

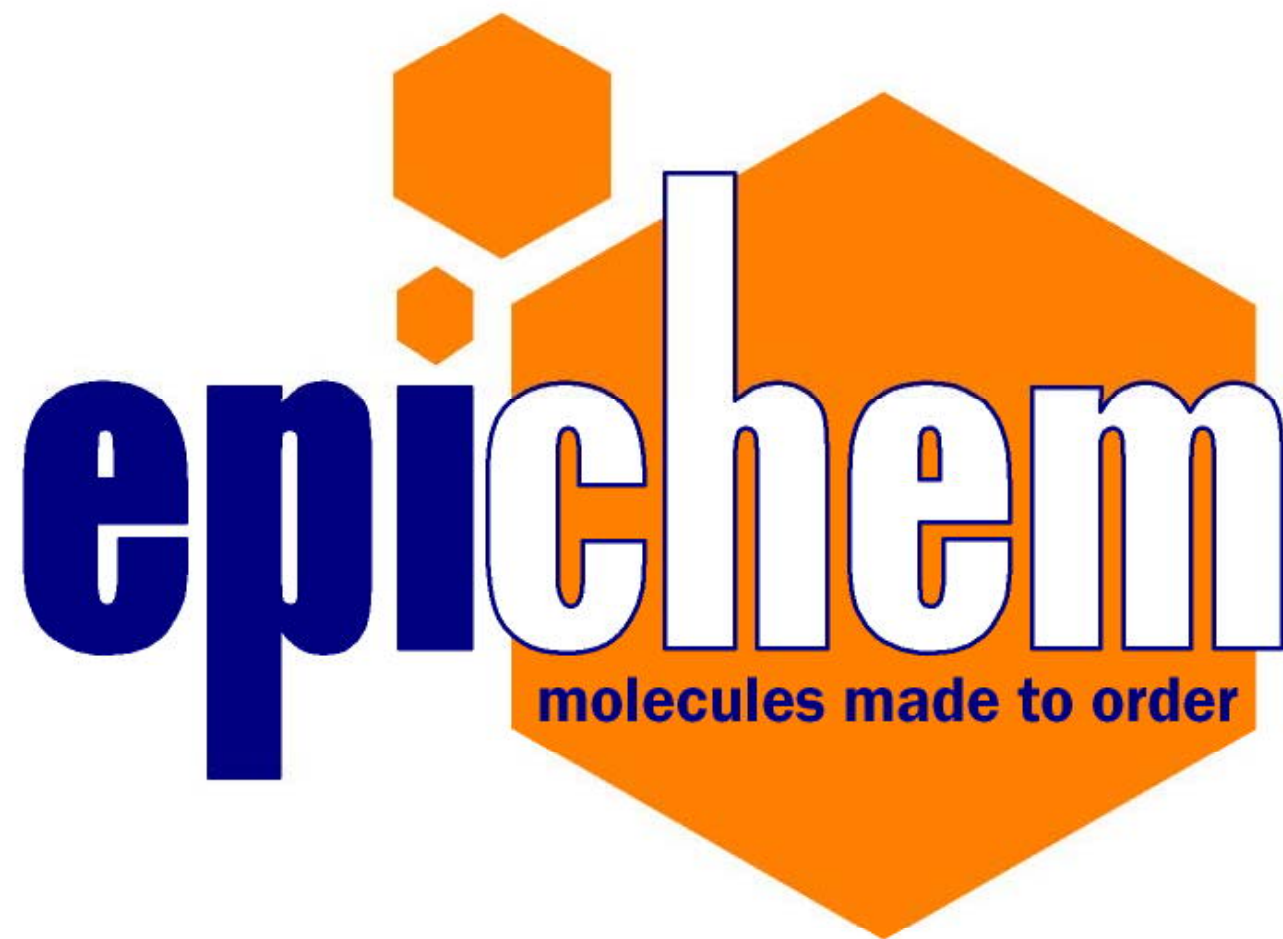


PRESENTATION

AGM 24th October 2014



ASX: PAA
ACN 094 006 023



About Epichem

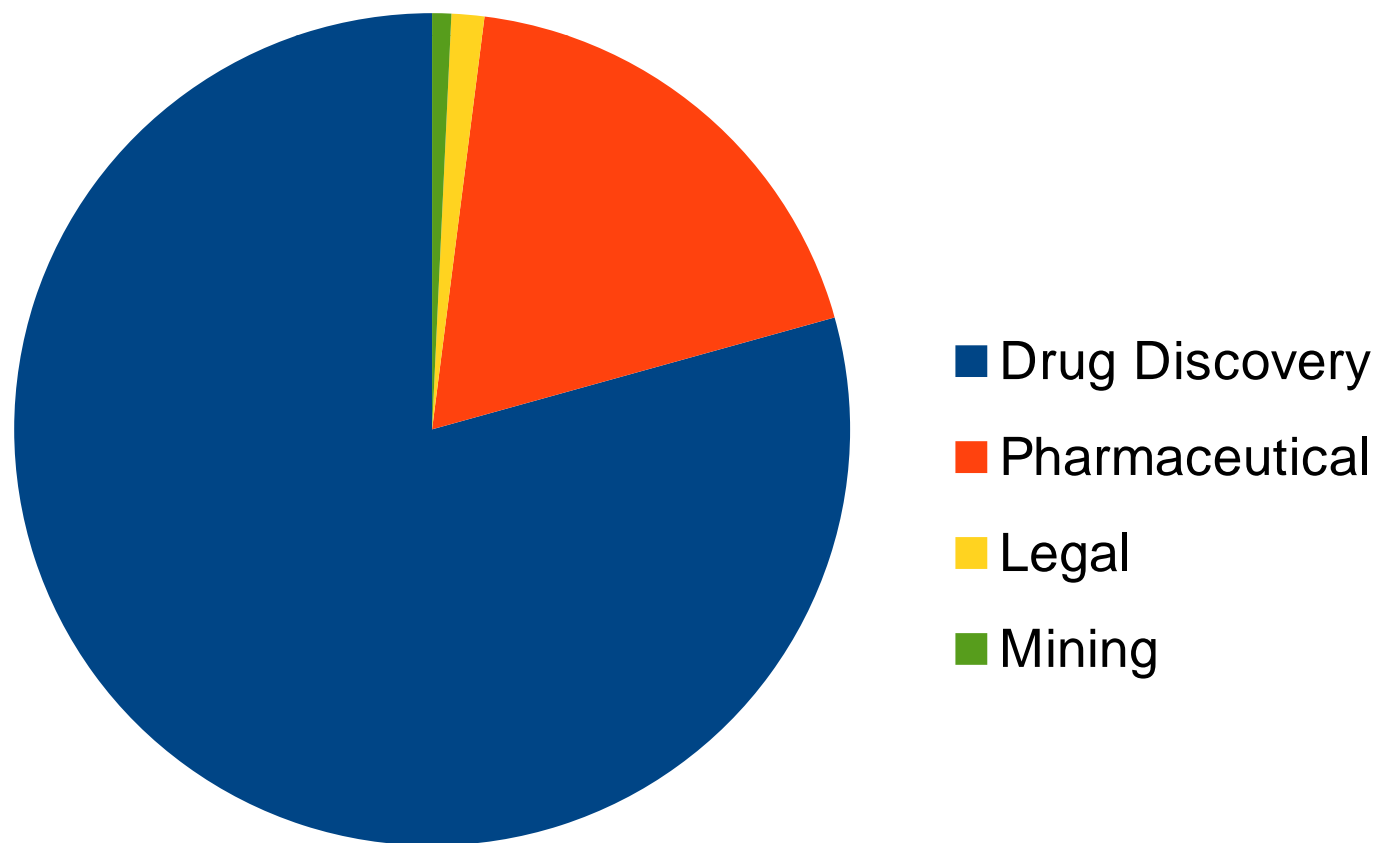
- Formed in 2003
- Wholly owned subsidiary of PharmAust Ltd
- Expertise in synthetic & medicinal chemistry
- 17 Employees (16 BSc, 12 PhD)
- Laboratories in Perth & Melbourne



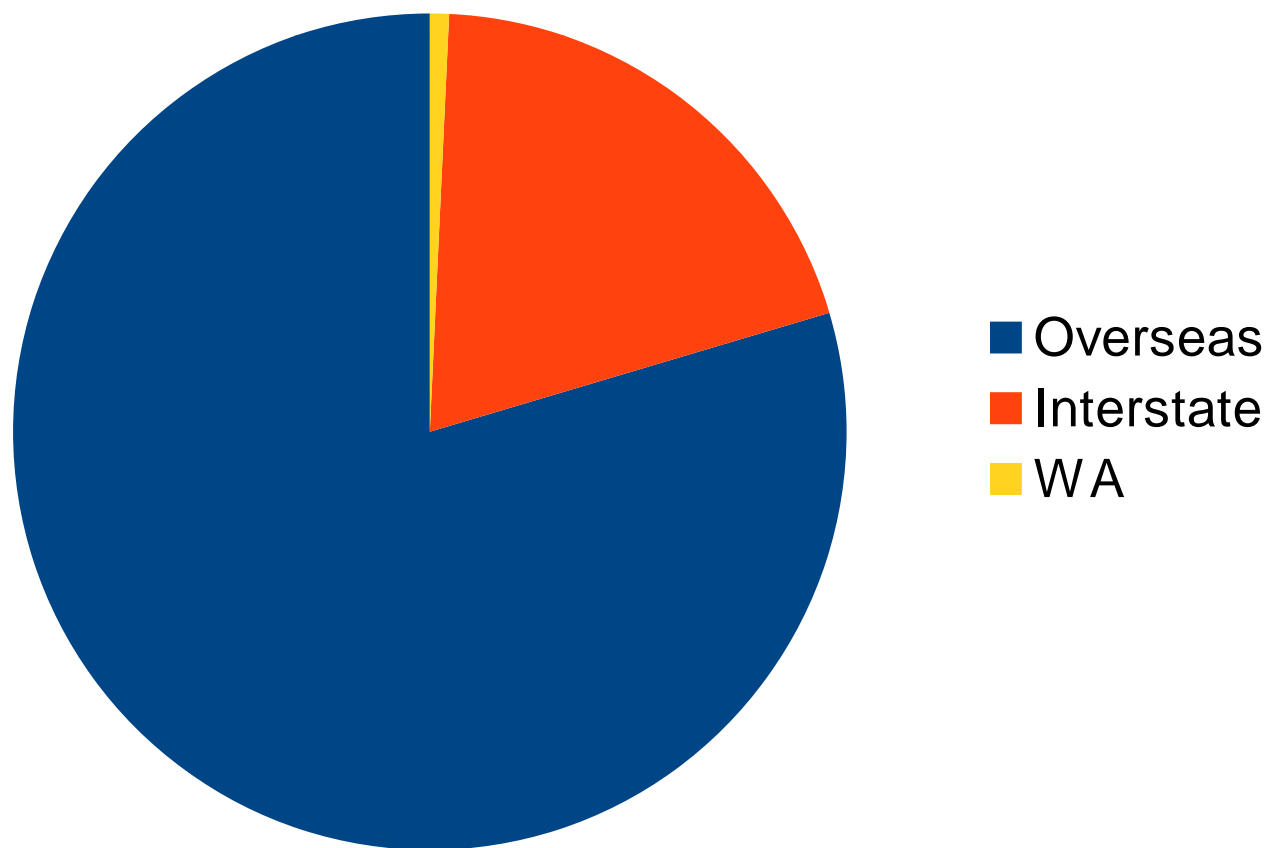
Our Business

- Contract research (fee-for-service)
 - predominantly for the drug discovery sector
- Collaborative research (IP generation)
 - with partners with expertise and assets in biology
- Manufacture reference standards
 - predominantly for the pharmaceutical sector
 - rapidly expanding catalogue of products
- **Revenue generating and profitable**

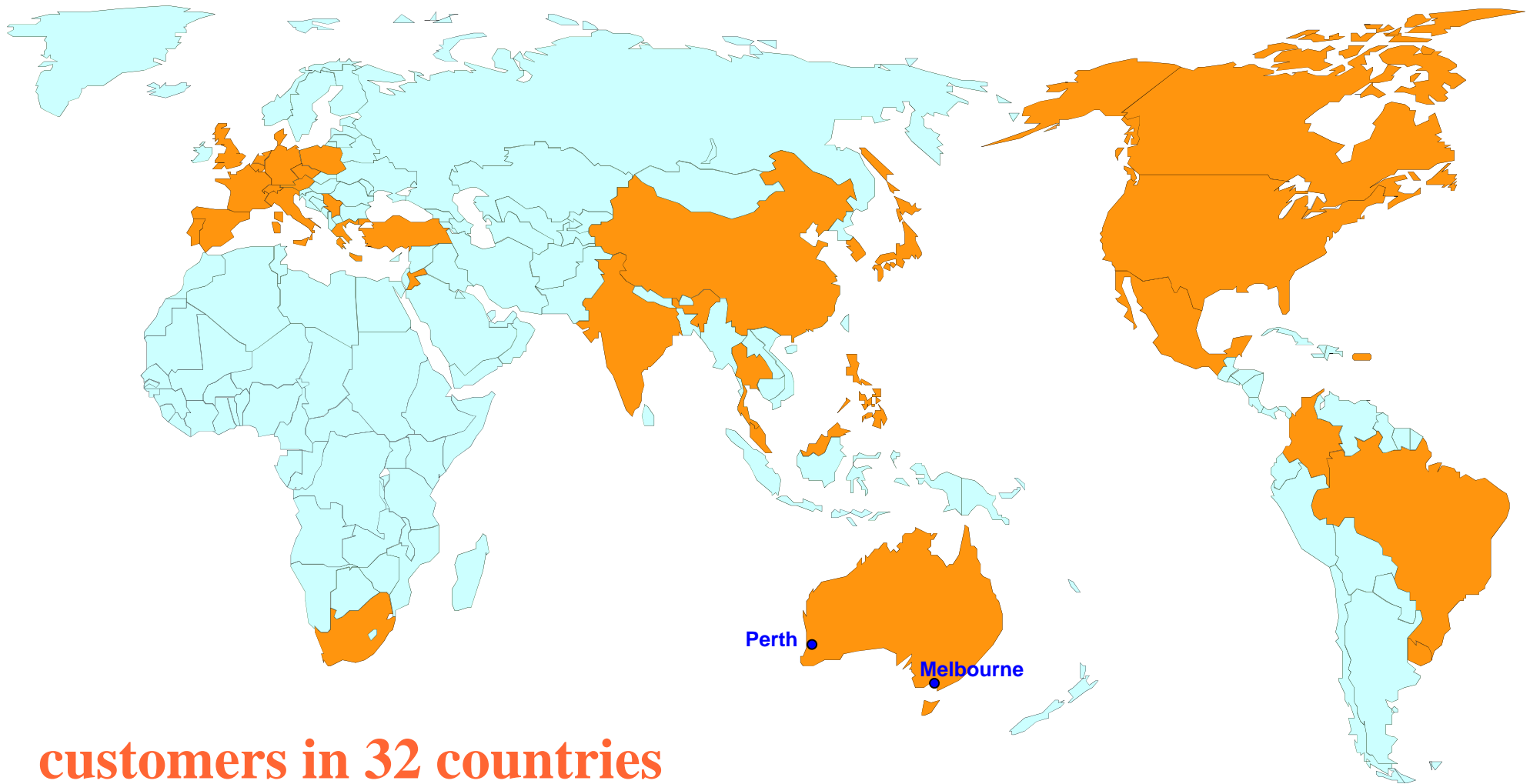
Revenues by Sector (2014)



Revenues by Region (2014)



World Class - Globally Competitive



customers in 32 countries



molecules made to order

Drugs by Design

Export Awards 2010-2013



Prospects for Contract Research Business

- Global market for chemistry outsourcing is US\$11bn
 - ...and growing at 10.5% p.a.
- Australian sector recovering following GFC
- The falling AUD and Epichem's growing reputation opens new opportunities in overseas markets
- Revenues and profitability from this business are good but constrained by the number of chemists/fumehoods
- Epichem is currently seeking extra laboratory space to exploit this market opportunity



Prospects for Reference Standards Business

- Global market > US\$1bn p.a.
- Highly fragmented market with 2 major suppliers
 - USP sales of ~US\$140M p.a.
 - LGC sales of ~US\$110M p.a.
- Significant market growth due to:
 - ever increasing regulatory requirements
 - new & improved analytical techniques
 - new drugs entering market, especially illicit drugs
- Epichem aiming for 1% of market (>\$10M) by 2020

Clients Include

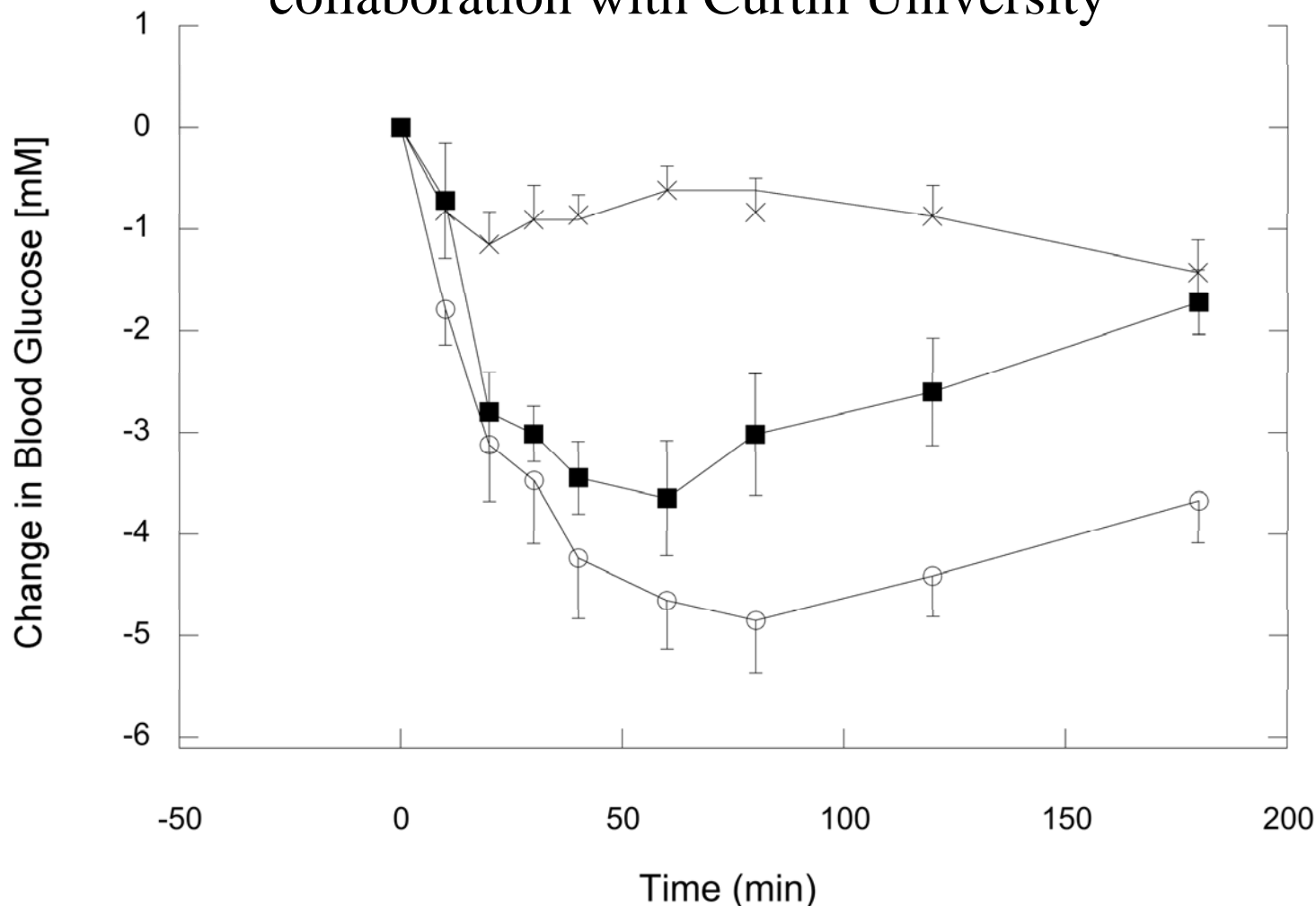


Epichem Research Projects

Epichem has a small number of early stage pre-clinical research projects where it has a share of the intellectual property and/or rights to any commercial outcomes.

Diabetes Project

collaboration with Curtin University



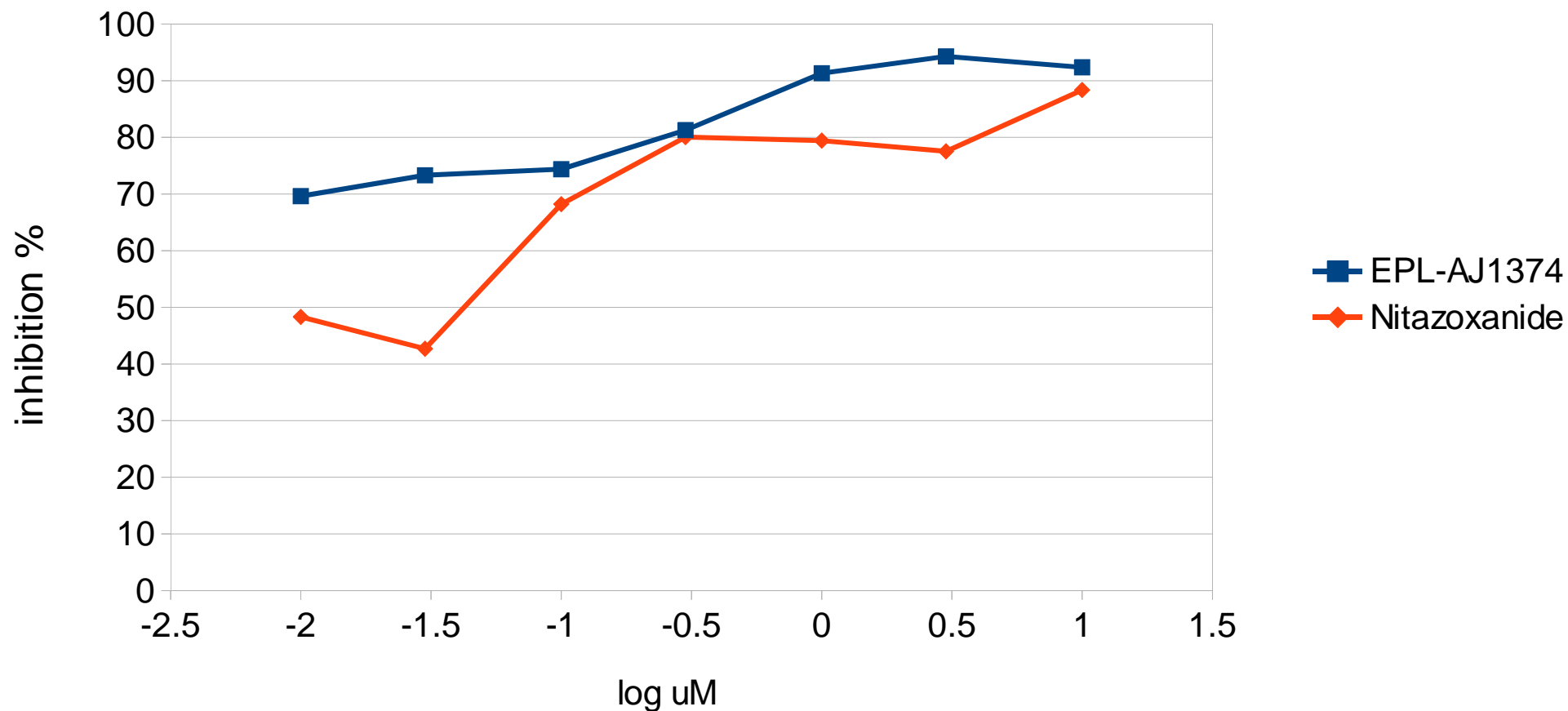
Blood glucose lowering comparison between EPL-BQ70 (33mg/kg or 72 μ M) and insulin (2.5nM) in anaesthetised, normoglycaemic rats.

Vehicle (X; $n = 8$ rats), human insulin (O; $n = 8$), or EPL-BQ70 (■; $n = 8$).

Cryptosporidium Project

collaboration with Murdoch University

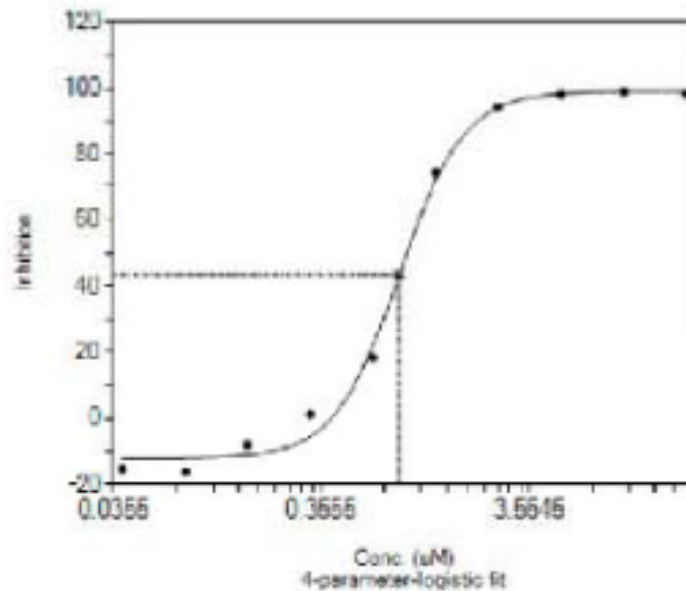
Inhibition of Cryptosporidium in vitro



Novel Anti Cancer Lead

Colo 320 Kras SL

IC50 0.836 μ M



We have identified a **highly novel**, small molecule that selectively kills a suite of oncogene-expressing engineered cell lines

Key Objectives for 2015

- Expand and promote Reference Standards business
 - launch US Distributor
 - target the growing SE Asian market
- Secure additional laboratory space
 - then promote Contract Research business
- Support Pitney's PPL-1 project
- Refocus research to maximise synergies with Pitney and exploit Pitney's oncology expertise

Find out more and stay in touch at...



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linkedin/company/epichem_2

**PRESENTATION TO
PHARMAUST LTD
ANNUAL GENERAL MEETING
24 OCTOBER 2014**

David Morris
Surgeon/Scientist
Professor of Surgery UNSW
St George Hospital
Sydney. Australia

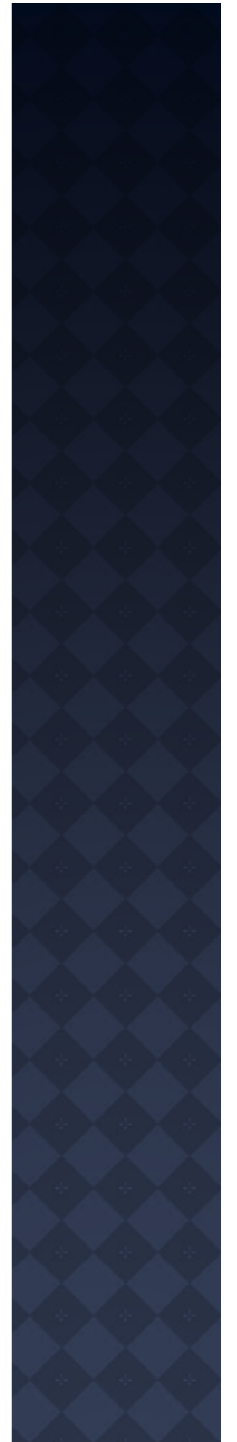
PHARMAUST CANCER

- ◎PPL-1 /AAD

- ◎Albendazole

- ◎Bromelain/Nac

- ◎Nanoparticles



MPL/AAD

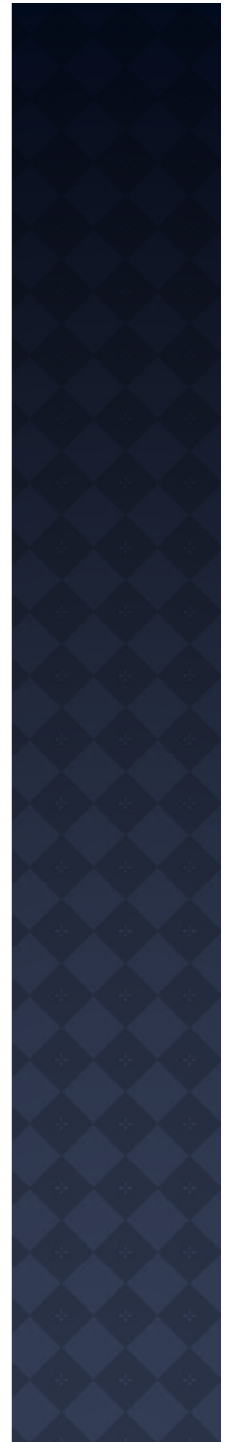
- ◎ Lab

- ◎ Animal

- ◎ Dog

- ◎ Clinical Trial

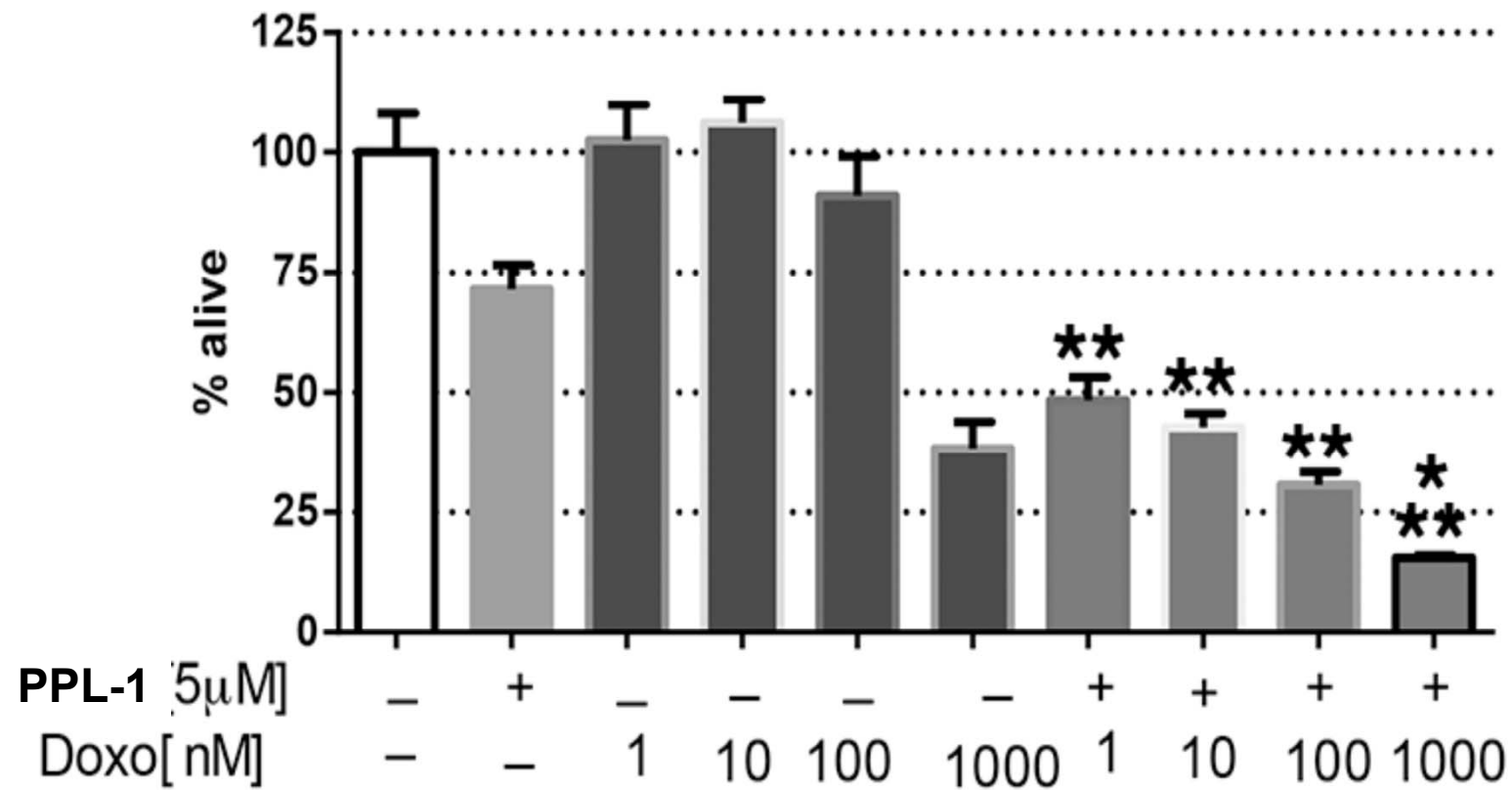
- ◎ Japanese Midsize Company



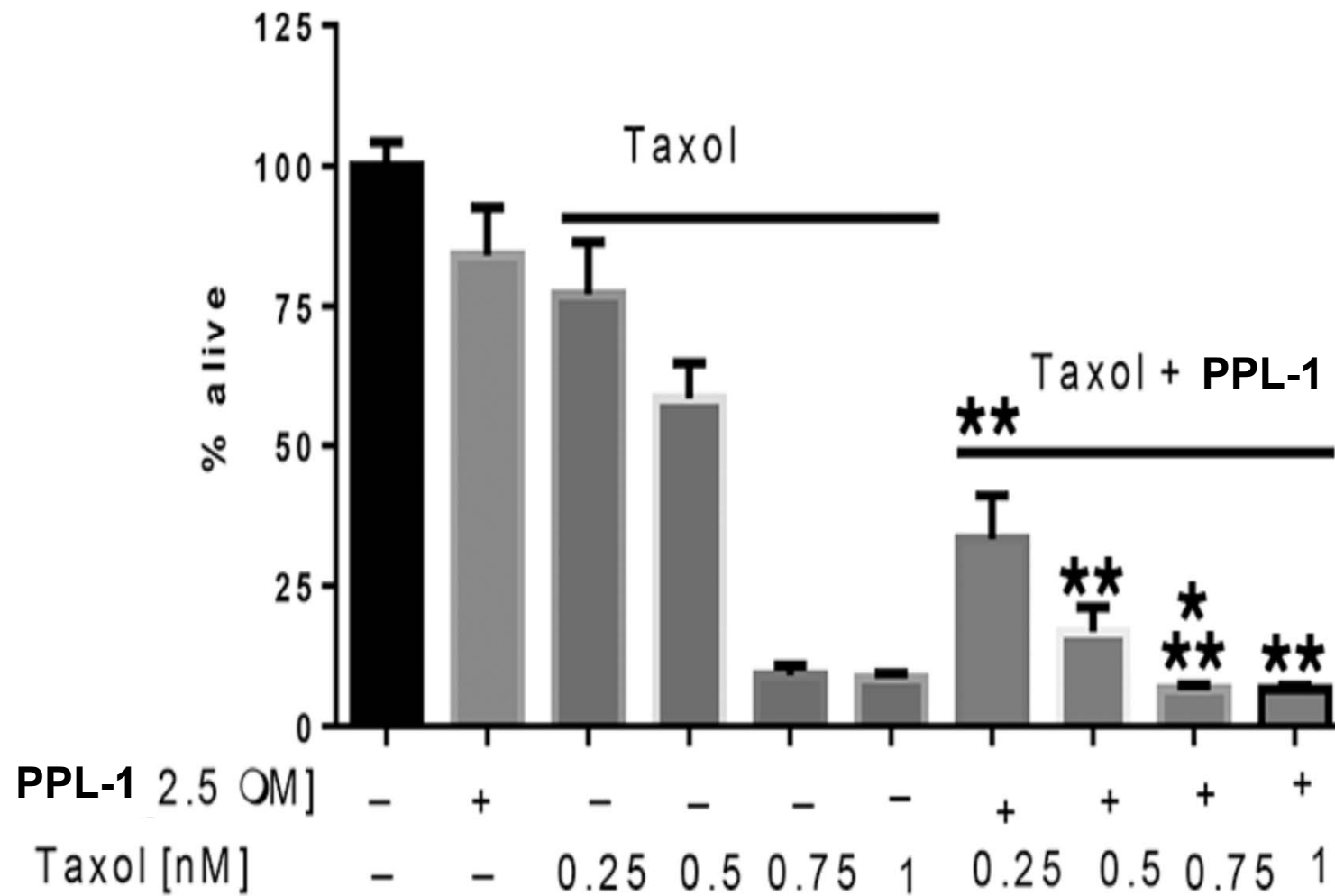
LAB

- ◎ >40 Different Tumor Cell Lines
- ◎ Combination Therapy
- ◎ Mtor Pathway
- ◎ p70s6K

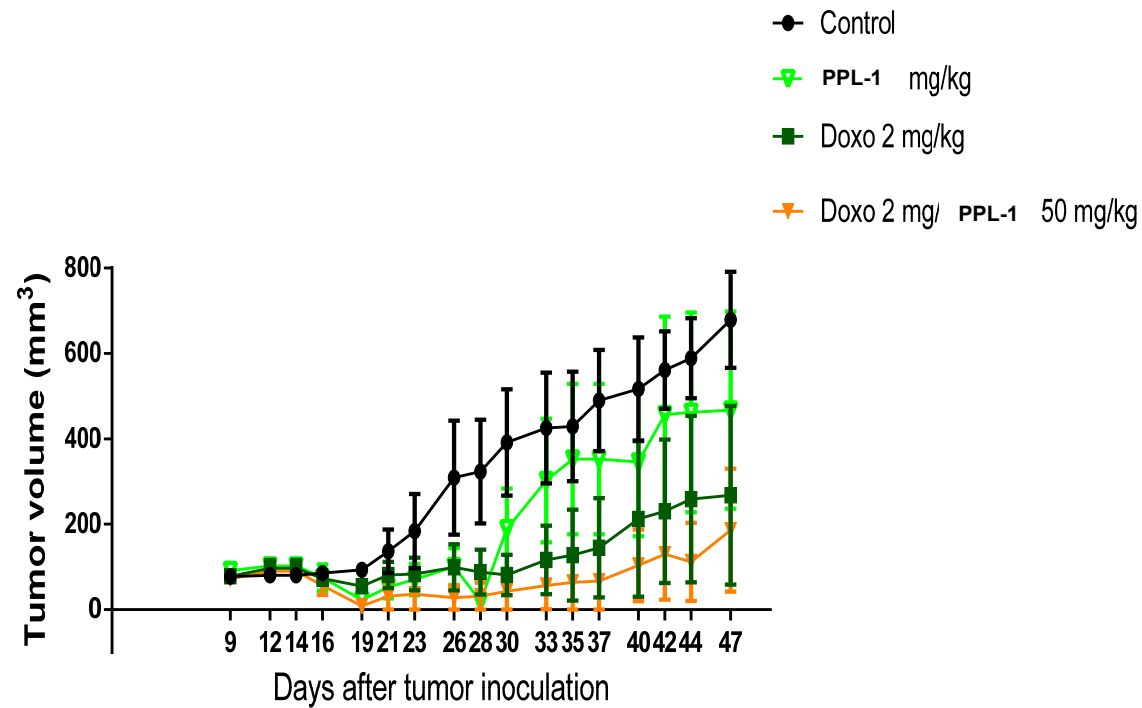
REN MESO COMBO



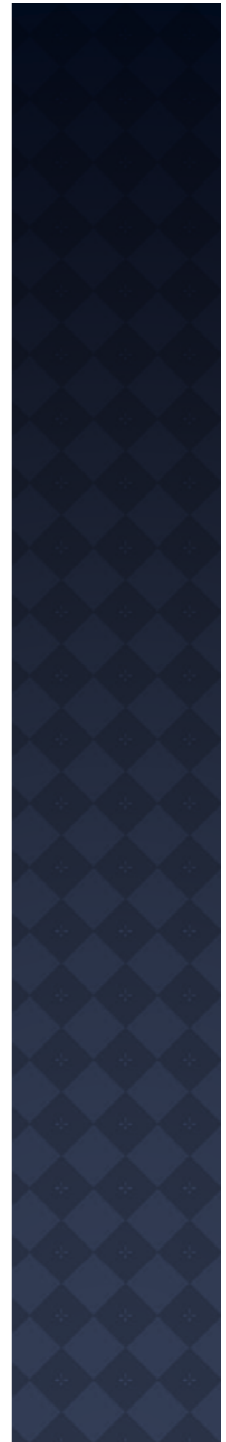
A2780, OV COMBO

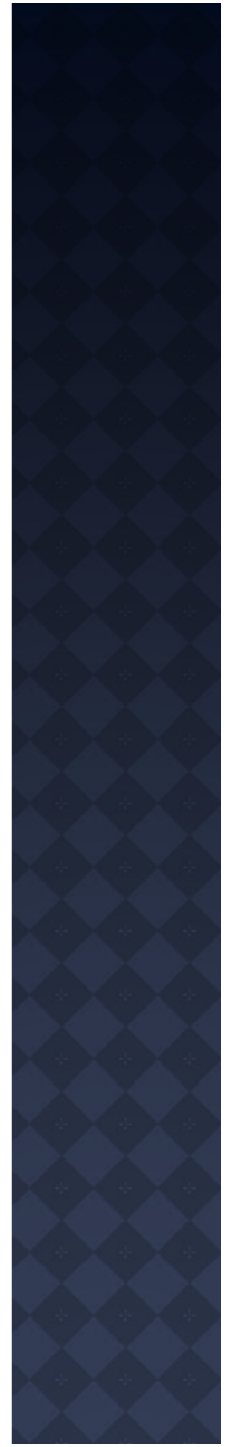


Comparison of tumor volume V.s. treatment time in mice treated with PPL-1 50 mg/kg alone or in combination with Doxorubicin 2 mg/kg.



- ◉ Dog (Lymphoma Sarcoma)
- ◉ 4 Dogs Treated (Compassionate Use)
- ◉ Trial Now Started (Corgi - Melanoma and Kelpie with chemo-resistant lymphoma)





CLINICAL TRIAL

- Phase I
- Adelaide
- Pt 1 Entered
- Death, Tumor Progression
- CRC Liver Mets

JAPANESE CO ANALOGUES

- ◉ Recent Visit Tokyo
- ◉ License AAD
- ◉ Joint Patent on AAD Library
- ◉ PAA 50% Ownership
- ◉ Very Exciting In Vitro Result in Human Brain Cancer

JAPANESE CO ANALOGUES

- ◉ PAA To Do Cell/Animal Work On AAD Analogue
- ◉ Re-asses Business Relationship in 6m
- ◉ Major Pharma

ALBENDAZOLE

- ⦿ Potent Inhibitor VEGF
- ⦿ Regulatory Submission Advanced
- ⦿ Work on New Delivery Mechanisms (Cyclodextrin, Albumin)
- ⦿ Clinical Trial For Ascites
- ⦿ US VEGF Patent



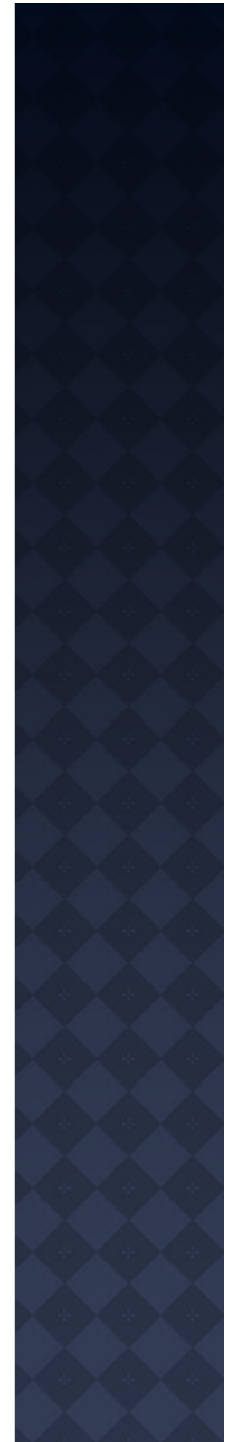
Control

MRC202

BROMELAIN/NAC

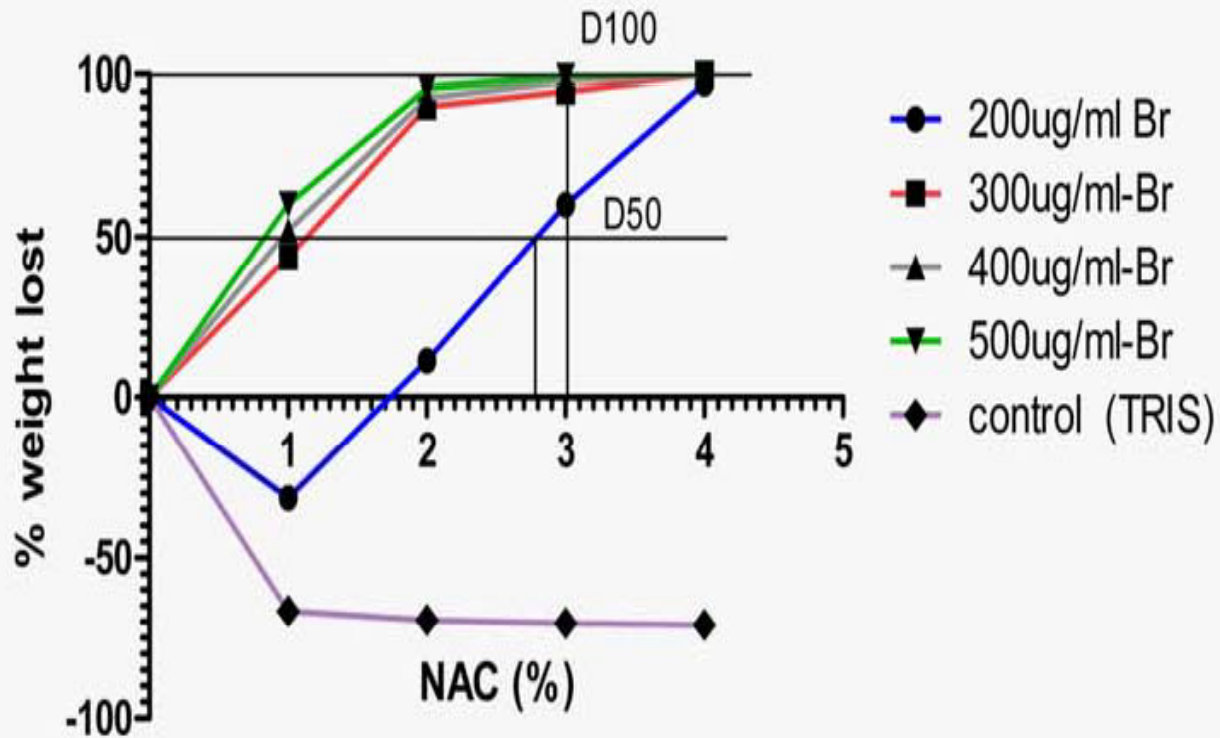
- ◉ Bromelain (Pineapple Stem Enzymes)
- ◉ NAcetylcysteine
- ◉ Synergistic Action On Tumor Mucous
- ◉ Patent Recently Published
- ◉ Cytotoxic Potentiator

**JELLY LIKE MUCIN IS TRANSFORMED TO AN AMBER COLOURED LIQUID
WITH 300UG/ML BROMELAIN + 4% NAC AT 37 DEG C - 3 HOURS**

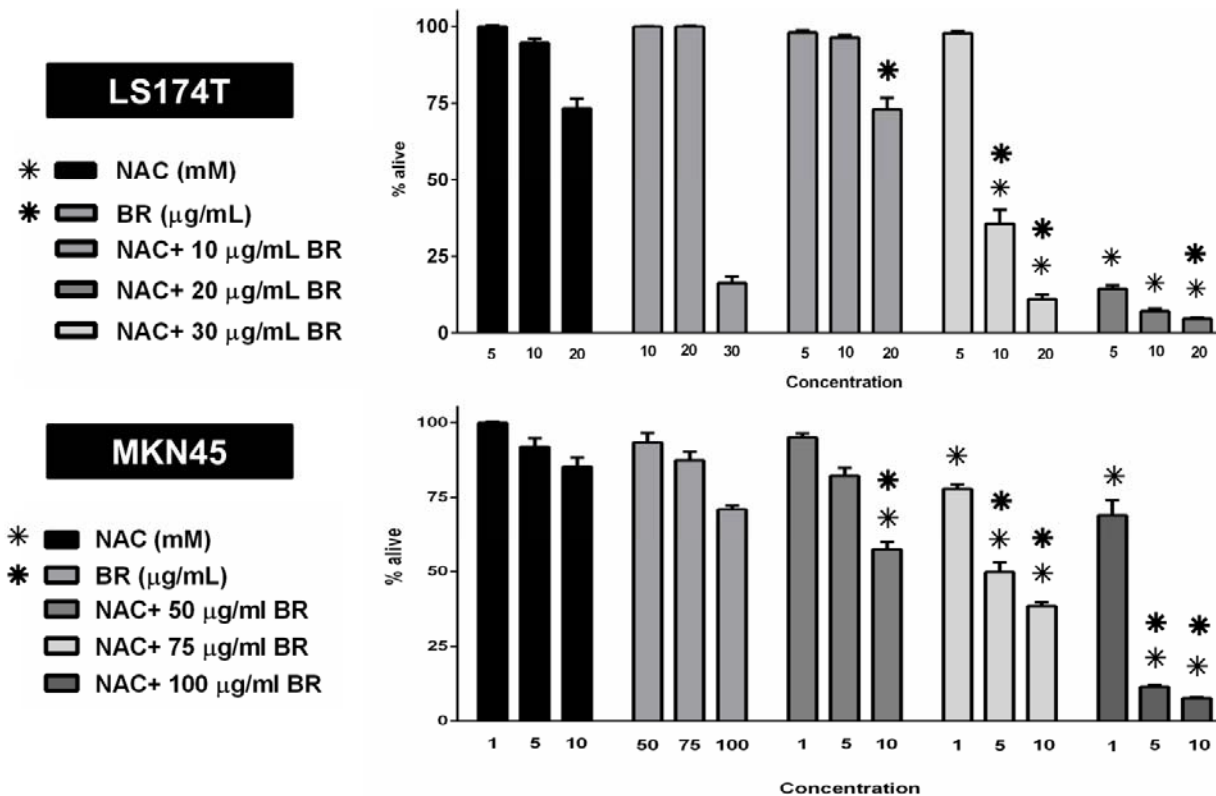


C

Total percentage weight lost by PMP mucin
incubated with Bromelain and NAC
at 37 deg C/4 hours



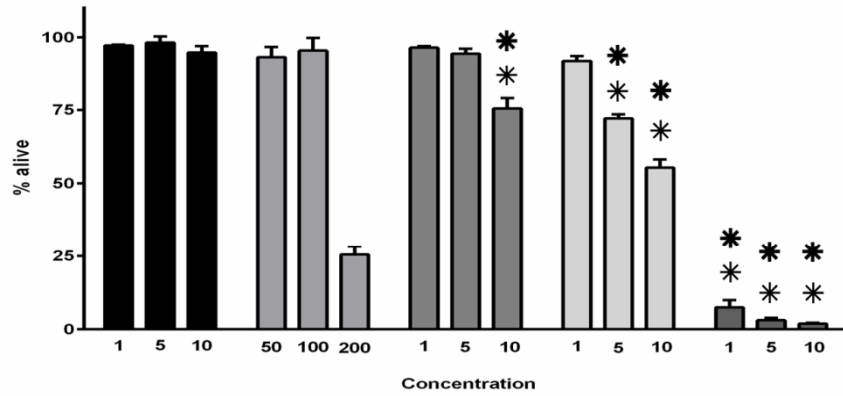
✓ Combination of bromelain and NAC results in significantly more potent growth-inhibitory effects on gastrointestinal cancer cells



Sulforhodamine B assay after single agent and combination treatment with bromelain and NAC for 72 hours. Significant changes ($p < 0.05$) are marked by bold and non-bold asterisks when single agent bromelain and NAC are considered as control, respectively

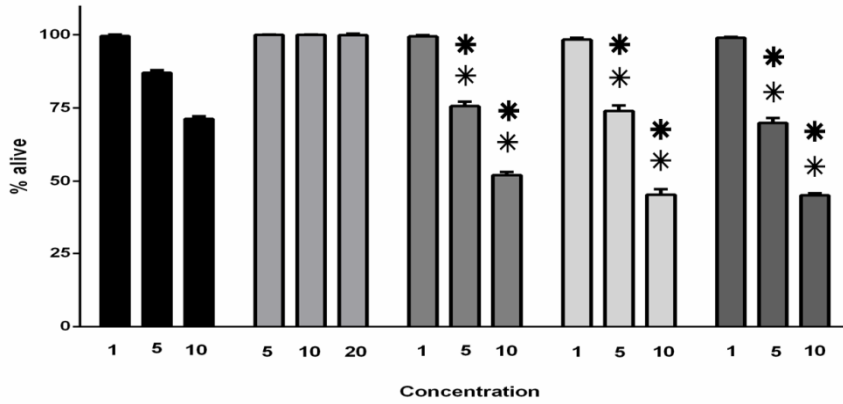
KATOIII

- * NAC (mM)
- * BR ($\mu\text{g}/\text{mL}$)
- NAC+ 50 $\mu\text{g}/\text{mL}$ BR
- NAC+ 100 $\mu\text{g}/\text{mL}$ BR
- NAC+ 200 $\mu\text{g}/\text{mL}$ BR



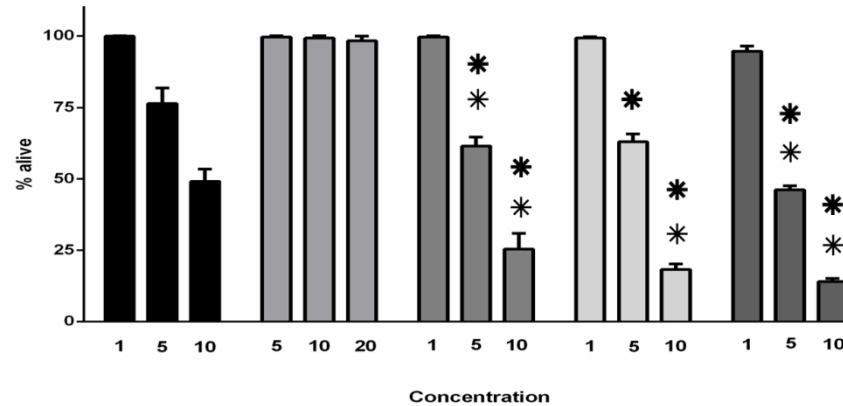
HT29-5M21

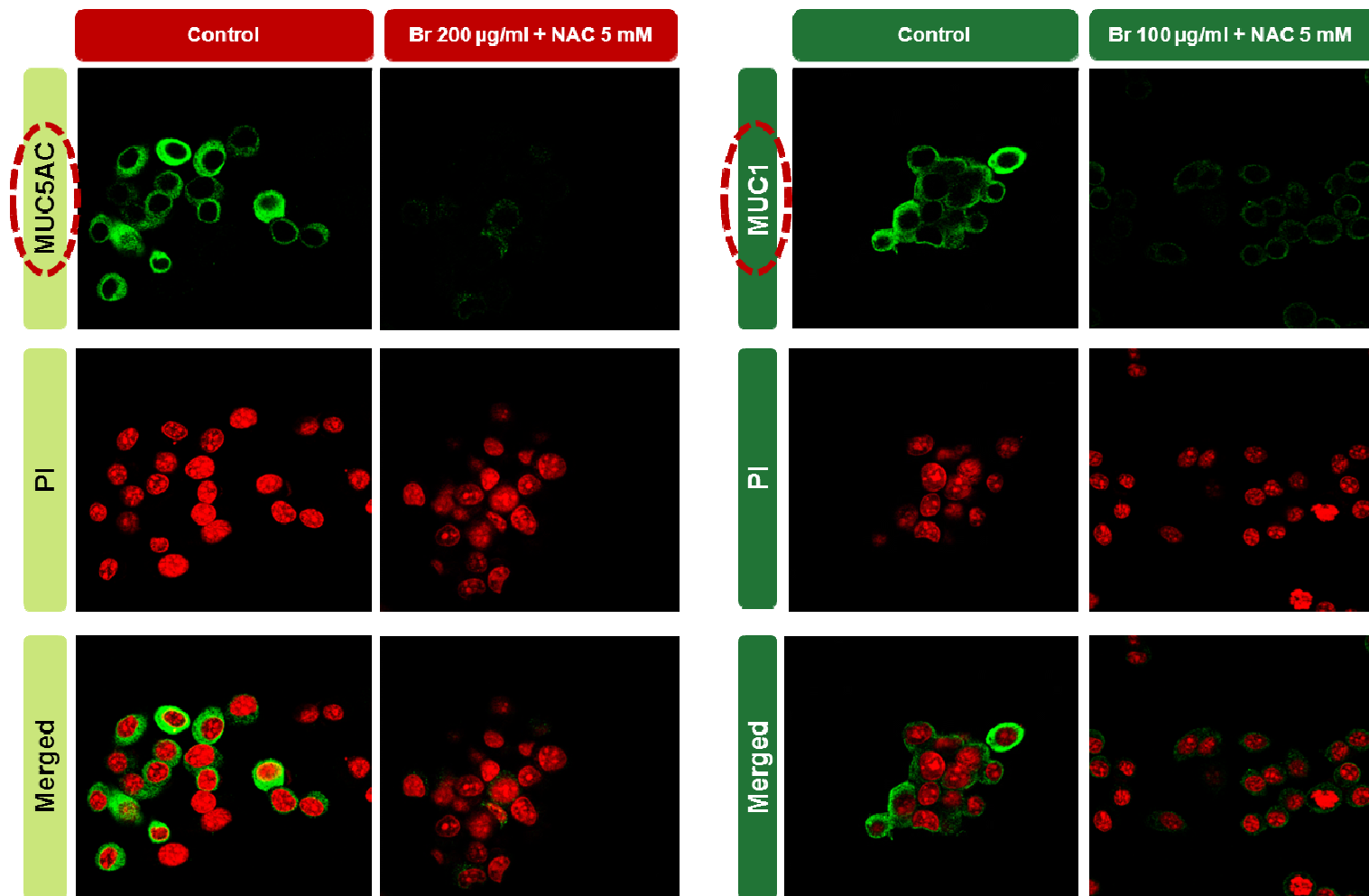
- * NAC (mM)
- * Br $\mu\text{g}/\text{mL}$
- NAC+ 5 $\mu\text{g}/\text{mL}$ BR
- NAC+ 10 $\mu\text{g}/\text{mL}$ BR
- NAC+ 20 $\mu\text{g}/\text{mL}$ BR



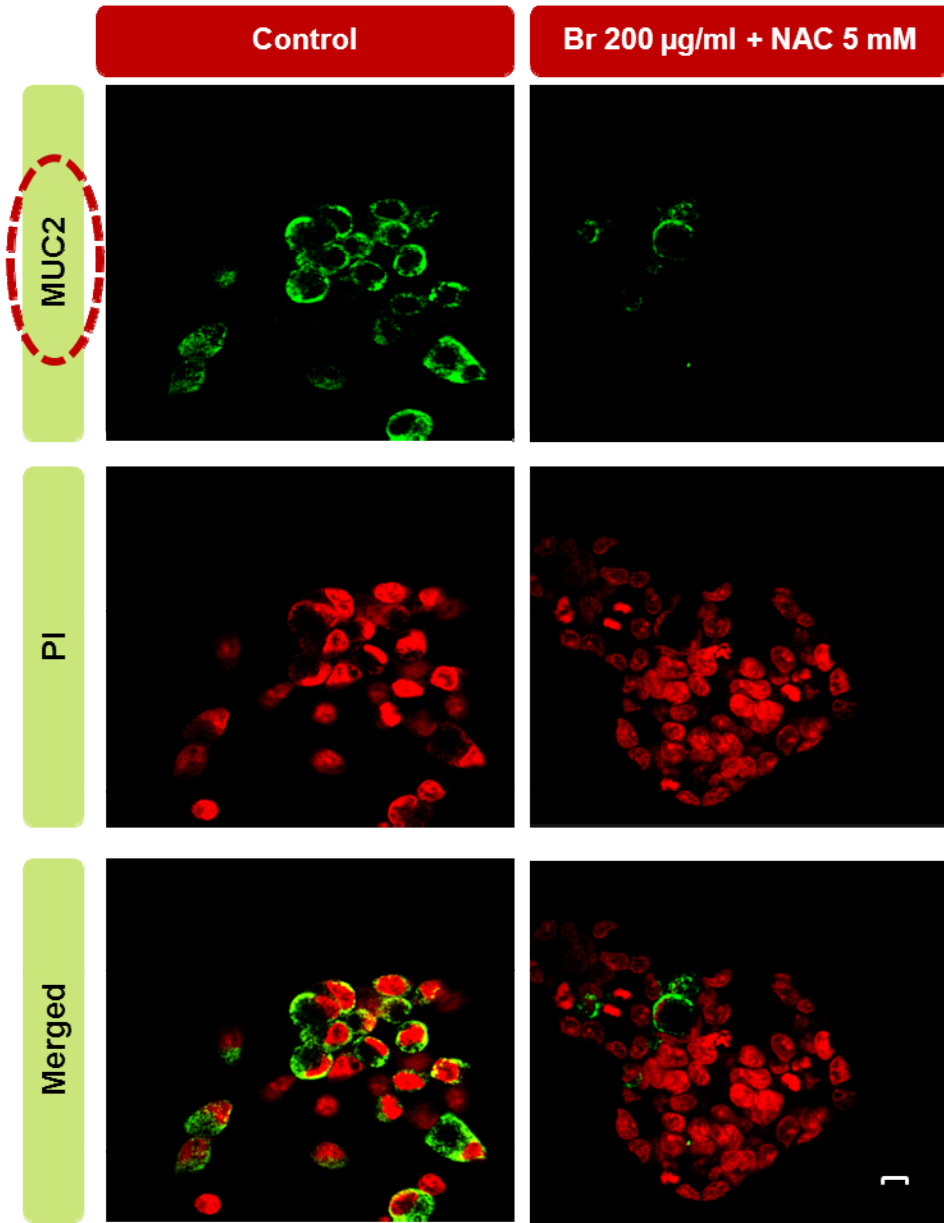
HT29-5F12

- * NAC (mM)
- * Br $\mu\text{g}/\text{mL}$
- NAC+ 5 $\mu\text{g}/\text{mL}$ BR
- NAC+ 10 $\mu\text{g}/\text{mL}$ BR
- NAC+ 20 $\mu\text{g}/\text{mL}$ BR



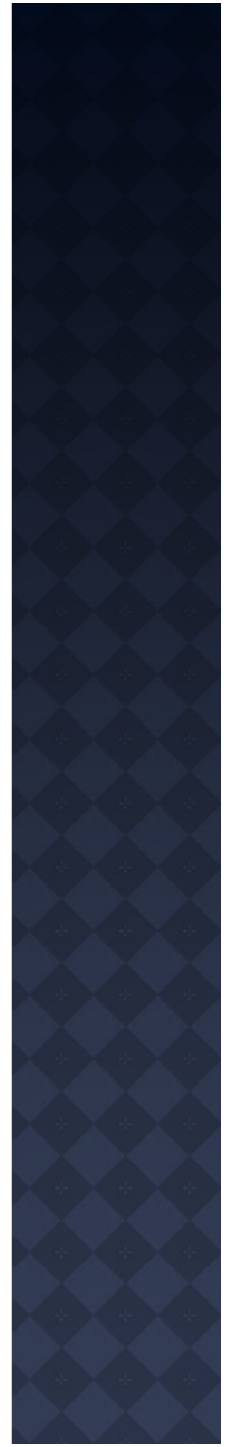


Representative photos of MUC5AC and MUC1 in MKN45 cells after 48h treatment with Br/NAC combination. Green and red fluorescence correspond to MUC5AC/MUC1 and propidium iodide, respectively. Scale bar: 50 µm.



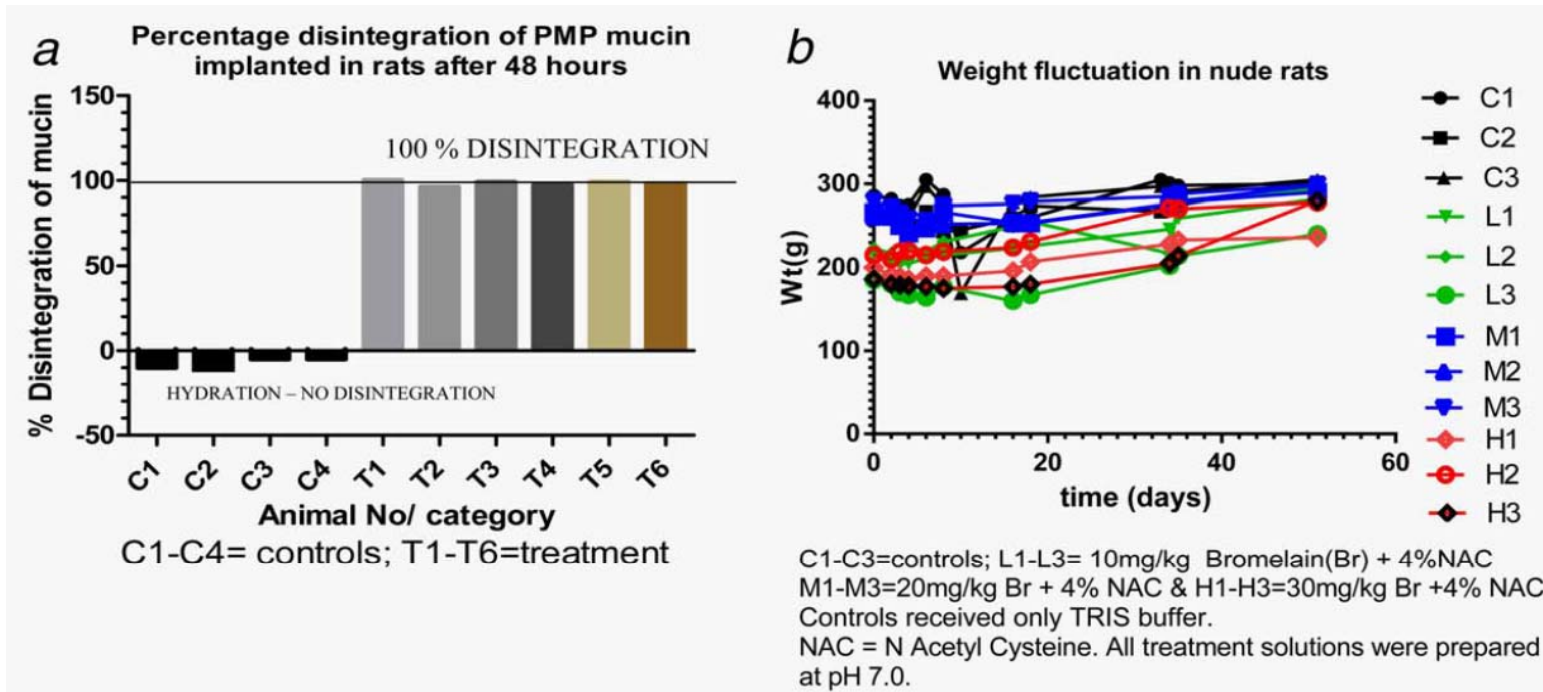
Representative photos of MUC2 in LS174T cells after 48h treatment with Br/NAC combination. Green and red fluorescence correspond to MUC2 and propidium iodide, respectively.

Scale bar: 50 µm.



In vivo testing of in situ lysis

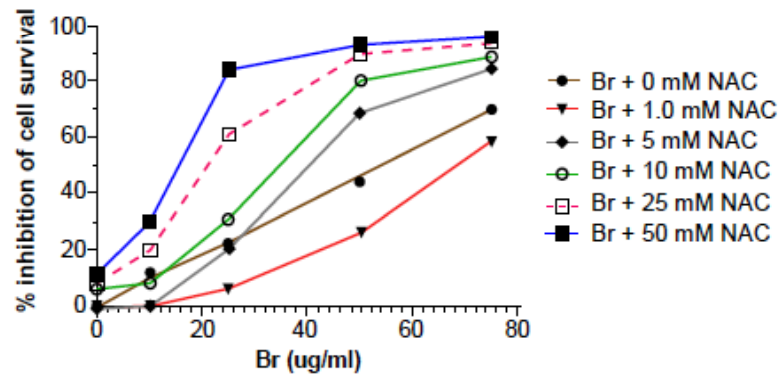
- ✓ IP administration of the combination effectively disintegrates mucin in rats bearing human PMP mucin implants



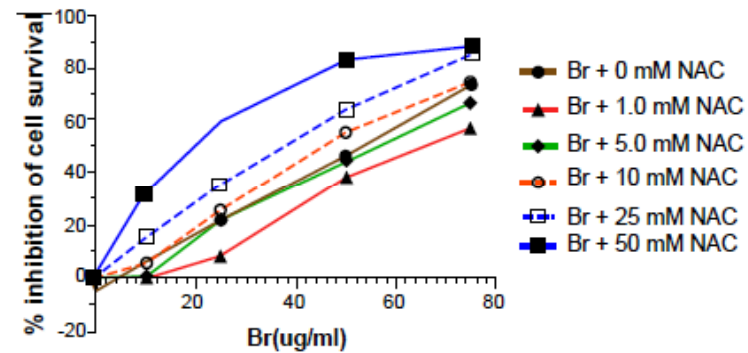
Graph (a) represents the percentage of mucin disintegration in rats treated every 12 hr for 48 hr. Graph (b) shows weight fluctuations in rats treated every 12 hr for 48 hr with various concentrations of bromelain and 4% NAC. Animals were monitored for 55 days for health-related parameters.

✓ **Combination of bromelain and NAC results in more potent growth-inhibitory effects**

Viability of YOU cells treated with bromelain or bromelain + various concentrations of NAC

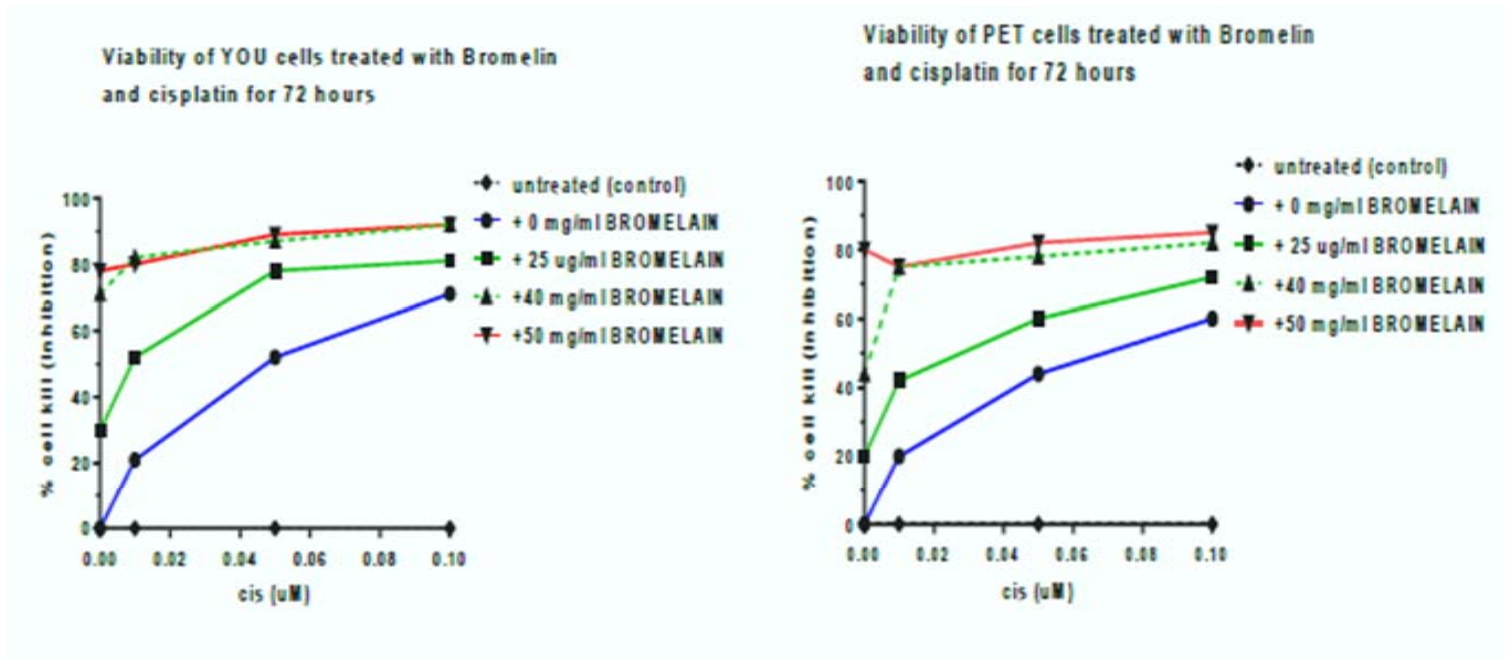


Viability of PET cells treated with bromelain or bromelain + various concentrations of NAC



Sulforhodamine B assay after combination treatment with bromelain and NAC for 48 hr.

✓ The addition of bromelain sensitized the MPM cells to cisplatin

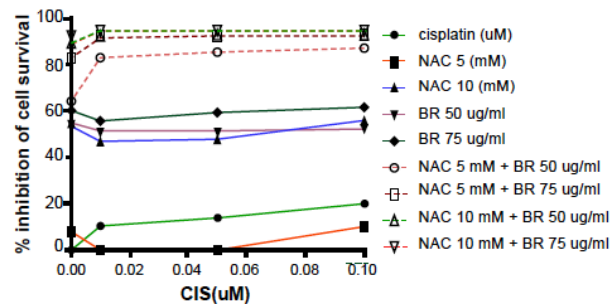


Sulforhodamine B assay after combination treatment with bromelain and Cis for 72 hours.

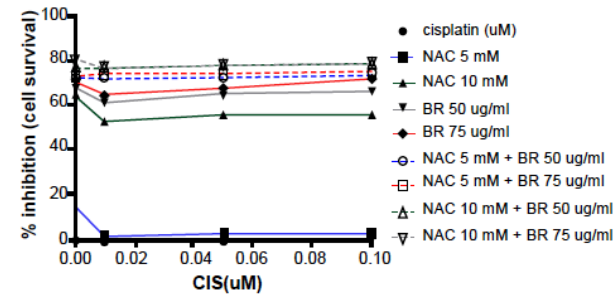


Combination of bromelain and NAC sensitized the MPM cells to cisplatin and 5-FU

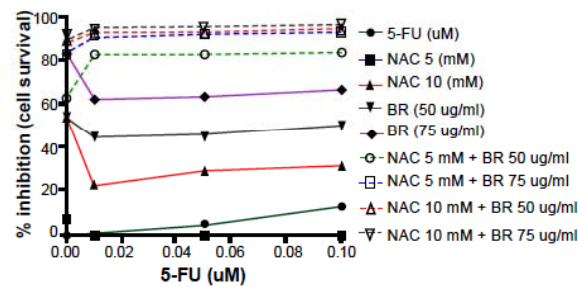
A Effect of cisplatin on YOU cells in combination with bromelain, NAC and NAC + Bromelain



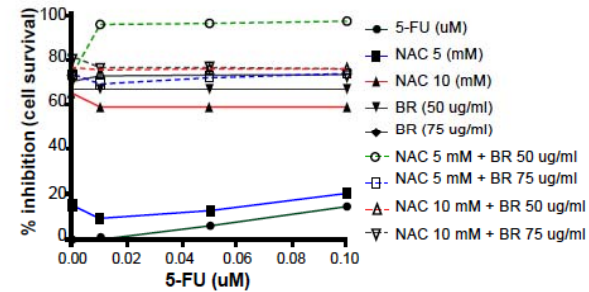
B Effect of cisplatin on PET cells in combination with bromelain, NAC and NAC + Bromelain



C Effect of 5-FU on YOU cells in combination with bromelain, NAC and NAC + Bromelain

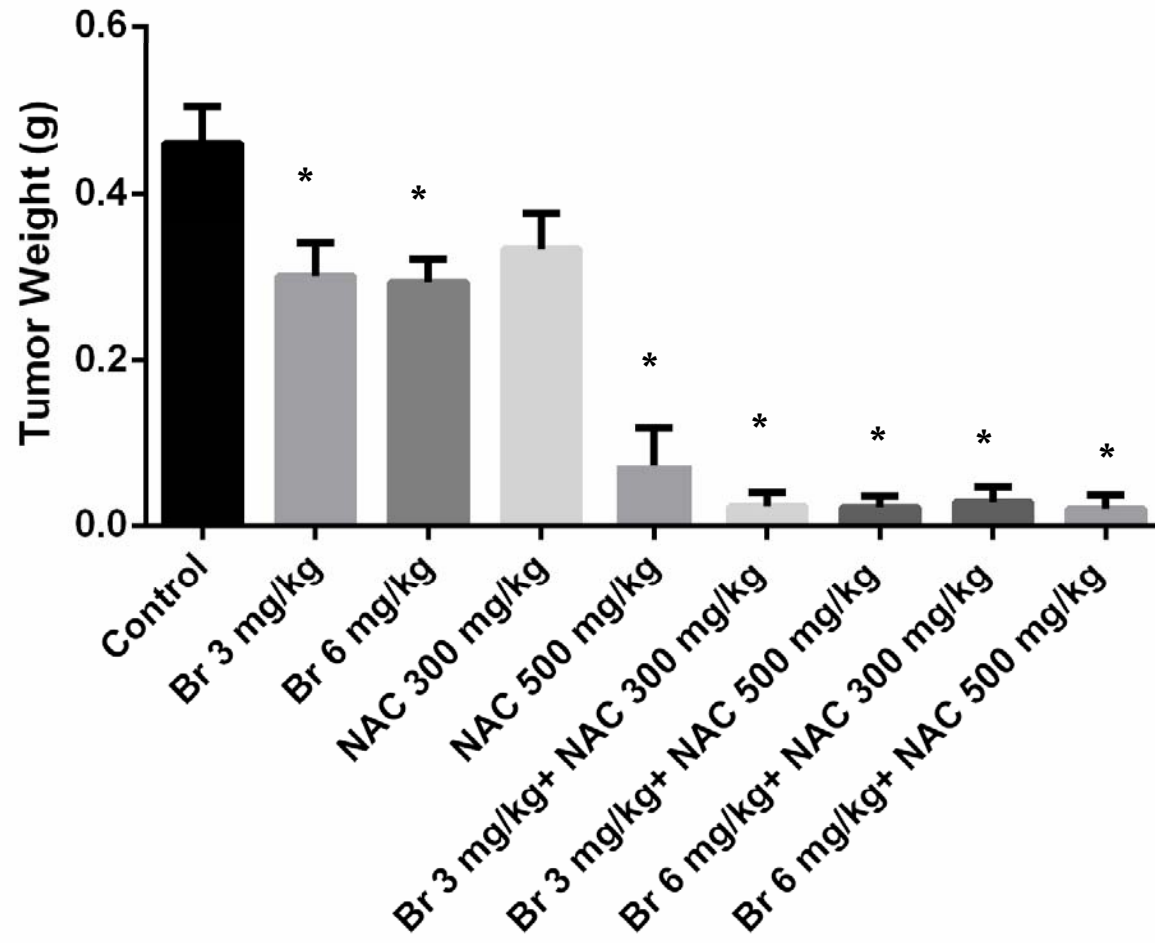


D Effect of 5-FU on PET cells in combination with bromelain, NAC and NAC + Bromelain



Sulforhodamine B assay after combination treatment with bromelain, NAC and Cis for 48 hr.

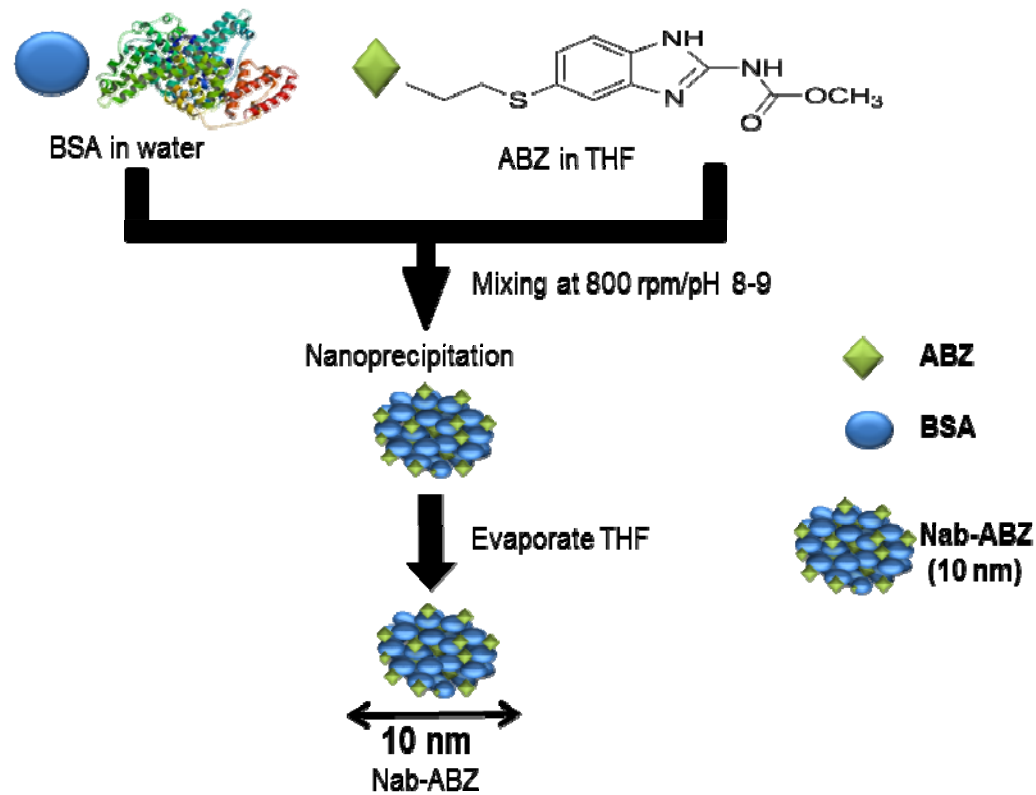
BR/NAC intraperitoneal treatment of LS174T nude mouse model of PC



NANOPARTICLES

- ◉ Work On Albendazole 200x ↑ effect
- ◉ Recent Work On An Established Cytotoxic Drug (\approx Bn/Yr)

Synthesis of nab-ABZ (10 nm)



Evaluation

Size - dynamic light scattering

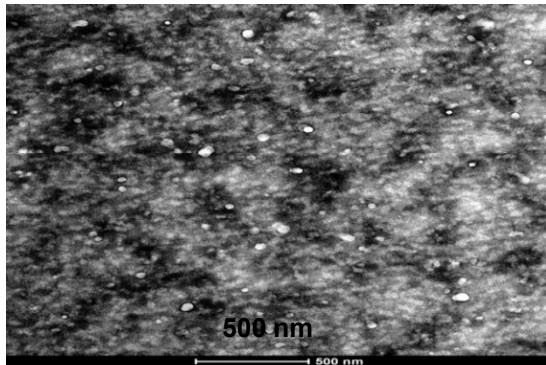
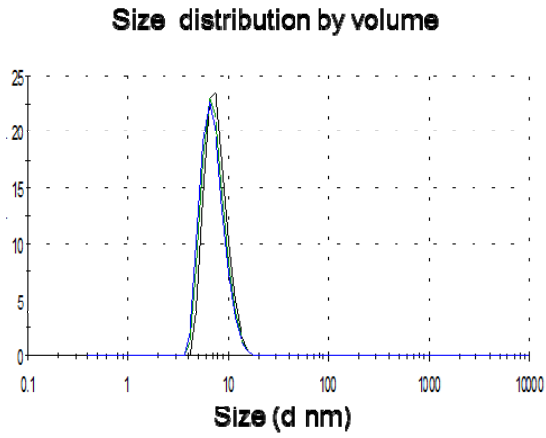
Morphology - TEM

HPLC drug encapsulation efficiency 60-90%

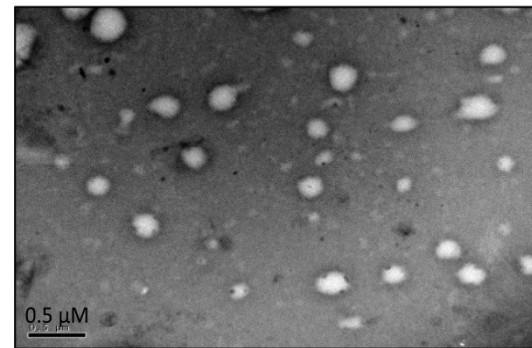
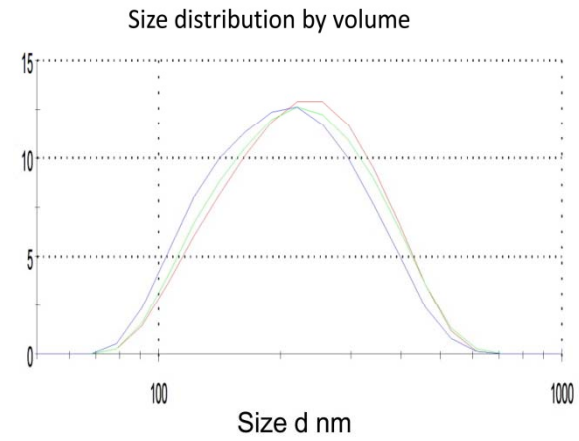
pH controls size + release

Drug release up to 7 days: 68% pH 5, 18% pH 7.4

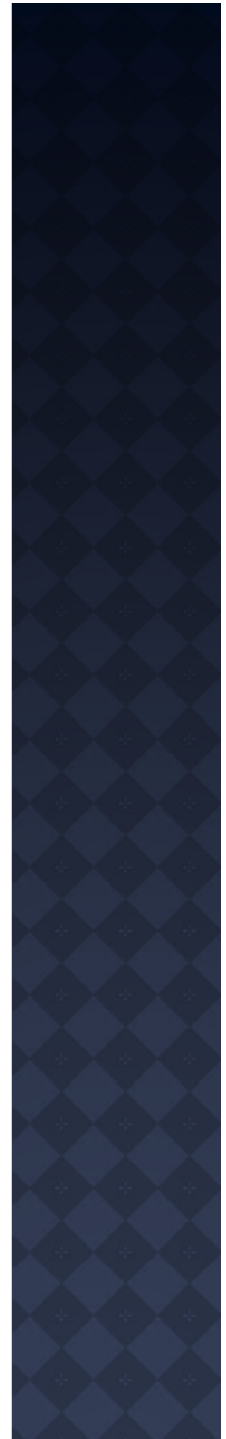
Characterization of nab-ABZ (DLS & TEM Picture)



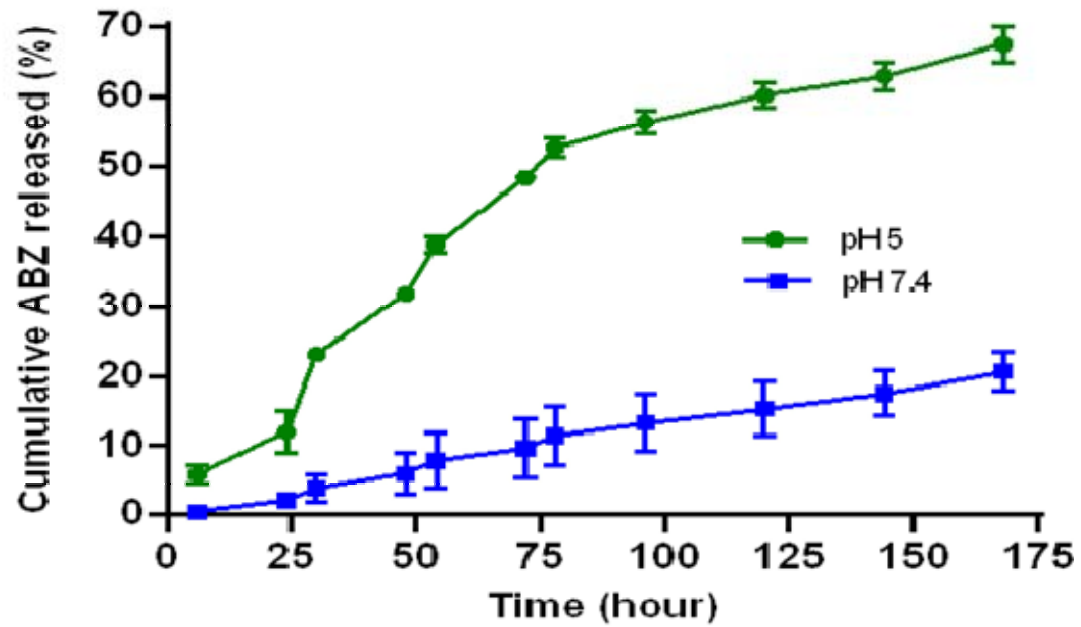
Nab-ABZ 10 nm



Nab-ABZ 200 nm



Release Study of nab-ABZ (200 nm)



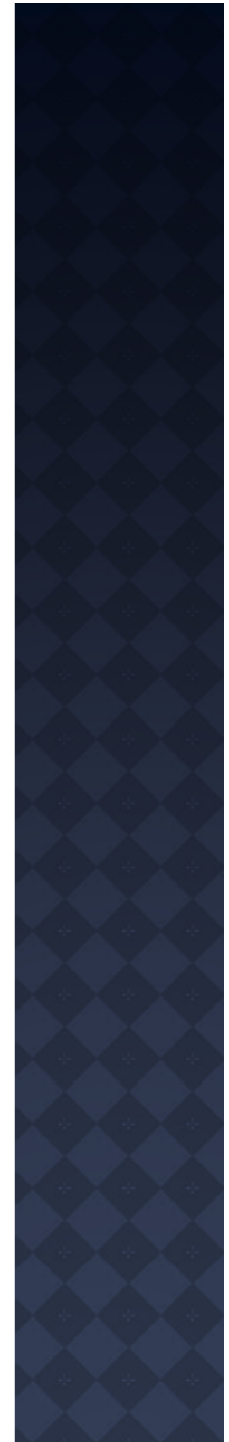
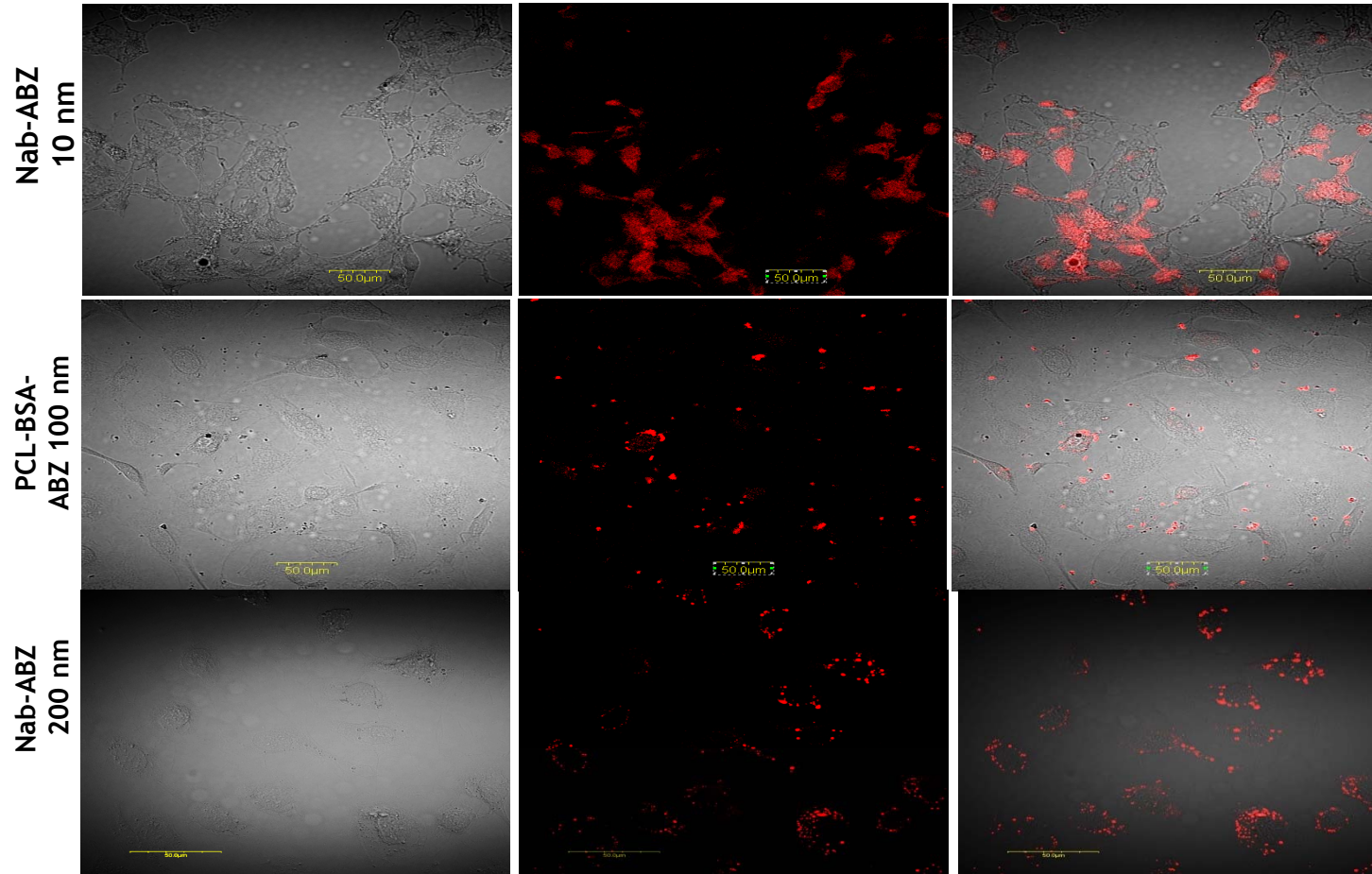
Internalisation

Nab-ABZ	15 min uptake
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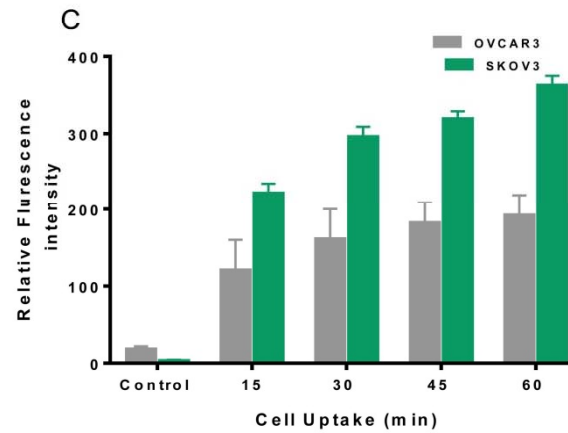
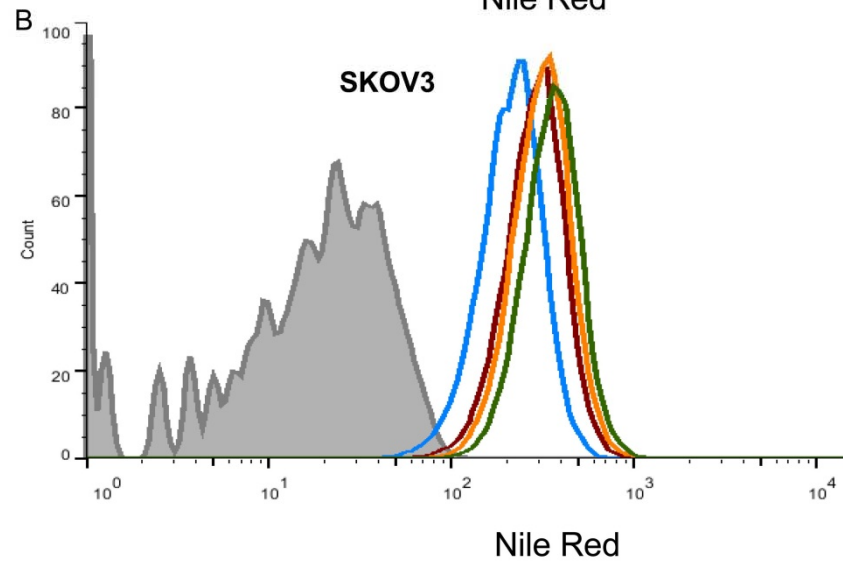
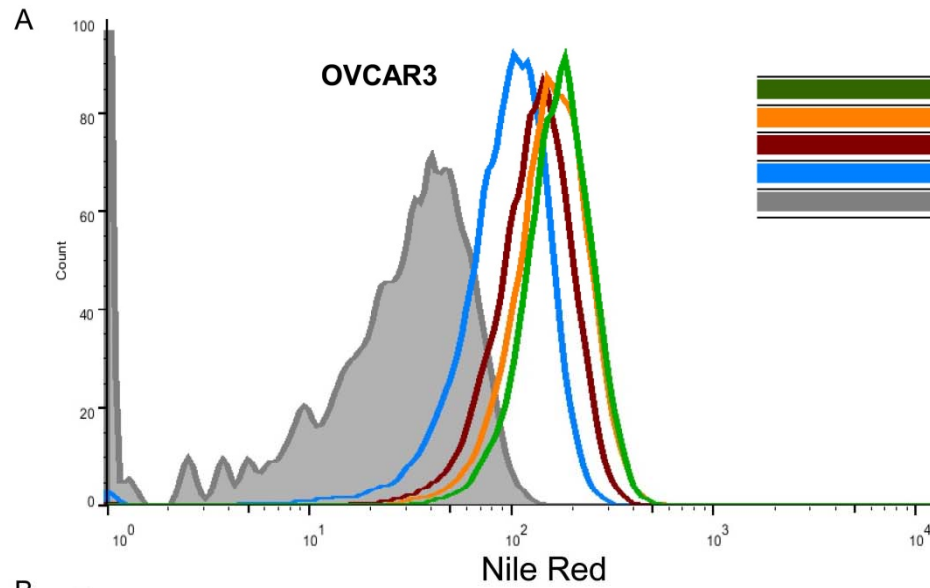
OVCAR3	37%, (88% 1 hour)
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SKOV3	99%
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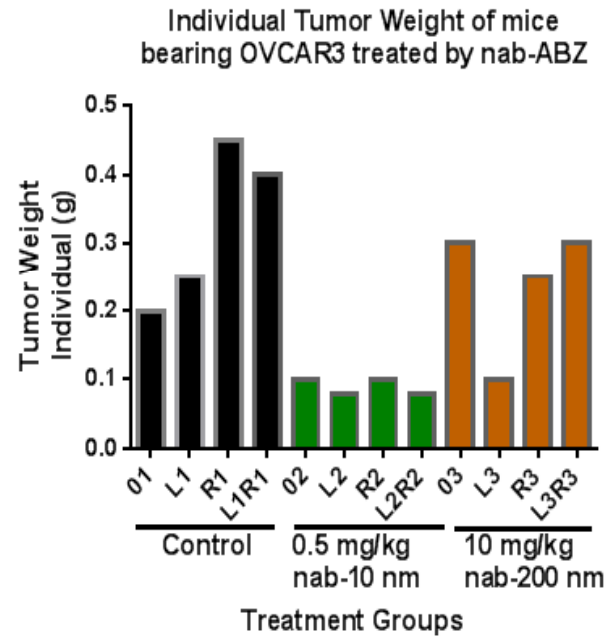
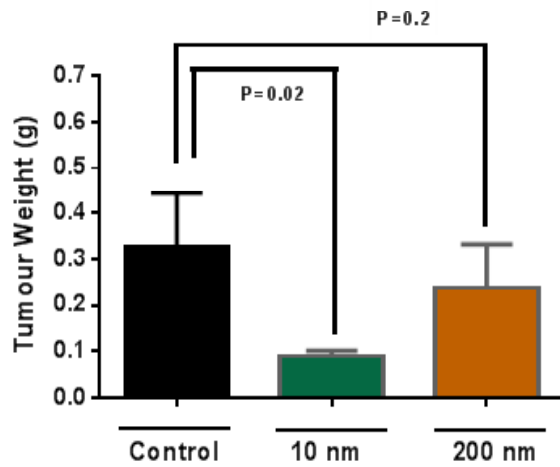
Cellular internalization nab-ABZ in SKOV3 cells (4 h Treatment)



Cellular Uptake study (nab-ABZ 200 nm) by FACS Analysis



In-vivo Comparative Study of nab-ABZ 10 nm & 200 nm (Tumour Weight)in OVCAR3 xenograft Tumor Model

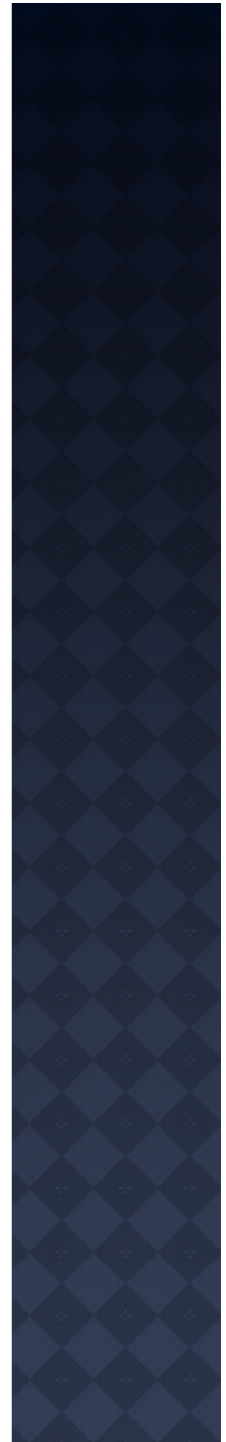


IC50 of Chemo Drug vs Albumin P10

nm	SKOV3	OVCAR3	CFPAC1	T407D
	Ov	Ov	Pancreas	Breast
Existing Drug 130nm	18	18	100	100
Albumin P10	4.4	1.9	5	13

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THANK YOU

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