± 1.23	4.91 ± 1.66
hivrt	8.59 ± 2.20	6.53 ± 2.17	5.59 ± 2.30	10.76 ± 2.24	8.68 ± 2.22	12.76 ± 2.81
inha	4.68 ± 1.05	8.75 ± 1.59	5.43 ± 1.24	5.47 ± 1.20	2.63 ± 0.31	5.65 ± 1.48
p38	3.25 ± 1.62	3.27 ± 1.61	3.26 ± 1.61	3.28 ± 1.59	11.34 ± 2.21	20.63 ± 4.47
pde5	0.00 ± 0.00	4.90 ± 1.72	2.58 ± 1.49	4.53 ± 1.57	1.91 ± 2.01	14.27 ± 3.61
pdgfrb	7.56 ± 1.33	11.29 ± 1.98	6.30 ± 1.36	6.16 ± 1.36	16.32 ± 1.92	21.58 ± 2.89
src	0.40 ± 0.23	18.72 ± 2.11	0.74 ± 0.21	5.30 ± 0.68	11.84 ± 1.93	0.00 ± 0.04
vegfr2	4.96 ± 1.29	12.06 ± 2.06	2.49 ± 0.96	7.07 ± 1.55	6.85 ± 1.57	12.70 ± 1.90

Table S4. awROCE enrichment at 5% of structure-based scoring functions and the combined scoring approach

target	XSCORE::HMSCORE	Fred::ChemScore	Fred::PLP	Fred::Chemgauss3	MedusaScore	MedusaScore + filter
ace	8.48 ± 1.00	5.84 ± 0.89	5.44 ± 0.96	9.18 ± 1.12	3.13 ± 0.71	7.04 ± 1.00
ache	3.09 ± 0.64	0.64 ± 0.28	4.08 ± 0.72	1.94 ± 0.32	4.35 ± 0.75	8.39 ± 1.12
cdk2	3.64 ± 0.62	6.92 ± 0.70	7.74 ± 0.82	7.40 ± 0.77	5.30 ± 0.69	5.14 ± 0.69
cox2	4.94 ± 0.56	1.61 ± 0.32	2.40 ± 0.40	5.38 ± 0.56	1.24 ± 0.35	1.66 ± 0.39
egfr	3.60 ± 0.37	9.56 ± 0.50	3.62 ± 0.40	4.36 ± 0.43	10.41 ± 0.49	9.25 ± 0.57
fxa	1.97 ± 0.72	5.79 ± 0.93	6.13 ± 0.91	3.16 ± 0.69	1.54 ± 0.60	4.18 ± 0.91
hivrt	4.32 ± 1.08	5.14 ± 1.03	3.07 ± 0.80	7.21 ± 1.05	4.56 ± 0.97	5.88 ± 1.01
inha	2.69 ± 0.57	5.54 ± 0.76	3.10 ± 0.46	3.99 ± 0.69	1.97 ± 0.43	4.18 ± 0.75
p38	1.30 ± 0.65	1.84 ± 0.65	2.64 ± 0.74	1.35 ± 0.64	5.85 ± 1.04	10.49 ± 1.49
pde5	0.00 ± 0.00	2.95 ± 0.76	2.00 ± 0.77	3.15 ± 0.69	3.57 ± 0.84	6.90 ± 1.36
pdgfrb	3.97 ± 0.62	6.68 ± 0.72	4.27 ± 0.75	4.57 ± 0.64	8.33 ± 0.77	8.63 ± 1.15
src	0.72 ± 0.10	9.67 ± 0.77	0.49 ± 0.12	3.28 ± 0.76	5.49 ± 0.78	0.19 ± 0.11

vegfr2	1.98 ± 0.52	6.65 ± 0.80	2.24 ± 0.58	2.92 ± 0.62	5.44 ± 0.75	6.27 ± 0.79
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Table S5. awAUC of structure-based scoring functions and the combined scoring approach

target	XSCORE::HMSCORE	Fred::ChemScore	Fred::PLP	Fred::Chemgauss3	MedusaScore	MedusaScore + filter
ace	0.69 ± 0.04	0.68 ± 0.03	0.64 ± 0.03	0.66 ± 0.04	0.52 ± 0.04	0.63 ± 0.04
ache	0.42 ± 0.03	0.47 ± 0.03	0.51 ± 0.03	0.47 ± 0.03	0.43 ± 0.04	0.73 ± 0.03
cdk2	0.60 ± 0.03	0.78 ± 0.02	0.61 ± 0.03	0.78 ± 0.02	0.57 ± 0.03	0.71 ± 0.02
cox2	0.68 ± 0.02	0.64 ± 0.01	0.61 ± 0.02	0.73 ± 0.02	0.27 ± 0.02	0.39 ± 0.02
egfr	0.57 ± 0.01	0.92 ± 0.00	0.67 ± 0.02	0.66 ± 0.01	0.83 ± 0.01	0.85 ± 0.01
fxa	0.57 ± 0.03	0.75 ± 0.02	0.76 ± 0.02	0.73 ± 0.02	0.52 ± 0.03	0.72 ± 0.02
hivrt	0.53 ± 0.04	0.68 ± 0.04	0.54 ± 0.04	0.75 ± 0.03	0.55 ± 0.04	0.64 ± 0.04
inha	0.29 ± 0.03	0.55 ± 0.03	0.45 ± 0.03	0.51 ± 0.03	0.44 ± 0.03	0.57 ± 0.03
p38	0.39 ± 0.03	0.42 ± 0.03	0.40 ± 0.03	0.35 ± 0.03	0.64 ± 0.03	0.81 ± 0.03
pde5	0.40 ± 0.03	0.70 ± 0.03	0.60 ± 0.03	0.61 ± 0.03	0.65 ± 0.03	0.75 ± 0.04
pdgfrb	0.44 ± 0.03	0.74 ± 0.01	0.64 ± 0.02	0.63 ± 0.02	0.60 ± 0.03	0.69 ± 0.03
src	0.44 ± 0.02	0.83 ± 0.01	0.45 ± 0.02	0.67 ± 0.02	0.50 ± 0.03	0.66 ± 0.05
vegfr2	0.43 ± 0.03	0.83 ± 0.01	0.58 ± 0.03	0.74 ± 0.02	0.65 ± 0.03	0.67 ± 0.03

Table S6. awROCE enrichment at 0.5% of FieldScreen, FLAP (LBX), FLAP(RBLB), MedusaScore + filter

target	FieldScreen	FLAP (LBX)	FLAP (RBLB)	MedusaScore + filter
ace	13.76 ± 7.42	28.56 ± 8.92	6.53 ± 1.96	36.95 ± 8.26
ache	15.88 ± 5.11	63.00 ± 8.16	48.39 ± 8.07	44.97 ± 10.16
cdk2	8.56 ± 3.29	27.66 ± 6.17	41.61 ± 7.53	26.73 ± 4.85
cox2	50.93 ± 4.67	57.33 ± 6.00	16.74 ± 5.59	8.29 ± 2.87
egfr	48.57 ± 5.22	47.96 ± 5.40	19.80 ± 2.89	41.61 ± 4.49
fxa	0.90 ± 2.54	9.57 ± 4.97	8.68 ± 1.81	9.69 ± 4.87
hivrt	39.99 ± 8.18	33.47 ± 7.44	27.59 ± 4.46	46.03 ± 9.60
inha	59.47 ± 7.05	70.23 ± 8.70	79.98 ± 8.20	21.66 ± 6.24
p38	3.99 ± 0.74	0.00 ± 0.00	5.56 ± 2.00	66.95 ± 17.33
pde5	8.19 ± 3.90	28.35 ± 5.61	73.64 ± 10.84	59.08 ± 13.50
pdgfrb	25.91 ± 5.38	1.61 ± 0.96	2.36 ± 0.57	86.46 ± 11.56
src	13.09 ± 4.78	0.00 ± 0.04	63.41 ± 8.08	0.00 ± 0.00
vegfr2	13.58 ± 4.51	6.34 ± 3.32	48.22 ± 6.28	30.00 ± 6.66

Table S7. awROCE enrichment at 1% of FieldScreen, FLAP (LBX), FLAP(RBLB), MedusaScore + filter

target	FieldScreen	FLAP (LBX)	FLAP (RBLB)	MedusaScore + filter
ace	12.23 ± 3.51	21.84 ± 5.58	11.15 ± 3.79	18.44 ± 4.13
ache	19.69 ± 5.55	34.58 ± 3.99	28.66 ± 4.07	26.22 ± 4.95
cdk2	4.27 ± 1.64	18.41 ± 3.28	22.11 ± 3.18	14.36 ± 2.33
cox2	30.33 ± 2.54	30.70 ± 2.77	14.98 ± 2.00	4.14 ± 1.44
egfr	28.04 ± 2.55	27.45 ± 2.75	14.66 ± 1.52	25.69 ± 2.13
fxa	3.36 ± 2.32	8.27 ± 3.81	9.67 ± 2.48	4.85 ± 2.44
hivrt	19.89 ± 4.07	16.64 ± 3.70	18.76 ± 3.59	22.88 ± 4.77
inha	11.77 ± 2.31	36.51 ± 3.98	44.46 ± 4.25	11.26 ± 2.91
p38	32.58 ± 3.81	0.00 ± 0.00	2.82 ± 1.00	35.65 ± 8.41
pde5	2.04 ± 0.36	14.13 ± 2.79	36.76 ± 5.43	26.49 ± 6.07
pdgfrb	5.70 ± 2.82	2.19 ± 0.67	1.19 ± 0.29	43.18 ± 5.77
src	13.00 ± 2.66	0.33 ± 0.18	37.53 ± 4.42	0.00 ± 0.00
vegfr2	6.77 ± 2.39	4.92 ± 1.96	24.12 ± 3.15	15.39 ± 3.23

Table S8. awROCE enrichment at 2% of FieldScreen, FLAP (LBX), FLAP(RBLB), MedusaScore + filter

target	FieldScreen	FLAB (LBX)	FLAP (RBLB)	MedusaScore + filter
ace	8.08 ± 2.84	17.00 ± 2.70	7.52 ± 1.74	11.53 ± 2.56
ache	14.14 ± 1.78	20.30 ± 2.01	16.68 ± 1.94	17.16 ± 2.60
cdk2	2.13 ± 0.82	10.23 ± 1.62	11.94 ± 1.68	7.18 ± 1.16
cox2	18.71 ± 1.62	16.28 ± 1.39	9.64 ± 1.07	2.07 ± 0.72
egfr	17.75 ± 1.40	15.49 ± 1.27	8.93 ± 0.90	15.78 ± 1.25
fxa	5.42 ± 1.35	7.15 ± 2.29	5.14 ± 1.23	4.91 ± 1.66
hivrt	11.77 ± 2.31	8.71 ± 2.14	9.57 ± 1.70	12.76 ± 2.81
inha	16.29 ± 1.91	18.26 ± 1.99	24.51 ± 2.15	5.65 ± 1.48
p38	1.14 ± 0.20	0.00 ± 0.00	4.41 ± 1.18	20.63 ± 4.47
pde5	10.12 ± 2.07	7.05 ± 1.39	20.61 ± 2.76	14.27 ± 3.61
pdgfrb	8.51 ± 1.55	3.20 ± 1.04	0.93 ± 0.18	21.58 ± 2.89
src	3.55 ± 1.20	1.07 ± 0.64	19.91 ± 2.03	0.00 ± 0.04
vegfr2	7.06 ± 1.56	3.38 ± 1.14	14.14 ± 1.69	12.70 ± 1.90

Table S9. awROCE enrichment at 5% of FieldScreen, FLAP (LBX), FLAP(RBLB), MedusaScore + filter

target	FieldScreen	FLAB (LBX)	FLAP (RBLB)	MedusaScore + filter
ace	4.64 ± 0.96	7.59 ± 0.98	3.28 ± 0.70	7.04 ± 1.00
ache	7.57 ± 0.80	8.71 ± 0.83	8.11 ± 0.82	8.39 ± 1.12
cdk2	0.85 ± 0.33	5.02 ± 0.69	6.18 ± 0.75	5.14 ± 0.69
cox2	10.49 ± 0.63	7.32 ± 0.59	5.72 ± 0.54	1.66 ± 0.39
egfr	9.34 ± 0.54	8.38 ± 0.57	5.10 ± 0.40	9.25 ± 0.57
fxa	5.14 ± 0.87	3.46 ± 0.84	4.29 ± 1.09	4.18 ± 0.91
hivrt	5.14 ± 0.99	6.63 ± 0.96	4.95 ± 0.82	5.88 ± 1.01
inha	6.85 ± 0.74	8.10 ± 0.82	10.21 ± 0.85	4.18 ± 0.75
p38	0.53 ± 0.08	0.11 ± 0.02	2.61 ± 0.54	10.49 ± 1.49
pde5	4.75 ± 0.96	5.49 ± 0.89	9.92 ± 1.06	6.90 ± 1.36
pdgfrb	3.56 ± 0.62	1.35 ± 0.43	0.74 ± 0.14	8.63 ± 1.15
src	2.40 ± 0.62	2.38 ± 0.69	9.67 ± 0.85	0.19 ± 0.11
vegfr2	3.57 ± 0.63	1.89 ± 0.59	7.69 ± 0.82	6.27 ± 0.79

Table S10. awAUC of FieldScreen, FLAP (LBX), FLAP(RBLB), MedusaScore + filter

target	FieldScreen	FLAP (LBX)	FLAP (RBLB)	MedusaScore + filter
ace	0.64 ± 0.04	0.69 ± 0.03	0.53 ± 0.03	0.63 ± 0.04
ache	0.63 ± 0.03	0.62 ± 0.04	0.74 ± 0.03	0.73 ± 0.03
cdk2	0.44 ± 0.02	0.68 ± 0.02	0.50 ± 0.03	0.71 ± 0.02
cox2	0.82 ± 0.02	0.69 ± 0.02	0.49 ± 0.02	0.39 ± 0.02
egfr	0.82 ± 0.01	0.70 ± 0.02	0.55 ± 0.02	0.85 ± 0.01
fxa	0.73 ± 0.02	0.61 ± 0.03	0.62 ± 0.03	0.72 ± 0.02
hivrt	0.64 ± 0.04	0.56 ± 0.04	0.61 ± 0.04	0.64 ± 0.04
inha	0.72 ± 0.02	0.66 ± 0.03	0.67 ± 0.03	0.57 ± 0.03
p38	0.28 ± 0.02	0.31 ± 0.02	0.45 ± 0.03	0.81 ± 0.03
pde5	0.62 ± 0.03	0.55 ± 0.04	0.64 ± 0.05	0.75 ± 0.04
pdgfrb	0.40 ± 0.03	0.44 ± 0.02	0.34 ± 0.03	0.69 ± 0.03
src	0.39 ± 0.03	0.44 ± 0.03	0.80 ± 0.02	0.66 ± 0.05
vegfr2	0.53 ± 0.03	0.59 ± 0.03	0.61 ± 0.03	0.67 ± 0.03

