

USING BIRD VIRUS TO TREAT CANCER

Professor Datin Paduka Dr Khatijah Mohamad Yusoff tells **Kasmiah Mustapha** more about her research on the use of an avian virus to treat cancer

FOR more than 30 years, Professor Datin Paduka Dr Khatijah Mohamad Yusoff has been researching the Newcastle Disease Virus (NDV), a contagious and deadly viral disease in birds. Humans infected with the virus will suffer from mild flu-like symptoms or conjunctivitis.

Researchers are interested in NDV as it can replicate more quickly in human cancer cells than in most normal human cells. It even kills the host cells.

Khatijah, dean of Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia, is now expanding her research into the novel use of NDV as an anticancer agent as well as a carrier for anticancer drugs in targeted chemotherapies.

The recipient of the Merdeka Award (2015) for health, science and technology, explains her research.

When did you begin your research on NDV?

I have been working on NDV for more than 30 years. It began when Professor Datuk Dr Abdul Latif Ibrahim introduced me to the virus at UPM.

I did my post-doctoral research on the virus under Professor Peter Emmerson at the University of Newcastle-upon-Tyne, UK. I was supported by the North of England Cancer Research Campaign.

Why are you looking into NDV virus-cancer cell interactions?

We started to look in-depth at the interaction between NDV and cancer cells in 2007. It was done by some of my students undertaking their PhD degrees.

The virus is able to establish syncytium-mediated cell lysis and are capable of modifying immune functions that dramatically enforce anticancer immunosurveillance.

The virus can be quickly modified and manipulated by recombinant DNA technology to enhance the immunomodulatory effects.

What inspired you to embark on this research?

The idea of using viruses in the treatment of cancers or oncolytic virotherapy is not new. Certain viruses like measles, mumps and NDV have a propensity to lyse cancer cells with high specificity and sensitivity. Some of these viruses can even indirectly stimulate the host anti-cancer immunological response. Side effects are extremely mild compared with those of chemotherapy or radiation.

This form of therapy works by exploiting viruses which can enter and replicate in cancer cells while leaving the normal cells unaffected.

The first of such viral cancer vaccines, IMLYGICTM, has been authorised for the treatment of metastatic melanoma in the United States. It uses herpes simplex virus-1 which has been engineered to encode human-macrophage colony stimulating factor (GM-CSF) and paved the way for other such vaccines to be in clinical practice.

How does the NDV work in treating cancer?

NDV is an avian virus, which is incapable of replicating in normal cells because of the presence of normal defence mechanisms like IFN type 1 and p53 pathways.

However, these defence mechanisms are not present in cancer cells and this

allows the virus to replicate specifically in the cancer cells.

These cells may be killed directly by overwhelming viral infection and lysis, which releases additional viral particles to infect neighbouring cells and distant metastases.

The viral infection may also activate the immune system, unmask stealthy tumour antigens, and aid the immune system to recognise and attack neoplasms.

When the cancer cells are killed, they are cleared by the immune system. These, in turn, act like a cancer vaccine. When the immune system detects similar cancer cells in the body, it will recognise these cells as foreign antigens and respond accordingly.

What do you hope to achieve in your research?

Our objective is to discover, invent and produce an effective NDV strain for use in cancer treatment. Despite the outstanding advances made in cancer treatments, the biggest challenges remain in early diagnosis, accessibility and affordability due to the excessive cost.

The production of the virus is well-established and cost is minimal, like the production of vaccines for chickens.

One day this treatment will be available for all cancer patients and the cost will no longer be an issue.

Imagine a time when people will no longer be fearful of cancer as it can be treated like a common flu by the doctors.

It has been reported that clinical trials on people using NDV as a cancer treatment have not worked. What is your comment on this?

Science is progressing every day. Negative results from previous clinical trials do not dictate the future of virus in cancer treatment.

Many modifications are done to improve the treatment including the virus, dosage, route of administration, and in combination with other treatments.

The future of cancer treatment with virus is very bright, more so after the US FDA approval of IMYLYGICTM for melanoma.

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