

# Pears

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Building

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Building soon  
to get power

Solving an auto-immune puzzle

Research update

**The laboratory and patient accommodation areas are taking shape and the Institute of Immunity and Transplantation (IIT) researchers can start to see what their new base will look like.**

Inside Professor Claudia Mauri talks about her hopes for her research into auto-immune disease, particularly rheumatoid arthritis and lupus.

And on the back cover we update you on some major funding which will help researchers find new treatments for patients.

## Coronavirus

The coronavirus pandemic poses unprecedented challenges for the Royal Free Hospital and UCL. Both organisations are working together to provide the best possible clinical care for our patients, including releasing all medically-trained academics from their university responsibilities to support NHS services.

We are also closely monitoring the impact that this pandemic may have on the construction timetable for the Pears Building. The safety of our construction workforce and minimising the impact on our neighbours are our top priorities.

For advice and more information about how the pandemic is affecting services at the Royal Free, see <https://www.royalfree.nhs.uk>

# Building update and IIT news



With the brickwork and glazing now almost complete, most effort is now focused on the internal fit-out of the laboratories and associated areas, and the patient accommodation.

The surfacing of the floors on levels 2 and 3 is complete, allowing floor coverings to be laid in preparation for the installation of the laboratory furniture. Electricity, gas and water

supplies will be installed soon which means the building can be powered up, facilitating further works.

The tender for facilities management is progressing: mid-tender briefings have taken place and a draft contract issued, as are fire and other safety plans. The security arrangements will be signed off soon.

## Other news

### Type 1 diabetes award

IIT researcher Natalie Edner in Professor Lucy Walker's group has been awarded the Dean's Research Prize for her postgraduate research on the immune response in type 1 diabetes.

Ms Edner, who joined the lab in 2016, has been studying the immune cells that cause type 1 diabetes and how they change when a patient receives immunotherapy. By using computational ways of analysing blood samples from people with diabetes she has been able to create a model that can help predict the patient's likely response to immunotherapy. This may improve the outcome of immunotherapy for type 1 diabetes, by identifying patients who are most likely to benefit.

### Symposium

The IIT is hosting its annual symposium and Pears Lecture on 18 June at the Royal Free Hospital.

Leading international researchers will present the latest findings in immunology and Professor Carl June of the University of Pennsylvania will give the Pears Lecture. Prof June was the first to perform successful CAR-T cell therapy in patients, which involves taking a patient's T-cells, a type of immune cell, and changing it so it will attack cancer cells.

## Focus on the IIT

# Claudia Mauri, Professor of immunology

When white blood cells leave the bone marrow - where they are made - a crucial decision is made by the body about what sort of cell they will become, and therein lies the key to whether someone may go on to develop auto-immune disease.

Puzzling out what are the mechanisms underlying the decision is the essence of the work of Professor Claudia Mauri, who will move with her team into the Pears Building.

Auto-immune diseases like rheumatoid arthritis (RA) and systemic lupus erythematosus (lupus) can be devastating for patients, particularly the younger women who suffer from lupus and for whom some of the treatment options are life changing.

"Although there have been great developments in the treatment of RA, a third of patients don't respond to the available therapies which is awful for them and very expensive for the NHS," said Prof Mauri.

It's even worse for lupus patients. "These are often young girls and the first line of treatment is immunosuppression that often includes steroids."

But it's also the fatigue. "They always tell you that the fatigue is beyond what anyone else can imagine - when they feel like that they just can't function. If you're healthy, you can't understand what level of impairment is involved."

Twenty years ago Prof Mauri's team made a seminal discovery about the function of a particular white blood cell, the B-cell. It was already known that the B-cell made antibodies to fight off infection caused by bacteria, viruses or other pathogens, and helped the body recognise infections that the body had been vaccinated against, like measles.

But the team discovered that a sub-set of B-cells, called regulatory B-cells (Bregs) make a powerful anti-inflammatory chemical mediator - a cytokine called Interleukin 10 (IL-10) - which suppresses the immune system.

"It's obviously important that the body recognises whether something is a threat from the outside, like a bacterial infection - which requires an immune response - or is a process that is happening within the body, which doesn't.



"Patients with RA and lupus don't have these IL-10 B cells, so they're missing an important part of the pathway that normally prevents the body from attacking itself."

The team then asked: if some people did not have the "on" switch to make these cells, couldn't they be given it, and that would solve their auto-immune disease?

"The answer is that it doesn't work - simply adding Bregs to the circulation doesn't help."

She and her team are now trying to see if they can identify the signals that instruct normal B cells to differentiate into these powerful anti-inflammatory Breg cells and why this does not happen in patients with auto-immune disease.

"We have identified some of the signals which lead the body to make the Bregs, which go on to make the anti-inflammatory IL-10. We know that patients with autoimmune disease have lots of plasma cells making lots of antibodies but they have very, very few Bregs, so very little capacity for making IL-10."

"We hope to understand why this is and find a way to restore the signal so that patients can produce their own Bregs."

# Research update

## £4m grant to study inherited disease

Professor Siobhan Burns, who leads a team of IIT researchers studying inherited disorders of the immune system, is part of a collaboration with scientists at Cambridge University who have just received a grant of nearly £4m from the Wellcome Trust to look at genes which regulate immunity.

"We want to improve the way we diagnose patients with primary immunodeficiency disorders so that we can tailor specific treatments to different conditions to improve health and quality of life," said Prof Burns, who is leading one strand of the research.

"We plan to use a combination of genetic, clinical and immune cell data to discover new genes that regulate the immune system. The role of my team will be to collect and classify the clinical information for more than 1,000 patients nationally, which will be needed to fully interpret genetic data."

The work, which is being led overall by Professor Ken Smith at Cambridge, will have implications for other areas of medicine. "Abnormal regulation of immunity is an important cause of many conditions including autoimmune disease and cancer," said Prof Burns.

## Team secures funds for major clinical trial

Professor Ron Chakraverty and his team have secured more than £400,000 for a 20-centre trial to test a potentially ground-breaking treatment for patients who have had a bone marrow stem cell transplant.

They will look at a new way of treating graft-versus-host-disease (GVHD), which can happen in patients after bone marrow transplantation and cause life-threatening complications.

"It's very difficult to treat this disease," said Prof Chakraverty. "It's caused when donor immune cells that are transplanted along with donor stem cells attack the skin and other organs in the patient. Although we use powerful drugs to suppress this immune reaction, many patients fail to respond well and have a much decreased quality of life."

One in three patients undergoing transplant is left with chronic disability due to GVHD. "The lack of effective therapies is frustrating for physicians, patients and their families," he added.

Prof Chakraverty's team pioneered the use of antibodies to overcome the immune cells that cause GVHD, but it has drawbacks as it leaves the patient vulnerable to infection for significant periods. Now he wants to trial a new treatment using a short course of chemotherapy to remove the donor immune cells reacting to the patient.

The team aims to start the trial in July 2020 in 20 UK centres and to complete the first analysis of results by March 2022.

## Volunteers needed for research

Patients with the immune deficiency XLA, and volunteers without the condition, are being sought to help find a cure which would require only one treatment session.

XLA is an immune system condition that occurs almost exclusively in men. Patients with XLA have no B cells - specialised white blood cells that help protect the body against infection.

Researchers at the Royal Free Hospital and the Institute of Child Health have secured funding from the Medical Research Council to develop a gene editing technique for XLA and the hope is that this could lead to a curative treatment.

Sameer Bahal, clinical training fellow, said: "Gene therapy has progressed in the past few decades and involves the use of a viruses to insert a correct version of the gene into stem cells. These stem cells are injected into patients and restore the immune system.

"However, we can't control where the gene is inserted and this risks damaging cells and causing them to act abnormally, so we use it only as a last resort. New advances in gene editing mean we can correct mutations in stem cells in a targeted way and this is less likely to cause problems."

They would like to test the technique on stem cells donated from patients with XLA and would also like members of the public without the disease to donate stem cells. The donation is the same process used when people donate stem cells to treat patients with some cancers of the blood.

**Anyone who would like to know more, particularly if they might be interested in taking part, please email [rf.clinicalimmunology@nhs.net](mailto:rf.clinicalimmunology@nhs.net)**