

# Pears

## Building

In association with



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**Construction has reached level 4, one of the two floors that will house the Institute of Immunology and Transplantation (IIT). Work is underway to consider numerous aspects of the way the building will operate.**

Meanwhile, the IIT has thrown open its doors to scientists and students at two annual events which help showcase its work and encourage potential researchers.

Finally, we look at the work of Dr Joe Grove, who's trying to work out exactly how a virus invades a cell, in the hope that one day a vaccine for hepatitis C will be found.

# Building update and IIT news



The construction remains on schedule with levels 1, 2 and 3 now cast and level 4 in progress. The basement plant room remains under construction and there are a number of additional contractors on site working on brickwork and scaffolding, as well as mechanical and electrical aspects.

Meanwhile, it has been agreed that the trust will manage the car park, whose management will be aligned with that of the hospital. The Royal Free Charity is almost ready to confirm the IT infrastructure requirements and is working towards a tender process for the management of the building's facilities. The contract for this will be awarded in May 2020 to start work in the September.

There is work underway on the branding for the patient accommodation and on some aspects of the interior design.

The institute is currently considering in detail which equipment it will take into the new building and what additional equipment will be needed, as well as continuing with the process of recruiting additional researchers.

## Immunity insight

IIT researchers have made an important discovery about how a natural regulator of the immune system works.

In an article published in *Science Immunology*, Professor Lucy Walker's team have discovered which type of immune cell is controlled by the important regulatory molecule CTLA-4.

Antibodies to block CTLA-4 function are used in cancer immunotherapy to increase immune responses against tumours.

"Immune cells use CTLA-4 to regulate the behaviour of other immune cells – but until now we didn't know the identity of these other cells," said Professor Walker. "We've now shown that a particular type of immune cell, a subset of dendritic cells, is the target for CTLA4's immunoregulatory activity."

"CTLA-4 is working inside us all the time to prevent us getting autoimmune diseases, so it's a key molecule to understand. It's also targeted by immunotherapy drugs so the more detail we have on how it works, the better we can deploy these drugs."

## Sharing knowledge with our peers...

In June the IIT threw open its doors once again for its annual IIT Symposium with Pears Lecture and for the annual Schools Open Day, great opportunities to share ideas, both with colleagues and with A-level students who may one day take up the mantle of the work we have begun.

**Professor  
Federica Sallusto**

from the Universita della Svizzera Italiana and ETH Zurich delivered the Pears Lecture at the symposium on 18 June.



Professor Sallusto is a world leader in immunology research. Her work has shown how a network of highly specialised cells regulate the immune system in healthy people and those with immunity problems.

Professor Hans Stauss, director of the IIT, said: "We are grateful to Professor Sallusto for joining the symposium and delivering the Pears Lecture. Her work illustrates the complexity of the human immune system and provides important information about how to exploit the immune system to treat disease."

A total of 14 other research scientists from a range of leading research institutes shared details of their work, either during lectures or while networking and visiting stands in the Sir William Wells Atrium.

# ...and the scientists of the future?

A week later, more than 100 A-level students attended the annual open day for schools and heard how Nobel prizewinning scientist Peter Medawar made his ground-breaking discoveries about the immune system after a plane crashed near his house during the Battle of Britain, changing the course of his research.

They also heard about how studies of twin cows led to major insights into organ rejection after transplantation and why older people are more prone to infection.

**Year 12 students** from Graveney School in Tooting, who have been doing a project with IIT professor

**Emma Morris**, gave a presentation on their investigation into CTLA4 deficiency, a rare disorder that severely impairs the normal regulation of the immune system leading to various disorders including intestinal disease, respiratory infections, autoimmune problems and enlarged lymph nodes, liver, and spleen.

**Rhian Fisher**, a biology teacher at Graveney, said how grateful she and her students were to have the chance to be involved in real research. "As well as the benefits for students, this project has enabled us to raise the profile of scientific research at Graveney and keep our teaching up to date."



**Students from Graveney School present their findings on research into a rare immune deficiency.**



# The IIT in focus

About 80 million people worldwide are infected with the hepatitis C virus. Dr Joe Grove, Sir Henry Dale fellow, is hoping that his team's research into the basic functioning of viruses may one day lead to a vaccine.

"Years of research into hepatitis C have led to the development of fantastically effective drugs which are helping many patients with this disease," said Dr Grove. "But the symptoms can take decades to develop and while people don't know they've got the disease they can pass it on."

## Life-threatening damage

Hepatitis C is transmitted through unsafe injection practices, sexual contact and transfusion of unscreened blood products (which continues in the developing world). Left untreated, the virus may cause serious and potentially life-threatening damage to the liver including cirrhosis and liver cancer.

With current treatments it's usually possible to cure the infection. However, most individuals don't know that they're infected. Consequently, HCV continues to kill more than 350,000 people per year, and establishes up to four million new infections.

"Before a vaccine can be found, we need to understand more about how viruses pass on infections," said Dr Grove. "The way the infection travels is always via a virus particle, a microscopic vehicle that invades and implants its genetic material into cells. It exists to reproduce itself."

Dr Grove and his team are focused on how virus particles work, particularly at the precise point where they infect a cell. "Viruses come in all shapes and sizes but they all contain genetic material protected in a shell surrounded by a bag of fats. Sticking out of this bag are what we can call "spikes" and it's these that target the host cell and allow the virus to get in.

"Our cells naturally import things from their outside world – outside their cellular wall – for example to bring in nutrients. The virus hijacks these normal pathways into the cell."

All this is happening on a microscopic scale. Dr Grove said: "Viruses are almost unimaginably small. If we were to expand an influenza virus particle to the size of an apple, in comparison a human being would be 1,000 miles tall - about as long as the UK."

Of course, most viruses are fought off by people with a healthy immune system. During an infection by, for

example, chickenpox, antibodies develop which, upon a subsequent attack, recognise and neutralise the viral "spike". "Vaccines take advantage of this process by teaching the immune system to make antibodies successfully; the immune system can then recognise the virus and stop it in its tracks."

But in some diseases the situation is not so straightforward. "Some viruses can mutate in order to evade the antibodies – change the shape of its spike – and then the immune system will try to learn this new shape. Then the virus mutates again. You end up with a kind of arms race between the virus and the antibodies. If the antibodies don't win, the virus can establish a chronic, sometimes lifelong infection, as with HIV and hepatitis C. However, if we had vaccines against these viruses we could prevent them ever establishing infection; we could essentially teach the immune system how to win the arms race."

The spike proteins that attach to the host cells are the particular focus of Dr Grove's research. "It seems that the spike proteins of hepatitis C are novel – in other words they don't follow the rules of other spike proteins.

"The spike proteins of a range of completely different viruses, like HIV, Ebola and influenza, all work in a similar way. But hep C doesn't, which suggests that we need to unravel some completely new biology."

Dr Grove's latest work suggests that the hep C spike protein has an extended flexible tail which, when bound to a receptor on the host cell surface, activates the spike protein and allows the virus to invade the cell.

## Vaccine needed



"If, as is likely, other viruses behave in a similar way to hep C, our work may teach us how they work too, and eventually lead to better treatments and vaccines," said Dr Grove. "Certainly we'll only eradicate a disease like hep C if we find a vaccine."

The move to the Pears Building will bring this a step forward. "A large part of what we're doing is integrating our basic lab work with different cutting edge techniques: computational biology (that is, developing computer simulations of virus proteins), mathematical analysis, and advanced microscope imaging. This approach takes a lot of teamwork and collaboration. The Pears Building will bring together a critical mass of really excellent scientists. I can't wait to build new collaborations, which will take our research in exciting directions and help us develop new treatments for patients faster."