SUPPORTING INFORMATION

Design of dual inhibitors of Histone Deacetylase 6 (HDAC6) and Heat Shock Protein 90 (Hsp90)

Luca Pinzi,[a†] Rosaria Benedetti, [a‡] Lucia Altucci, [‡] Giulio Rastelli[†*]

[†]Department of Life Sciences, University of Modena and Reggio Emilia. Via G. Campi 103, 41125 Modena, Italy.
[‡]Department of Precision Medicine, University of Campania "*Luigi Vanvitelli*". Via L. De Crecchio 7, 80138 Naples, Italy.

* Correspondence to Prof. Giulio Rastelli, Department of Life Sciences, University of Modena and Reggio Emilia. Via Giuseppe Campi, 103. 41125 - Modena, Italy. Phone: +39 035 2058564; e-mail: giulio.rastelli@unimore.it

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Table S1. Representative HDAC6 and Hsp90 crystal structures employed in the study.

Protein	*Cluster ID*	*Number of the waters*	*PDB code*	*Chain*	*Ligand ID*	*Resolution (Å)*	*RMSD of redocking*
Hsp90	Ia	4	1UY6	A	PU3	1.90	0.788
Hsp90	IIa	3	2YKI	A	YKI	1.67	1.006
Hsp90	IIIa	3	2XHR	A	C0P	2.2	0.759
Hsp90	IVa	3	2BYI	A	2DD	1.6	0.123
Hsp90	Va	3	3OWD	A	MEY	1.63	0.303
Hsp90	VIa	1	3RLR	B	3RR	1.7	0.115
Hsp90	VIIa	4	4YKW	A	4ES	1.85	0.083
Hsp90	VIIIa	3	2VCI	A	2GJ	2.00	0.557
Hsp90	IXa	3	4AWO	A	99B	1.7	1.557
Hsp90	Xa	3	3K99	A	PFT	2.1	0.195
Hsp90	XIa	3	3TUH	A	TUH	1.8	0.166
HDAC6		0	5EDU	A	TSN	2.79	1.42

Note: * RMSD of redocking poses was evaluated after binding site alignment.

Table S2. Hsp90 ligands that resulted similar to the identified compounds, according to MACCS and ECFP4 fingerprint similarity estimations.

Compound ID	*Number of ChEMBL ligands (actives)*[a]	*MACCSfp score range (max - min)*	*MACCSfp mean (± St.Dev.)*	*ECFP4fp score range (max - min)*	*ECFP4fp mean (± St.Dev.)*
4	760 (666)	0.842 - 0.23	0.546 ± 0.094	0.593 - 0.3	0.378 ± 0.057
5	632 (574)	0.721 - 0.158	0.555 ± 0.078	0.553 - 0.3	0.367 ± 0.043
8	796 (713)	0.69 - 0.197	0.475 ± 0.07	0.622 - 0.3	0.394 ± 0.066
9	866 (742)	0.647 - 0.179	0.506 ± 0.077	0.564 - 0.3	0.378 ± 0.056
10	930 (812)	0.647 - 0.179	0.507 ± 0.075	0.575 - 0.3	0.394 ± 0.062

Note: [a] Ligands whose activity annotations have been reported in terms of IC_{50}, K_I, K_d or EC_{50}, and their activity values on Hsp90 are below 5 μM.