Engineering antibodies to block viruses

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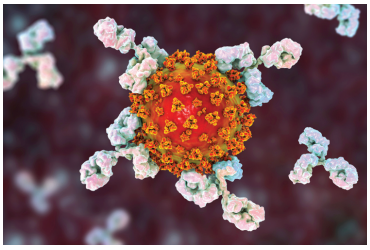
Scientific knowledge of our complex immune system has flourished over the past two decades. Our scientific progress, catalysed by fundamental research, is now being applied to treating infections, immune-mediated diseases and cancer. Immunotherapies are coming to the forefront as a way to manipulate our immune system for our benefit. While standard drugs targeting the immune system remain an important component of clinical medicine, doctors are excitedly adopting so-called biological therapeutics or biologics due to their higher precision and lower side effects. And scientists in Malta are playing a role in this process of discovery.

Chief among the biologics are engineered antibodies. We produce antibodies naturally to fight off pathogenic organisms, in response to infection or vaccination. Antibodies are proteins possessing the ability to bind the surfaces of foreign organisms entering the body. They coordinate the immune system's defences against invaders. Inspired by nature, scientists have been exploring ways to manufacture antibodies for the treatment of complex human diseases. Four Nobel prizes awarded for the research and manufacture of antibodies are testament to this endeavour's success. These antibodies are used in the clinic to treat metastatic cancer, neutralise viruses and manage autoimmune disorders. Latest in the line of innovations in antibody engineering, and awarded the 2018 Nobel prize in Chemistry, is a technique developed by George Smith and Sir Gregory Winter called 'Phage Display', based on a kind of virus called a bacteriophage that infects bacteria. These bacteriophages can be modified to generate a myriad of antibodies, each of which can home in on a specific target. Scientists can then fish out individual and highly specific antibodies – termed monoclonal antibodies – for the target of interest. The fishing process is referred to as 'biopanning' because of the resemblance to the process used in finding gold from a river bed. Scientists start off with a collection of antibodies called an antibody-phage library containing 10 billion different antibodies and gradually isolate monoclonal antibodies with the highest specificity.



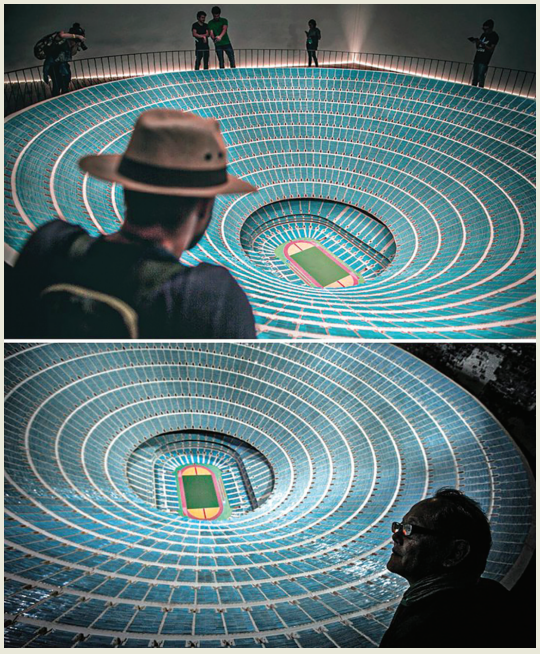
Antibodies attacking a virus.

Using phage display, a team of scientists at the University of Malta, led by Professor David Saliba, are on the hunt for antibodies that neutralise vulnerable structures on dangerous viruses such as SARS-CoV2 and Zika virus. The project, entitled ACCELERATE, is funded by the Malta Council of Science and Technology and is performed in collaboration with scientists from the University of Edinburgh and the International Centre for Cancer Vaccine Science. The international team has already generated antibodies that specifically bind these viruses. They are now verifying if these antibodies can block these viruses from entering human cells.

Having set up this pivotal platform at the University of Malta, local scientists from the Department of Applied Biomedical Science, Department of Clinical Pharmacology and Therapeutics, and the Centre for Molecular Medicine and Biobanking are also expanding the use of this technique to isolate antibodies that bind to key therapeutic targets found on cancer cells. In the journey of innovative applications of antibody screening against human diseases, this is only the beginning.

Project ACCELERATE (IDP.RP.2021-01) is financed by the Malta Council for Science and Technology for and on behalf of the Foundation for Science and Technology, through the Infectious Disease Programme.

PHOTO OF THE WEEK



American artist Paul Pfeiffer's one-million-seater stadium concept. Not sure about the visual from the last row though. PHOTO: PAUL PFEIFFER

DID YOU KNOW?

- Word of the Day: Autotonsorialist – someone who looks like they cut their own hair.
- Starting this fall, NASA will have a team investigating UFOs.
- Not flushing a public toilet after you have used it is a crime in Singapore.
- Eighty five per cent of people secrete a chemical that reveals their blood type to mosquitos.

For more trivia, see: www.um.edu.mt/think.

SOUND BITES

- A fossilised lower jaw has led an international team of palaeontologists to discover a new species of predator that once lived in Europe. These large predators belong to a group of carnivores colloquially known as 'bear dogs'. They could weigh around 320 kilograms, appeared 36 million years ago, before becoming extinct around 7.5 million years ago.

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- Engineers have developed a new design strategy and 3D printing technique to build robots in one single step. The breakthrough enabled the entire mechanical and electronic systems needed to operate a robot to be manufactured all at once by a new type of 3D printing process for engineered active materials with multiple functions (also known as metamaterials). Once 3D printed, a 'meta-bot' will be capable of propulsion, movement, sensing, and decision-making.

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MYTH DEBUNKED

An overactive immune system is a good thing

What you feel when you are "coming down with something" such as a raised temperature, sore throat or a sniffly nose is actually the effects of the immune system battling the invaders.

Orchestration of the body immune defence mechanisms to destroy invaders is one of the most complex biological responses in the human body.

Organs including the skin and airways act as a barrier to pathogenic invasion while billions of immune sentinel cells constantly patrol tissues and release trillions of molecular weapons. Inflammation plays a central role in the communication of the different facets of the immune system to direct its destructive power to the site of infection.

This response is only beneficial if temporary, and the immune system is restored to a baseline level once the invaders are eliminated.

If prolonged indefinitely, this response can be more harmful than beneficial. The latter is a salient feature of conditions such as autoimmune diseases, in which healthy tissue is attacked, as opposed to invaders.

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