Global team targets new cancer therapies
By Anne Sarzin

For people struggling to come to terms with the harsh treatments associated with cancer, it must seem to them that nothing much has changed since the early days of slash, burn and poison—as surgery, radiotherapy and chemotherapy still constitute the bulk of conventional treatments in the cancer arena.

But while responsible scientists shy away from an emotive word such as “breakthrough” and are reluctant to trigger premature hope in the masses of patients hungry for new and less invasive solutions to their health problems, at last new treatment methodologies are truly on the horizon.

In a powerful research initiative spanning continents, an international team of leading Australian and Israeli researchers—world leaders in their respective fields— aims to develop revolutionary therapies for treating cancer and autoimmune diseases.

Israel’s **Professor David Naor**, a renowned authority in the field of immunology, and his group at the Hebrew University in Jerusalem will collaborate with immunologist and clinical oncologist **Dr Galina Kaseko** and biophysicist **Dr Tohsak Mahaworasilpa**, Directors of the **Stephen Sanig Research Institute,** a non-profit independent research organisation. Dr Kaseko and Dr Mahaworasilpa are Adjunct Lecturers in the School of Physics at the University of New South Wales in Sydney.

This international development is a potent shot in the arm for research into potential **therapies for cancer and autoimmune diseases**. The team will merge their expertise to streamline and validate therapies that promise to transform the treatment of **cancer** and autoimmune diseases such as juvenile onset diabetes and rheumatoid arthritis.

Their collaborative project hinges on the use of advanced biotechnology techniques pioneered at the Institute, which will complement Professor Naor’s acclaimed research into antibodies that target and eradicate cancer cells.

In a career that spans four decades, Professor Naor’s research interests have focused on how the body defends itself, which led him to a study of cancer and autoimmune diseases and the associated failure of the immune system.

In a sense, cancer and autoimmune diseases are at opposite ends of the immunological spectrum. Our immune system responds to diseases by sending killer cells to the site under attack. In autoimmune diseases such as Rheumatoid Arthritis (RA), the immune system perceives as foreign the body’s own cells and develops antibodies to attack and destroy body tissue. With cancer, however, the immune system fails to recognise or attack the abnormalities of the cancer cells.

Intrigued by these immunological contradictions, Professor Naor identified for the first time an adhesion molecule called CD44, a receptor that latches onto cells of the immune system. He demonstrated conclusively that this CD44 receptor plays a vital role in facilitating the migration of the immune system’s blood cells, enabling them to leave the blood vessels and circulate through the body to sites perceived to be under attack.

He has also identified variants of CD44, all of which have immunological functions specific to particular tissues in the body. In the synovial fluid of people with RA, for example, he discovered that they share a variant of the CD44 receptor responsible for the migration of inflammatory cells to the joints, where they release destructive toxins. He reasoned that monoclonal antibodies could block that specific variant, thereby preventing the migration of inflammatory cells to the joints.

His team induced arthritis in mice and treated the mice with anti-CD44-variants antibodies. According to Dr Galina Kaseko, Professor Noar's discoveries were groundbreaking and set the scene for a radically new approach to treatments for autoimmune diseases and cancer.

"Professor Noar's team reduced by very large margins the inflammation in the joints of mice with arthritis but, most importantly, they discovered that the mice antibodies they developed to inhibit the migration via the CD44 variant did not have side effects and did not interfere with any other CD44 functions around the body," Dr Kaskeo explains. "This knowledge is vital because you don't want to stop the migration of inflammatory cells, for example, to other parts of the body where there might be bacterial infection."

Currently in the global marketplace, there are humanisation techniques that can replace a substantial part of the mouse molecule sequence with a human molecule sequence. The process is laborious, however, and some of the mouse version of the antibodies remains, which can trigger adverse reactions in humans.

While Professor Noar's research so far has won worldwide acclaim, the translation of his research from a mouse model to human clinical trials is dependent on extremely advanced biotechnology involved in humanisation techniques, which Dr Kaseko and her colleague, biophysicist Dr Mahaworasilpa, can provide at the Stephen Sanig Research Institute.

"That's where we come in," Dr Kaseko says. "For human trials you need a human version of the monoclonal antibody because a mouse monoclonal antibody injected into humans will cause toxic reactions and will be eliminated by the patient's immune system. We specialise in human proteins and we have a unique technology that allows us to generate a fully human monoclonal antibody."

The implications of this new research for the future of cancer therapies is immense. As Dr Kaseko points out, oncologists aim to stop the invasion of cancer and its migration through the body. Professor Naor, she says, has shown for the first time that patients with aggressive cancer have a variant of the CD44 molecule, so by developing antibodies specific to that variant it becomes possible not only to treat the primary cancer but also to prevent it spreading invasively.

"The CD44 molecule could be involved in many more diseases connected to the malfunction of the immune system, so scientists could develop therapies that would target only the variant without blocking any other functions in your body," Dr Kaseko says. "I'm a clinician oncologist and an immunologist by training, so I always knew the immune system was the key to many diseases especially cancer.

" I believe the emerging field of monoclonal antibodies is potentially a new bullet for treating cancer, nobody doubts its potential. We've been in this area for some time, but the moment we met Prof Naor we knew we had at last found an important application for our technology.

"Any novel breakthrough in scientific and medical fields comes from collaborative effort, and sometimes it takes cross-country relationships and effective links. Israel is second only to the United States in the quality of scientific publications; we hear of Israel as a country of conflict and forget that this country has given us top scientific research in the medical field."

Dr Kaseko concedes, however, that the road ahead is not an easy one. She estimates that the international team will require a minimum of five years to validate their approach and to negotiate the clinical development of their findings. But they have faith in their unique approach and especially the proven absence of the side effects that currently bedevil cancer therapies.