

# S'pore scientists extend lifespan of lymph nodes outside the body to test vaccines

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Singapore researchers have managed to extend the lifespan of lymph nodes outside the body, allowing them to study how the immune system reacts to vaccines and immunotherapies.

To do this, the scientists have, once again, used a locally created, tissue-like, bioengineered hydrogel to preserve the lymph nodes for up to seven days, enabling functional studies to be carried out.

The jelly-like hydrogel is made from hyaluronic acid, a water-retentive substance found naturally in human tissues and fluids in the skin, joints and eyes. Without the hydrogel, a lymph node deteriorates once it is removed from its blood supply and does not “survive” outside the body.

The hydrogel was previously used to preserve cancer tumour cultures for better targeted drug testing outside the body. This was

to prevent cancer patients from receiving unnecessary and expensive treatments, or wasting time on therapies that prove to be ineffective.

It was later used in the search for individualised treatment for advanced cancer in the abdominal lining, giving hope to some patients who face an average survival rate of just several months.

Assistant Professor Eliza Fong from the department of biomedical engineering in the College of Design and Engineering (CDE) at NUS said: “With the hydrogel, we are now able to significantly extend the viability of the lymph nodes *ex situ* (outside the body), preserve its ‘architecture’, and reduce the rate of tissue decline. This will offer a stable window for monitoring the immune responses to vaccines.”

For example, researchers can map how the lymph node fragments mount immune responses after they are exposed to mRNA vaccines such as the one for the Covid-19 virus, added Prof Fong, a

co-author of the study.

Lymph nodes act as sieves for foreign substances such as germs and contain immune cells that help the body fight infection closest to them.

The lymph nodes are scattered throughout the body in clusters, and are commonly found in areas where they can be felt, such as the neck, armpits, groin and under the chin. There are others found deeper in the body, filtering fluid from areas like the chest, abdomen and pelvis.

Professor Gopal Iyer, a co-author of the study and head of the department of head and neck surgery at the National Cancer Centre Singapore, likened the immune system and lymph nodes to police headquarters and police posts in different precincts.

“Should the ‘crime’ in your body affect the head and throat areas, it is dealt with locally by the lymph nodes located there (police posts). It is only when the ‘crime’ has infiltrated the entire body, then the whole immune system (the police



NUS PhD trainee Elektutige Anton Kanishka Fernando (left) preparing the tumour samples for drug testing. Beside him are Professor Gopal Iyer and Assistant Professor Eliza Fong. PHOTO: NUS-CDE

headquarters) will be activated. That is perhaps when it sends out the Swat (Special Weapons And Tactics) team,” he said.

As lymph nodes are usually removed during surgery primarily to determine if a cancer has spread from a primary tumour, Prof Iyer said they could be used to test for personalised and precision cancer vaccines.

“With the technology and a validated system, the hydrogel-based

lymph node allows functional studies of how one’s immune system reacts to vaccines and tumour antigens. One area that is of high interest is the body’s response to the recent mRNA vaccine such as the one for Covid-19,” he said.

“The mRNA vaccine provides our cells with instructions to make the harmless spike protein from the Sars-CoV-2 virus, while the immune system recognises and produces antibodies to fight it.”

Prof Fong said the hydrogel model “addresses the gaps in current *in vitro* and *in vivo* studies”.

*In vitro* studies use artificial laboratory settings like test tubes or petri dishes to study cells, tissues or molecules in a controlled environment. *In vivo* research is done on living organisms to obtain complex, real-world data on the effects of treatments or substances within their natural environment.

A key limitation of *in vitro* studies is that it can be difficult to predict how cells will behave within a living system. *In vivo* studies, however, are complex and costly.

“With hydrogel, we are able to provide a human lymph node avatar (outside the body) and ... investigate immune responses and accelerate research from bench to bedside in cancer and infectious disease,” Prof Fong said.

The lymph node samples outside the body were able to show strong immune activity and produce antibodies when exposed to tumour material and to mRNA from the Sars-CoV-2 virus, she added.

The research was published on Aug 29 in ScienceDirect, a database platform from Elsevier, a Dutch academic publishing company specialising in scientific, technical and medical content.

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