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Building

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The construction site has been transformed as the emerging building takes up much of the available space

The construction of the institute's new home has almost reached the halfway point, which means that it is bang on schedule.

Inside this issue, we talk to Professor David Sansom about his work on immune "checkpoints" and how they help trigger T-cells.

And Drs Clare Bennett and Joe Grove explain why it's so important to take time away from their labs to work with primary schoolchildren who may be inspired to become the next generation of scientists.

Building update and IIT news

Halfway point nears

The construction remains on schedule and will soon reach the halfway point for the main build.

Levels 1 and 2 are almost complete and level 3 is in progress, with preparations underway for the three further floors and roof. The basement plant room is under construction and will house major mechanical plant which is expected to arrive in the next few weeks.

Off site, pre-cast units which will be used in the external façade, are expected to begin production soon with delivery expected in early July.

From early August, the erection of the steel frame for the upper two floors, which will include the patient accommodation, will begin and this will coincide with another milestone when work on the building's external features can begin.

The safety of the public and the workforce, as well as minimising the impact on our neighbours, remain the highest priorities. The work is constantly monitored to ensure that agreed thresholds of noise, vibration and dust are not exceeded.

Prof Federica Sallusto

Update on our researchers

Reza Motallebzadeh, who is investigating the role that the micro-organisms in our body (microbiome) play in the long-term outlook of patients who have had an organ transplant, has been awarded a grant of £148k.

The grant, from the NIHR UCL Hospitals Biomedical Research Centre, will enable him to investigate the role of the gut and urine microbiome in what happens to patients after a kidney transplant.

Two of our investigators have been sharing their insights with the wider scientific community. Last month, **Anne Pesenacker's** work to puzzle out the mechanisms which cause some people's bodies to attack themselves featured in a panel discussion during BioTrinity, a major investment and biopartnering conference for European life sciences, in London.

And **Emma Morris**, who is working on novel gene and cell therapies for blood cancers and inherited immune deficiencies, took part in a panel discussion during World Immunology Day last month at the Frances Crick Institute in London.

Prof Federica Sallusto from the Universita della Svizzere Italiana and ETH Zurich will deliver the PEARS lecture at the IIT Science Symposium on 18 June 2019.

Prof Sallusto's research focuses on the identification of particular cell types that regulate the immune response in humans.

Prof Hans Stauss, director of the IIT, said: "Her research has made critical contributions to our understanding of the complexity of the immune system which underpins the development of novel immunotherapies for patients. We are very much looking forward to her lecture."

The IIT in focus

When a healthy body recognises a threat like infection or cancer it usually fights it off. What happens when things don't go to plan is the job of David Sansom, professor of transplant immunology, and his team.

His work focuses on a series of immune "checkpoints" and how they influence the body's decision to activate T-cells, a type of white blood cell and a critical part of the immune response. Without T-cells we couldn't fight infection and vaccines wouldn't work. But they can also be a danger to us, by mistaking our own cells for a threat and attacking our own tissues, as in autoimmune diseases like Type 1 diabetes and arthritis. They can also start a series of reactions that could lead to a transplanted organ being rejected.

"My lab works on fundamental aspects of how T-cells determine whether to make an immune response or not," said Prof Sansom. "In particular we focus on the interplay between two receptors on T-cells – CD28 and CTLA-4 – and two triggers that enable them to respond.

"We're one of the few labs in the world trying to figure out exactly how this checkpoint works. If we can understand the fundamental mechanisms at play in these checkpoints, we can manipulate them and help patients with immune-related disease."

The team has discovered a mechanism by which CTLA4 acts as brake on the immune system when a full response isn't needed, preventing it from attacking the body's own tissues, as in autoimmune disease.

"We've found a sort of molecular "hoover" that helps prevent autoimmunity. Under the microscope you see that when the CTLA4 expressing T-cell touches the cell – that should provoke an immune response – it hoovers up the triggers that should stimulate T-cells and disposes of them. Because they're no longer there, the immune system isn't stimulated and doesn't make a response – in other words, it's suppressed. This system prevents our immune system attacking our own tissues.

"We have been able to identify patients with "hoovers" that are faulty, understand what goes wrong and this will help us understand these diseases and identifybetter treatments."

Of course, often the body does need to mount a full immune response and this knowledge of the role of CTLA4 has enabled the development of immunotherapy which blocks CTLA4, allowing the body to do all it can to attack the threatening cancer cells. "But if you block CTLA4, as we do in some cancer treatments for example, you may well get rid of your cancer but you run a risk of autoimmune problems as a side effect.

"This is because if you take the brakes off your immune system – which CTLA4 provides - it attacks things at a lower threshold. So you want the threshold set at a point low enough to activate your cells against a real threat but not so low that your own, healthy, cells are attacked. You have to find the right set point."

He explains that we all sit somewhere on the immune spectrum and, as usual, somewhere in the middle seems like it might be a good place to be. "For example, we think that if you sit at the high end and make it easy to trigger immune responses all the time, you may be susceptible to auto-immunity, although you may get fewer infections or be less likely to get cancer.

"However, there's no guarantee that you'd suffer from auto-immunity because the environment will always be a factor and we can't control that. For example, we know that there are people with half the amount of the T-cell CTLA4 they should have. This should mean they would certainly become autoimmune but some people still don't get it. They are, genetically, right at the most susceptible level you can be but still it doesn't happen. Maybe they don't encounter the right environment or possibly they compensate in another way.

"So we need to understand how immune systems are wired up, what makes some people make immune response easily and what stops others. If we understand how that works, we can manipulate it to help patients."

He, like his colleagues, is immensely grateful to the patients who enable this work to be done. "We're learning the biology of this system from patients with these rare mutations who visit the clinic here – they're crucial to our understanding of the entire system. We are always very grateful that they're happy to help us learn more."

He's equally glad of the planned move to the Pears Building. "The move will enhance the overall potential we have to do this work. It will be a large, well-equipped, multidisciplinary environment that will help us take the work forward. We'll have more space, more equipment and a generally fantastic facility to do the kind of patient-relevant but basic immunological science that needs to be done to further our understanding of immunological disease."

Tomorrow's science: inspiring our future scientists

Joe Grove sometimes wonders whether a tube of Smarties might lead to some important scientific research of the future.

"I wanted to explain the concept of a hypothesis to a class of six and seven-year-olds," said Joe, whose laboratory at the IIT investigates how viruses enter human cells and how they evade the immune system.

"So I took a Smartie out of the tube – it was a pink one – and ate it. I then explained that we could have two hypotheses about this situation: 1) All Smarties are pink and 2) All Smarties are made of chocolate.

"We were able to disprove hypothesis 1 almost immediately just by tipping out the other sweets and they really enjoyed proving hypothesis 2!"

Joe was at his son's school in Enfield where he ran five half-hour lessons, reaching 150 children on that day alone. In common with many of his colleagues at the IIT, he thinks it's important to take time away from the lab to try to inspire today's schoolchildren to consider science as a career.

One of the barriers can be clichés about those who work in science, so he was careful to ensure that his slides didn't reinforce them. "In a slide of scientists I included Marie Curie, who was the first woman to win a Nobel prize; and the American biochemist Jennifer Doudna, who helped discover an important technology in genome editing and who is still relatively young so also doesn't fit the stereotype."

Making science attractive to women is a particular interest of his colleague, Clare Bennett, who as well as leading research investigating how the immune cells in our skin protect us from diseases, is an ambassador for in2science, a charity which promotes social mobility and diversity in science.

"We get lots of requests for lab experience from students from privileged homes who've decided to become doctors. But this scheme is for children who haven't had that sort of start in life, whose parents haven't been to university and who may be struggling financially.

"They come in for a week or two and see what a career in science could be like. They love it and so do we. I helped one girl write her personal statement for her UCAS application and I think we both got a lot out of it."

Clare's work in immunology means that she is particularly driven to educate students – and perhaps their parents – about the benefits of vaccination. "We're in a world where people are suspicious of information and I think that people need to understand much better how science works and that it's the way we design experiments and test things that leads to good information.

"Vaccination is a classic example. Millions of lives have been saved and there's so much data out there showing that but then you get just one small bit of misinformation and it has a massive effect so that measles, for example, is now returning as a real threat in this country.

"People don't realise that if your child isn't vaccinated and carries the virus, they can infect other people, quite apart from possibly getting ill themselves. So if you're around young children or other vulnerable people like those on chemotherapy, an unvaccinated child could make them ill."

Researchers regularly talk about their work at the IIT's annual schools open day for secondary school students, which will take place next month and which we will report on in the next issue. It includes a series of talks about the different types of work the scientists do and provides the opportunity for some hands-on experience. Last year students were able to view live cells under a microscope, separate blood into its different components and inflate a sheep's lung.

Clare said: "It's all about showing what science and being a scientist is, that it's a job for the future, that it's a job for women and for people with no previous links to the world of science – and that it's a fun job."