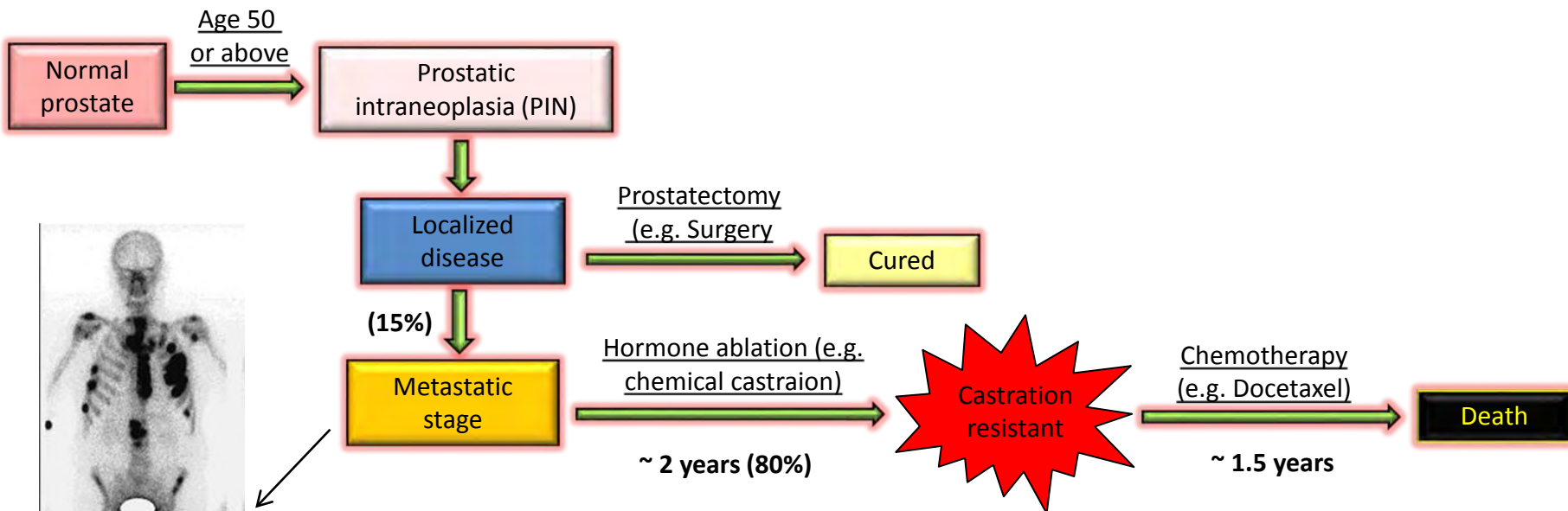


Dissecting the mechanism responsible for the anti-cancer stem cell properties of gamma-tocotrienol

Development and progression of prostate cancer



- Late onset (99.5% are diagnosed at age of 45 or older).
- Early stage with locally confined tumor
 - Prostatectomy produces a five-year survival rate of >90%
 - Around 15% of patients will have disease relapse
- When diagnosed at advanced stage
 - Hormone ablation produces immediate tumor regression
 - Most of patients will progress to castration resistant (terminal) stage
 - Currently incurable (Docetaxel, the best ever chemodrug, can only extend survival for ~ 2 months)

Roxburgh et al., *The Internet Journal of Urology*, 2007

Laboratory of Cancer Therapeutic Development



Royal Brisbane and Woman Hospital

Clinical Sample



Clinical Sample



Princess Alexandra Hospital

Clinical Trial

Clinical Trial

Basic Research

Basic Research



Translation Research Institute

Anti-cancer drug screening with >200,000 natural product extracts



Institute of Health and Biomedical Innovation

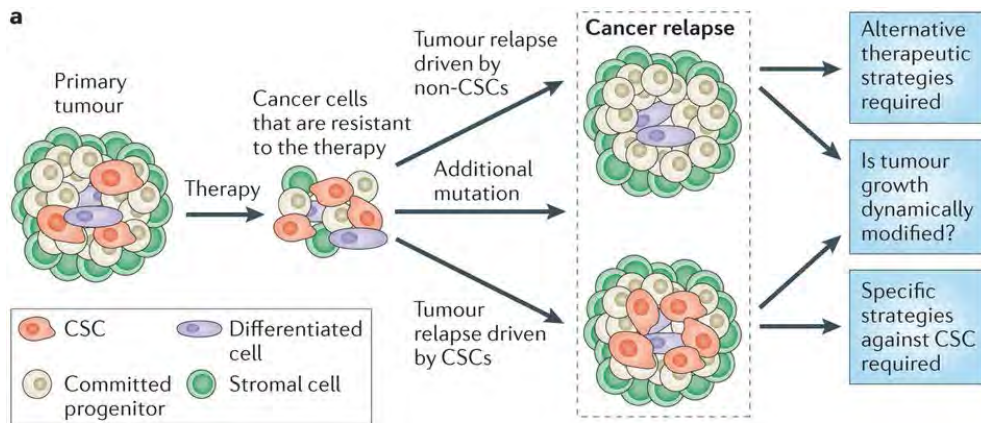


Queensland Institute of Medical Research

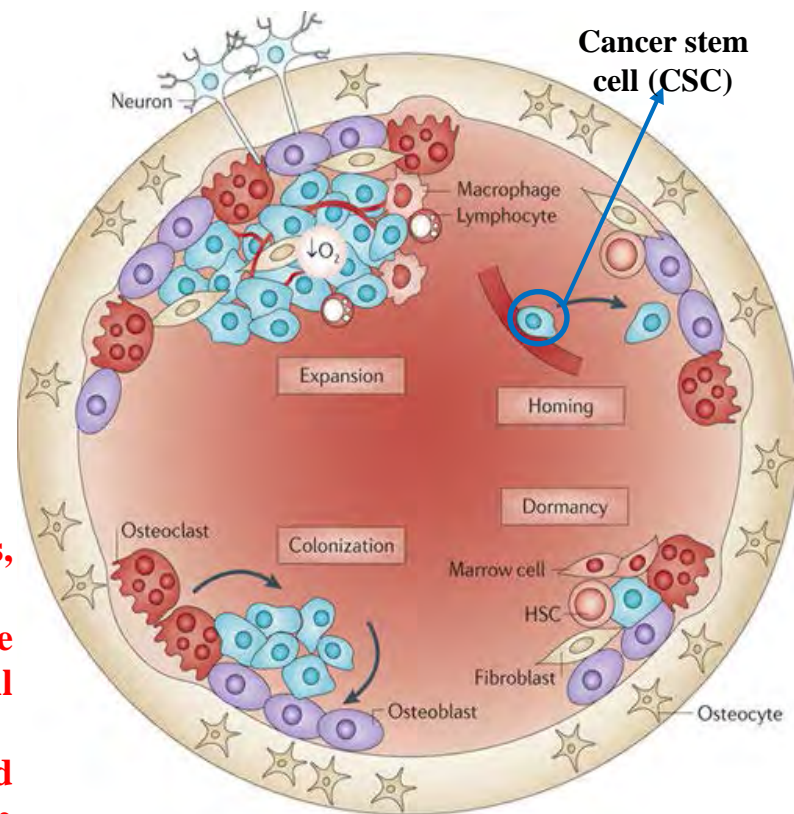


Eskitis Institute

Current Research Programme: Targeting cancer stem cells (CSCs) and their niche



Benjamin B et al.
Nature Reviews Cancer 2013



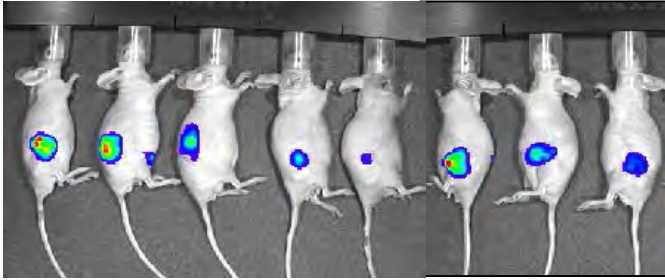
Modified from Weillbaecher KN
et al. *Nature Reviews Cancer* 2011

Creating a favourable environment:

- **Highly tumorigenic and resistant to conventional treatments**
- **Actively socializing with the neighbours such as osteoblasts, adipocytes or tumor-associated macrophage**
- **Blocking out “enemies” through inhibiting lymphocyte infiltration, suppressing T-cell activation or accelerating T-cell exhaustion**
- **Identifying the signalling pathways that help CSCs to grow and manipulates the surrounding microenvironment may open up new opportunities for novel therapeutic development**

Potent anti-cancer stem cell properties of T3

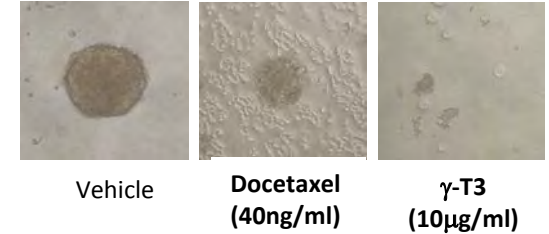
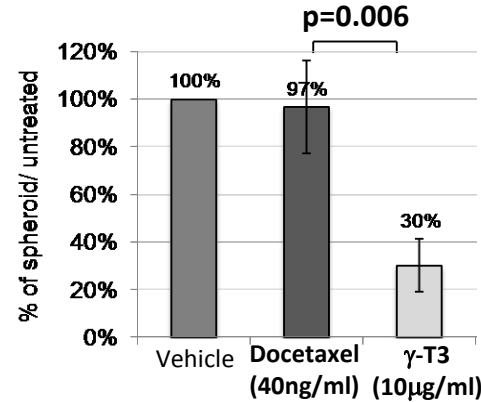
Mice injected with vehicle pretreated cancer cells



Mice injected with γ -T3 pretreated cancer cells



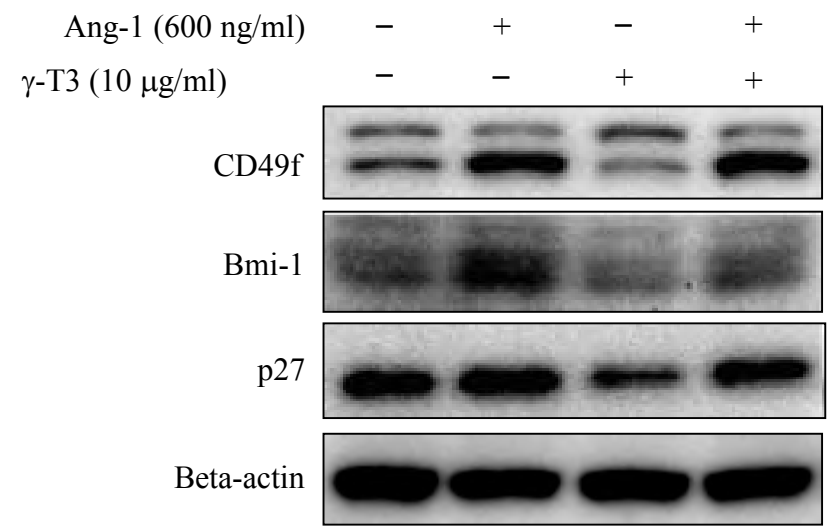
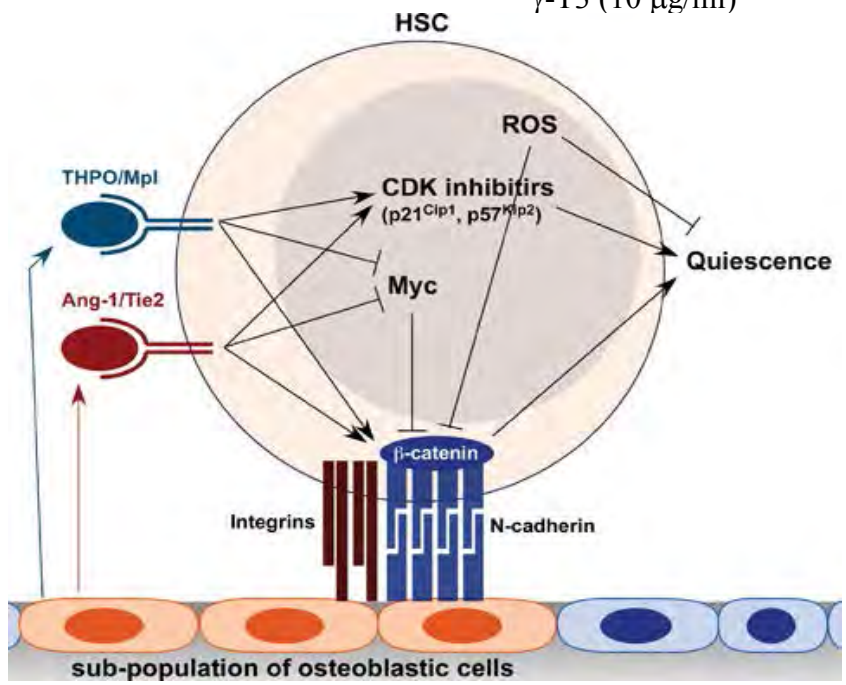
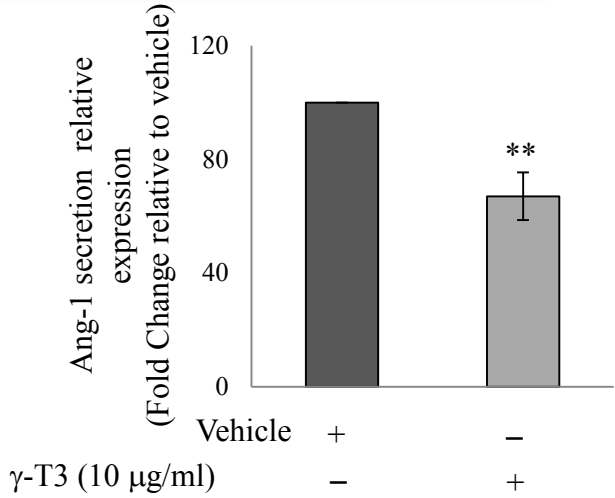
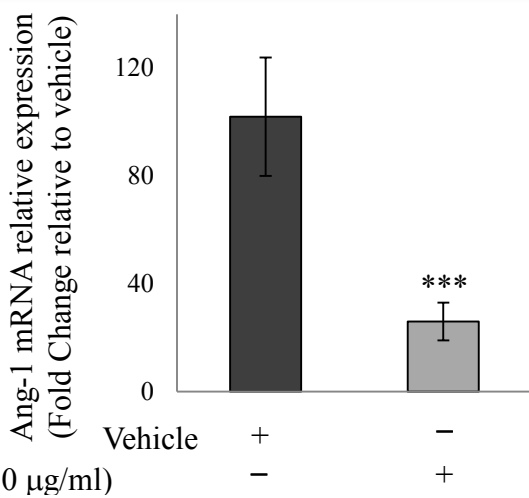
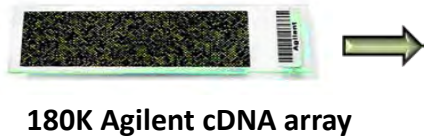
Mice orally fed with γ -T3



	Group 1	Group 2	Group 3
Total no.of mice	8	8	8
Mice with visible tumour at week 4	8	3	2
Percentage of tumour initiation	100%	38%	25%
Average size of tumors (mm ³)	421± 31	<25	<25

Luk et al 2010. *Int J Cancer*.
Ling et al 2011. *Carcinogenesis*.
12/599486: Patent approved.

Identification of Ang-1 as a novel T3-downstream target



Arai F et al. Stembook.

Ang-1/Tie-2 promotes prostate tumor bone metastasis



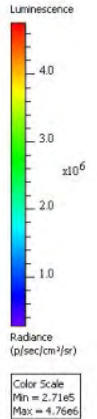
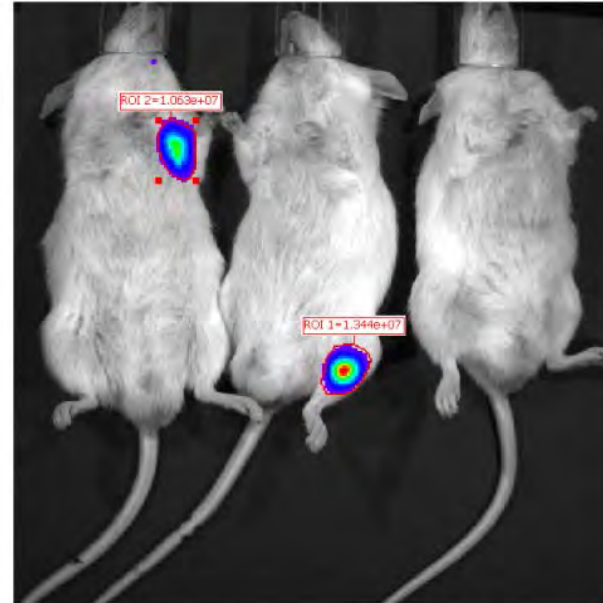
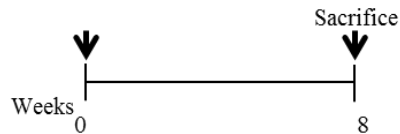
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PC-3 (Tie-2 ⁻) cells: n=8

PC-3 (Tie-2 ⁺) cells: n=8



3,000 cells per mice

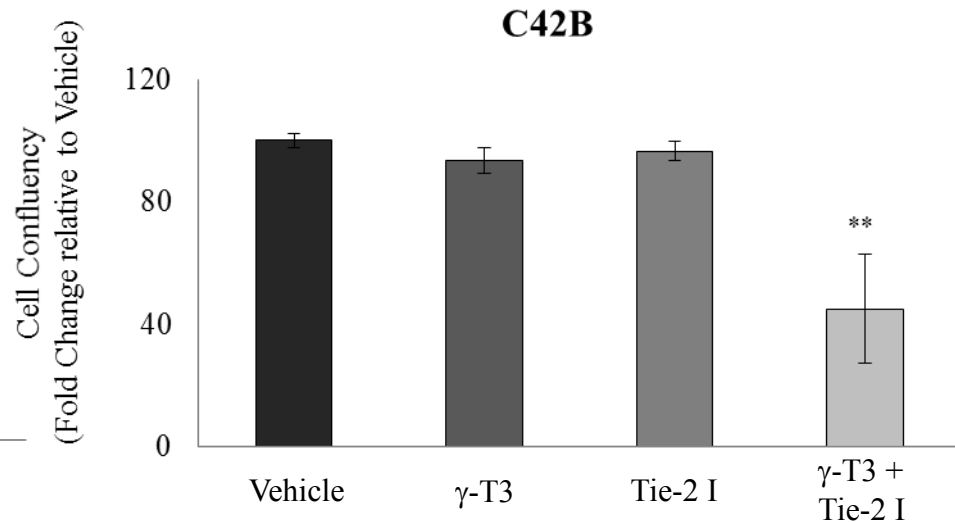
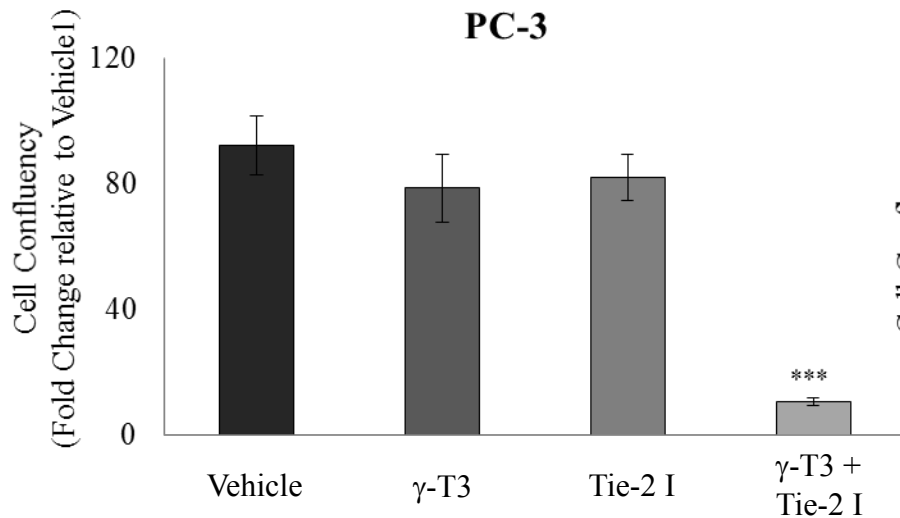
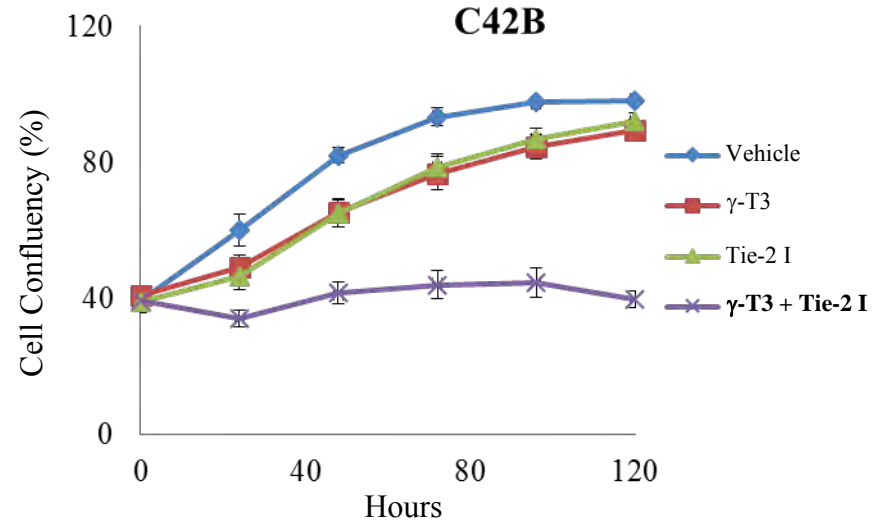
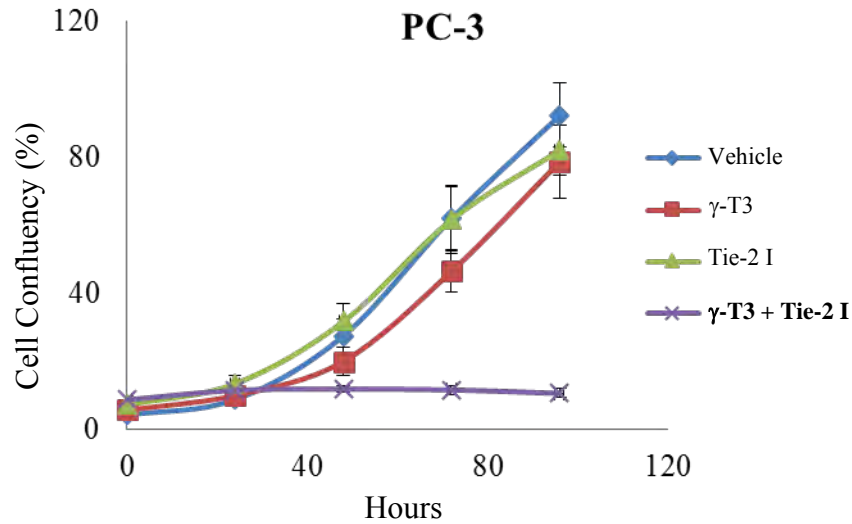


Incidence of metastasis

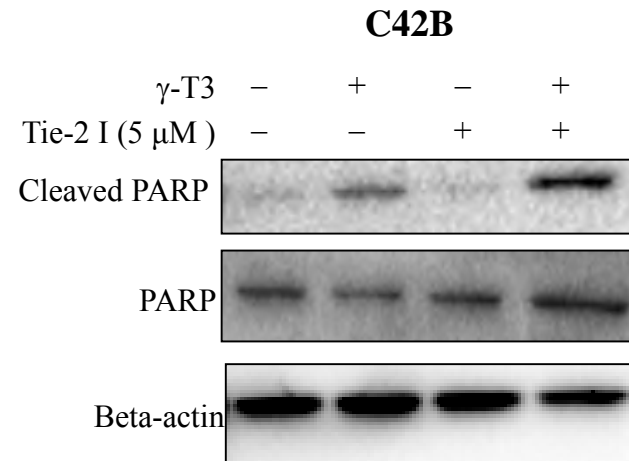
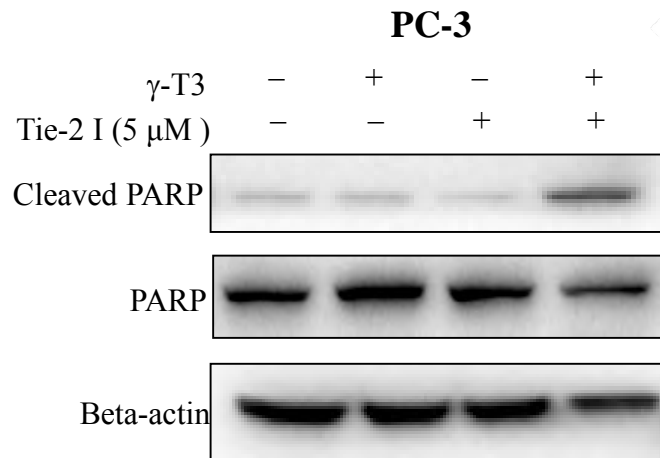
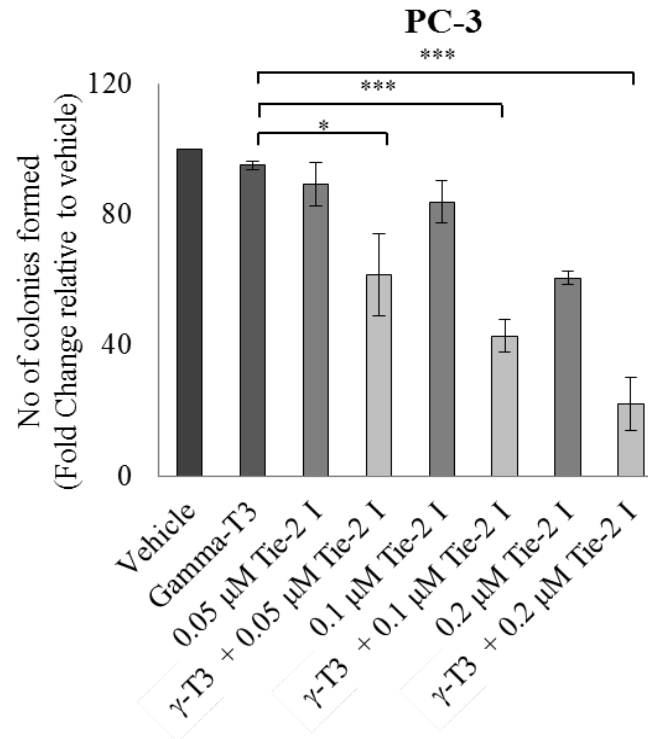
Cells injected (3,000 cells per mouse)	No. of mice	Bone metastasis	Soft tissue metastasis
Tie-2 ^{Low}	n=8	0	0
Tie-2^{High}	n=8	2	1

P value < 0.05

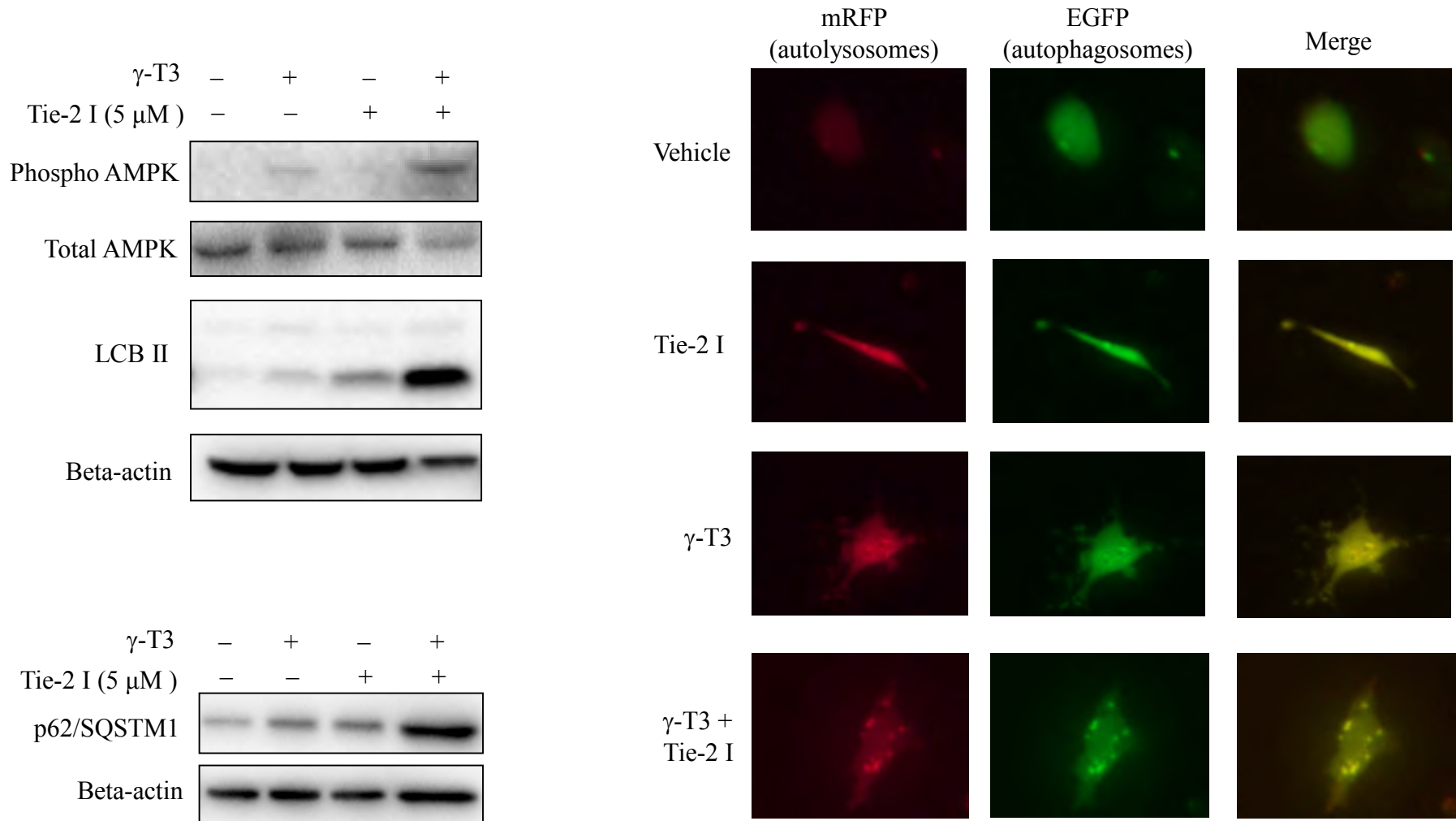
T3 synergize the anti-cancer effect of Tie-2 inhibitor



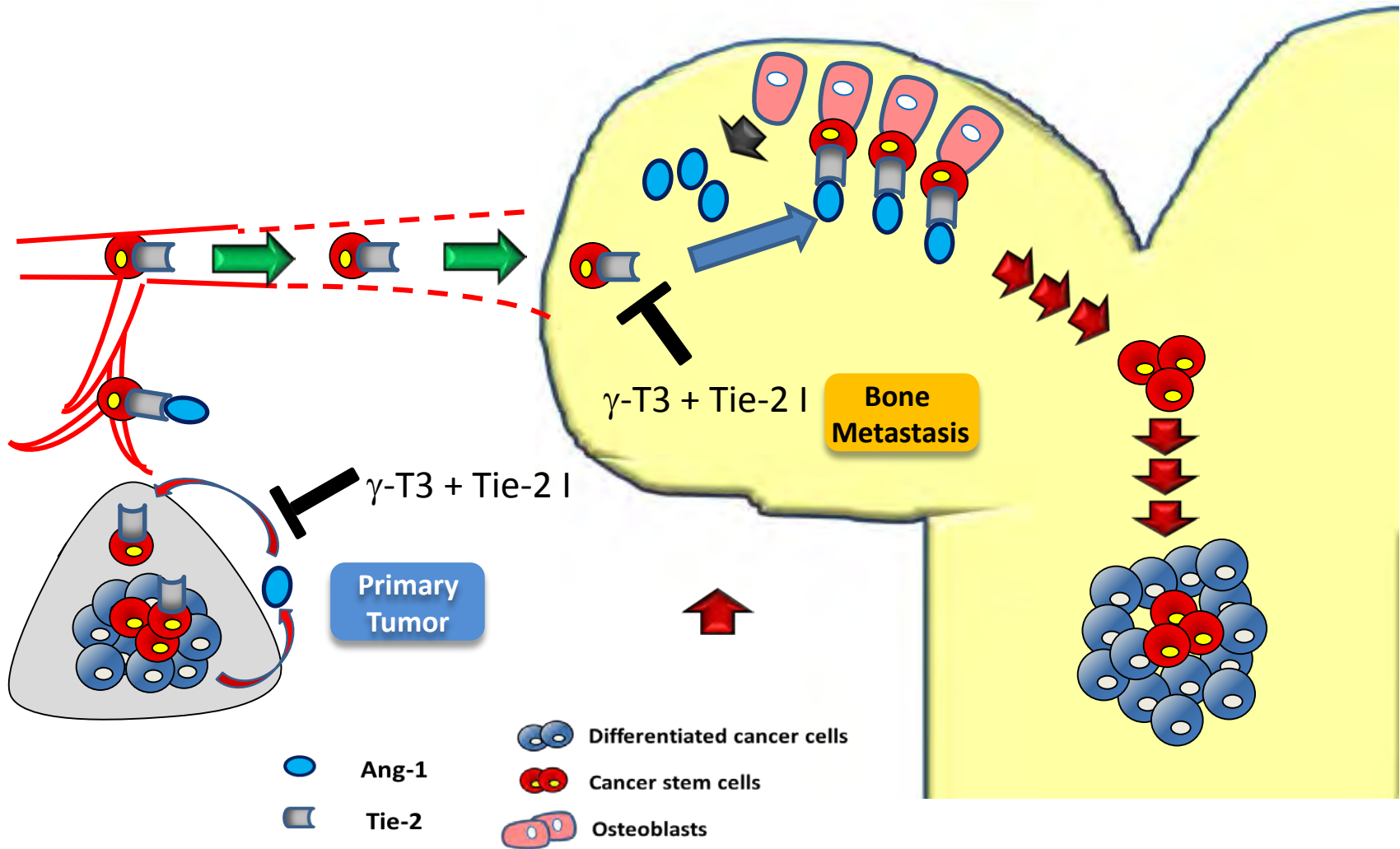
T3 synergize the anti-cancer effect of Tie-2 inhibitor



Tie-2 inhibitor promotes T3-induced autophagy



Therapeutic potential of T3 against metastatic prostate cancer



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Australian Government

National Health and Medical Research Council



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