IMMUNOTHERAPY

TREATMENT FOR CANCER

Dr Marco Matos, Medical Oncologist

Cancer is the result of the accumulation of changes in the genetic material (mutations) that allow the cancer cell to survive, proliferate and invade other healthy organs. Environmental factors (smoking, sun exposure, radiation etc), chronic inflammatory processes (viral infections, etc) and host-related factors (obesity, hereditary conditions, etc) are important in the carcinogenesis process (formation of cancers).

The human body has more than one hundred trillion cells, dividing every day from the very first day we are born, except for brain and nerve cells. Every second of our lives, one million cells die (apoptosis) due to aging, and new cells replace them with the exact same DNA material. During this process, things can go awry and the body (including immune system) attempts to rectify the mistakes or destroy those wrongdoings.

Cancer occurs when an altered DNA sequence (mutation) remains occult or disguises itself to allow that cell to survive. The newly formed mutated cell then will have to learn many other abilities (further mutations) before it becomes malignant and proliferates and invade other organs.

The immune system plays an important role in protecting our organisms from external invaders (bacteria, viruses, fungus, etc) and also maintaining the balance among other cells, destroying unwanted extras. The immune system has the ability to recognise every molecule in the universe (diversity), to react to a specific event (specificity) and to memorise that event (memory) so it can mount a big defence if confronted again.

Immunotherapy is an anti-cancer approach that complements traditional ways of fighting cancer such as chemotherapy and radiotherapy. Over 120 years ago, Dr William B. Coley - considered the father of cancer immunotherapy - injected a mixture of dead bacteria into patients with cancer after observing that some cancers regressed in the presence of streptococcal infections. Since then we have learned a lot that allows us to manipulate the immune system with more specificity to a variety of antigens, including cancer antigens (proteins sitting in the surface of cancer cells), activating or inactivating mechanisms that allow the immune system to recognise cancer cells as wrong cells, developing antibodies that slow down pathways that are overactive and creating vaccines that induce the formation of a robust army against cancer cells.

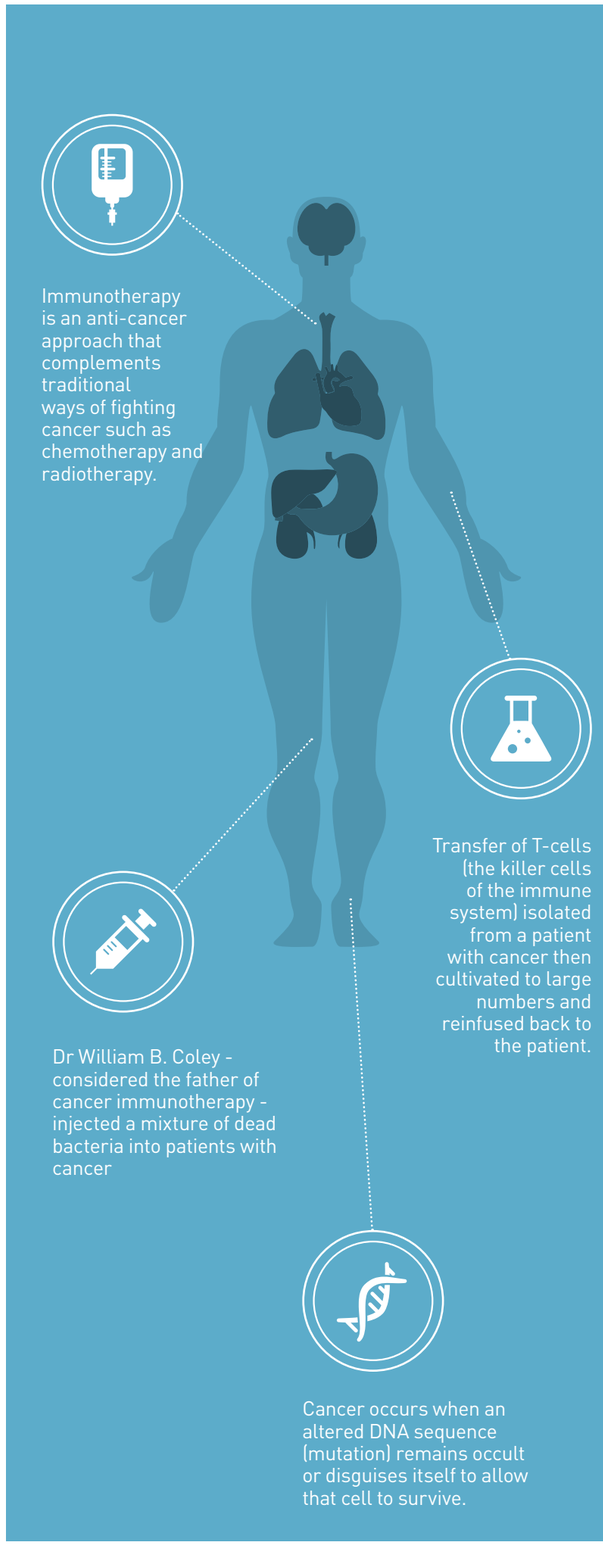
The main types of immunotherapy can be divided into non-specific immunotherapies, antigen specific antibodies and cancer vaccines.

Non-specific Immunotherapy

Antigen therapy, such as BCG therapy, uses a weakened strain of mycobacteria originally designed to produce immunity against tuberculosis, which also produces an immune response when injected into early bladder cancers.

Cytokines such as interferon alpha IFN, tumour necrosis factor TNF and interleukins IL 4 and 6 have a direct anti-tumour effect as well as an indirect effect, enhancing the immune response. Used to treat kidney cancers and melanomas.

Cell therapy, such as dendritic cell therapy, cultivates and multiplies cells that recognise cancer cells, and are then infused back into the patient.



Antigen Specific Immunotherapies

Antibody therapy uses different immune proteins that attack specific molecular targets such as Herceptin, which targets a type of breast cancer that overexpresses a growth factor receptor (Her2) or panitumumab - an antibody that targets the gene RAS, present in half of colorectal cancers.

Transfer of T-cells (the killer cells of the immune system) isolated from a patient with cancer then cultivated to large numbers and reinfused back to the patient. The results are good but short-lived. Enormous efforts are put into expanding and maintaining the killer effect of the T cells.

Specific Immunotherapy

Vaccination of tumour-based vaccines, virus-based vaccines or protein and peptide-based vaccines.

Check-point inhibitors act by releasing the brakes that stop the immune system unleashing the immune system to attack cancer cells. Cancer cells use check points to escape the detection of the immune system. CTLA4 and PD-1 are the most studied and drugs and include Pembrolizumab (Keytruda), Nivolumab (Opdivo) and Ipilimumab (Yervoy), which are currently routinely used to treat melanomas.

As evidence emerges that other cancers (lung cancer, head and neck carcinomas, bladder cancer, kidney cancer, some types of breast cancer and prostate cancer) can also respond to check point inhibitors, the management of cancers have changed dramatically. Patients that respond to these drugs have less side effects, and respond for longer periods of time, providing new hope for cancer sufferers around the world.