# Novel intracellular immune checkpoints for T cell therapy

**THERAPEUTIC:** Cancer Immunotherapy

<table>
<thead>
<tr>
<th>Product Type</th>
<th>CD8 T cell-based immunotherapy (e.g. CAR T cells, TCR T cells, etc)</th>
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</thead>
<tbody>
<tr>
<td>Indication</td>
<td>Cancer, Infectious Disease</td>
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<tr>
<td>Target</td>
<td>Phosphatases PTPN2 and PTPN1 (PTP1B)</td>
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<tr>
<td>Development Stage</td>
<td>Pre-clinical</td>
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**Brief Description & Differentiation**

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. Apart from its potency and safety, targeting PTPN2 and/or PTPN1 in T cell immunotherapy offers the following benefits:

- A lower dose of T cell infusion is needed, due to increased T cell function and proliferation *in vivo*
- Enhanced T cell infiltration in solid tumours
- Overcomes T cell exhaustion
- Advantageous over targeting traditional surface immune checkpoints
- Flexible choice between gene deletion and small molecule inhibition

**Research Team**

Professor Tony Tiganis (Monash University & Peter MacCallum Cancer Centre)

**Intellectual Property**

- PTP1B: PCT/AU2019/050565, PCT patent application filed.
- PTPN2 + PTPN1 combination: Australian provisional patent application filed, covering inhibiting both PTPN2 and PTPN1 to enhance T cell activity

**Key Publications**

Wiede et al., PTPN2 phosphatase deletion in T cells promotes anti-tumour immunity and CAR T-cell efficacy in solid tumours. *EMBO J* (2020) 39:e103637

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**Key Data**

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

HER-2-E0771 mammary tumour cells (2x10⁵) 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 6x10⁶ HER-2 CAR T cells generated from Ptpn2²ff versus Lck-Cre;Ptpn2²ff splenocytes. HER-2 mice were monitored for tumour growth. Significance was determined using 2-way ANOVA Test; ***p<0.0001.*