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Supplementary material

SUPPLEMENTARY MATERIAL TO

Antiproliferative activity of NCI-DTP glutarimide derivatives. An alignment independent 3D QSAR study

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An alignment-free three dimensional structure-activity relationships (3D QSAR) of the antiproliferative potency of twenty-two glutarimide-containing compounds towards eight representative human tumour cell lines are reported.

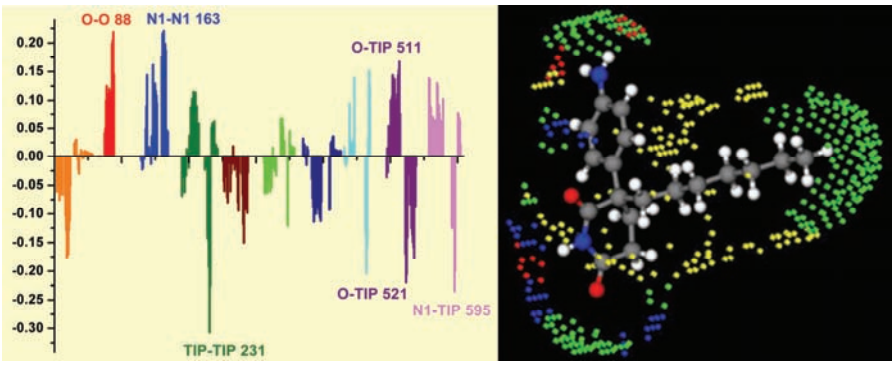

TABLE OF CONTENTS

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TABLE I-S. p(GI_{50}) Values for **1**–**22** towards: K562 (leukaemia), A549 (non-small cell lung), malme-3M (melanoma), COLO205 (colon), UO31 (renal), U251 (CNS), IGROV1 (ovarian), and MFC 7 (breast) human tumour cell lines

Cmpd. No.	Class	NSC No.	Model							
			A	B	C	D	E	F	G	H
			K-562	A549	COLO-205	U251	Malme--3M	IGROV1	UO-31	MFC07
1	I	39147	7.510	7.290	7.419	7.505	7.263	7.534	7.260	7.421
2		185	7.277	7.437	7.453	7.220	7.051	7.274	7.542	/
3		32743	8.000	8.000	8.000	8.000	8.000	8.000	8.000	8.000
4	II	636355	4.562	4.342	4.347	/[a]	4.450	4.193	4.561	/
5		636351	4.000	4.000	4.000	/	4.000	4.000	4.077	/
6	III	622730	4.564	4.500	4.660	/	4.552	4.491	4.688	/
7	IV	645461	4.252	4.000	4.000	4.232	4.000	4.000	4.000	/
8		645462	4.538	4.000	4.434	4.000	4.034	4.014	4.000	/
9	V	655763	4.691	/	4.753	4.358	4.770	4.350	4.747	/
10		653947	4.599	4.000	4.000	4.000	4.000	4.000	4.010	/
11		656924	4.000	4.000	4.000	4.120	4.000	4.000	4.000	4.000
12		671764	5.196	/	4.037	4.000	4.000	4.000	4.000	4.000
13		671765	5.760	5.108	5.717	5.259	5.410	4.803	5.337	5.248
14		655764	4.236	/	4.000	4.000	4.242	4.000	4.080	/
15		655766	4.487	/	4.000	4.000	4.000	4.000	4.137	/
16	VI	66645	4.363	4.290	4.467	4.462	4.795	4.702	4.311	4.561
17		248958	4.688	4.667	4.767	4.506	/	4.721	4.697	4.677
18	VII	677677	4.521	4.517	/	4.689	4.703	4.641	4.567	4.701
19	VIII	679266	4.766	4.256	5.019	5.007	4.696	5.268	5.353	4.525
20	IX	679109	4.709	/	4.682	4.827	4.730	4.705	4.780	4.714
21		677755	4.267	4.171	/	4.253	4.184	4.000	4.117	4.355
22	X	355461	8.618	8.550	8.534	8.561	8.545	8.417	8.691	8.572

[a]Data not available

TABLE II-S. PCA models for K562 and IGROV1. *SSX* – Percentage of the *X* sum of squares; SSX_{acc} – accumulative percentage of the *X* sum of squares; *VarX* – percentage of the *X* variance; $VarX_{aac}$ – accumulative percentage of the *X* variance

Comp.	K562				IGROV1			
	SSX	SSX_{acc}	*VarX*	$VarX_{acc}$	*SSX*	SSX_{acc}	*VarX*	$VarX_{acc}$
1	38.95	38.95	35.82	35.82	41.58	41.58	38.55	38.55
2	13.48	52.43	11.47	47.29	14.85	56.43	13.13	51.68
3	8.14	60.57	6.53	53.82	8.29	64.72	6.95	58.64
4	6.44	67.01	5.22	59.04	6.32	71.04	5.35	63.99
5	5.28	72.29	4.36	63.40	4.15	75.19	3.18	67.17

TABLE III-S. PCA models for A549atcc and COLO205. *SSX* – Percentage of the *X* sum of squares; SSX_{acc} – accumulative percentage of the *X* sum of squares; *VarX* – percentage of the *X* variance; $VarX_{aac}$ – accumulative percentage of the *X* variance

Comp.	A549atcc				COLO205			
	SSX	SSX_{acc}	*VarX*	$VarX_{acc}$	*SSX*	SSX_{acc}	*VarX*	$VarX_{acc}$
1	33.04	33.04	28.46	28.46	43.50	43.50	40.26	40.26
2	18.13	51.17	15.56	44.02	15.65	59.15	13.93	54.20
3	10.36	61.53	8.41	54.42	8.55	67.70	7.26	61.46
4	7.89	69.43	6.55	58.97	6.56	74.26	5.72	67.18
5	5.03	74.46	3.58	62.54	4.24	78.50	3.40	70.58

TABLE IV-S. PCA models for U251 and malme-3M. *SSX* – Percentage of the *X* sum of squares; SSX_{acc} – accumulative percentage of the *X* sum of squares; *VarX* – percentage of the *X* variance; $VarX_{aac}$ – accumulative percentage of the *X* variance

Comp.	U251				malme-3M			
	SSX	SSX_{acc}	*VarX*	$VarX_{acc}$	*SSX*	SSX_{acc}	*VarX*	$VarX_{acc}$
1	48.48	48.48	45.36	45.36	41.93	41.93	38.77	38.77
2	10.59	59.08	8.45	53.81	14.20	56.13	12.32	51.09
3	8.73	67.80	7.36	61.17	8.77	64.90	7.41	58.50
4	5.25	73.05	3.95	65.12	6.39	71.28	5.37	63.87
5	4.59	77.64	3.66	68.78	4.37	75.65	3.40	67.27

TABLE V-S. PCA models for UO31 and MFC-7. *SSX* – Percentage of the *X* sum of squares; SSX_{acc} – accumulative percentage of the *X* sum of squares; *VarX* – percentage of the *X* variance; $VarX_{aac}$ – accumulative percentage of the *X* variance

Comp.	UO31				MFC-7			
	SSX	SSX_{acc}	*VarX*	$VarX_{acc}$	*SSX*	SSX_{acc}	*VarX*	$VarX_{acc}$
1	41.58	41.58	38.55	38.55	54.66	54.66	50.05	50.05
2	14.85	56.43	13.13	51.68	12.96	67.62	10.25	60.30
3	8.29	64.72	6.95	58.64	7.14	74.77	4.83	65.13
4	6.32	71.04	5.35	63.99	6.17	80.94	4.72	69.85
5	4.15	75.19	3.18	67.17	4.56	85.50	3.34	73.19

TABLE VI-S. PLS models. *SSX* – Percentage of the *X* sum of squares; SSX_{acc} – accumulative percentage of the *X* sum of squares; *SDEP* – standard deviation of error of the predictions; R^2 – coefficient of determination; R^2_{acc} – accumulative coefficient of determination; Q^2_{acc} – accumulative squared predictive correlation coefficient

Comp.	*SSX*	SSX_{acc}	*SDEC*	*SDEP*	R^2	R^2_{acc}	Q^2_{acc}
				K562 for **1**–**22**			
1	37.13	37.13	0.97	1.19	0.47	0.47	0.21
2	13.46	50.59	0.46	0.86	0.41	0.88	0.59
3	7.84	58.43	0.34	0.84	0.05	0.93	0.60
4	6.83	65.26	0.23	0.87	0.04	0.97	0.58

TABLE VI-S. Continued

Comp.	*SSX*	SSX_{acc}	*SDEC*	*SDEP*	R^2	R^2_{acc}	Q^2_{acc}
			IGROV1 for **1**–**22**				
1	40.22	40.22	0.99	1.20	0.50	0.50	0.26
2	9.26	49.48	0.58	1.04	0.33	0.83	0.44
3	5.80	55.28	0.34	1.05	0.11	0.94	0.43
4	11.50	66.78	0.24	1.09	0.03	0.97	0.40
			A549atcc for **1**–**22**				
1	26.22	26.22	0.84	1.10	0.70	0.70	0.49
2	17.88	44.10	0.42	0.83	0.22	0.93	0.71
3	13.57	57.66	0.33	0.80	0.03	0.95	0.73
4	7.01	64.68	0.21	0.83	0.03	0.98	0.71
			COLO205 for **1**–**22**				
1	41.69	41.69	1.02	1.25	0.50	0.50	0.25
2	10.05	51.74	0.57	1.06	0.35	0.85	0.46
3	6.10	57.84	0.37	1.06	0.09	0.94	0.46
4	11.53	69.37	0.26	1.10	0.03	0.97	0.42
			U251 for **1**–**22**				
1	50.04	50.04	1.00	1.22	0.53	0.53	0.30
2	12.58	62.62	0.48	0.83	0.36	0.89	0.68
3	3.91	66.54	0.26	0.82	0.08	0.97	0.69
4	6.36	72.90	0.18	0.81	0.02	0.98	0.70
			malme-3M for **1**–**22**				
1	44.02	44.02	0.92	1.09	0.55	0.55	0.38
2	16.48	60.50	0.54	0.78	0.29	0.85	0.69
3	6.74	67.24	0.39	0.82	0.07	0.92	0.65
4	5.07	72.31	0.26	0.85	0.05	0.96	0.62
			UO31 for **1**–**22**				
1	45.69	45.69	1.03	1.22	0.47	0.47	0.26
2	12.35	58.04	0.62	0.92	0.34	0.81	0.57
3	7.45	65.49	0.45	0.93	0.09	0.90	0.56
4	4.85	70.34	0.31	0.97	0.06	0.95	0.52
			MFC-7 for **1-22**				
1	52.12	52.12	1.06	1.34	0.54	0.54	0.25
2	14.50	66.62	0.57	1.10	0.33	0.86	0.49
3	5.32	71.94	0.23	1.15	0.11	0.98	0.45
4	4.27	76.21	0.09	1.14	0.02	1.00	0.46

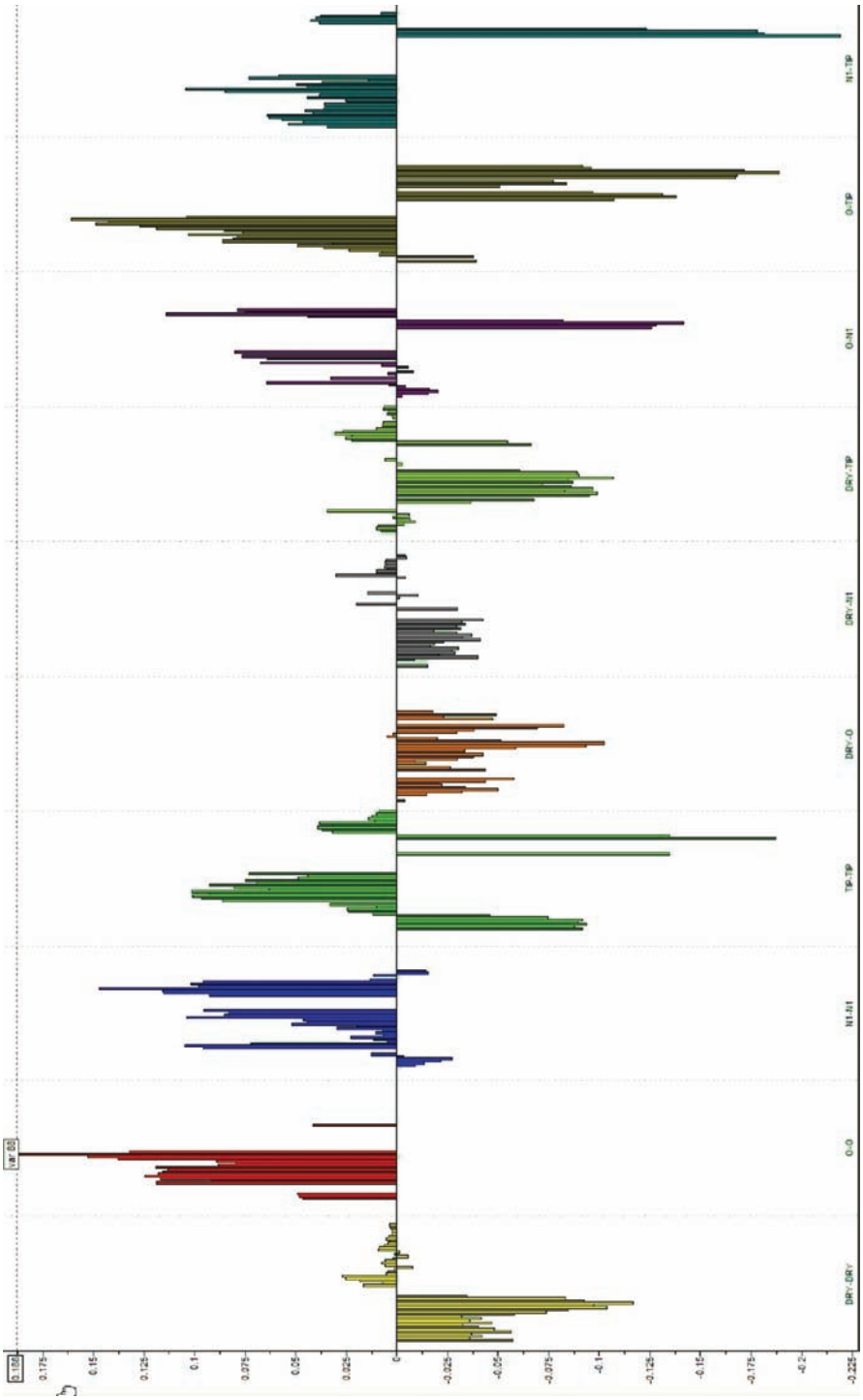


Fig. 1-S. 4LV PLS plot for IGROV1.

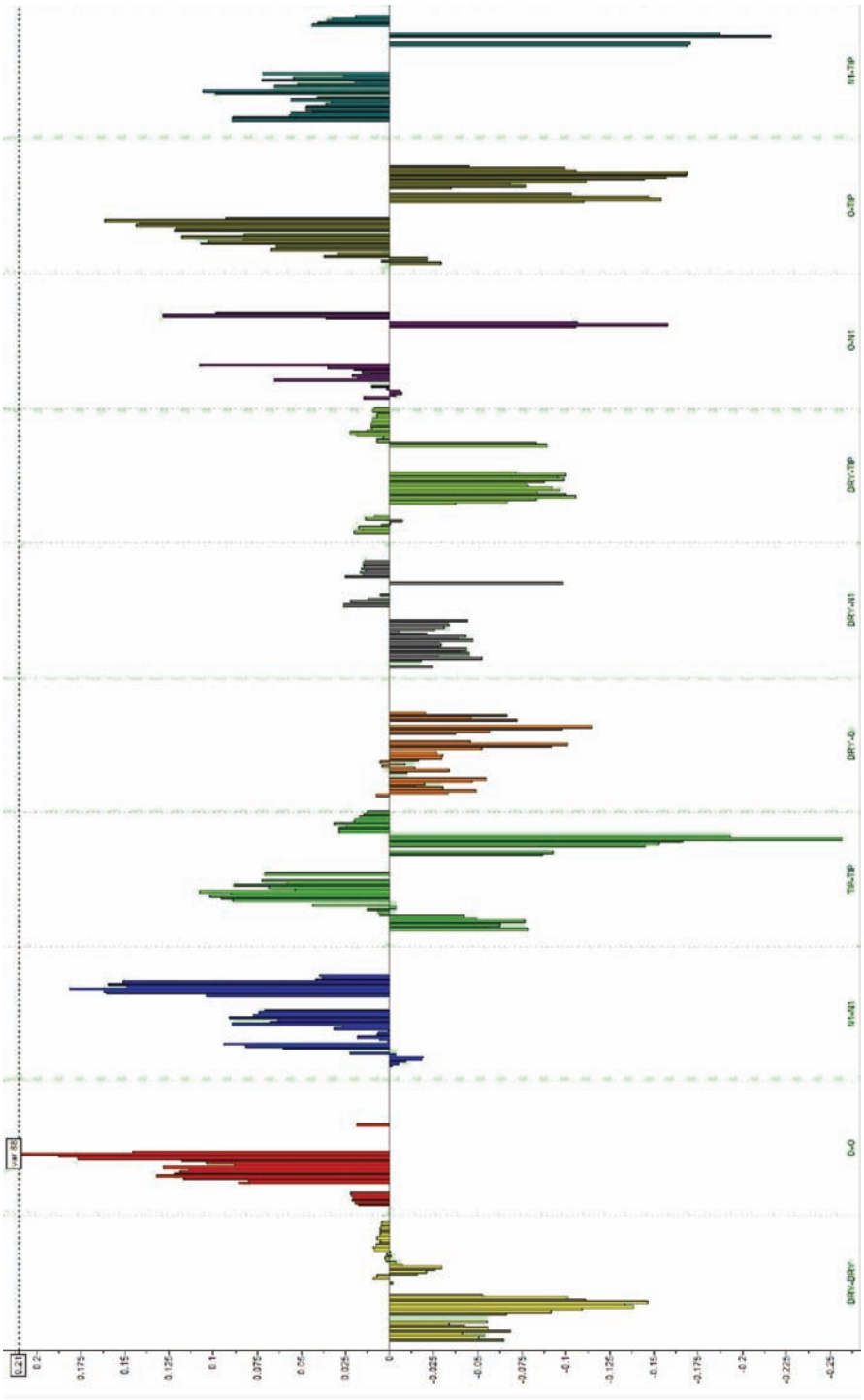


Fig. 2-S. 4LV PLS plot for A549.

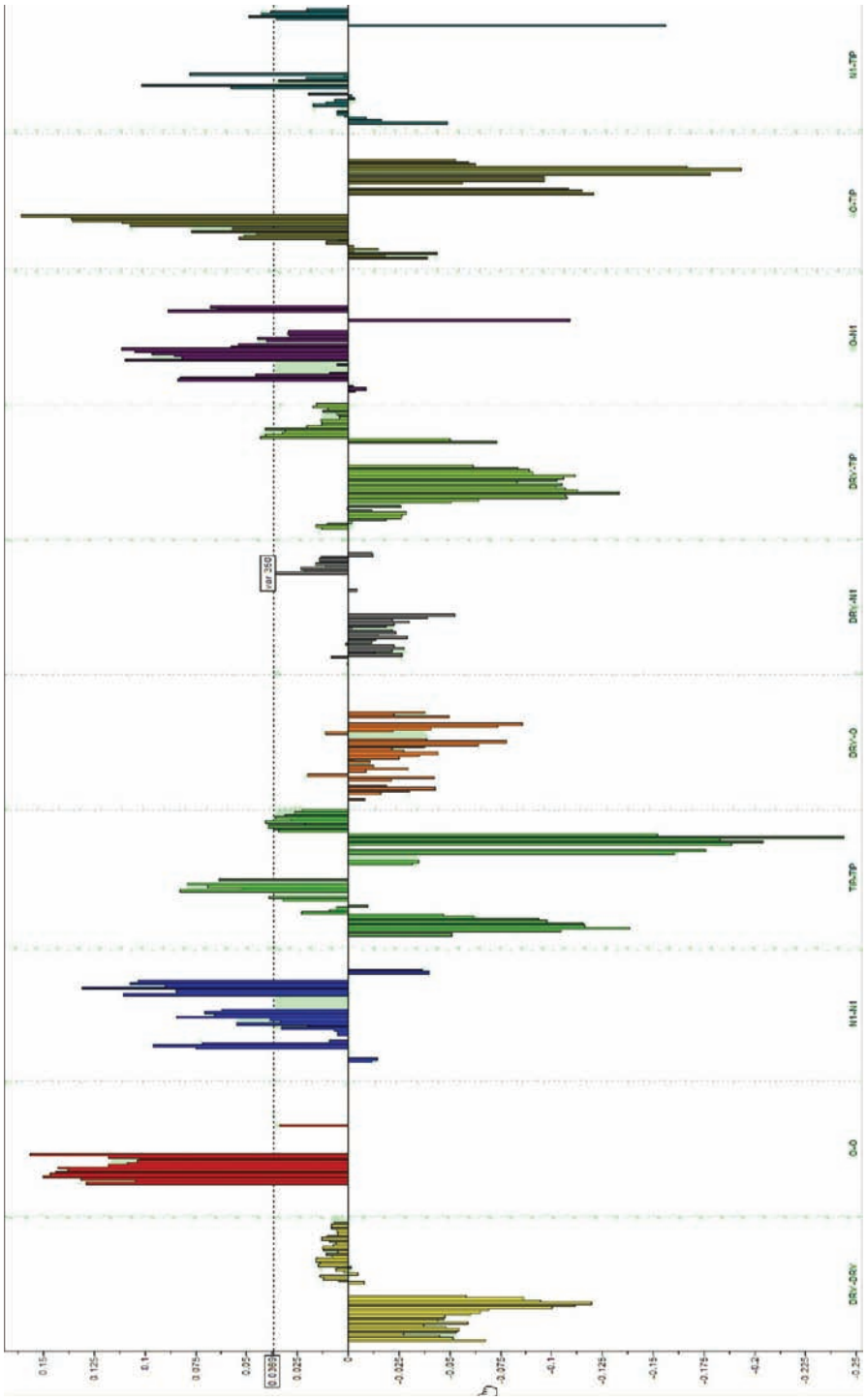


Fig. 3-S. 4LV PLS plot for COLO205.

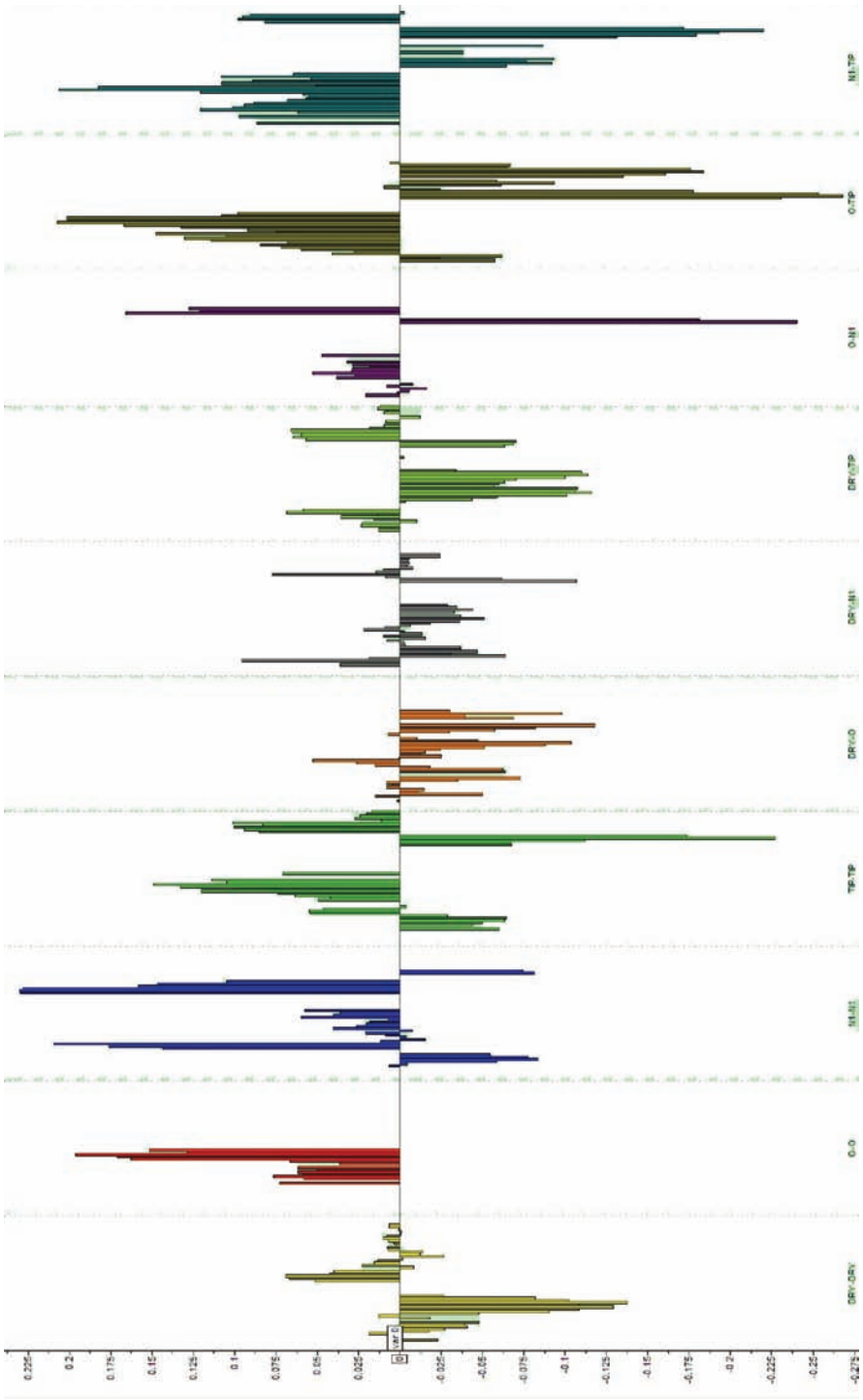


Fig. 4-S. 4LV PLS plot for U251.

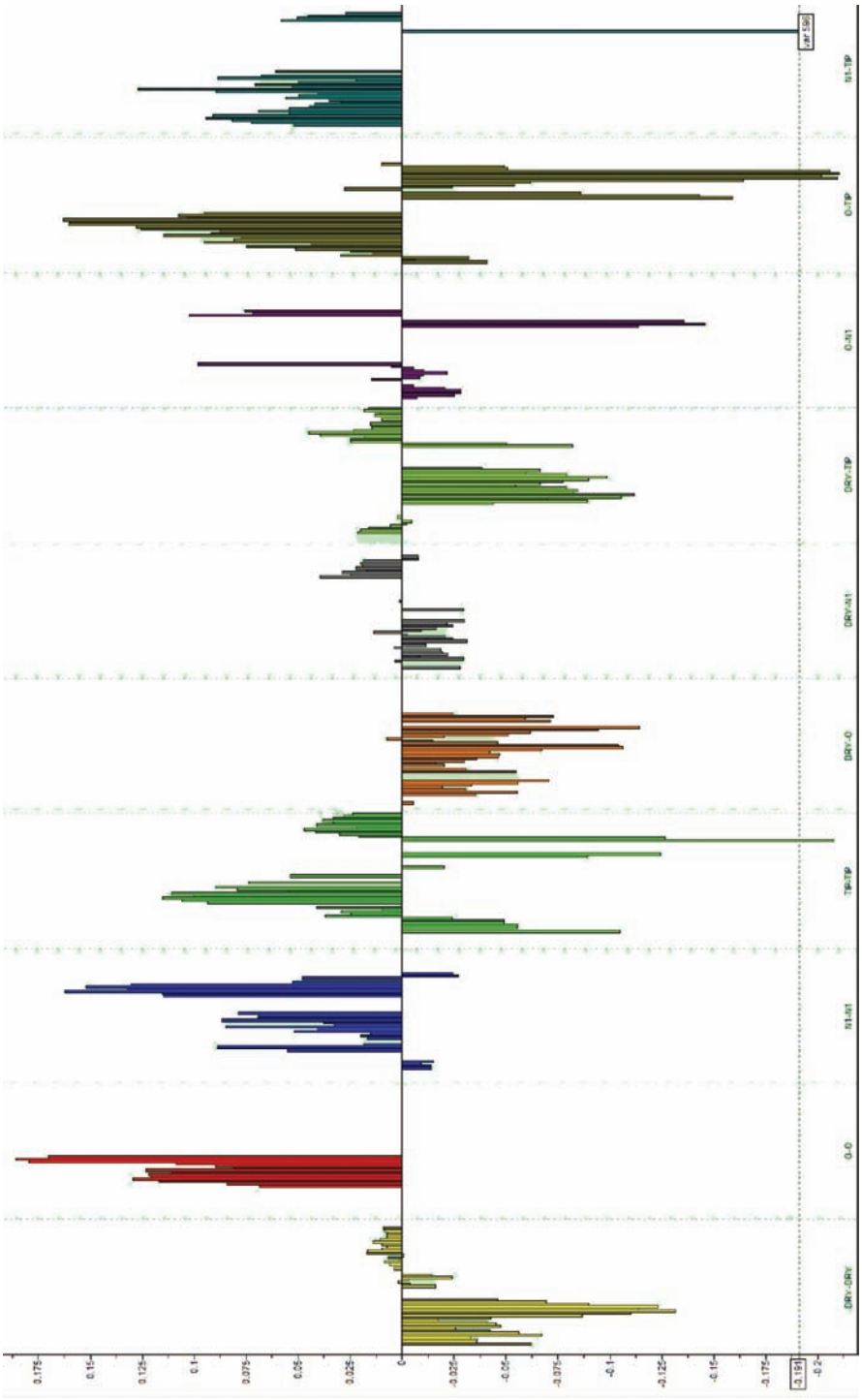


Fig. 5-S. 4LV PLS plot for malme-3M.

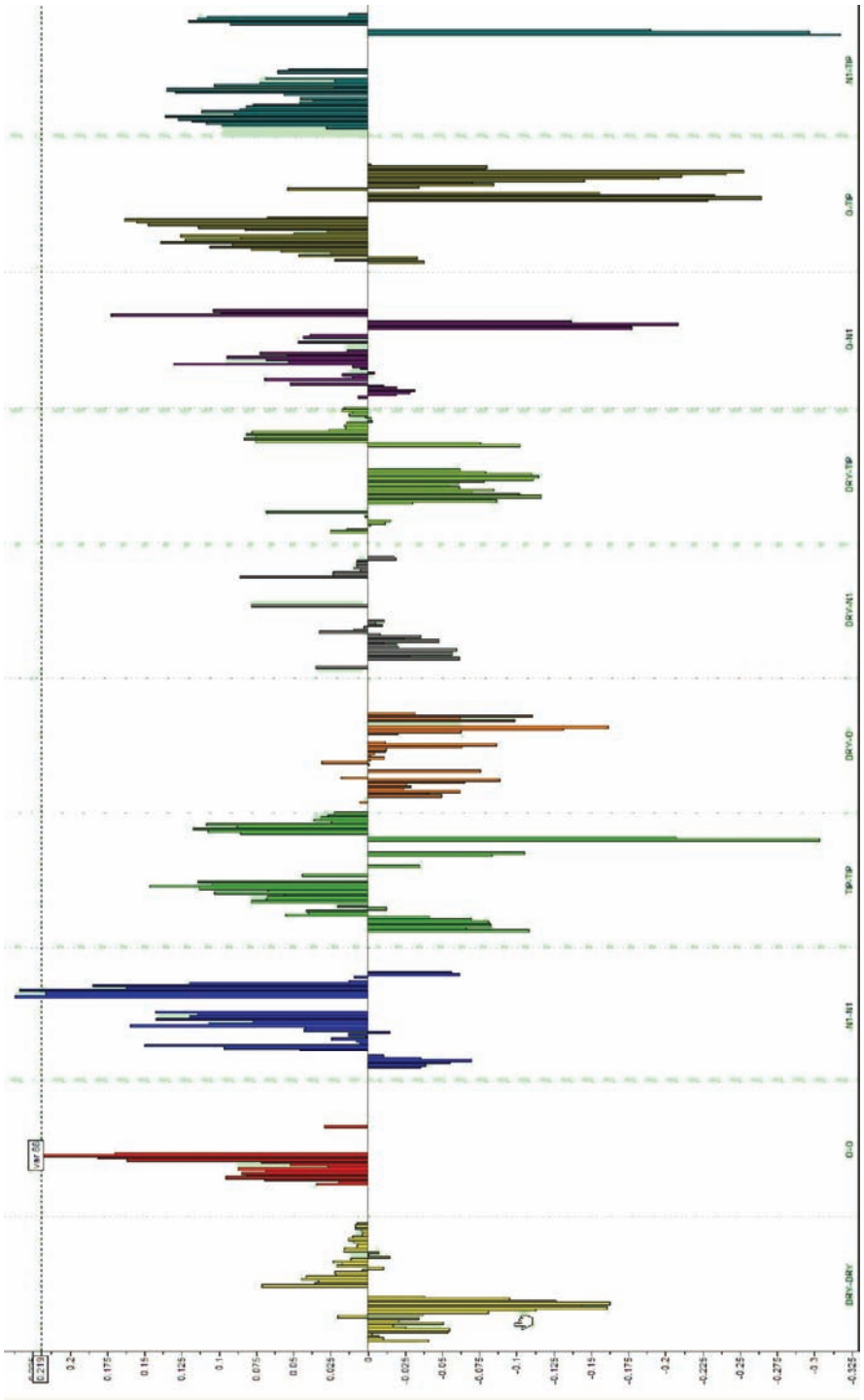


Fig. 6-S. 4LV PLS plot for UO31.

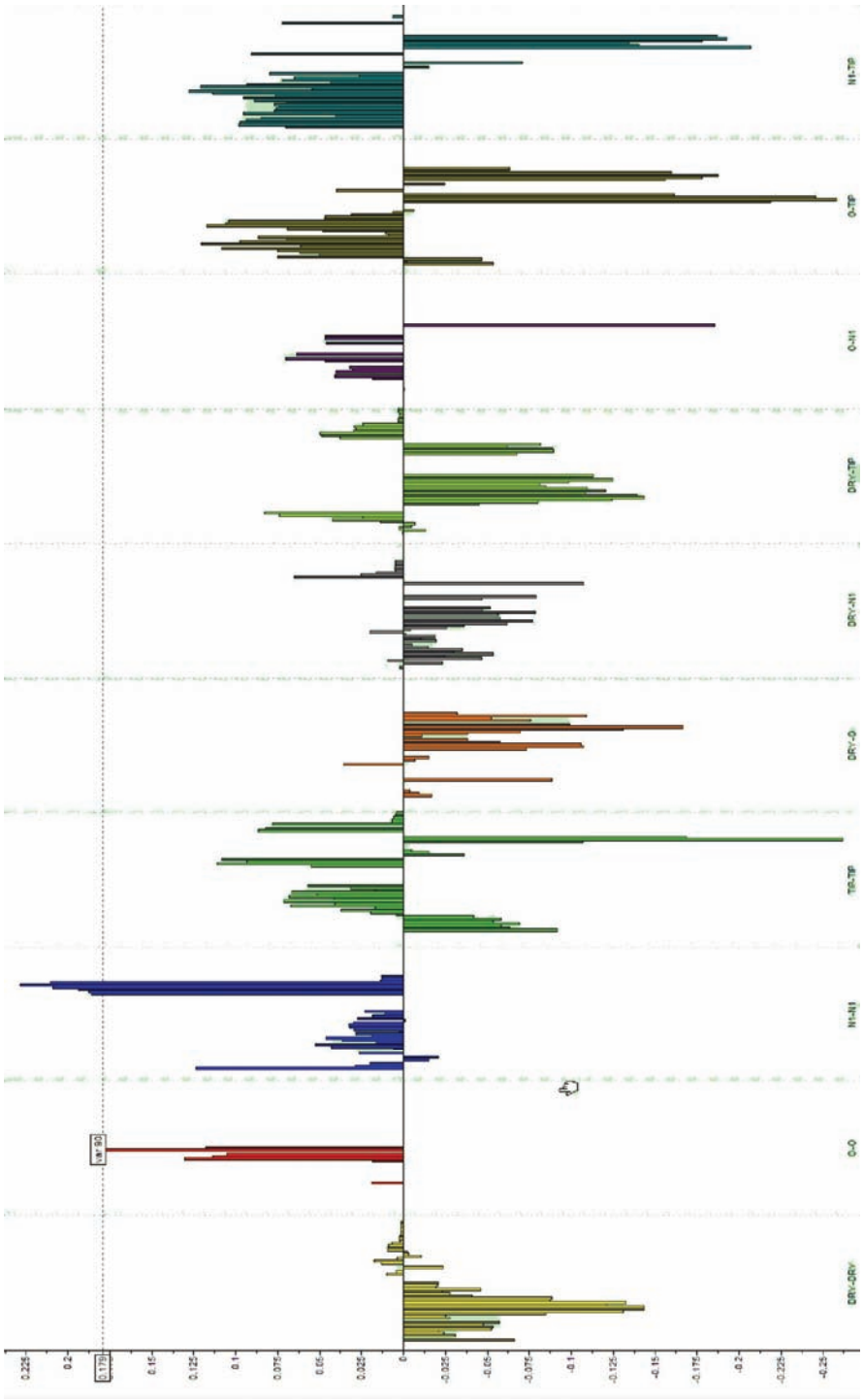


Fig. 7-S. 4LV PLS plot for MFC-7.

TABLE VII-S. Leukaemia K-562

Probe block	Variable No.	Impact	Distance Å	Regions
DRY–DRY	26	–	8.32–8.64	$–CH_2–$ of glutarimide ring and: alkyl part of cyclohexanone ring (I), phenyl (II, III, V), double bond of ring B dodecahydrophenanthrene system (IV), conjugated double bonds (VI), oxybenzyl group (VII), glutarimide naphthyl moiety (VIII), substituted cyclohexanone or cyclohexanol ring (IX).
O–O	111	+	10.88–11.20	Glutarimide (NH) hydrogen and: hydroxyl group on $–(CH_2)_2–$ bridge (I), hydroxyl group (VI), –OH group on 1,3-dioxane ring (X), amino group (III)
N1–N1	205	+	16.32–16.64	Glutarimide >C=O and: ester group (I), oxygen of alkoxy substituents or tertiary-N (**13**) (V)
TIP–TIP	290	–	18.80–19.20	Length of molecule: substituent on glutarimide ring and alkoxy group on benzene ring (V) *N*-Phenyl and *t*-butyl group on cyclohexanone or cyclohexanol ring (IX) Glutarimide ring and terminal methyl group (VI) Glutarimide ring and glutarimide naphthyl moiety (VIII)
O–N1	590	+	16.64–16.96	Glutarimide (NH) hydrogen (**10**) or *N*-amino group (**15**) and methoxy group (V) Glutarimide (NH) hydrogen and ester group (**3**) or *t*-hydroxyl group and glutarimide (NH) hydrogen (**1**) (I)
O–TIP	638	+	7.04–7.36	*t*-Hydroxyl group and glutarimide ring (X) Hydroxyl group of $–(CH_2)_2–$ bridge and glutarimide ring (I), *N*-phenyl group (IX) Glutarimide (NH) hydrogen and: cyano groups (II), aminophenyl group (III), *t*-butyl group (VII), ethyl group (VIII) Amino glutarimide group and carbonyls of glutarimide group (V) Hydroxyl group and glutarimide ring (VI)
O–TIP	672	–	17.92–18.24	Glutarimide (NH) hydrogen and methyl ester group (I), nitro group (VIII), methylene oxybenzyl group (VII), ester group (IV), terminal double bond (VI) *p*-Hydroxyl group and *N*-phenyl group (IX) *N*-Amino group and methoxy group (V)

TABLE VII-S. Continued

Probe block	Variable No.	Impact	Distance Å	Regions
N1–TIP	746	–	16.96–17.28	Glutarimide >C=O and: ester group (I, IV), *n*-heptyl group (III), terminal double bond or terminal methyl group (VI), methylene oxybenzyl group (VII), naphthyl moiety (VIII), *t*-butyl group (**20**) Glutarimide >C=O or *N*-glutarimide substituents and alkoxy substituent (V) Hydroxyl group and *N*-phenyl (**21**) (IX)

TABLE VIII-S. Non-small cell lung cancer A549

Probe block	Variable No.	Impact	Distance Å	Regions
O–O	88	+	10.80–11.20	Glutarimide (NH) hydrogen and: hydroxyl group on 1,3-dioxane ring (X), hydroxyl group of $-(CH_2)_2-$ bridge (I, VI), amino group (III)
N1–N1	163	+	16.40–16.80	Glutarimide >C=O and: ester group (**3**) or *t*-hydroxyl group (**1**) (I), alkoxy substituent (**10**, **11**) or *t*-N (**13**) (V)
TIP–TIP	231	–	19.20–19.60	Length of molecule: substituent on glutarimide ring and alkoxy groups (V) *N*-phenyl and *t*-butyl group (IX) Glutarimide ring and terminal methyl group (**17**) or terminal double bond (**16**) (VI) Glutarimide ring and aminonaphthyl moiety (VIII)
O–TIP	511	+	9.20–9.60	*t*-Hydroxyl group and glutarimide ring (X) Hydroxyl group of $-(CH_2)_2-$ bridge and glutarimide ring (I), *N*-phenyl group (IX) Glutarimide (NH) hydrogen and: cyano groups (**5**) or Cl-phenyl (**4**) (II), *t*-butyl group (VII), ethyl group (VIII) Aminophenyl group and *n*-heptyl group (III) Hydroxyl group and glutarimide ring (VI)
O–TIP	521	–	13.20–13.60	Hydroxyl group and ester group (**3**), glutarimide (NH) hydrogen and *o*-methyl group (**2**), *t*-hydroxyl group and glutarimide ring (**1**) (I) Aminophenyl group and glutarimide ring (III) Hydroxyl group and: glutarimide ring (**8**) or glutarimide (NH) hydrogen and ring D (**7**) (IV) Hydroxyl group and terminal double bond (**16**) or terminal methyl group (**17**) (VI), *N*-phenyl group (IX)

TABLE VIII-S. Continued

Probe block	Variable No.	Impact	Distance Å	Regions
O–TIP	521	–	13.20–13.60	Glutarimide (NH) hydrogen and benzyl ring (VII), naphthyl moiety (VIII) glutarimide (NH) hydrogen and furan ring (X)
N1–TIP	595	–	18.40–18.80	Glutarimide >C=O and: ester group (I, IV), terminal double bond or terminal methyl group (VI), amino naphthyl moiety (VIII) Hydroxyl group and *N*-phenyl group (IX) *t*-Nitrogen and *N*-butyl group (**13**) or amino and methoxy group (**11**) (V)

TABLE IX-S. Melanoma malme-3M

Probe block	Variable No.	Impact	Distance Å	Regions
O–O	87	+	10.40–10.80	Glutarimide (NH) hydrogen and: hydroxyl group of $–(CH_2)_2–$ bridge (I), amino group (III), hydroxyl group (VI), *t*-hydroxyl group (X)
N1–N1	163	+	16.40–16.80	Oxygen of glutarimide group and: (C=O) of ester group (**3**) or *t*-hydroxyl group (**1**) (I) Oxygen of glutarimide group and methoxy group (**10**, **11**, **12**) (V) *N*-Amino group and methoxy group (**15**) (V) *tert-N* of glutarimide ring substituents and methoxy group (**9**, **14**) or glutarimide oxygen (**13**) (V)
TIP–TIP	231	–	19.20–19.60	*N*-Substituent on glutarimide ring and substituents on benzene ring (V) Glutarimide ring and terminal double bond (VI) Glutarimide ring and amino naphthyl moiety (VIII) *N*-Phenyl and *t*-butyl group (IX)
O–TIP	510	+	8.80–9.20	Hydroxyl group of $–(CH_2)_2–$ bridge and glutarimide ring (I, X) Glutarimide (NH) hydrogen and aminophenyl group (III), cyano groups (II), *t*-butyl group (VII), ethyl group (VIII) Hydroxyl group and glutarimide ring (VI) Hydroxyl group of $–(CH_2)_2–$ bridge and *t*-butyl group (IX)
O–TIP	533	–	18.00–18.40	Glutarimide (NH) hydrogen and: ester group (I, IV), terminal double bond (VI), benzyl group (VII), aminophenyl group (VIII) Amino group hydrogen and methoxy group (V) Hydroxyl group and *N*-phenyl group (IX)

TABLE X-S. Colon COLO205

Probe block	Variable No.	Impact	Distance Å	Regions
DRY–DRY	21	–	8.40–8.80	$–CH_2–$ of $–(CH_2)_2–$ bridge and *p*-methyl group (**3**) or $–(CH_2)–$ groups of the glutarimide ring and cycloalkyl groups (**1**, **2,** respectively) (I) Aromatic moiety and: cyano groups (II), *n*-heptyl group (III) Glutarimide ring and double bond of ring C (IV) $–(CH_2)–$ Groups of glutarimide ring and aromatic moiety (V), conjugated double bonds (VI), cycloalkyl groups (IX), glutarimide naphthyl moiety (VIII)
O–O	88	+	10.80–11.20	Glutarimide (NH) hydrogen and: hydroxyl group on $–(CH_2)_2–$ bridge (I), amino group (III), hydroxyl group (VI), 1,3-dioxane ring (X)
N1–N1	163	+	16.40–16.80	Glutarimide >C=O and: ester group (**3**) or *t*-hydroxyl group (**1**) (I), alkoxy group (**10**, **11**, **12**, **15**), pyrrolidine nitrogen (**13**) (V) Alkoxy group and pyrrolidine nitrogen (**14**) or piperidine nitrogen (**9**) (V)
TIP–TIP	231	–	19.20–19.60	*N*-Glutarimide ring substituents and alkoxy group (V) Glutarimide ring and terminal methyl group or terminal double bond (VI) Glutarimide ring and glutarimide naphthyl moiety (VIII) *N*-Phenyl group and *t*-butyl group (IX)
O–TIP	532	–	17.60–18.00	*t*-Hydroxyl group and glutarimide ring (X) Hydroxyl group of $–(CH_2)_2–$ bridge and glutarimide ring (I), *N*-phenyl group (IX) Glutarimide (NH) hydrogen and: *t*-butyl group (I), ester group (IV), alkoxy group (**10**) (V), terminal methyl group or terminal double bond (VI), amino group (VIII)
N1–TIP	596	–	18.80–19.20	*N*-Amino group and alkoxy group (V) Glutarimide >C=O and ester group (I, IV), butoxy group (**12**) (V), terminal methyl group or terminal double bond (VI), amino naphthyl moiety (VIII) Pyrrolidine nitrogen and *N*-alkyl group (**13**) (V), Piperidine nitrogen and alkoxy group (**14**) (V) Methoxy oxygen and pyrrolidine ring (**9**) (V)

TABLE XI-S. Renal UO31

Probe block	Variable No.	Impact	Distance Å	Regions
O–O	88	+	10.80–11.20	Glutarimide (NH) hydrogen and: hydroxyl group on $–(CH_2)_2–$ bridge (I), amino group (III), hydroxyl group (VI), 1,3-dioxane ring (X)
N1–N1	160	+	15.20–15.60	Glutarimide >C=O and: ester group (**3**) or hydroxyl group (**1**) (I), ester group (IV), *t*-hydroxyl group (IX), >C=O of glutarimide naphthyl moiety (VIII)
				Alkoxy group and: glutarimide >C=O (**10**, **11**, **12**, **13**, **15**) or piperidine N (**14**) or pyrrolidine N (**9**) (V)
TIP–TIP	231	–	19.20–19.60	Length of molecule: substituent on glutarimide ring and substituent on benzene ring (V)
				Glutarimide ring and terminal methyl group (VI), aminonaphthyl moiety (VIII)
				N-Phenyl and *t*-butyl group (IX)
O–N1	464	–	14.60-15.20	*t*-Hydroxyl group and glutarimide oxygen (I, IX)
				N-Amino hydrogen and methoxy group (**15**) or glutarimide (NH) hydrogen and methoxy group (**10**) (V)
				Glutarimide (NH) hydrogen and ester group (**7**) or hydroxyl group and glutarimide (NH) oxygen (**8**) (IV), keto group (VI)
O–TIP	521	–	13.20–13.60	Hydroxyl group of $–(CH_2)_2–$ bridge and ester group (**3**), *t*-hydroxyl group and glutarimide ring (**1**), glutarimide (NH) hydrogen and *o*-Me group (**2**) (I)
				Amino group and glutarimide ring (III)
				Glutarimide (NH) hydrogen and: ring C (**7**) or hydroxyl group and glutarimide ring (**8**) (IV), benzyl group (VII), naphthyl moiety (VIII), substituted pyrrolidine ring (X)
				N-Amino group and benzene ring (V)
				Hydroxyl group and: terminal double bond or terminal Me group (VI)
				Hydroxyl group of $–(CH_2)_2–$ bridge and aromatic ring (IX)
N1–TIP	595	–	18.40–18.80	Glutarimide (NH) hydrogen and ester group (I)
				t-Hydroxyl and *N*-phenyl group (IX)
				Glutarimide >C=O and: nitro group (VIII), terminal methyl group or double bond (VI), alkoxy group (**11**, **12**) (V)
				Pyrrolidine N and *n*-butyl (**13**) (V) or methoxy group (**9**)

TABLE XII-S. CNS U251

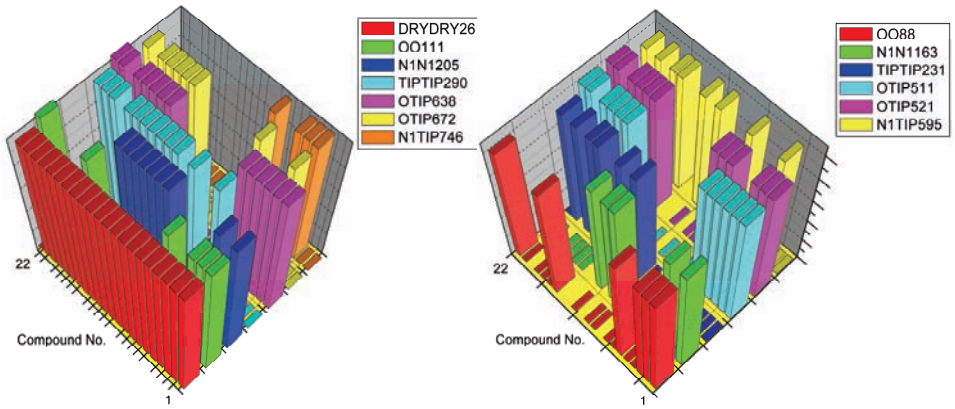
Probe block	Variable No.	Impact	Distance Å	Regions
O–O	88	+	10.80–11.20	Glutarimide (NH) hydrogen and: hydroxyl group on $–(CH_2)_2–$ bridge (I), hydroxyl group (VI), 1,3-dioxane ring (X)
N1–N1	163	+	15.60–16.00	Glutarimide >C=O and: ester group (**3**) or *t*-hydroxyl group (**1**) (I), pyrrolidine N (**13**) (V)
				Alkoxy group and: glutarimide >C=O (**10**, **11**, **12**, **15**) or piperidine N (**14**) or pyrrolidine N (**9**) (V)
TIP–TIP	231	–	19.20–19.60	Length of molecule: *N*-substituent and alkoxy substituent (V)
				Glutarimide >C=O and: *t*-Me or double bond (VI), nitro group (VIII)
				N-Phenyl and *t*-butyl group (IX)
O–N1	464	–	14.80–15.20	*t*-Hydroxyl group and glutarimide oxygen (I)
				Glutarimide (NH) hydrogen and ester group (**7**) or hydroxyl group and glutarimide >C=O (**8**) (IV)
				N-Amino hydrogen and methoxy group (**15**) or glutarimide (NH) hydrogen and methoxy (**10**) (V)
				Glutarimide (NH) hydrogen and keto group (VI)
				Hydroxyl group and glutarimide oxygen (IX)
O–TIP	509	+	8.40–8.80	*t*-Hydroxyl group and glutarimide ring (X), hydroxyl group on $–(CH_2)_2–$ bridge and glutarimide ring (I, VI)
				Glutarimide (NH) hydrogen and *t*-butyl group (VII), ethyl group (VIII)
				Hydroxyl group of $–(CH_2)_2–$ bridge and aromatic ring (IX)
O–TIP	521	–	13.20–13.60	Glutarimide (NH) hydrogen and substituted pyrrolidine ring (X)
				t-OH and glutarimide ring (**1**), or glutarimide (NH) hydrogen and *o*-Me (**2**), or hydroxyl and ester group (**3**) (I)
				Glutarimide (NH) hydrogen and ring C (**7**) or hydroxyl and glutarimide ring (**8**) (IV)
				N-Amino group and aromatic ring (V)
				Hydroxyl group and terminal methyl group or terminal double bond (VI)
				Glutarimide (NH) hydrogen and benzyl ring (VII), naphthyl moiety (VIII)
				Hydroxyl group on $–(CH_2)_2–$ bridge and aromatic ring (IX)

TABLE XIII-S. Ovarian IGROV1

Probe block	Variable No.	Impact	Distance Å	Regions
O–O	88	+	10.80–11.20	Glutarimide (NH) hydrogen and: hydroxyl group on 1,3-dioxane ring (X), hydroxyl group of $-(CH_2)_2-$ bridge (I), hydroxyl group (VI), amino group hydrogens (III)
N1–N1	163	+	16.40–16.80	Glutarimide >C=O and: ester (C=O) group (**3**) or *t*-hydroxyl group (**1**) (I), or *t*-nitrogen (**13**) (V)
				Alkoxy group and: glutarimide >C=O (**10**, **11**, **12**, **15**), piperidine N (**14**), pyrrolidine N (**9**) or glutarimide >C=O and pyrrolidine N (**13**) (V)
TIP–TIP	231	–	19.20–19.60	Length of molecule: substituent on glutarimide ring and alkoxy group (V)
				Glutarimide ring and terminal methyl group (**17**) or terminal double bond (**16**) (VI)
				Glutarimide ring and aminonaphthyl moiety (VIII)
				N-Phenyl and *t*-butyl group (IX)
O–TIP	511	+	9.20–9.60	Hydroxyl group of $-(CH_2)_2-$ bridge and glutarimide ring (I), *N*-phenyl group (IX)
				Glutarimide (NH) hydrogen and: cyano groups (**5**) or Cl-phenyl (**4**) (II), *t*-butyl ester group (VII), ethyl group (VIII)
				Aminophenyl group and *n*-heptyl group (III)
				Hydroxyl group and glutarimide ring (VI)
				t-Hydroxyl group and glutarimide ring (X)
O–TIP	532	–	17.60–18.00	Glutarimide (NH) hydrogen and methyl ester group (I, IV), terminal methyl group or terminal double bond (VI), methylene oxy-benzyl group (VII), nitro group (VIII)
				N-Amino and alkoxy group (V)
				t-Hydroxyl group and *N*-phenyl group (IX)
N1–TIP	594	–	18.00–18.40	Glutarimide >C=O and: ester group (I, IV), terminal double bond or terminal methyl group (VI), aminonaphthyl moiety (VIII), oxybenzyl group (VII)
				Hydroxyl group and *N*-phenyl group (IX)
				Glutarimide >C=O and alkoxy group (**10**, **11**, **12**, **15**) or *t*-nitrogen and: alkoxy (**9**, **14**), *N*-alkyl group (**13**) (V)

TABLE XIV-S. Breast MFC7

Probe block	Variable No.	Impact	Distance Å	Regions
O–O	90	+	11.60–12.00	Glutarimide (NH) hydrogen AND: *t*-hydroxyl group (I), 1,3-dioxane ring (X)
N1–N1	165	+	17.20–17.60	Glutarimide >C=O and: ester (C=O) (I), pyrrolidine N (V)
TIP–TIP	231	–	19.20–19.60	*N*-Alkyl and alkoxy group (V)
				Length of molecule: glutarimide ring and: double bond or terminal methyl group (VI), aminonaphthyl moiety (VIII)
				N-Phenyl and *t*-butyl group (VII)
O–TIP	521	–	13.20–13.60	Hydroxyl group on $–(CH_2)_2–$ bridge and methyl ester (**3**) or glutarimide >C=O and *t*-OH group (**1**) (I)
				Hydroxyl group and terminal methyl group or double bond (VI)
				Glutarimide (NH) hydrogen and oxybenzyl ring (VII), naphthyl moiety (VIII)
				Hydroxyl group on $–(CH_2)_2–$ bridge and aromatic ring (IX)
N1–TIP	590	–	16.40–16.80	*t*-OH or ester carbonyl and glutarimide ring (**1**, **3,** respectively) (I)
				Glutarimide oxygen and: alkoxy group (**11**, **12**) (V), terminal methyl group or double bond (VI), benzyl ring (VII), aminonaphthyl moiety (VIII), *t*-butyl group (**20**) (IX)
				t-OH and aromatic ring (**21**) (IX)
				Alkoxy and *N*-alkyl group (**13**) (V)



K562 A549

Fig. 8-S. Association of variables with **1**–**22** for the model on the studied cell lines.

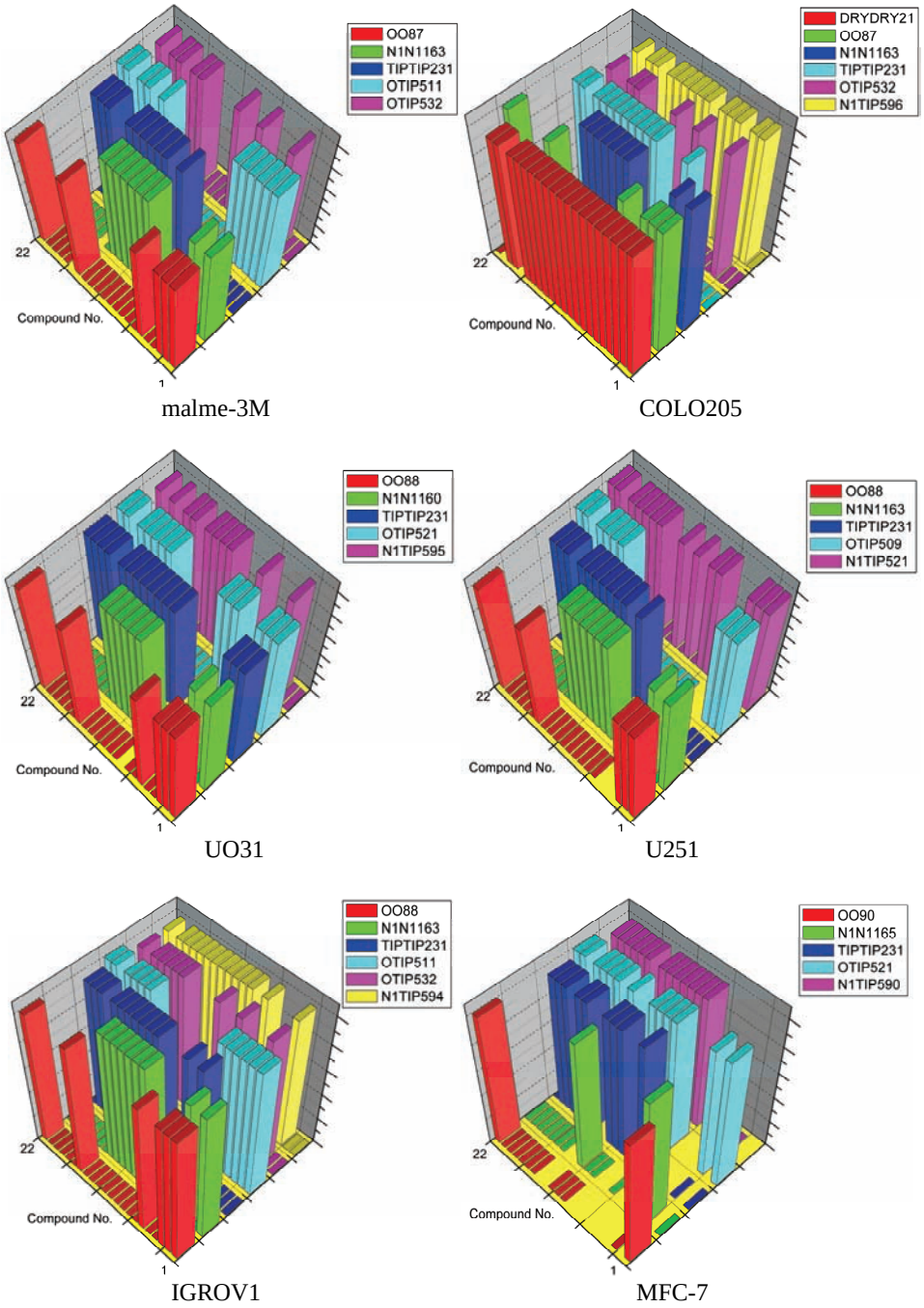


Fig. 8-S. Association of variables with **1**–**22** for the model on the studied cell lines (continued).

TABLE XV-S. Intercorrelation matrix of p(GI_{50}) values for **1**–**22**

	Leukaemia K-562	Non-small cell lung cancer A549	Colon cancer COLO-205	CNS Cancer U251	Melanoma Malme-3M	Ovarian cancer IGROV1	Renal cancer UO-31	Breast cancer MFC-7
Leukaemia K-562	1							
Non-small cell lung cancer A549	0.988	1						
Colon cancer COLO205	0.976	0.989	1					
CNS cancer U251	0.972	0.991	0.991	1				
Melanoma malme-3M	0.971	0.992	0.992	0.992	1			
Ovarian cancer IGROV1	0.962	0.982	0.985	0.993	0.986	1		
Renal cancer UO-31	0.969	0.985	0.992	0.992	0.988	0.989	1	
Breast cancer MFC-7	0.971	0.998	0.992	0.994	0.997	0.983	0.985	1