



Cancer Research Wales aims to reduce the impact of cancer on the people of Wales through supporting world class cancer research and education. In recent years intense interest has focussed on the role of the immune system and ways to harness its power in order to eradicate cancer. With the ever increasing number of new therapies and treatment strategies (immuno-therapies) that target the immune system, we at CRW believe it will be important to:

- Enhance our knowledge of how cancers and the immune system interact.
- Gain a better understanding of when and how best to use cancer vaccines and other immuno-therapies in the treatment pathway.
- Discover reliable immune system biomarkers for clinical use in oncology.
- Rationally design improved immuno-therapies based upon novel scientific and research findings.



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The immune system consists of several specialised cell and tissue types, distributed throughout the body which co-operate to remove infected or damaged and diseased tissues including cancer cells. However, immune abnormalities are common hallmarks of most, if not all cancers. Cancer Research Wales (CRW) fund a number of immuno-oncology projects which aim to:

-  Determine the role and impact of regulatory immune cells (T-reg cells) in colon cancer progression.
-  Reveal processes that alter immune responses in patients with prostate cancer.
-  Understand how chemotherapy and radiotherapy alter immune responses in prostate cancer patients.
-  Examine the function and prognostic value of specific subsets of immune cells in Chronic Lymphoblastic Leukaemia.

Colon Cancer

Immuno-therapies such as vaccines are gaining acceptance as a viable treatment option for different malignancies. These newer therapies seek to harness the power of the immune system in order to aid the eradication of cancer cells. The full benefits of immuno-therapies are reliant upon a fully functional immune system that is capable of generating a robust immune response against cancerous cells. Pioneering projects funded by CRW are providing vital and much needed insights into the processes that control immune responses in various cancers. One such study has shown that the blood and tumours of some colon cancer patients harbour increased numbers of immuno-suppressive T-regulatory (T-reg) cells, which in line with their function, invoke immuno-suppression in and around the tumour. An ongoing CRW sponsored cancer vaccine trial in patients with inoperable colon cancer is combining the use of vaccines with chemotherapy agents (cyclophosphamide) that are shown to selectively eradicate the detrimental T-reg cell population. It is hoped that this treatment combination will better stimulate the immune system, resulting in greater tumour control.

Prostate Cancer

Scientists working at the CRW laboratories have discovered previously unrecognised benefits of radiotherapy to the immune system of prostate cancer patients. Treatment with radiotherapy stimulates key anti-tumour immune cells several weeks following initial therapy. Importantly, these findings reveal ideal windows of opportunity that can be exploited therapeutically to maximize the effects of cancer vaccines and other immune based therapies currently used for advanced prostate cancer (for more information please refer to the prostate cancer leaflet in this series).

Leukaemia

Chronic Lymphocytic Leukaemia (CLL) is the most common form of leukaemia in the UK. In the early stages of the

disease most patients remain well for long periods. It can frequently take over 12 years for people with early stage CLL to develop a level of advanced disease that will require treatment. However, not an insignificant number of patients have a more rapid onset of symptoms that will require therapy sooner.

CRW funded research has found that the ratio of CD4 and CD8, two molecules found on the surface of types of white blood cells, known as T cells, can accurately identify CLL patients that have a shorter time to first treatment. A higher proportion of CD8 cells relative to CD4 T cells (termed an inverted ratio), pinpoint patients who require therapy on average 3-5 years earlier than those patients with normal ratios. The CD8 positive T cells of patients with inverted ratios display markers of 'exhaustion'. Essentially, the very cells responsible for keeping cancerous blood cells in check had literally become 'worn out', leading to loss of immunological control of the leukaemia. Further studies of the prognostic value of this unique immune profile in patients undergoing conventional chemotherapy for CLL are ongoing. It is hoped this work will identify markers of treatment resistance, allowing clinicians to tailor therapies to better meet individual needs.

