

Supplementary Information

In silico and in vitro Studies of the (+)-2,3,9-Trimethoxypterocarpan and Vorinostat Association as an Epigenetic Strategy to Inhibit Human Cancer Cells

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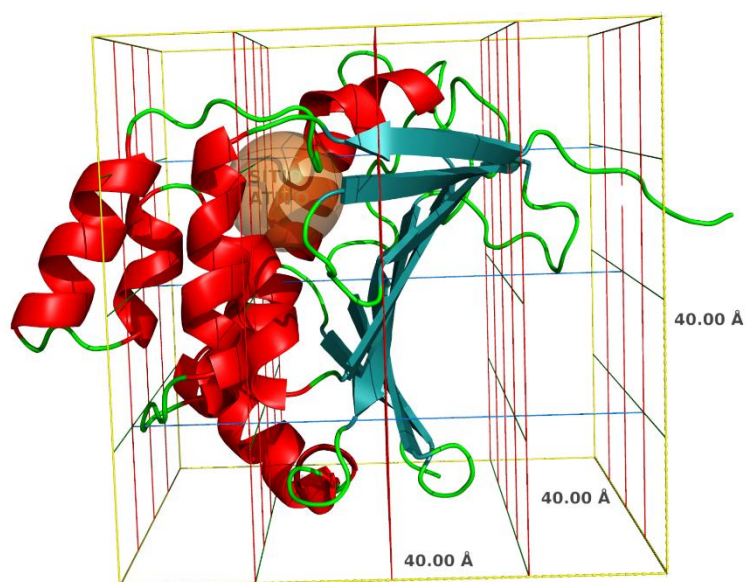


Figure S1. Illustrative representation of the Gridbox, generated in the PyMol software. The image shows the spatial configuration applied to one of the target proteins (HSP90) subjected to broad search docking, representing the procedure adopted for all other structures analyzed. The orange sphere represents the protein's active site, always included in all assays.

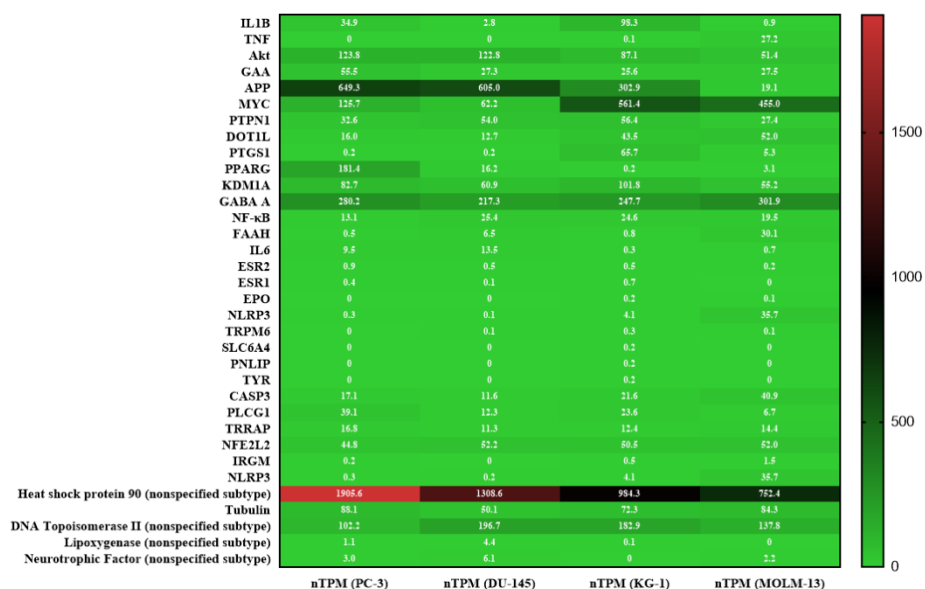


Figure S2. Possible targets with expression modulated by the suggested treatment, according to the basal expression in each lineage (normalized transcripts *per* million - nTPM).

Table S1. DockThor software default parameters for the wide search docking procedure

Parameter	Value
XYZ box dimension	40
Discretization	0.42
Number of evaluations	1,000,000
Population size	750
Number of runs	24

Table S2. Human cell line origins and plating concentrations

Cell line	Histological type	Origin	Seeding concentration / (cells mL ⁻¹)
PC-3 (prostate carcinoma)	prostatic adenocarcinoma	BCRJ	0.1×10^6
DU-145 (prostate carcinoma)	prostatic adenocarcinoma	BCRJ	0.8×10^5
KG-1 (acute myeloid leukemia)	myeloblast	NCI	0.3×10^6
MOLM-13 (acute myeloid leukemia)	monoblast	NCI	0.1×10^5

US-NCI: United States National Cancer Institute; BR-BCRJ: Cell Bank of Rio de Janeiro.

Table S3. Target fishing for pterocarpan in the platform TargetNet, Swiss, and Cortellis Drug Discovery Intelligence (CDDI)

TargetNet	Swiss	CDDI
P08183	P08183	P05067
P03372	P18031	P09917
Q92731	Q14432	P06276
P09917	Q13370	P42574
P35463	Q9Y233	P01588
P26684	P12931	P03372
P21728	P35968	Q92731
P18031	Q5S007	B4DQM1
Q6B856	P09874	P19113
Q03181	P47869	A1A4Y4
Q3KRE8	P49798	P01584
Q9UNQ0	Q04759	P05231
P02550	O60885	P01106
P37231	O60674	Q16236
Q07869	Q9H8M2	P16233
P11511	Q9Y5Y9	P37231
P05979	P45983	P27815
P14174	P53779	Q07343
O42713	P49841	Q08493
P35869	P24941	Q08499
P12527	P11802	P23219
P23219	P23219	P31645
Q14432	P10721	P12931
P35398		Q9Y4A5
	P08581	H0Y4W2
O43353	P16234	Q9BX84
P63000	P28907	P01375
P51452	P23443	Q8NHX9
P27338	O14965	P12023
P35236	P24941	
O14842	Q9H4B4	
P18825	Q9NYY3	
P63001	P46098	
Q04206	P43405	
P04058	O76074	
P16050	O00408	
P55211	P21554	
P24468	P34972	

Q63470	P07333
P23280	P09619
P21397	P35916
Q16548	P36888
P05177	P30411
P21396	Q13255
P22303	P23946
Q9HC97	P30281
P33261	P42574
Q01959	P21980
P14061	P22735
P47936	Q08188
Q9NR96	Q02750
P21918	P10275
P35367	P28472
P10275	P28472
P06401	P28472
P28566	P18507
P31645	P06239
P49759	Q08493
P05067	Q16769
P18089	Q02156
P04150	P24723
P22086	Q9Y463
O60755	P15538
P16234	Q9UBU7
P08173	P19099
P08235	Q08881
P15121	Q9UGN5
P29477	P32246
Q07343	P55210
P08913	P49759
O42275	Q8NER1
Q08499	P07949
P01375	P37059
O60240	Q15303
Q05769	P68400
P19643	Q8IXJ6
P04054	Q12866
P41235	P15311
P37059	P14867
P79208	Q13133

Q00G26	P00558
P13866	Q15349
P18901	P55055
P34995	P25090
P08575	Q99572
P18130	P31644
P10827	P06213
P10826	O14920
P10828	P62136
P10276	P04629
P19327	P05362
Q15722	P16581
Q07820	P33981
P12268	P00918
P43140	P43166
P35563	P00915
P23944	O43570
P31639	O43293
P43119	P29274
P13631	P19320
P43088	P42336
P80457	P28472
P20288	P18507
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P61169	P20248
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P15207	P11802
P28564	P30279
P22001	P34903
P23141	P18507
Q9Y271	P18507
P43116	P14867
Q96RI1	P18507
P31388	P31644
P05129	P28472
P16581	Q16445
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P07943	
P30305	
P31652	

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P09958
P15056
Q9UKP6
P06241
P42574
P21554

Table S4. Target fishing for vorinostat in the platform TargetNet, Swiss, and Cortellis Drug Discovery Intelligence (CDDI)

TargetNet	Swiss	CDDI
Q9BY41	O15379	P22303
P08575	Q9UBN7	P15121
Q9Y2R2	Q92769	P10253
P08253	Q9Y618	P16050
P17706	Q9UQL6	P16220
Q8IXJ6	Q8WUI4	O43889
P34913	O75376	Q02930
O42713	Q9BY41	P25774
P04054	Q13547	P11597
Q04609	Q96DB2	P08684
P04058	P56524	Q13822
P16050	Q9UKV0	Q02790
Q5RAG0	Q969S8	P23771
Q9GZU7	P34913	P43220
P49840	Q99572	Q14833
P97612	P08246	P49841
P23141	P45452	Q13547
P31941	Q9NPA2	Q969S8
O15379	P51512	Q92769
P08254	P50281	O15379
Q9Y5X4	P13497	P56524
P56524	P35610	Q9UBN7
O00748	O75908	Q8WUI4
P14780	P08253	Q9BY41
O00519	O75460	P14902
P35236	P14780	P01584
Q9HC97	P28062	O60725
Q13547	Q7Z2W7	P17275
P03956	O14672	P17535
Q92769	P20839	P09960
P22894	P12268	O60341
O14746	P15311	P08253
Q9UBN7	P10275	P14780
P09960	P18405	P50579
P35869	P46098	P21397
Q9NR96	P30291	P01106

P51452	Q05193	Q13469
P12527	P06734	P20393
Q05941	P39900	Q13526
O95977	P07949	P09874
P39900	P35968	O43526
P05121	Q9H4B7	P56696
P18031	P49841	Q99572
P08311	P42892	P19793
Q99685	P29274	P28702
P21453	Q02750	P48443
		Q01196
P15144		H9KVB1
	P22736	A8MZI9
P26358	Q13557	Q13950
P00915	P00918	Q13761
P35610	P15121	P08842
O60240	P12931	P35610
Q9Y2D0	P42345	Q7Z2W7
P42892	O00329	Q8NER1
P15917	P78527	P01375
P09237	P42338	P14679
P00918	P08631	Q9NUW8
P22303	P48736	P17861
		Q76R61
O43497	Q9UBF8	Q89656
P14174	P42336	Q7K6A1
O43570	P54760	P14756
Q16790	Q9UNQ0	
O14684	Q07343	
P07861	Q07820	
P30305	Q15118	
O95136	P31213	
O43353	P17948	
P55211	P27986	
P35218	Q13946	
P22748	P24941	
P00749	P29323	
O95180	Q14833	
Q8TDS4	P08254	
Q9H228	P30542	
P07943	P17252	
Q9QZN9	P06493	

P05177	P22001
P45452	Q9UBU7
P05106	P03956
P24468	P24385
P35398	P21397
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Q04206	Q9UNA0
Q99572	O75173
P23280	P25101
O60725	Q16790
P60953	O14965
P43166	P35354
P20231	P55072
P05186	P14635
Q8T6T2	P27815
P30551	Q08499
Q9JI35	Q08493
Q15722	P37058
P50579	P14061
P68400	Q9Y233
Q96RJ0	P14222
P35439	P15538
P20309	P00742
Q07820	P05093
P25779	Q8WWL7
P30553	O95067
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P47898
P04150
Q13627
P34969
Q01959

P20292
P08482
P08483
P30560
P47871
O96020
P23975
P23977
O96017
P41231
O96013
P19156
P18405
Q96RI1
Q6V1X1
P55210
P55212
O77636
P51681
P28845
P51685
P31648
P08909
P08908
Q07343
P31645
P31424
P31389
P31388
P18901
P56481
Q60492
P05129
P09483
P07948
P07949
P16581
Q969F8
Q3KRE8
P11387
P29466
P61073

P28482
Q14432
P06493
P08238
Q95136
P28335
Q9HAZ1
P13945
O95822
P20648
P07308
P48067
Q9QYJ6
Q8TDU6
P10635
P49146
P30530
P46663
P32238
P30874
P15538
P30872
P16257
P42785
P06239
P50750
P31751
P32305
P33533
P32300
P33535
P24557
Q9GZT9
P13726
P14061
P50130
P07607
P42262
P51661
P18825
P97266
P19020

P10415
P55263
P07900
O00311
P31421
P02550
Q05655
P13612
O14842
P51812
P21836
O14920
P49430
Q15858
P11086
P11712
P47811
Q05769
P35372
Q8N1Q1
Q86TI2
P08246
Q9H3N8
P17948
P55157
Q9NWZ3
Q96BI3
Q92542
P37231
P42338
P42336
P30989
Q08499
P00734
P00735
P23946
P34975
P34976
Q9Y233
P50406
P43235
Q99808

P43681
P28190
P50613
Q9UHL4
P63000
P48443
Q00987
P46925
Q63470
P05771
P11309
Q13093
P31652
P62943
P62942
P41597
P16753
P09874
P07384
P14842
O00329
P27815
Q16539
Q28156
Q06418
P30968
P30969
P11597
Q13224
Q07817
Q07869
P04818
P00517
Q9Y5N1
O75907
Q29010
Q99835
P13922
P09958
P15056
Q9UKP6
P06241

P37059

P37058

Table S5. Potential targets of vorinostat potentiated by pterocarpan

Target fishing from three platforms
Q9UNQ0
P22303
O14672
P30542
P15121
P16050
P13497
Q16790
O96020
P06493
P11597
P25774
P05093
P08684
P42892
P25101
P08246
P54760
P34913
P00742
P17948
Q14833
P08631
Q13547
Q92769
P56524
Q9UBN7
Q9BY41
P14061
P37058
O60725
P12268
P22001
P09960
P21397
Q07820
P50579
P03956

P39900

P45452

P08253

P08254

P14780

P42345

Q13946

P42338

O00329

P48736

P35354

P19793

P28702

P48443

P35610

P18405

P31213

P08842

P30291

