- Virus

Researchers looking to viruses to beat cancer

Cape Argus · 7 Jun 2022 · 10 · LOUIS FOURIE Professor and technology strategist Professor Louis C H Fourie is an extraordinary professor, University of the Western Cape.

MICROSCOPIC viruses, such as the ones causing influenza, smallpox, Aids and Covid-19, are often feared by human beings since they are well known for causing destructive diseases.

However, viruses are simple systems that are easily manipulated for beneficial purposes. In medicine, viruses have been used in vaccines since the 18th century. But in the past few years, viruses are increasingly being used as vectors to carry genetic material to specific cells for the treatment of diseases, such as cancer.

Medical practitioners use several types of viruses in gene therapy, such as the adenovirus (causing cold- and flulike illnesses), lentivirus (cause chronic and deadly diseases and includes HIV), and adeno-associated virus (AAV) (does not cause illnesses in humans). The virus infects certain cells and then make copies of themselves and spread to surrounding uninfected cells.

AAV are the primary platform for gene delivery for the treatment of a variety of diseases. Luxturna is one such gene therapy product that uses AAV to deliver a functional copy of a genetically mutated gene into retinal cells to restore the vision of patients with progressive vision loss due to the mutation of a specific gene.

Another valuable application of viruses for gene therapy is to treat cancer, since viruses can target specific cells infected with cancer without damaging the healthy cells.

More recently, viruses have been used to attack cancerous tumours.

These, often modified, viruses are known as oncolytic viruses and are a promising approach to treat cancer since cancer cells often have impaired antiviral defences.

The viruses can also deliver therapeutic payloads to tumours and kill the cancer cells, which releases cancer antigens that stimulate immune responses.

Scientists from Imugene Limited (an Australian biotech company specialising in novel therapies that activate the immune system against cancer) and City of Hope (a cancer research and treatment institute in the US) used a genetically modified smallpox virus known as Vaxinia, to infect, replicate and kill cancer cells without effecting healthy cells.

According to Professor Daneng Li, a principal researcher at City of Hope, oncolytic viruses can stimulate the immune system to respond to and kill cancer, while stimulating the immune system to be more responsive to other immunotherapies such as checkpoint inhibitors that block proteins that stop the immune system from attacking the cancer cells.

Until now, patients often relapsed and eventually stopped responding to or developed resistance to checkpoint inhibitor treatment.

However, Vaxinia stimulates the patient’s immune system and increase the level of the PD-L1 protein in tumours, thus making immunotherapy more effective against cancer than with pre-

vious generations of oncolytic viruses.

When an oncolytic virus replicates, it disintegrates and kills infected tumour cells, which release tumour proteins or antigens when they burst. The antigens are recognised by the immune system as foreign and the immune response is triggered, resulting in the further death of tumour cells. Tests in the laboratory and on animals have indicated that Vaxinia can significantly reduce the size of colorectal, lung, breast, ovarian and pancreatic cancer tumours.

After the very successful studies on animals, Imugene and City of Hope have started with a 24-month phase 1 clinical trial of a hundred cancer patients with metastatic or advanced solid tumours in the US and Australia.

In the trial, patients will be receiving a low dose of Vaxinia intravenously or directly into the tumours.

Once the safety of Vaxinia has been established, some participants will receive pembrolizumab, an immune checkpoint inhibitor or immunotherapy drug that improves the immune system's ability to fight cancer-causing cells.

Cancer cells usually express certain checkpoint proteins to prevent their elimination by T-cells of the immune system. Immune checkpoint inhibitors are drugs that block such proteins' function to enhance the immune cells' ability to destroy tumour cells.

The importance of Vaxinia, according to Dr Yuman Fong, the chair of the department of Surgery at City of Hope, is that the virus is designed to target all types of cancers. This approach makes cancer into one disease with a targeted agent to obliterate it. The new generation of therapeutic viruses is thus much more potent than prior viruses and also more selective.

A separate study, by scientists from Leeds University and The Institute of Cancer Research in London, discovered that the reovirus (a non-enveloped virus) could cross the blood-brain barrier to reach tumours, where it replicates and kills the cancer cells. Simultaneously, it activates the body's immune system to attack the cancer as in the case of immunotherapy treatment. If similar cancer cells try to regrow, the immune system will be ready to shut it down.

Last year, one of the viruses causing the common cold, the coxsackievirus in combination with pembrolizumab, showed tremendous promise in treating advanced skin cancer that could not be treated with surgery. During the clinical trial, the combination reduced the size of melanoma tumours by 47 percent.

A genetically engineered herpes virus is also used to treat late-stage melanoma, the deadliest form of skin cancer. This is the first oncolytic drug to be approved by the American Food and Drug Administration.

It thus seems certain that virotherapy and immunotherapy will play an increasingly important role in the treatment of a wide variety of life-threatening and advanced-stage cancers. Oncolytic virus therapy, in particular, is a promising new class of drugs that could bring hope to numerous cancer patients.

Unfortunately immunotherapy is hugely expensive in South Africa and not covered by most medical aids.