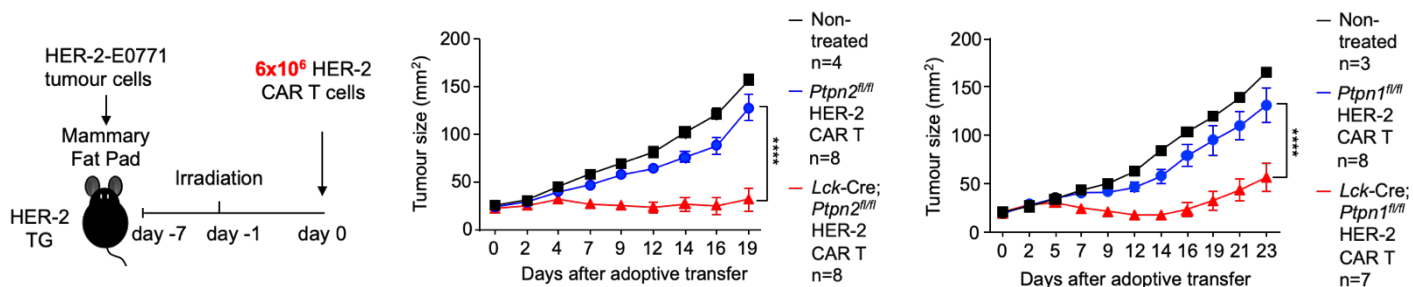


# Novel intracellular immune checkpoints for T cell therapy

## THERAPEUTIC: Cancer Immunotherapy

Product Type	CD8 T cell-based immunotherapy (e.g. CAR T cells, TCR T cells, etc)
Indication	Cancer, Infectious Disease
Target	Phosphatases PTPN2 and PTPN1 (PTP1B)
Development Stage	Pre-clinical
Brief Description & Differentiation	<p>We have identified two targets in T cells, PTPN2 and PTPN1, which are critical in controlling T cell activation and function. Deletion of either PTPN2 or PTPN1 drastically improves the ability of CD8 T cells to inhibit solid tumour growth. Strikingly, inhibiting both PTPN2 and PTPN1 in CAR T cells leads to the complete eradication of solid tumours in an orthotopic syngeneic mouse model of breast cancer, even when very low numbers of CAR T cells are used. In addition, our pre-clinical data shows targeting either phosphatase in T cells is safe, establishes long-lived memory and does not worsen inflammatory responses.</p> <p>Apart from its potency and safety, targeting PTPN2 and/or PTPN1 in T cell immunotherapy offers the following benefits:</p> <ul style="list-style-type: none"> <li>• A lower dose of T cell infusion is needed, due to increased T cell function and proliferation <i>in vivo</i></li> <li>• Enhanced T cell infiltration in solid tumours</li> <li>• Overcomes T cell exhaustion</li> <li>• Advantageous over targeting traditional surface immune checkpoints</li> <li>• Flexible choice between gene deletion and small molecule inhibition</li> </ul>
Research Team	Professor Tony Tiganis (Monash University & Peter MacCallum Cancer Centre)
Intellectual Property	<ul style="list-style-type: none"> <li>• PTPN2: PCT/AU2015/050318, national phase patent applications filed for US, EP, JP and AU.</li> <li>• PTP1B: PCT/AU2019/050565, PCT patent application filed.</li> <li>• PTPN2 + PTPN1 combination: Australian provisional patent application filed, covering inhibiting both PTPN2 and PTPN1 to enhance T cell activity</li> </ul>
Key Publications	Wiede <i>et al.</i> , PTPN2 phosphatase deletion in T cells promotes anti-tumour immunity and CAR T-cell efficacy in solid tumours. <i>EMBO J</i> (2020) 39:e103637

### ➤ Key Data



### ***PTPN2- or PTPN1-deficiency enhances CAR T cell responses to solid tumours in vivo.***

HER-2-E0771 mammary tumour cells ( $2 \times 10^5$ ) were injected into the fourth inguinal mammary fat pads of female HER-2 TG mice. Seven days after tumour injection HER-2 TG mice received total body irradiation (4 Gy) followed by the adoptive transfer of  $6 \times 10^6$  HER-2 CAR T cells generated from *Ptpn2*<sup>fl/fl</sup> versus *Lck-Cre; Ptpn2*<sup>fl/fl</sup> splenocytes. HER-2 mice were monitored for tumour growth. Significance was determined using 2-way ANOVA Test; \*\*\*\*p<0.0001.