

Pears

In association with



Building

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Building outline emerges

App is 'game changer' for patients

New treatment for rare disease

The building is now clearly visible from one end of the site and will emerge from above the hoarding in a few weeks' time.

The weather has continued to be largely kind, keeping construction on schedule, and planning for the inside of the building and for the recruitment of new research staff is well underway.

Meanwhile, work continues on new treatments and better care for patients. In this issue we focus on the rare but life-limiting diseases known as lysosomal storage disorders.

Building update and IIT news



Construction of the concrete frame is well underway, creating a very different look to the site. This will continue over the coming months up to level 5 and the frame should become visible above the hoarding from sometime next month.

A series of 3-D model images and photographs have been uploaded to the charity's website to show where we are now and how the building will progress.

A "topping out" ceremony will take place later in the year once the highest point has been reached.

Resisting death - research reveals surprising link

A paper by **Benedict Seddon**, professor of immune cell homeostasis, and his team, which describes work on a critical component of the immune system, was published in the journal *Immunity* last month.

It looks at how important immune cells, called T-cells, are made and reveals an unexpected link between the inflammation that is seen in many diseases and the production of healthy T-cells.

"We've known for some time that immune inflammation is an underlying cause of many diseases. In particular, secretion of an immune hormone called TNF can be a major driver of disease and blocking the activity of this hormone can be a very helpful therapy," said Prof Seddon.

"TNF contributes to disease by causing cells to die, which in turn can feed more inflammation. To our surprise, we found that our immune system also uses TNF when making new T-cells. Instead of killing T cells, the TNF stimulates them to live and work normally, ensuring they are ready to fight infections."

The discovery may reveal a new way in which the immune system can respond to disease. "There may also be implications for our understanding of how TNF intervention therapies work in the treatment of conditions such as rheumatoid arthritis, and how they might be improved," he added.

Prize-winning research

An IIT student has been awarded a UCL Dean's Research Prize for her work on natural killer (NK) cells that live in the liver.

Yuyan Duan completed her masters research project with Dr Victoria Male in the IIT, on the role of NK cells in liver repair, and won the prize in the 'postgraduate taught' category.

NK cells kill infected and cancerous cells and those that live only in the liver behave differently from those which circulate in the rest of the body. Yuyan's work looked at the role of these cells and how they affect other immune cells, which may have implications for treating chronic liver fibrosis.



Yuyan Duan

The IIT in focus

Uma Ramaswami is the clinical lead for the lysosomal storage disorders unit (LSDU) at the IIT, one of eight centres in the UK. It sees around 600 patients with these rare, inherited conditions from all over the country and is constantly working on ways to improve treatments and care for patients.



"Patients with lysosomal storage disorders (LSD) are affected by a range of symptoms including pain, gastrointestinal symptoms, tiredness, muscle weakness, problems of the heart, brain, lungs, kidneys, liver, spleen and joints," said Dr Ramaswami.

Each disease involves an enzyme deficiency in the lysosome - "the binman of the cell". She added: "Cells accumulate waste and have to be cleaned up and that's what lysosomes do. Within the lysosomes there are about 50 enzymes which do this. But in LSD patients, a particular enzyme is missing and the waste builds up, affecting all the organs."

For a small proportion of lysosomal disorders, the missing enzymes can be replaced or a medication given to reduce the amount of waste that builds up.

There are other approaches. "For example, in Fabry disease, we have chaperone therapy. Sometimes the patient's enzyme hasn't been made quite right and can't get into the lysosome to do its job. The easiest way to explain this is that the enzyme hasn't been folded correctly to fit through the cell "letter box". The oral chaperone therapy attaches itself to the faulty enzyme and folds it correctly so it can get into the lysosome."

Gene therapy is also in the offing and the IIT will be participating in a Fabry disease gene therapy study this year. "In our centre, we continue to be actively involved in many translational research studies for lysosomal disorders – meaning we're involved in clinical trials for new therapies that are delivered to patients in clinics. This research relies to an enormous extent on the generosity of our patients for their participation."

The IIT clinics are organised as efficiently as possible

to minimise the time that patients have to spend there. Those coming for an annual review, for example, attend a one-stop clinic and have all their assessments and multidisciplinary clinical reviews organised over two days.

Trying to find other ways to improve the day-to-day for patients with debilitating diseases is an abiding concern and last year Dr Ramaswami launched a Fabry patient phone app.

"Patients could have a variety of symptoms. But when you see them only once or twice a year, it's difficult to get a clear picture of symptoms since the last visit. With the app, they can track their symptoms and I can review them remotely and intervene before their next appointment if necessary.

"It empowers patients to monitor their symptoms and it gives us a better understanding of longer-term symptom management and treatment effects."

Much work is underway to find better treatments and Dr Ramaswami is clear on the benefits of doing this work within the IIT. "We have access to facilities and other researchers whose expertise we seek when our patients have particular health issues.

"We have a unique set-up with close links between academics and clinicians. Doctors from Europe and further afield join us to train in lysosomal disorders. In the new building, we'll be able to provide more of this.

"The Pears Building will enable us to provide the best care for these patients in a research setting. Having patient accommodation will be a massive advantage for those participating in research."



Q&A



with **David Bleloch**,
Fabry Disease patient

Fabry disease is a rare, inherited and often life-threatening disorder characterised by the build-up of a substance known as GL-3 within the cells. It is one of the lysosomal storage diseases treated at the IIT (see p3).

When did you realise something was wrong?

Even as a child, I knew things weren't right. I couldn't cope with getting hot and this stopped me going on family holidays or playing sport. But I put it down as a curiosity.

Around the age of 25 the symptoms got worse but again I found an explanation – I thought my hearing difficulties and balance problems were probably due to a motorbike accident I had shortly before they appeared.

And then what happened?

One day in November 2015 I suddenly developed a racing heart and my cheek and arm went numb, so I called emergency services. I live in Fareham, Hampshire, and after lots of tests I found myself in front of Peter Howarth, consultant cardiologist at Queen Alexandra Hospital in Portsmouth, who amazingly spotted Fabry disease among all these symptoms. I was so lucky to find the right person.

He put me in touch with the LSDU at the IIT and then I had a lot of things done from having my genome analysed to tests on my heart, hearing, kidneys, skin, questions about my diet...you name it.

The LSDU staff are brilliant, super effective, clever people whose care was unaparalleled in the, by then, 40 years I'd been receiving treatment. They have pretty much all the answers for me.

What treatment did the LSDU offer?

First they put me on a drug called Fabrazyme, which was administered as an infusion by the wonderful nurses from the Healthcare at Home service, but it gave me some weird side effects. However, as soon as I saw the consultants at the LSDU, they switched me to Replagal, another enzyme replacement therapy, which has been fine.

The LSDU has also developed this great app. It used to be the case that when I saw the consultant every six months, I would have to fill in a questionnaire about how things had been over the previous 24 hours, which was only a snapshot of the time since I'd last been to the clinic.

But with this app I do a weekly update about the levels of pain and other symptoms. Over 40 years I've got to know my triggers pretty well but it's a difficult disease and it is up and down. Then when I go to the IIT I sit down with my consultant, we look at the data together and I explain what was going on when symptoms flared up.

The great thing is that there's a cohort of Fabry patients all over the country putting in their data and this will be a great resource to help the doctors find ways to help LSDU patients further.

How does your disease affect you now?

Because I'm pretty good at avoiding my triggers, flare-ups are rare, but they do happen. Hot days are difficult because I don't sweat so I have no cooling mechanism. I have to make sure that if I'm going out when it's hot I'm always near an air-conditioned building or water which I can use to cool down. If I do get too hot, I get pain and tingling in my jaw, scalp, hips, hands and feet – they feel like they're being burnt – and I get shooting pains in my legs and feet. If things progress to the next stage, which they did most recently during a trip to Mexico, I get tunnel vision and dizziness. If I can cool down it starts to reverse but it can take up to two days to get back to normal. I also have to make sure I get at least eight hours' sleep. If I don't I start losing my balance.

It all makes for a rather staid life, but at least I know now what the cause is, thanks to the LSDU. Anything that happens, they sort it out. They've been faultless. For the first time since it all started going seriously wrong in my 20s, I feel like what is going on is understood because they know more about it than anyone else. I'm very lucky indeed to be treated by them.