Anti-NPY/PYY Antibody for the Treatment of Cancer

Garvan researchers have demonstrated that the neutralisation of NPY/PYY neuropeptides increases survival and reduces tumour burden in many cancer models.

- NPY/PYY knock-out mice survive lethal tumour challenge
- Novel mAb (5E12) effectively neutralizes NPY/PYY
- 5E12 treatment reduces tumour growth and increases survival in aggressive orthotopic models

Garvan researchers have found a link between neuropeptide Y (NPY) and the closely related peptide YY (PYY) and tumour growth. NPY and PYY belong to the neuropeptide Y family of peptides and receptors (Y1 – Y6) involved in a wide variety of biological processes including metabolism, angiogenesis and immunity. NPY & PYY signal through receptors NPY-R Y1, Y2 and Y5. Receptors Y1, Y2 & Y5 are expressed on immune cells and various tumours including neuroblastoma, Ewing sarcoma, pheochromocytoma, and many prostate and breast cancer cell lines.

NPY-/- PYY-/- double knockout mice survive lethal doses of B16 melanoma and LL2 lung carcinoma cells

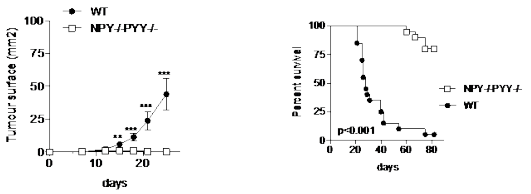


Figure 1. *Mice deficient in NPY and PYY injected with a lethal dose of melanoma cells (B16) display higher survival rates and reduced tumour growth.*

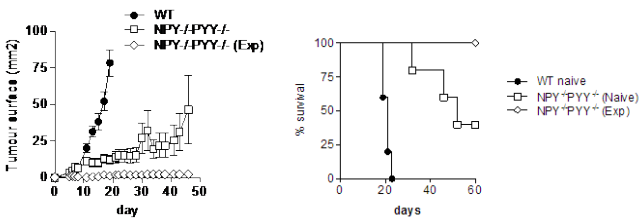
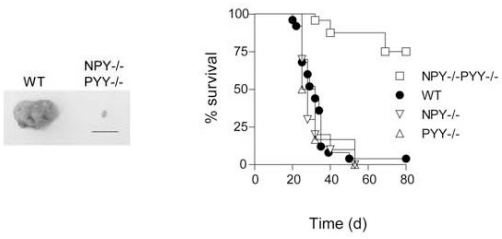


Figure 2.

Figure 2. *Induction of protective immunity. Mice re-challenged with B16 cells 100 days after initial dose completely reject tumours (in contrast to mice that had not previously been exposed to B16 cells).*



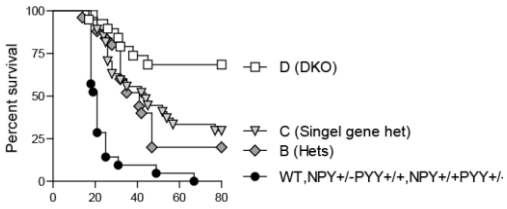


Figure 3. *Lack of NPY and PYY is required for higher survival rates and reduced tumour growth. Shown are mice after injection of a lethal dose of Lewis lung carcinoma (LL2) cells.*

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Mab 5E12 neutralises NPY/PYY activity with high affinity and specificity

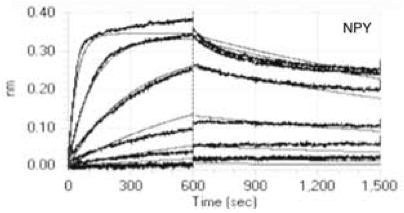

Figure 4. *5E12 binds to NPY and PYY with high affinity and specificity. It does not bind to other peptides (such as PP).*

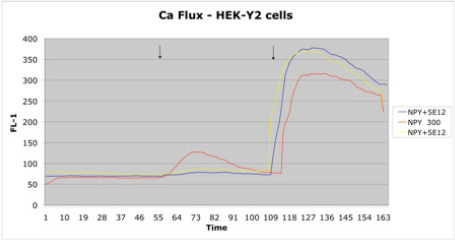

Figure 5. *5E12 inhibited NPY-induced calcium flux in HEK cells expressing NPY-Y2 receptor.*

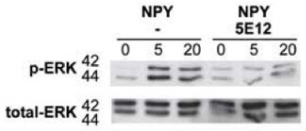

Figure 6. *5E12 neutralises NPY-induced ERK phos-phorylation.*

5E12 treatment reduces tumour growth and increases survival in animal models

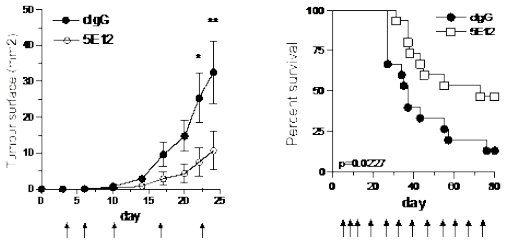

Figure 7. *5E12 treatment reduces tumour growth and increases survival in the LL2 lung cancer model of disease (therapeutic).*

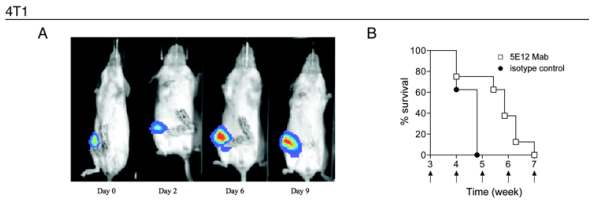

Figure 8. *5E12 treatment increases survival in the aggressive orthotopic 4T1 model of basal breast cancer. Growth is monitored by whole animal imaging and treatment is only initiated once detectable tumours are established.*

Intellectual Property: PCT/AU2012/001464

Opportunity: Licensing or Collaborative Research

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