A chance at better life after organ transplant

Study's findings could lead to new inhibitors to prevent or treat chronic transplant rejection

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A team led by researchers from the National University Hospital (NUH) and the National University of Singapore (NUS) has discovered the structure of proteins associated with organ transplant rejection, which could lead to the development of inhibitors that can prevent chronic transplant rejection.

The study was led by Professor A. Varibhava, co-director of the National University Centre for Organ Transplantation at NUH, and Associate Professor Paul Mackay, director of the NUS Life Sciences Institute. The researchers used X-ray crystallography to unravel the secrets of an antibody-binding partner called human leucocyte antigen (HLA), a transplanted donor organ in the patient. The findings could lead to better treatments and clinical potential therapies.

Transplant rejection is a phenomenon's immune system attacks the new "foreign" organ, resulting in damage. Patients can experience both acute rejection, which happens within weeks, and chronic rejection, which can happen many years later.

Professor Varibhava said acute rejection -- which is due to white blood cells called T cells attacking the organ -- can be treated with "calcineurin inhibitors" that suppress the immune system, or immunosuppressants.

He added that there were no causes of acute rejection at the centre in the last two years.

Chronic rejection, caused by another type of white blood cell known as B cells releasing antibodies, is harder to diagnose, predict and treat.

This is because chronic rejection is less well understood than acute rejection, as the process by which antibodies bind to HLA and cause inflammation was previously unknown.

The paper authored by Prof Mackay, Prof Varibhava and Singapore scientists was published in the journal Nature Communications on Feb 23, is the first to describe the interaction between the antibody and the HLA antigens.

Between 50 per cent and 60 per cent of all transplanted kidneys fail due to chronic rejection, said Prof Varibhava. The more similar the recipient's HLA molecules are to the donor's, the less likely it is that the organ will be rejected.

Most doctors learn that rejection has happened only after the organ begins to fail, he said. Checking for antibodies is one way to prevent it, but if rejection is likely, the patient will be treated.

The team observed that some types of antibodies can transiently attack the patient's organs, but preserve other types of harmful antibodies from binding.

Prof Mackay said the knowledge could be used to develop inhibitors in future that can prevent or treat chronic rejection by simply hormones.

The team was also able to define the structure of one particular type of HLA which is commonly found in Chinese populations and is the most common among Singaporeans.

Over the next three to five years, the researchers hope to find drugs that would work on the majority of all other antigens, he said.

The methodology can be made standard for all transplant patients. Understanding which specific antibodies are harmful or harmless will also allow doctors to better the immune suppression in patients undergoing treatment.

Under the current approach, some patients who receive an organ from their own donors take powerful immunosuppressors for their entire life to minimize the risk of rejec-
tion, even if they might not need it.

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More customized treatment

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