THE UNIVERSITY OF MELBOURNE

Research, Innovation & Commercialisation

CRICOS 00116K

Opportunity

To accelerate the development of this innovation, through licensing or direct investment, contact

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New therapeutics for autoimmune diseases

Novel therapeutics with reduced side effects for systemic lupus erythematosus (SLE)

Clinical Need

- Current approved therapeutics for SLE result in loss of B-cells and have profound side effect profiles. Many therapeutics in late clinical stage development also suffer from B-cell depletion, broad cytokine inhibitions resulting in major side-effects. This impairs the body's defence to infections and cancer. There is unmet clinical need to develop novel therapeutics without depleting beneficial B-cells.

The Technology

- We have identified and validated a novel way to treat SLE. Using our unique targeting approach we can selectively inhibit a highly inflammatory component of B-cell activating factor (BAFF) which is differential to the BAFF targeting approaches that are currently in the market or in development.

Technology Status

- We have identified and validated novel allosteric site on BAFF for development of new therapeutics. We have developed a proprietary cyclic peptide and have identified a small molecule compound with affinity in low micromolar range. Both cyclic peptide and a small molecule hit have been validated in disease animal model compared to standard approved therapeutics for efficacy and reduced side effects.

To find out more about our licensing opportunities, scan this QR code

Market Need

Lupus erythematosus (SLE) is a debilitating and chronic autoimmune disease affecting >5 million people worldwide, predominantly women. By 2025 annual drug sales for the SLE market are expected to reach USD$3B.

State-of-the-art treatments include biologics Belimumab (BAFF inhibitor) and Anifrolumab (type I interferon receptor inhibitor). Unfortunately, the efficacy rates are modest and Belimumab depletes beneficial B cells, greatly weakening the immune system and increasing risk of infections. Additionally, high annual treatment costs limit Belimumab's and Anifrolumab's use. Therefore, the mainstay of SLE therapeutic options is delivered by cheaper off-label therapies (eg. anti-malarials) and immunosuppressive steroid treatments that possess undesirable safety profiles, particularly with long-term use. Another factor that is impacting the health of patients is the absence of a reliable biomarker to assess disease severity.

Key Proof-of-Concept Validation Data

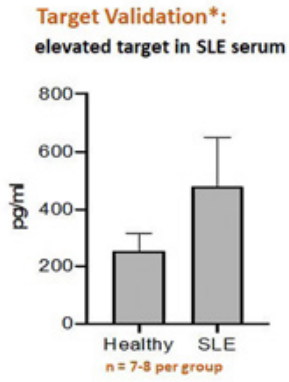

*Figure 1. Target validation. *More target validation data has been generated (confidential information).*

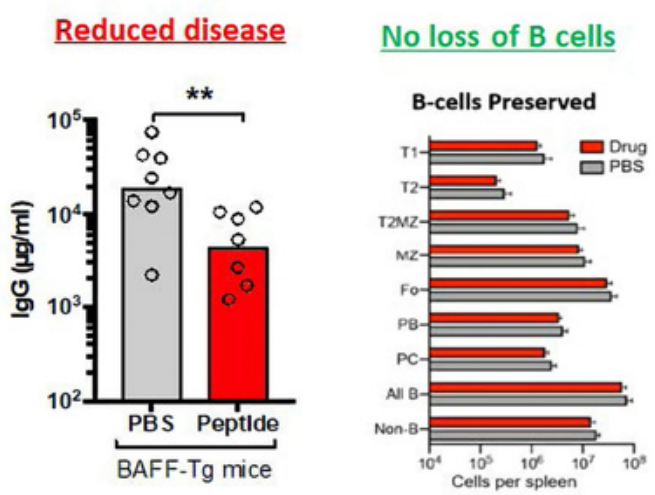

Figure 2. Proof-of-concept data from the in vivo experiment using lupus mice: cyclic peptide reduces disease (measured as IgG concentration in cellular assay, on the left) without detrimental impact on the immune system (on the right).

Solution

The University of Melbourne team has identified a new targeting approach (confidential know-how) associated with the BAFF protein which was under-appreciated in previous anti- BAFF strategies. In a key proof-of-concept experiment, University of Melbourne researchers successfully utilised a novel cyclic peptide to specifically inhibit the identified pathway. The in vivo mechanism of action for the cyclic peptide was further validated using the BAFF-overexpressing SLE- prone mice. The novel treatment showed markedly reduced autoimmunity without compromising B-cell survival and thus represents a critical shift in the current paradigm.

The research team has now progressed from cyclic peptides to drug-like small molecules and has identified hit compounds with affinity in uM range. A biomarker to stratify patients for the disease severity and the pathogenic mechanism has also been identified. This biomarker will enable the most relevant subgroup of patients (~60%) to be targeted in clinical trials to improve response rates.

Technology and IP Status

The advantages of the University of Melbourne novel targeting mechanism for the SLE and the proprietary technology are:

- novel differentiated mechanism of action allowing for the best-in-class anti-SLE therapeutic;
- not compromising B-cell survival and thus alleviating side effects of the existing therapies, such as immunity suppression;
- cyclic peptide or small molecule approach;
- companion diagnostic for patient stratification.

Tech name and number	2021-094 - Novel BAFF inhibitors for stopping autoimmunity in patients with SLE
Research Leads	Prof. Michael Parker, Dr. Tracy Nero
Keywords	Lupus, Sle, Autoimmune, Baff, Small Molecule, Cyclic Peptide