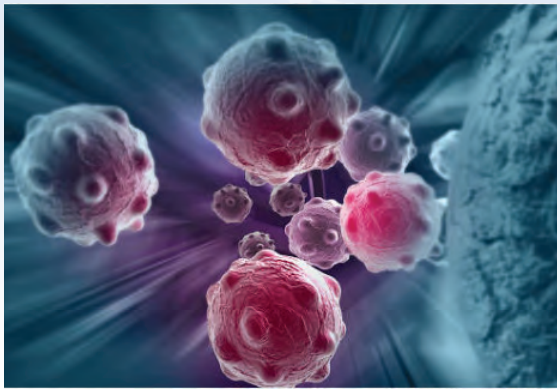
CONNECTGENE Genomics Oncology

Unlock the Power of Genomics

TCR-BETA ASSAY



What are T-Cells?

T-cells are part of our body's immune system and play a key role in enabling the immune system to recognise foreign particles they come into contact with, allowing our bodies to fight foreign invaders such as bacteria and viruses.

How do T-Cells detect cancer?

T-cells can recognise foreign particles through their T-cell receptors (TCRs) which have variable ends enabling the recognition of millions of antigens (foreign molecules). If a T-cell is activated, by coming into contact with an antigen that matches its variable region, this will trigger clonal expansion - a process generating many more copies of that specific T-cell (clone) to be able to fight off the foreign particle. The sum of all the different TCRs by the T-cells of one individual is termed the TCR repertoire. [1]

It is often difficult for the immune system to detect cancer, as cancer cells are abnormal versions of our own normal cells, and our body has mechanisms in place to stop our immune system attacking our own cells. Tumour neoantigens (new molecules generated by tumour cells) may activate T-cells triggering an immune response. Tumours with more mutations (a high mutational load) are more likely to have a neoantigen that will stimulate the T-cell.

Using immunotherapies to remove checkpoints that prevent recognition of cancer cells by T-cells can further assist the immune system to identify cancer cells and remove them.

What is the TCR-Beta Assay?

Our TCR-Beta Assay utilises next generation sequencing technologies to look at all the different TCRs in the patient's representative sample (TCR repertoire) assessing diversity and clonal expansion and allows for identification of allele-specific polymorphisms. This allows doctors to see how your immune system is recognising and responding to the cancer.

The extreme diversity of the TCR repertoire requires specialized methods to characterize the TCR repertoire in-depth. [1] Currently, next generation sequencing based technologies are the most widely employed for the high-throughput analysis of the immune cell repertoire. [1-5]

How can I use the results of the TCR-Beta Assay?

The TCR-Beta assay can be used to assess if the immune system is recognising the tumour and generating more cells directed at fighting the tumour. Clonal convergence can be used along with other indicators of the T-cell repertoire such as diversity and evenness to predict the likely response rate to immunotherapies. High TCR-Beta clonal convergence and low evenness indicates there are multiple clones targeting the same antigen and suggest a better response to immune checkpoint inhibitors. Low TCR-Beta clonal convergence and greater diversity indicates there are few clones targeting the same antigen and is associated with a low response to immune checkpoint inhibitors. [7]

Tumour mutational Load is also associated with a higher response to immune checkpoint inhibitors, however the T-cell repertoire is a more direct measure of the immune systems actual response to the cancer and may enable a more informative evaluation of the response to immune-oncology agents. A strong association has been observed between T-cell diversity and tumour mutation load. [4]

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Why is it important to have genomic testing?

Our TCR-Beta assay has been designed in response to the need to determine if treatment utilising immune checkpoint inhibitors is likely to be of benefit in your particular clinical circumstances. For some cancer types, the immunotherapy drugs are not listed on the Australian Pharmaceutical Benefits Scheme, and they would incur a large out-of-pocket expense. We consider this test an important step in gaining as much information as possible prior to making a decision on whether to progress with this particular group of drugs.

If immune checkpoint therapy is being considered, ctDNA tracking and blood TCR-Beta testing is recommended at 0, 4 and 8 weeks as a predictor of response to immunotherapy. [6] Testing is performed prior to any treatment to establish a baseline and then again and 4 and 8 weeks into treatment to assess response. Patients who respond to therapy are more likely to clear or reduce ctDNA and will increase or sustain clonal expansions. [6,8]

By 4-8 weeks of treatment CG Genomics Oncology TCR-Beta assay, in combination with TML assay and ctDNA tracking, can give an indication of the efficacy of treatment and whether patients should continue with this particular therapy.

Investing in genomic testing, to obtain a complete diagnosis and to select appropriate therapy is a small investment compared with the money that may be wasted on ill-chosen therapies. Genomic testing provides a powerful diagnostic tool, and every patient with cancer deserves an accurate diagnosis.

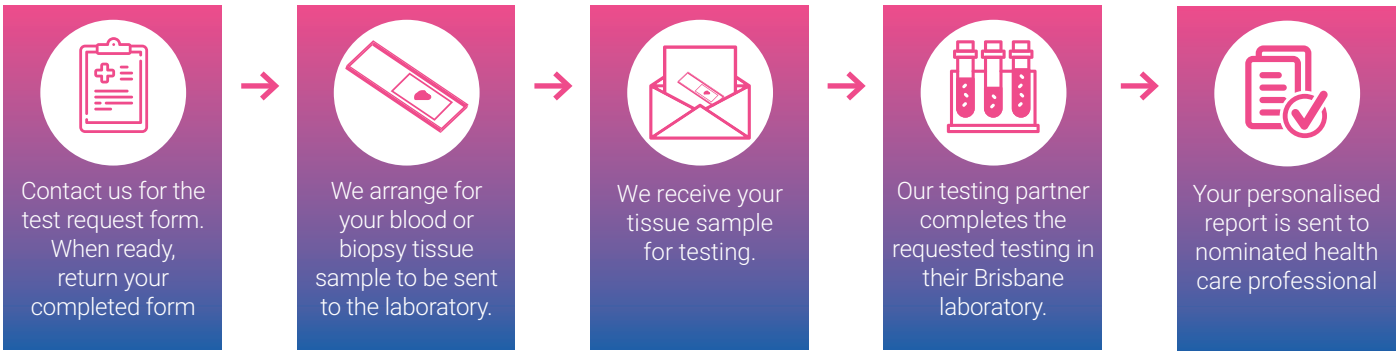
Sample Requirements

To perform this test we require a fresh blood sample. If immune checkpoint therapy is being considered, TCR-Beta testing is recommended at 0, 4 and 8 weeks as a predictor of response to immunotherapy. [6]

Technical Information

The assay uses next generation sequencing to measure T cell repertoire diversity, clonal expansion, and identify allele-specific polymorphisms. For medical practitioners seeking further technical information regarding the assay, please contact CG Genomics Oncology.

How to organise testing



References

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