220 Rethinking CD52: a therapy for autoimmune disease

Asset Overview

Product Type	Peptide
Indication	Metabolic Diseases, Infectious diseases
Current Stage	Preclinical
Target(MoA)	CD52 inhibitor
Brief Description	CD52 is a small GPI-anchored glycopeptide expressed on leukocytes, and up-regulated and shed by activated T cells. CD52 suppresses T cell function by binding the Siglec-10 receptor and also suppresses the innate immune response. Administration of soluble hCD52-Fc reduces incidence of diabetes and sepsis in pre-clinical models, with no demonstrable adverse effects. Ongoing studies characterizing key co-factors, CD52 glycosylation structure-function may yield new IP.
Organization	Walter and Eliza Hall Institute of Medical Research

Differentiation

□ **Immune inflammatory disease is an area of high unmet medical need**

- Immune inflammatory disorders are responsible for substantial morbidity and mortality, and affect at least 4% of the global population
- Current B cell therapies have limitations in their efficacy and side effects; and certain patient populations remain underserved
- Immune disorders mediated by activated T cells need to be addressed

□ **CD52-Fc exerts a dual mechanism of action targeted to activated T cells and HMGB1**

- Soluble CD52 acts on activated T cells and other immune cells by mimicking a natural physiological mechanism of immune homeostasis, thus likely to have fewer
- CD52-Fc inhibits T-cell activation by suppressing TCR signaling to inhibit T cell proliferation and cytokine secretion
- CD52-Fc bound to HMGB1 suppresses HMGB1 pro-inflammatory activity

□ **Opportunities for partnership**

- Unique MOA: sCD52-Fc functionally targets overactivated T cells, neutralizes HMGB1, and suppresses innate responses
- Extensive patent protection (WO2014075125, WO2013071355)
- A world-leading understanding of CD52 biology and unique pre-clinical models

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Key Data

CD52-Fc directly suppresses T-cell proliferation and effector function

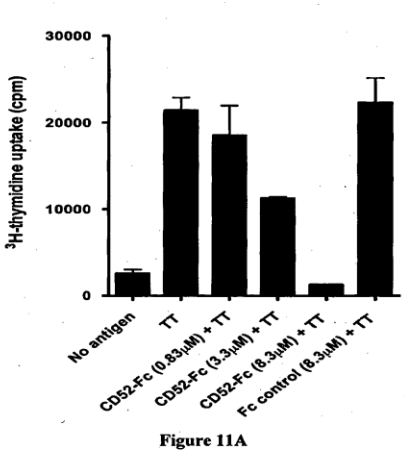

Figure 11A

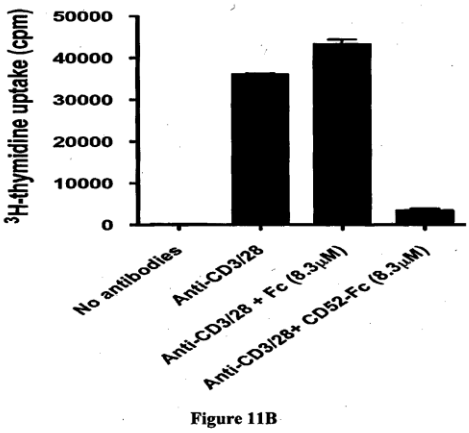

Figure 11B

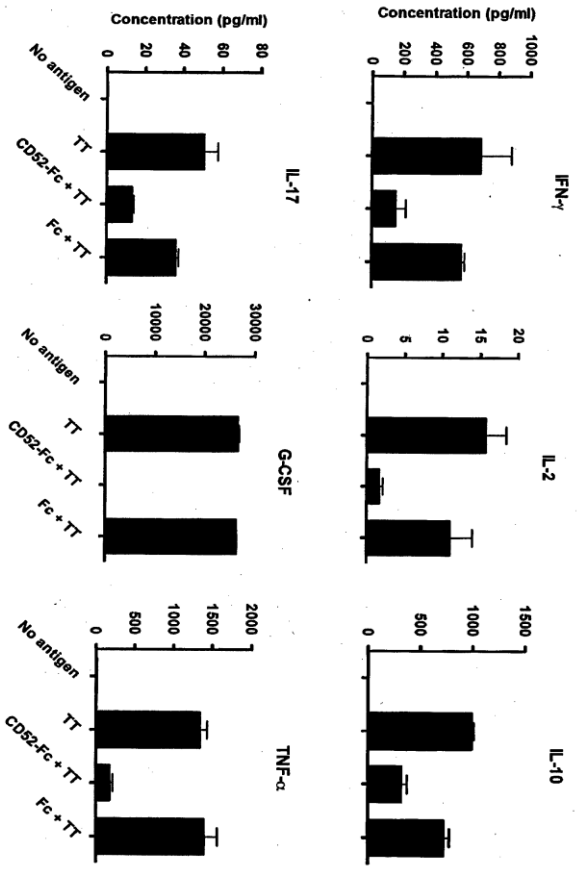

Figure 11C

Suppression of T-cell proliferation by recombinant CD52-Fc. PBMCs (200,000) were cultured with TT for 7 days (A) and purified CD4+ T-cells (20,000) with anti-CD3 (100 ng/ml) and anti-CD28 (200 ng/ml) antibody for 48 hrs (B), with 4 times the number of irradiated PBMCs in 200μl round bottom wells, in the presence of recombinant CD52-Fc or Fc protein control protein at the indicated concentrations. 3H-thymidine uptake was measured over the final 16 hrs of incubation. Results (mean±sem of triplicates) are representative of six independent experiments. (C) Suppression of cytokine secretion by recombinant CD52-Fc. Media from PBMCs activated with TT in (C) ± 3.3 μM CD52-Fc or Fc proteins were sampled after 48 hrs incubation and assayed for cytokines by multiplex bead array.

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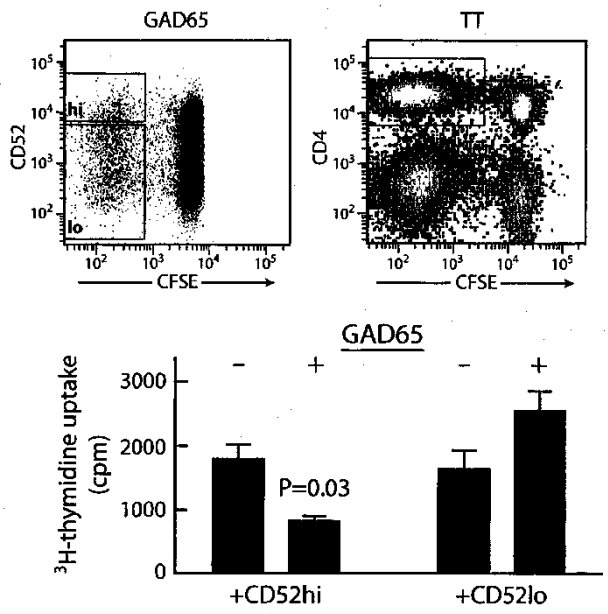
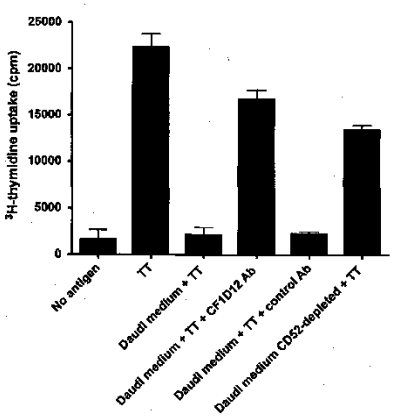
CD52 is a marker of antigen-activated blood CD4+ T-cells with suppressor function



Proliferation of tetanus toxoid (TT)-stimulated, FACS-sorted CD4+ T-cells re-activated with TT in the presence of GAD65-activated and sorted CD52hi or CD52lo CD4+ cells.

CD52 produced from Daudi cells directly suppresses T-cell proliferation and effector function.



Suppression of T-cell proliferation by Daudi cell conditioned medium. PBMCs (200,000 cells) were cultured for 7 days in IMDM containing 20% Daudi cell conditioned medium with TT and either anti-CD52 (CF1D12) or isotype control antibody (10 μg/mL). Results (mearttsem) are representative of three independent experiments.

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Intellectual Property

Patent No.	PCT/AU2012/001411 PCT/AU2013/000292
Application Date	2012.11.15 2013.03.25
Status	Registered
Country	US, EP, JP, CN, KR, AU, SG, RU, MX, HK, CA, BR

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