Biomarkers of regulatory T cells and disease risk

- Regulatory T cells (Tregs) play a pivotal role in maintaining immune homeostasis
- Potential use as biomarkers of immune status in autoimmune and inflammatory diseases and cancer

Scientific team

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The opportunity

Autoimmune diseases are one of the most important health issues in the world. Over 80 autoimmune diseases have been described, and there are estimated to be over 23 million sufferers in the USA alone. Examples of autoimmune diseases include type 1 diabetes, rheumatoid arthritis and multiple sclerosis.

Regulatory T cells (Tregs) are critical in the maintenance of immune cell homeostasis and play a pivotal role in preventing autoimmune diseases. Tregs maintain order in the immune system by enforcing suppression of other immune cells (e.g. effector T cells). When Tregs are unable to provide this protection, autoimmune diseases can develop.

Current therapies for autoimmune diseases: (i) are varied depending on the stage of disease; (ii) relieve only some of the symptoms; and (iii) can have serious side effects particularly if used long term (due to their non-specific immunosuppressive function).

Early or pre-symptomatic detection of an increased risk for immune system dysfunction as assessed by Treg activity potentially provides a powerful tool to facilitate clinical management of autoimmune diseases.

Researchers at the Walter and Eliza Hall Institute and the Murdoch Childrens Research Institute have identified a novel methylation signature of Tregs, which may serve as biomarkers of autoimmune diseases.

The technology

To identify distinguishing features of Tregs, one focus of the scientific team was the epigenetic landscape.

Global DNA methylation profiling was conducted, seeking to identify differentially methylated CpGs between human naïve Tregs and Naïve T cells, before and after activation in vitro.

The researchers detected 2,315 individual differentially methylated probes comprising 127 regions of differential methylation. To validate these findings, the locus of TIGIT, a known suppressive receptor expressed by Tregs, was examined. In general, it is thought that a reciprocal relationship exists between methylation and gene expression. The scientific team discovered that the TIGIT locus was: (i) one of the most significantly differentially methylated regions; and (ii) was hypomethylated.

This suggests the 2,315 differentially methylated CpGs and the nearby regions, as well as the 127 regions of differential methylation can be used as biomarkers of Treg activity.

In order to capture this set of differentially methylated genes in a more convenient and clinically-translatable manner, researchers have developed and validated a multiplex PCR-based method.

Applications

The present technology can be applied in diagnostic, prognostic, agent-screening and therapeutic protocols, as well as reporting systems:

- Method of identifying the level of T-regulatory cell activity in a test biological sample comprising immune cells
- Method of determining whether or not a subject has or is at risk of developing an autoimmune condition
- Method of treatment or prophylaxis of a subject
- Method of screening for an agent which modulates immune cell function

Opportunity for partnership

The Walter and Eliza Hall Institute and Murdoch Childrens Research Institute are seeking:

- a partner to co-invest in the development of a diagnostic assay; and/or
- to out-license intellectual property associated with this technology

Intellectual property

Intellectual property is protected by a PCT application (PCT/AU2014/000730) that protects assays identifying the level of immune cell activity in a biological sample, based upon methylation profiles of a pre-selected genetic locus/loci/regions.
Key publications


Walter and Eliza Hall Institute of Medical Research

The Walter and Eliza Hall Institute is Australia’s longest-serving medical research institute, celebrating its centenary in 2015. Our multidisciplinary research teams are focused on solving complex biological questions, and effectively linking laboratory research to the clinic. With a strong collaborative focus, the institute is a founding member of Biomedical Research Victoria, Cancer Trials Australia, BioGrid Australia and the Victorian Comprehensive Cancer Centre.

Research

- 750 research staff trained nationally and internationally
- 81 research laboratories

The institute’s scientists are driving innovative programs aimed at understanding, preventing and treating:

- Cancer: especially leukaemia, lymphoma, breast cancer, bowel cancer, ovarian cancer, lung cancer, pancreatic cancer and stomach cancer
- Immune disorders: including diabetes, rheumatoid arthritis, coeliac disease, rheumatic fever and other inflammatory conditions
- Infectious diseases: focusing on malaria, HIV, tuberculosis and hepatitis viruses

Research outcomes

- More than 300 publications annually
- 74% of publications in biomedical journals with an impact factor >15
- 34% of publications in the top 10% of their field

Strong translational focus

- Discovery pipeline fed by more than 300 projects
- Institute research is the basis of more than 100 clinical trials, and has resulted in 4 start-up companies and 5 spin-out companies
- Institute research has benefited more than 20 million people worldwide
- More than 470 collaborative partners across 120 cities in 43 countries

Opportunities for partnership

- Therapeutics
- Biomarkers and diagnostics
- Unique pre-clinical models
- Access to platform technologies including
  - bioinformatics
  - clinical translation centre
  - drug discovery including high-throughput screening and medicinal chemistry
  - systems biology including proteomics

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