24 October 2012

ASX Market Announcements
Australian Securities Exchange Limited
10th Floor, 20 Bond Street
SYNDEY NSW 2000

Dr Robin Scaife to Present at National Melanoma Conference

BPH Energy Limited (ASX:**BPH**) investee company Molecular Discovery Systems Limited ("**MDS"**) is pleased to provide a copy of Dr Robin Scaife's presentation that he will present today at the inaugural National Melanoma Conference hosted by the Scott Kirkbride Melanoma Research Centre (SKMRC). SKMRC supports research that is aimed at providing breakthroughs for improved diagnosis and treatment of melanomas.

Dr Scaife was awarded an SKMRC Discovery Research Grant in 2011 to use the high-content imaging analysis platform at MDS to screen new drug-like molecules for inhibitors of melanoma cell survival and proliferation.

MDS is continuing to invest in the discovery of new oncology drug candidates via its in-house screening program.

Yours sincerely,

David Breeze
Chairman

For Further Information
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Chairman
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Background:

***MDS**:*

MDS has core expertise in high-content and high-throughput imaging and analysis. Central to the MDS drug screening platform is a semi-automated cellular imaging and analysis facility that provides access to complex drug targets. BPH Energy has a 20% residual interest in MDS after the spin-off of MDS in 2010. BPH Energy is working towards a listing of MDS on the Australian Securities Exchange.

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SKMRC
Scott Kirkbride Melanoma Research Centre

Inaugural Melanoma Conference 2012

23rd and 24th October 2012,
Esplanade Hotel Fremantle, Western Australia

SUNCORP BANK

SKMRC
Scott Kirkbride Melanoma Research Centre

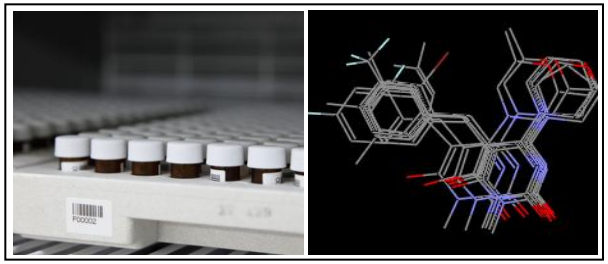
WAIMR
Western Australian Institute for Medical Research
FOR HEALTHIER LIVES

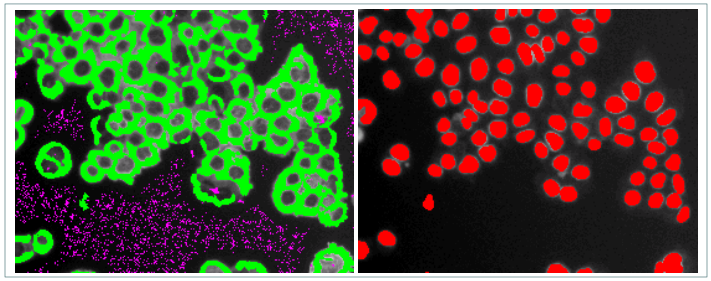
Robin M. Scaife

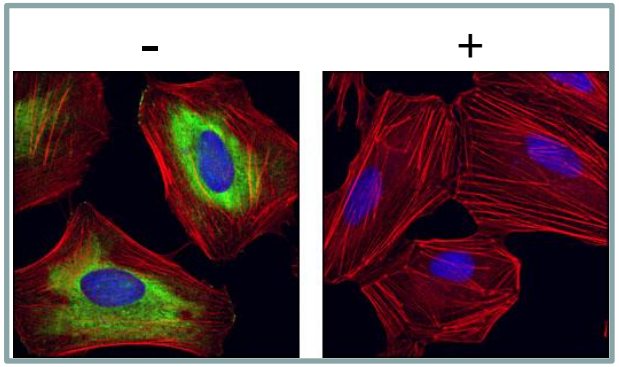
Molecular Discovery Systems (BPH Energy)
WAIMR

"Screening for new oncology drug candidates by imaging of molecular and cellular targets"

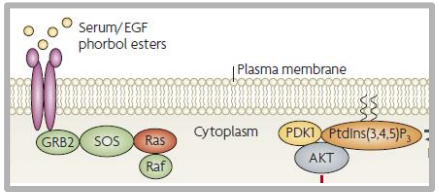
Oncogene and non-oncogene screening

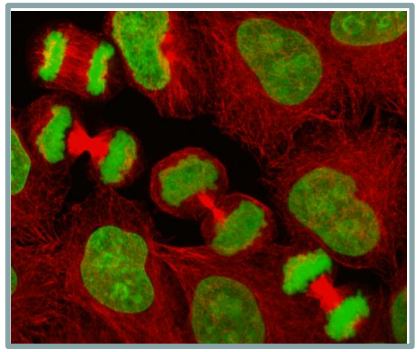


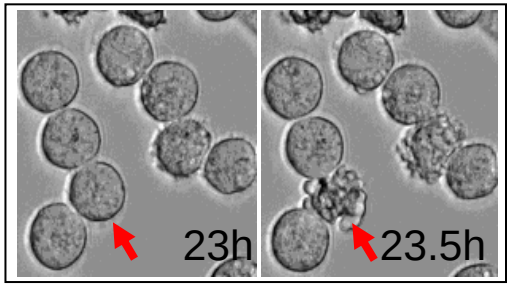




Inhibition of growth signal

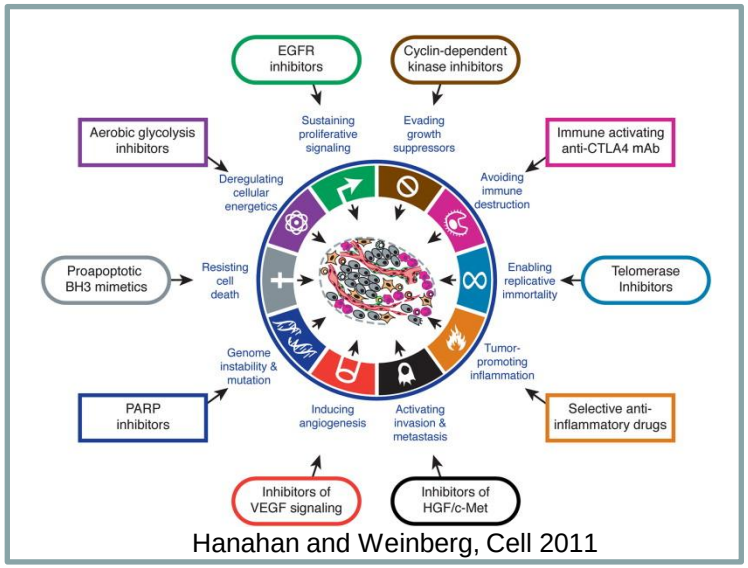




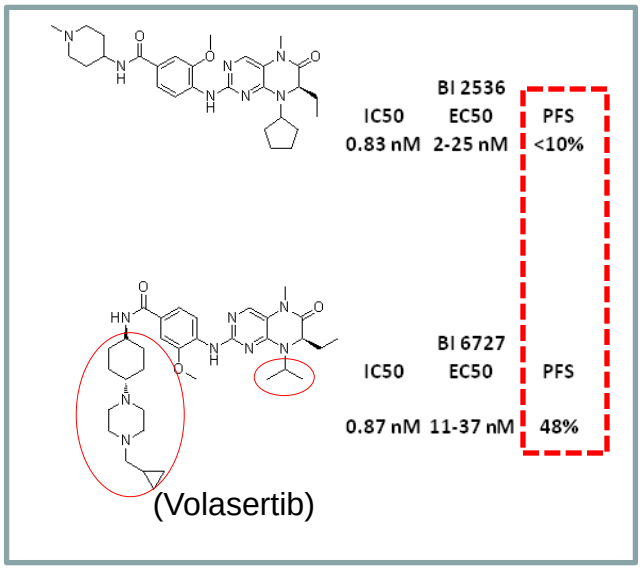


Induction of cell death

Molecular Targets and Drugs

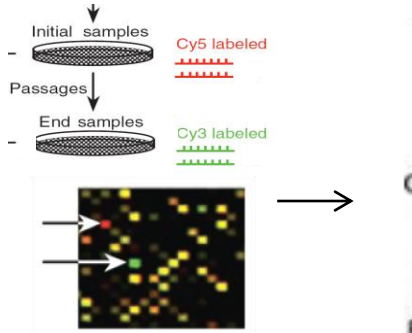


Hanahan and Weinberg, Cell 2011

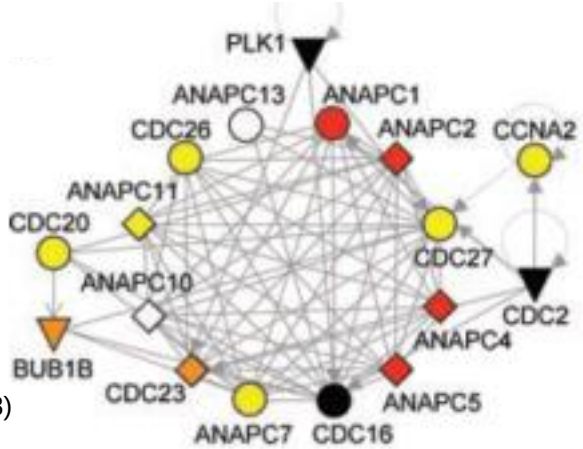


(Volasertib)

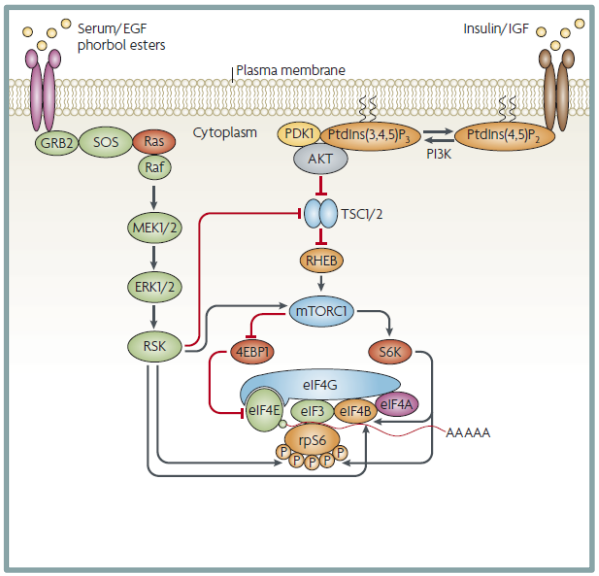
Jones et al., Science (2008)

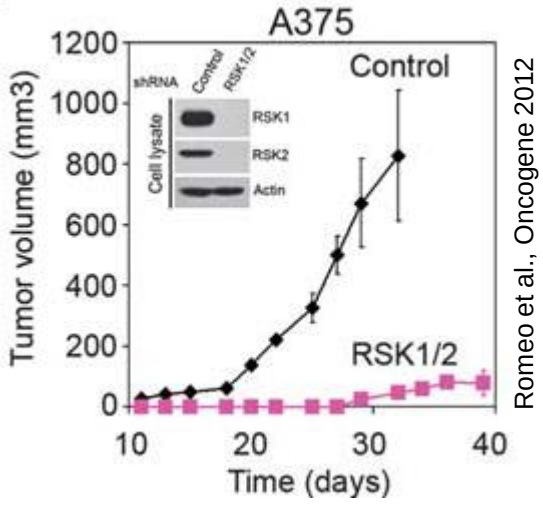


Schlabach et al., Science (2008)

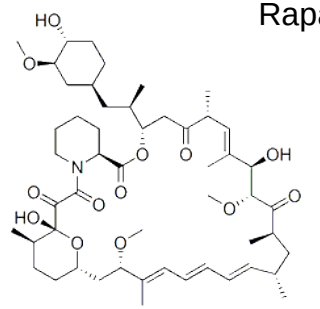


Melanoma Oncogenic Signaling

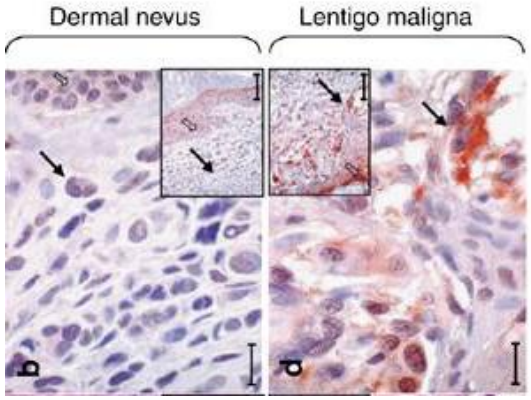




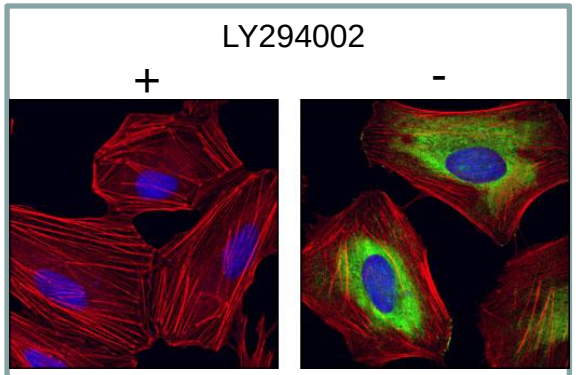
Romeo et al., Oncogene 2012



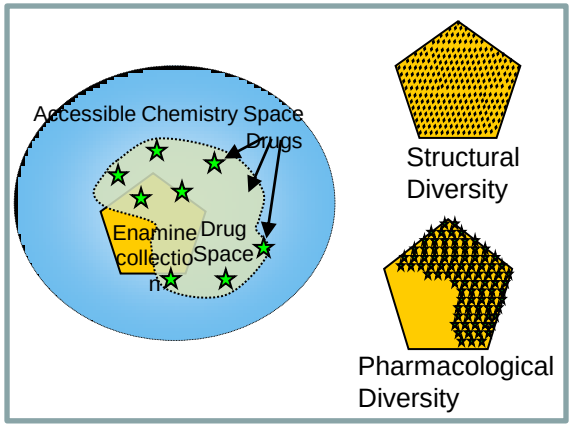
17/20 mTOR inhibitors =
Pyrimidine or Quinolines



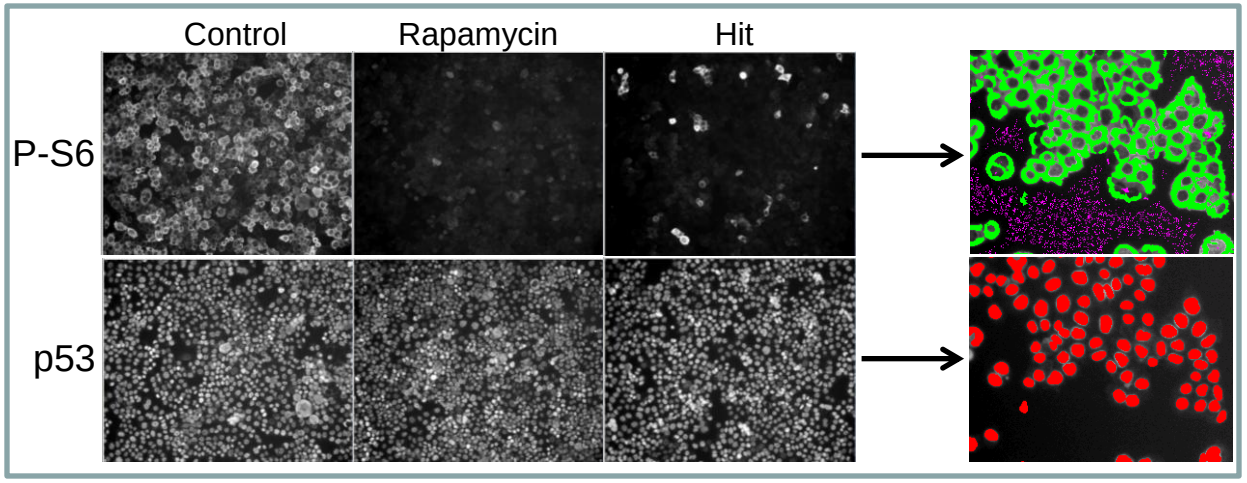
Karbowniczek et al., JID (2008)

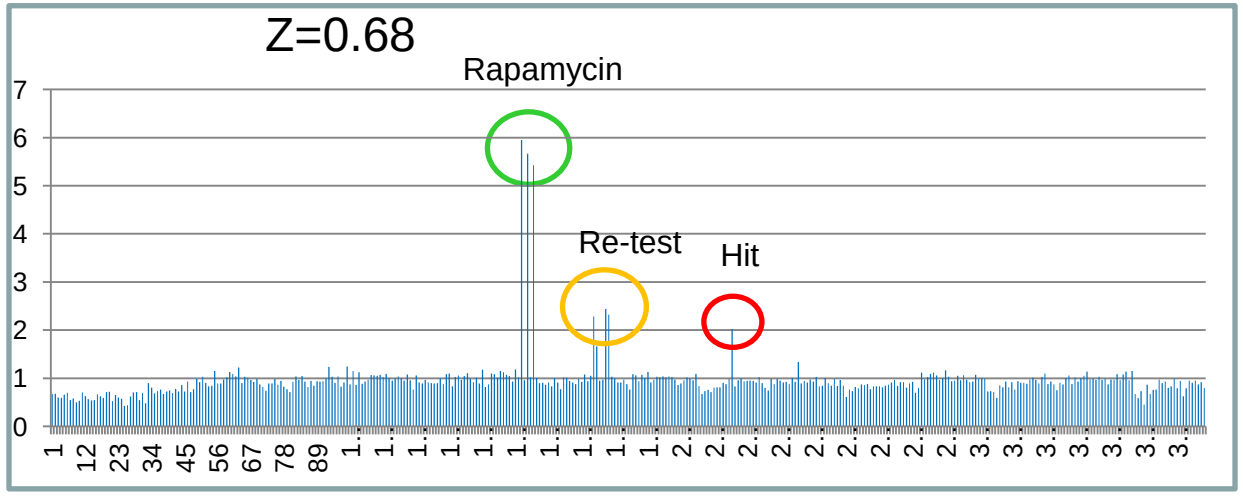


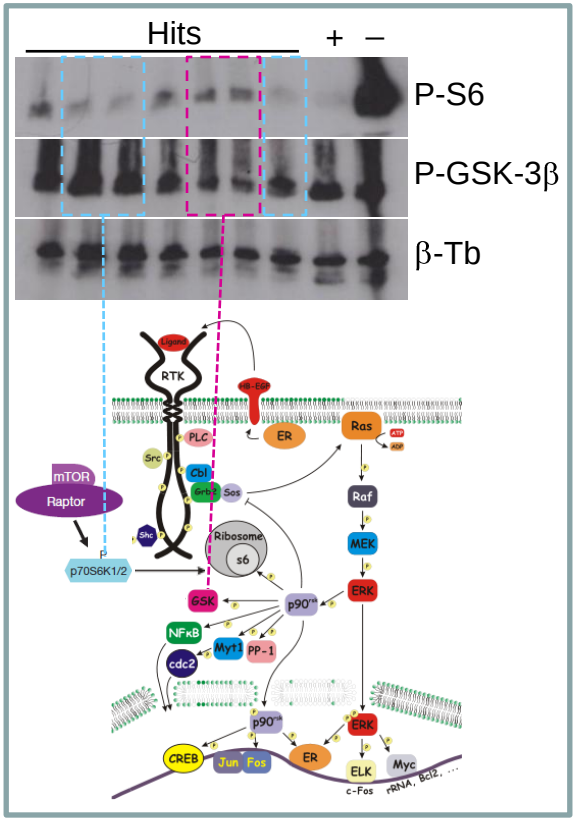
Anti-phospho S6



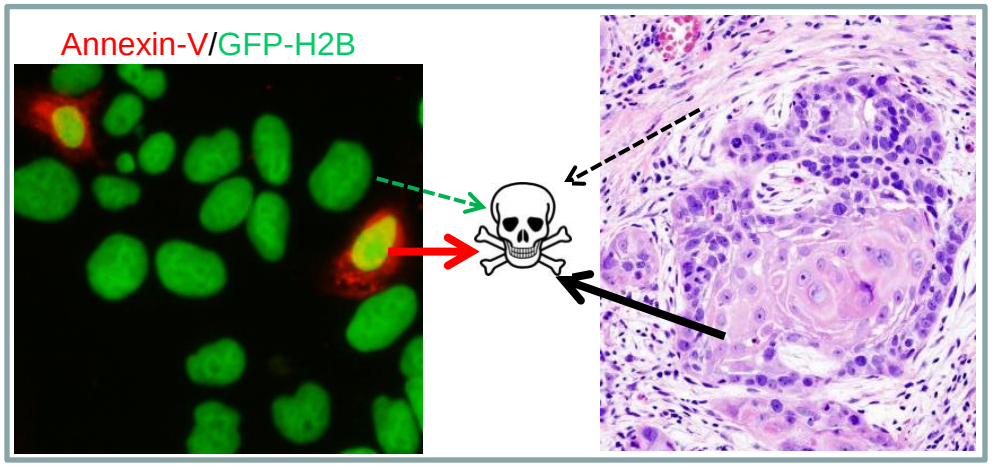
S6 Phosphorylation Screen

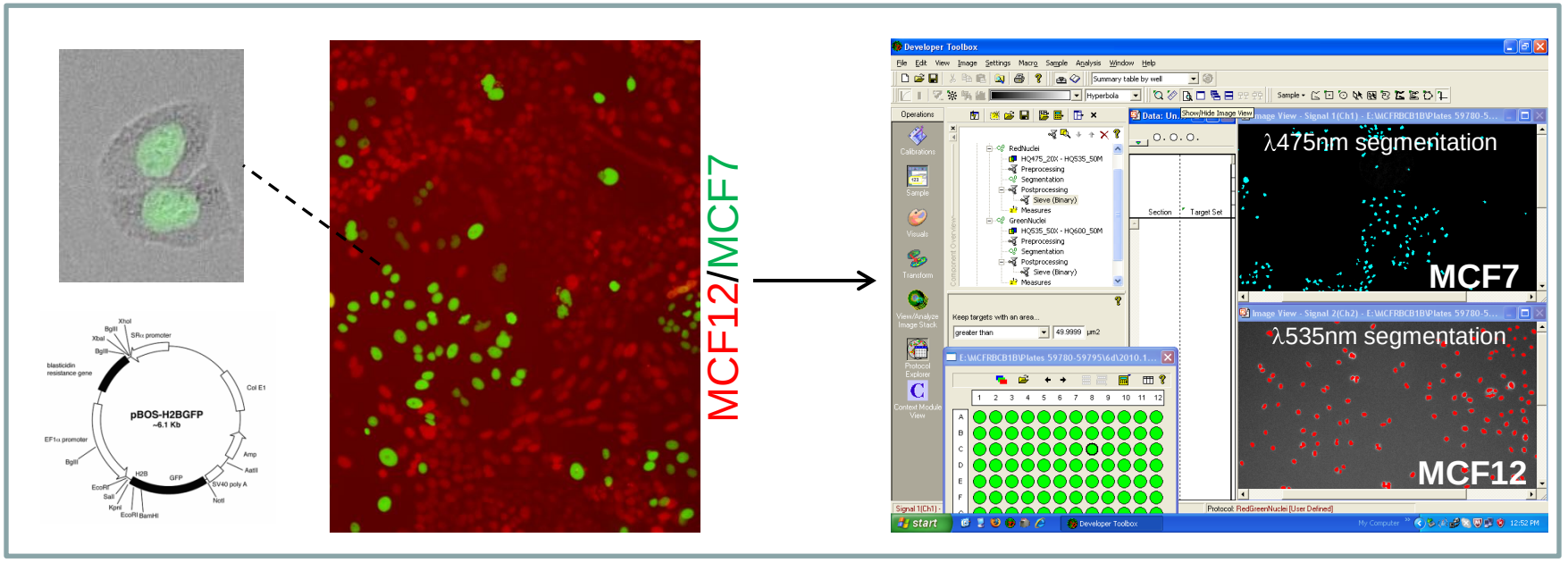






Induction of Cell Death

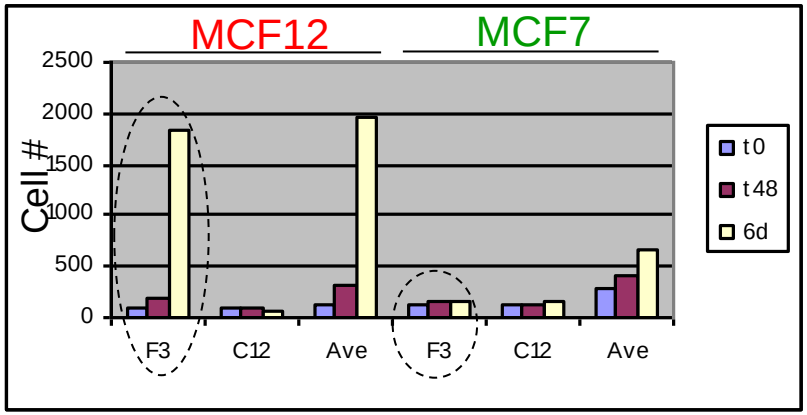




Selective Induction of Cell Death

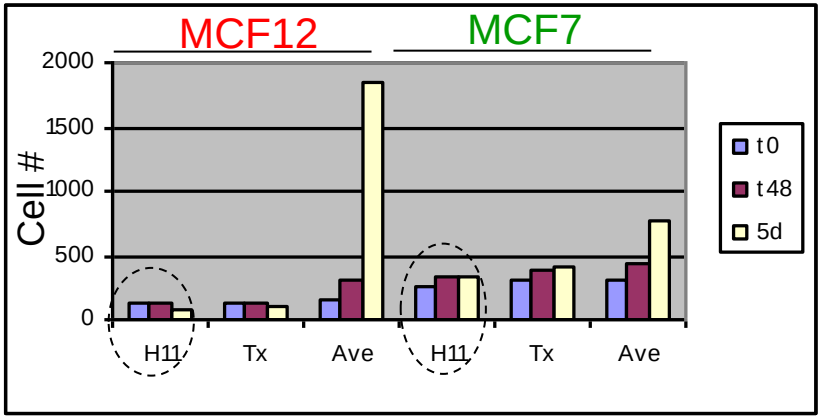
~2/10,000 compounds

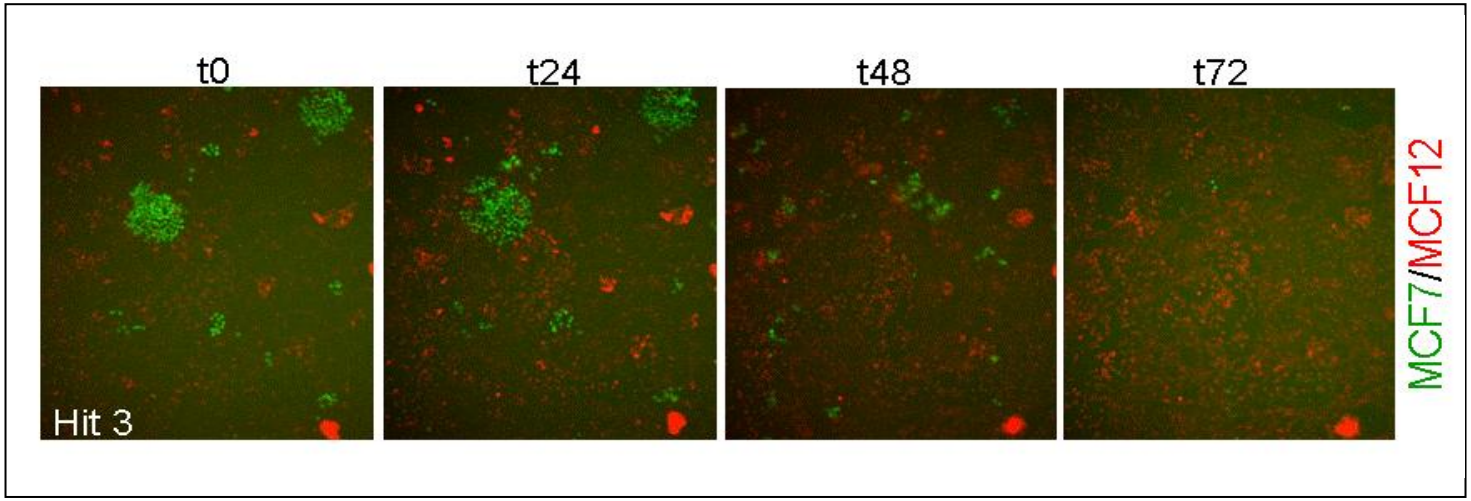
Selective inhibition



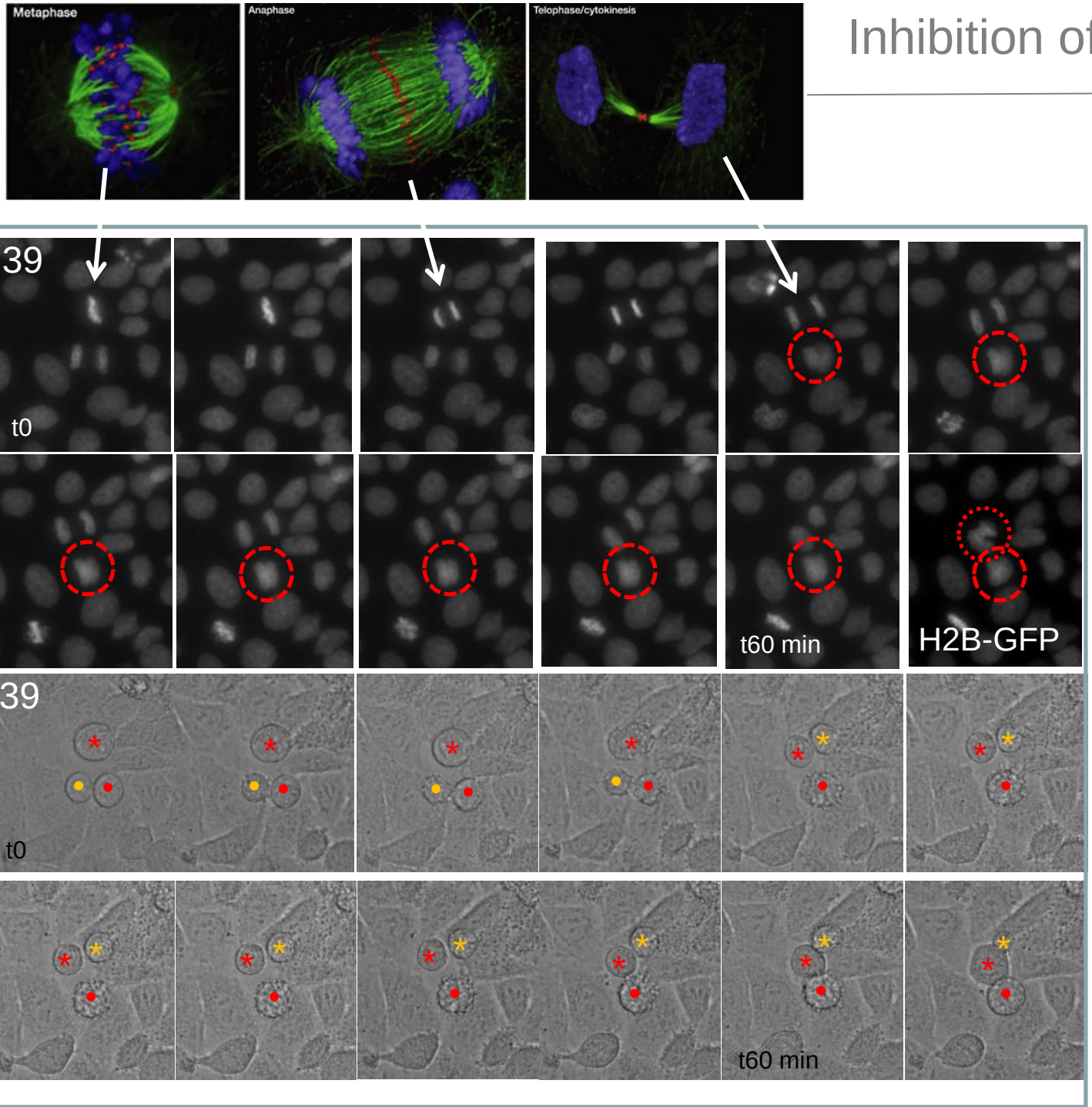
~50/10,000 compounds

Non-selective inhibition

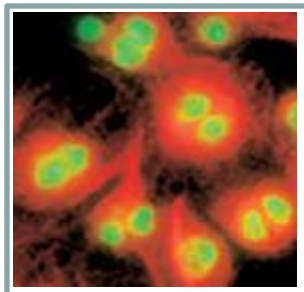


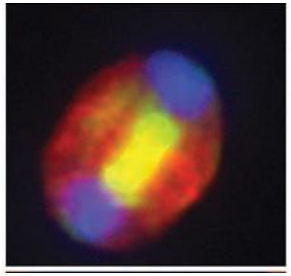


Inhibition of Cytokinesis



Actin and Endocytosis





Eggart et al. , PLoS, (2004)

Binucleines → Aurora B

Binucleines ⊣ Swinholide, Jasplakinolide

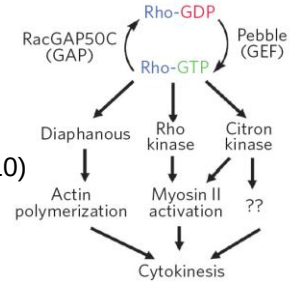
↓

F-Actin

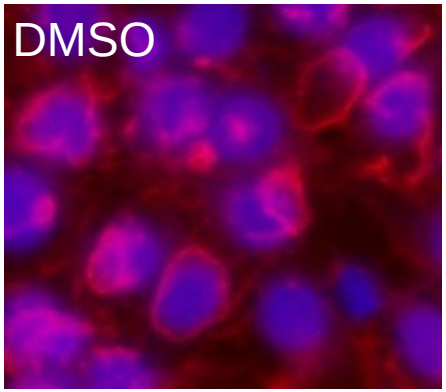
↑

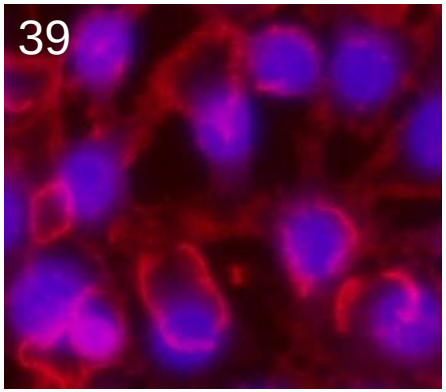
Rhodblocks

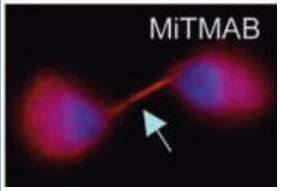
Castoreno et al., NCB (2010)

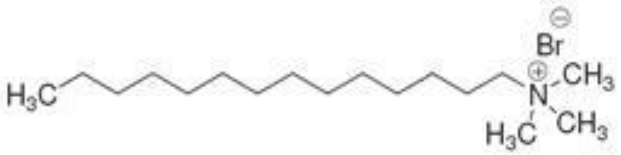


Tritc-phalloidin/Hoescht



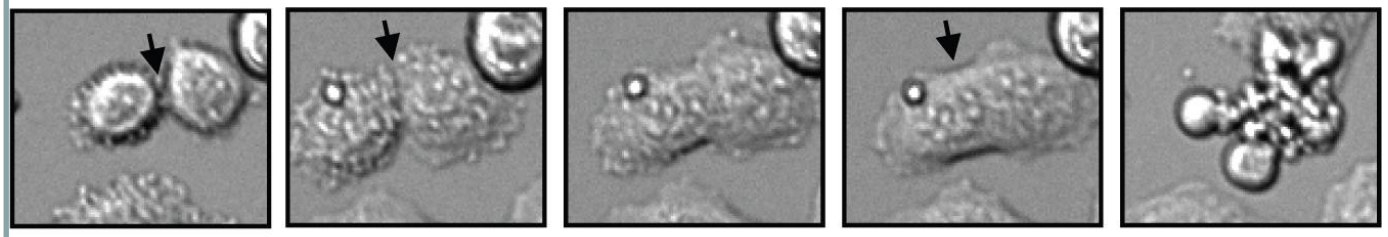




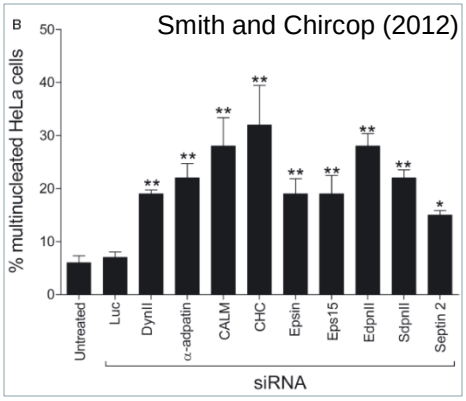


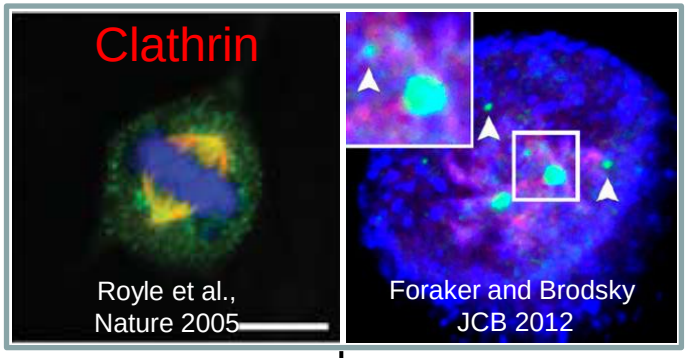
Dynamin

(Joshi et al .,Mol Cancer 2011)

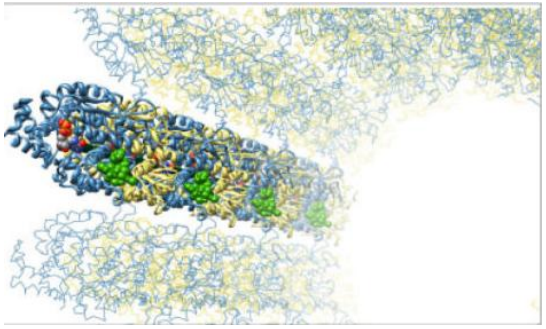


Inhibition of Mitosis





CKAP5/ch-TOG



Supplementary Table 12 | Agents that disrupt mitosis: limited activity to date

	Compound	Company	Comment	
Aurora	*Aurora inhibitors*			
	MK-0457 (VX-680)	Vertex/Merck	Response in 3 patients with imatinib-resistant T315I CML, suspended due to cardiac safety;[1] SD in 3/16 patients[2]	0%
	AZD 1152	Astra Zeneca	No activity reported	
	PHA 680632	Nerviano	No activity reported	
	PHA 739358	Nerviano	SD in 7/42 patients[3]	
	MLN8054	Millenium	SD in 3/43 patients[4]	
	MLN8237	Millenium	SD in 5/23 patients; 1 case of PR and 8/65 patients with SD[5]	13%
	R763	Merck/Serono	PD in 2/15 patients[6]	
	AT9283	Astex	HR in 2/29 patients;[7] SD in 3/22 patients;[8] 1 case of PR and 4/33 patients with SD[9]	11%
	SNS-314	Sunesis	SD in 6/32 patients[10]	
	SU 6668	Sugen/Pfizer	SD in 4/35 patients;[11] SD in 3/19 patients[12]	14%
	ENMD-2076	EntreMed	SD in 4/14 patients[13]	
	BI 811283	Boehringer Ingelheim	SD in 33.3% of 57 patients;[14] SD in 29% of 52 patients[15]	31%
	CYC116	Cyclacel	One study ongoing, one study terminated	
	ENMD 981693	Entremed/Miikana	Ongoing	
	MKC 1693	Entremed/Miikana	Ongoing	
Polo	*Polo-like kinase inhibitors*			
	ON01910	Onconova	SD in 1/23 patients;[16] SD in 2/5 patients;[17] no response[18]	
	BI-2536	Boehringer	PR in 4/95 patients;[19] PR in 2/33 patients;[20] SD in 7/23 patients[21]	
	GSK-461364	GlaxoSmithKline	SD in 2/27 patients[22]	
	HMN-214	Nippon Shinyaku	No activity;[23] MR and SD;[24] 1 TR and 2 SD out of 33 patients[25]	6%
	BI-6727	Boehringer	3 PR, 48% SD and PFS in 6 out of 65 patients[26]	
KSP1	*Kinesin spindle protein inhibitors*			
	Ispinesib (SB-715992)	Cytokinetics	SD in 4/42 patients;[27] SD in 3/27 patients;[28] unconfirmed MR in 3/24 patients;[29] SD in 2 and MR in 1 out of 27 patients;[30] SD in 7/19 patients;[31] 3 PR and SD in 4/16 patients[32]	17%
	SB-743921	Cytokinetics	1 PR and SD in 1/32 patients;[33] PR in 2/51 patients with lymphoma[34]	4%
	MK-0731	MRK	SD in 16/35 patients[35]	45%
	ARRY-520	Array Biopharma	PSD in 3/34 patients;[36] PR in 1/13 patients[37]	8%

Komlodi-Pastzor et al., NRCO (2011)

Taxol Resistance

Perez, The Oncologist (1998)

Evaluable patients	Overall response (%)
227	22
223	29
521*	29
	32
325*	21
	28
	22
516*	40
	50
88	23
91	30

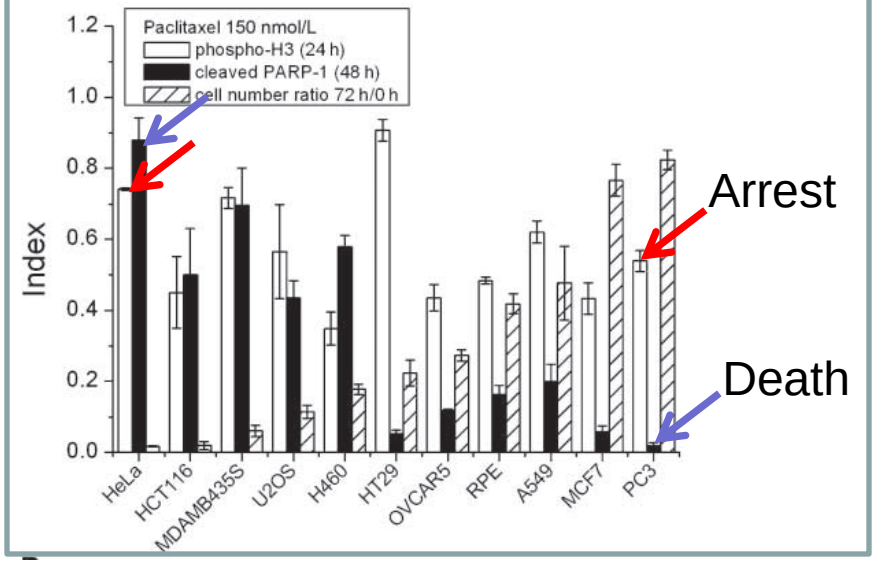
30-60%

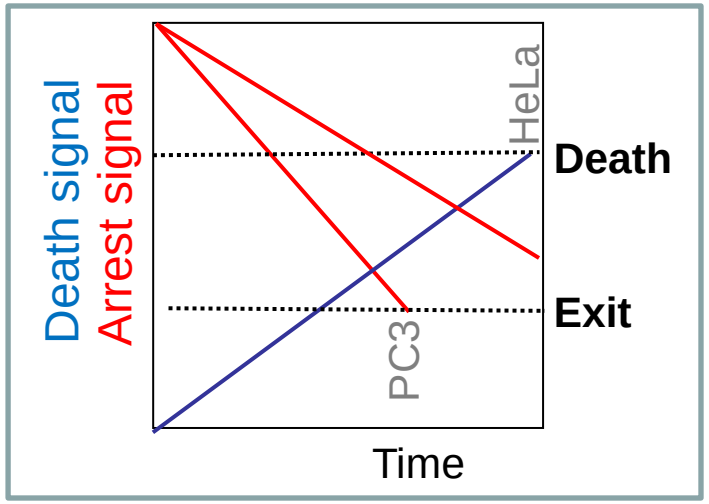
Table 1 | **Characteristics of microtubule-binding agents**

Agent	Sensitivity to ABC efflux pumps	Sensitivity to β-tubulin content
Vinca alkaloids	MDR sensitive MRP sensitive	Sensitive to βIII-tubulin content
Cryptophycins	MDR insensitive	Not determined
Dolastatins	MDR sensitive	Not determined
Taxanes	MDR sensitive MRP2 and MRP7 sensitive	Sensitive to βIII-tubulin content
Epothilones	MDR sensitive	No
Discodermolides	MDR sensitive MRP1 sensitive	Sensitive to βIII-tubulin content
Cyclostreptin	MDR insensitive	Not determined
Laulimalides	MDR insensitive	Not determined
Taccalonolide	MDR insensitive	More active if high βIII-tubulin content
Peloruside	MDR insensitive	Not determined
Hemiasterlin	MDR insensitive	Not determined
Combretastatins	MDR insensitive	Yes
2-Methoxyoestradiol	MDR insensitive	Inactive against βI-tubulin

Dumontet and Jordan NRDD (2010)

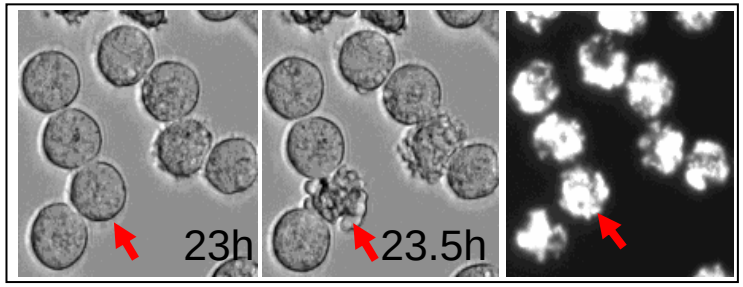
Shi et al., 2008

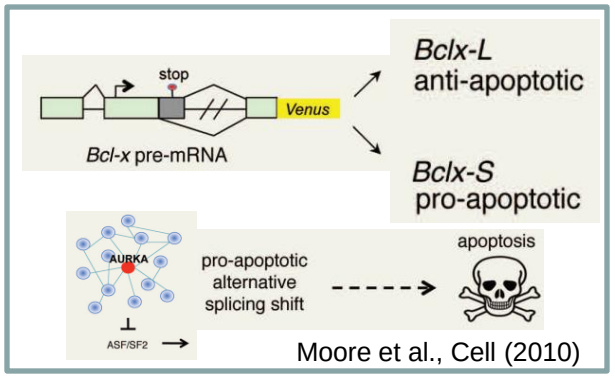




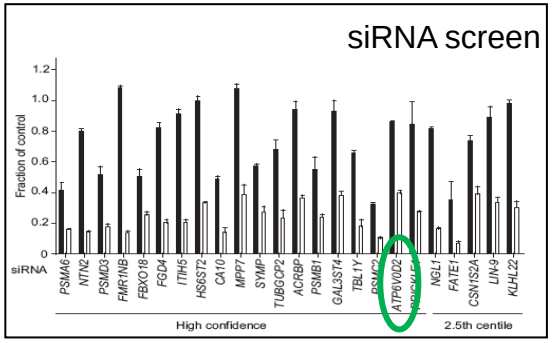
Taxol Synthetic Lethality

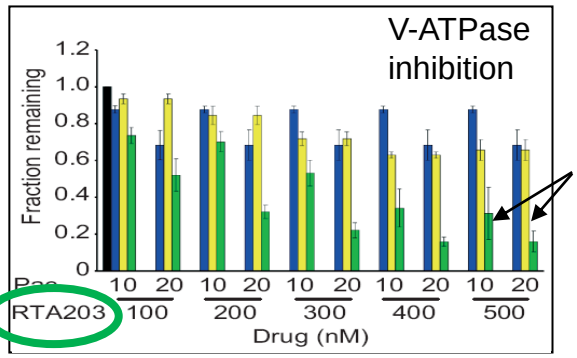
Mitotic Death



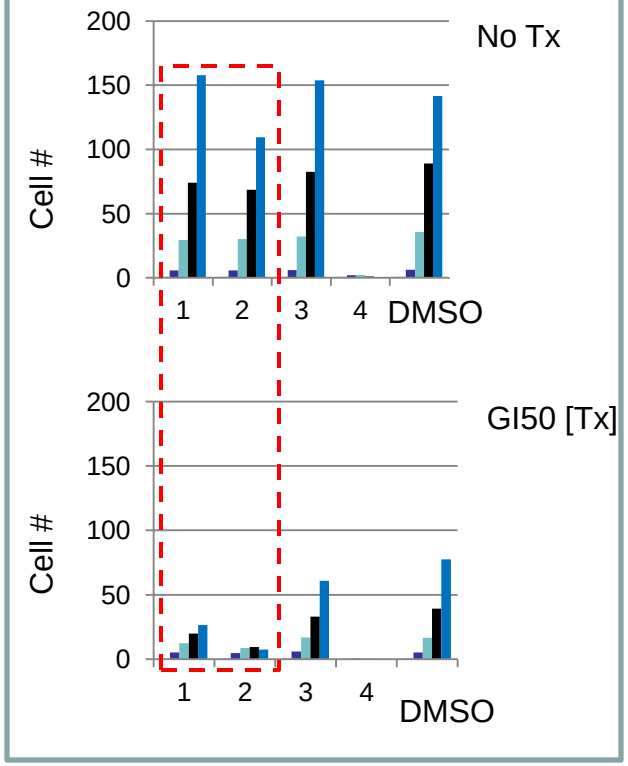


Whitehurst et al., Nature (2007)



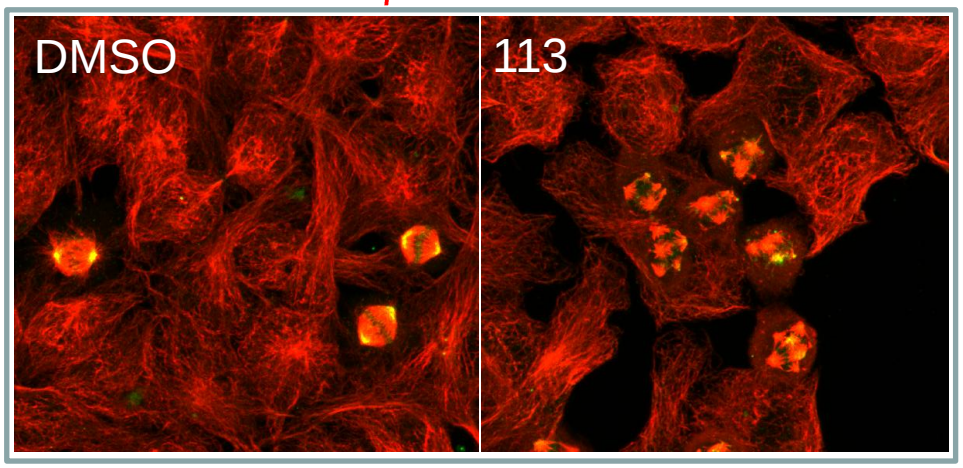


Taxol+
RTA203

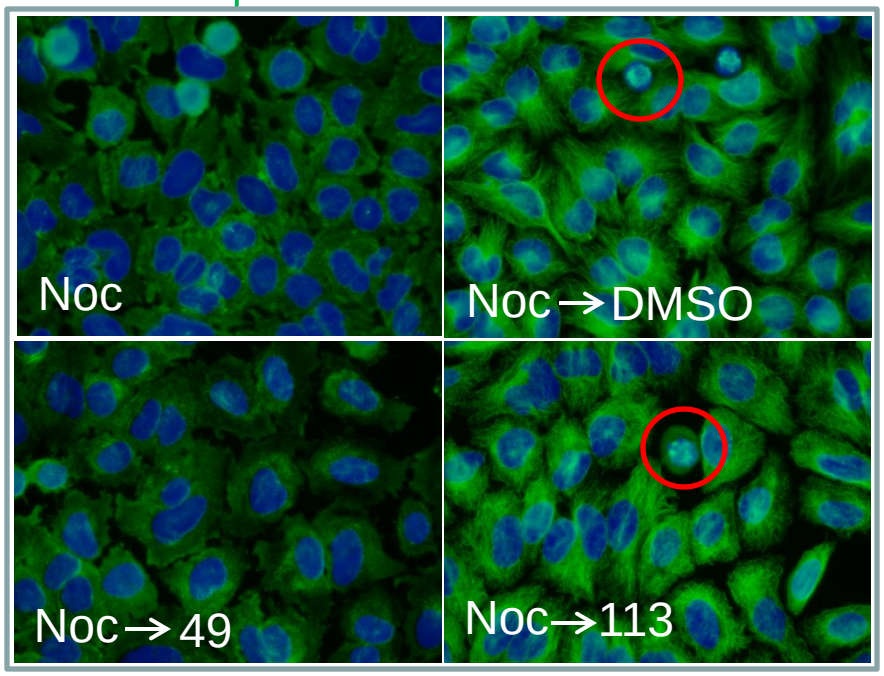


Selective Targeting of Microtubules

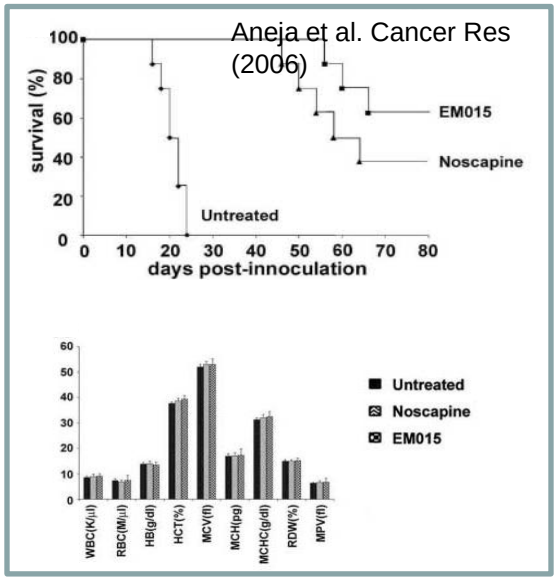
β-Tb/P-AU

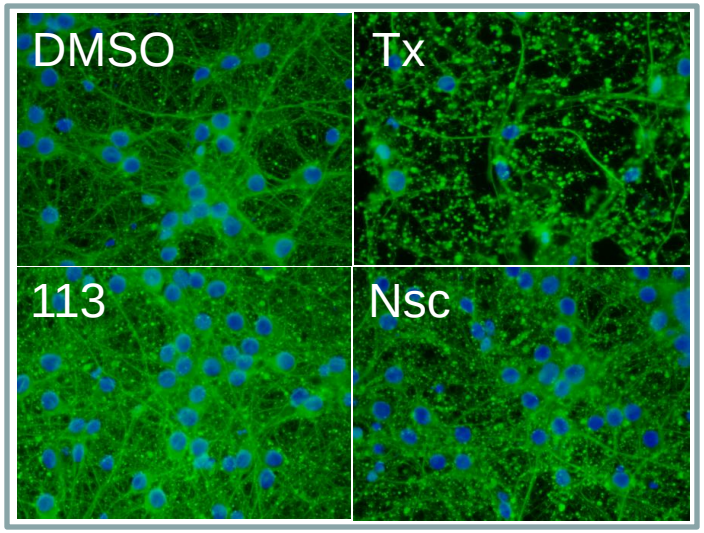


β-Tubulin/Hoescht

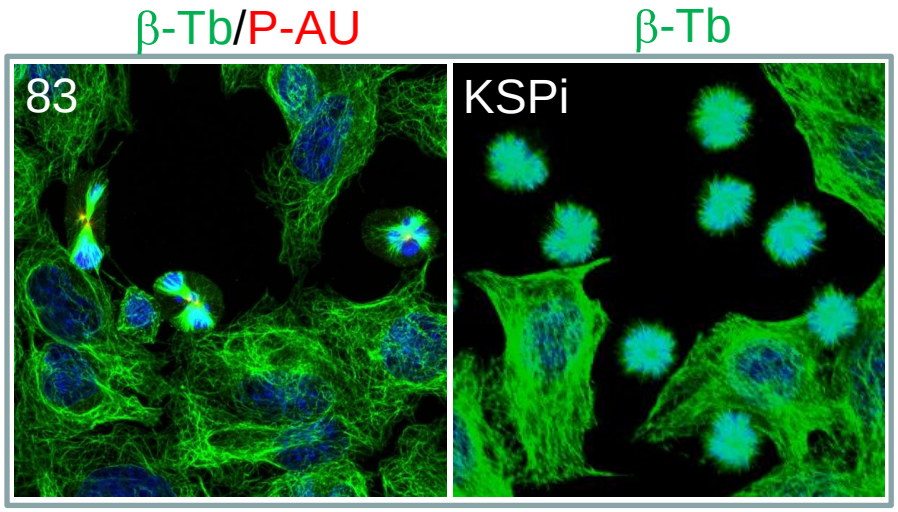


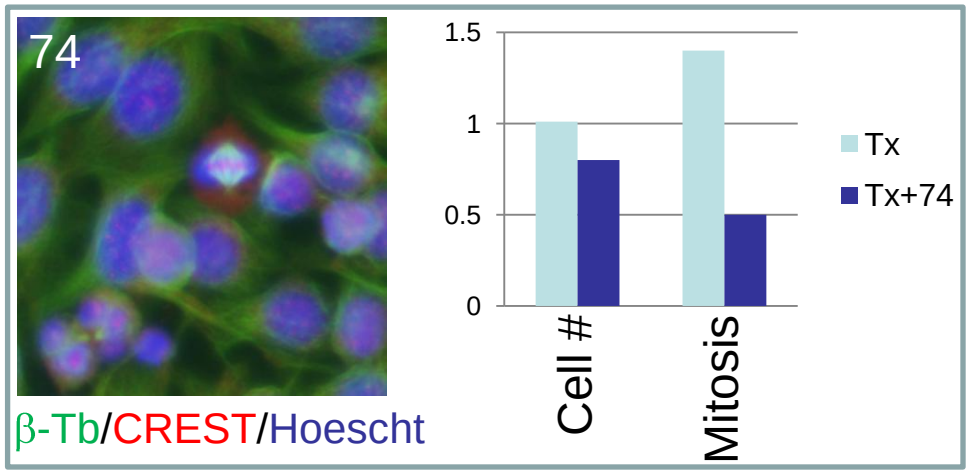
A *Papaver somniferum* 10-Gene Cluster for Synthesis of the Anticancer Alkaloid Noscapine
Thilo Winzer *et al.*
Science **336**, 1704 (2012);

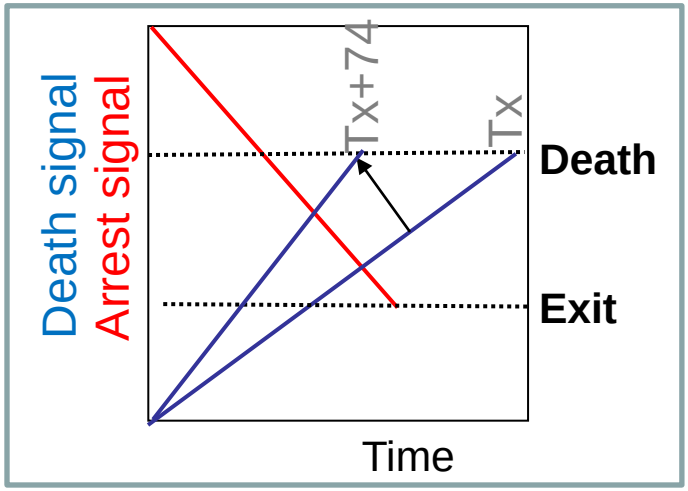




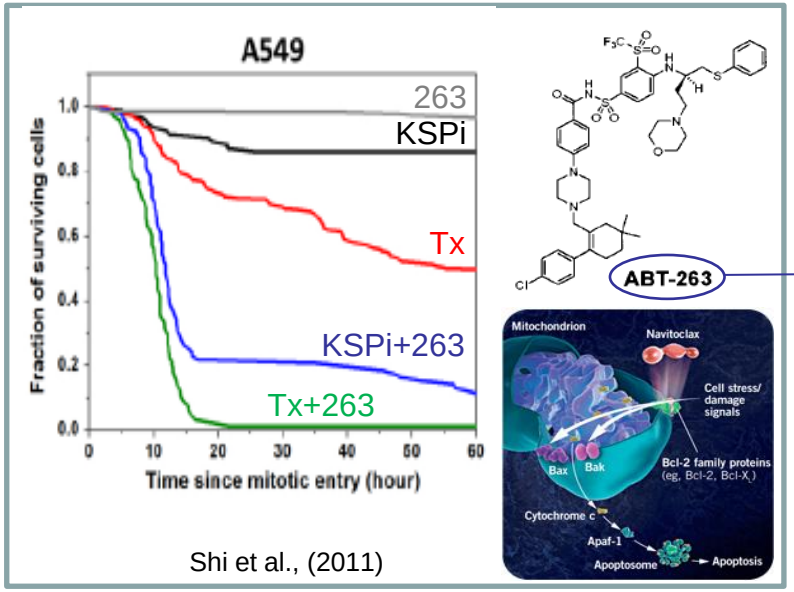
New Cellular Targets



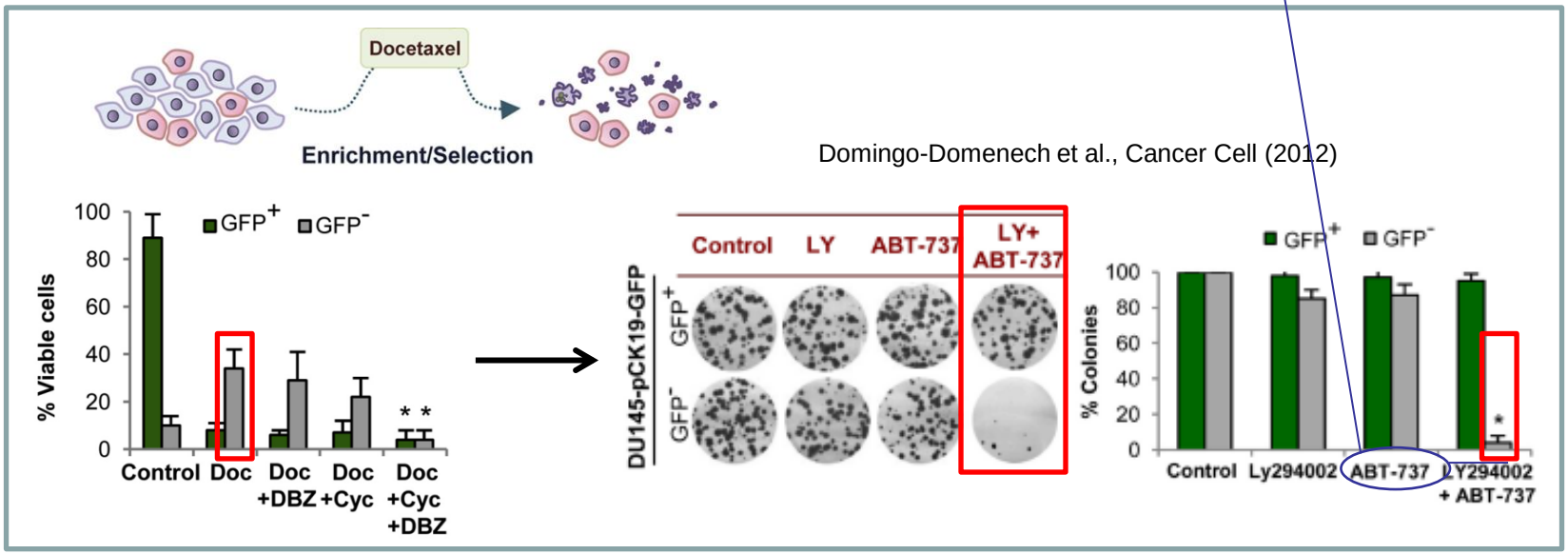




Induction of Death Signal



Shi et al., (2011)



Domingo-Domenech et al., Cancer Cell (2012)

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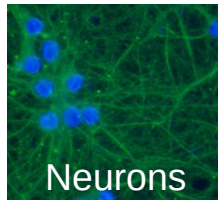
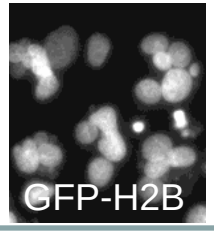
Rachel Ramsdale (PMCC)

Bruno Meloni (CNND)



Brian Gabrielli (UQ)



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