

Pears

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Building

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Moving inside
the building

£500,000 to study skin cells

HIV research –
the patient's role

With the external façade nearly finished, attention is now turning to fitting out the inside of the Pears Building.

The building is on target for completion in the autumn and researchers at the UCL Institute of Immunity and Transplantation (IIT) are looking forward to the increased collaboration their new space will allow.

On page 3 Professor Ariberto Fassati explains the implications for his HIV research. And on page 2 we hear how a major grant will help other IIT research.

On page 4 the crucial role that patients play in research is described by Graeme Long, an HIV patient determined that future generations will benefit from scientific discovery, as he has.

Building Update and IIT news

The building remains on target to be “practically complete” as planned in September 2020, and as everyone can see, the external façade is nearly finished.

Attention is now being focused on the interior: the fit-out of the institute floors is well underway and installation of the furniture in the laboratories will start soon. Work is also starting on the patient accommodation areas and the atrium roof is being finished.

Mock-ups of a typical laboratory work station and a typical patient bedroom/bathroom are helping to show what they will look like and how the different aspects of the design will interact with each other. Work is continuing on the design of the café and tendering for facilities management is in hand.



The fundraising and communications sub group will, next month, consider the branding of the building. It has already been agreed to adopt UCL's signage system throughout the building, the design of which allows for the differentiation of the various organisations.

Searching for the signals of change

A research team has received a grant of more than £500,000 to further its work on a group of cells that sit in the skin, protecting us from infections.

Langerhans cells, in the outer layer of the skin - the epidermis - ensure that our immune system fights off things it should, like infections, but doesn't react to everyday minor injuries, which could cause autoimmune problems like allergies.

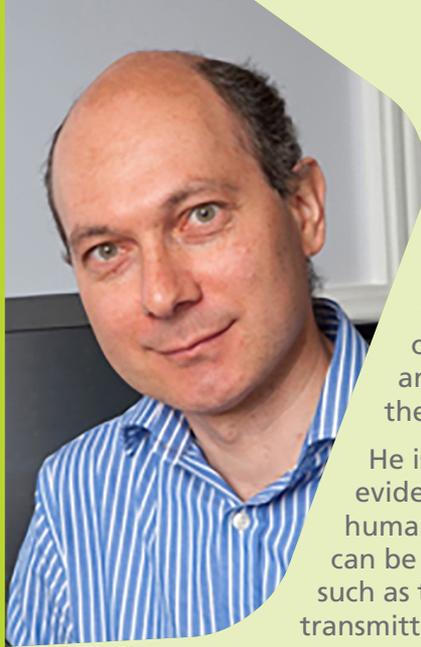
“Unfortunately some treatments, especially for cancer, kill these cells off,” said Dr Clare Bennett, principal researcher at the IIT. “But if circumstances are right, they can be replaced by other cells, monocytes, changing themselves to become identical to Langerhans cells.”

The £525k grant, from the Biotechnology and Biological Sciences Research Council, to fund a post-doctorate scientist for three years, will mean Dr Bennett and her team can focus on what it is in the skin that allows monocytes to become Langerhans cells. “We think that there's a particular type of place where they feel very comfortable to start the process of changing themselves. We want to know how they find that place, attach to it and start receiving the signals from the cells around them, that enables them to start the process.”

She hopes that the work will pave the way for new treatments for a poor immune response, which is common in the later years. “We know that in older people this process is not so good and it's one of the reasons that vaccination doesn't work as well for them. By answering some basic questions about how these cells work, we may be able to find ways to keep an efficient process going longer.”

FOCUS on the IIT

There are two different strands to the research by **Professor Ariberto Fassati** and his team, both related to the IIT's mission to find new ways to treat cancer and chronic infections.



Many people are living long lives with HIV infection thanks to highly successful antiretroviral therapy (ART) which at best can cut the virus in the blood to undetectable levels so it cannot be passed on.

"However, HIV patients still have to take ART for the rest of their lives," said Prof Fassati. "This means seeing doctors regularly and dealing with the side effects, but in less wealthy areas there is also a problem with accessing the drugs. And if people don't take their ART regularly we get drug resistance, which is spreading."

Worldwide, scientists are looking at two potential solutions, both aimed at tackling the problem of "latent" infection – the continued presence of the virus in the body. "We don't know enough about this yet but we do know that when you stop ART, the virus comes back – almost every time. So we can treat it but we can't cure it."

The first approach, being studied by teams at other centres, is to try to flush out the virus to expose it to the immune system so that it can kill the latent infection. This has been dubbed the "shock and kill" strategy.

The other strategy, which his team is studying, is to induce a state of "superlatency". "This we are calling 'block and lock' - in other words, we render the virus harmless. It's still there, but it can't cause problems. We have lots of viruses in this sort of state in our bodies."

The team has found that certain drugs can block the reactivation of the virus from the latent state and in mice has kept it dormant for the rest of their lives. "This may not be a cure but it could be a very long-term remission, which means people have longer between check-ups and the resistance problem goes away because they won't need to take drugs for years."

The compounds found to have these properties were being tested on tumours and blood cancers

and it was just chance that their effect on HIV infection was discovered.

The second plank of Prof Fassati's work concerns the phenomenon of transmissible cancer – in dogs. "This cancer can be passed from one dog to another, not through a virus but because the cancer itself is transmissible."

He is quick to point out that there is no evidence that this dog cancer can be passed to humans, and no evidence that cancers in people can be passed on, other than via familiar routes such as the human papilloma group of viruses transmitting cervical cancer.

He, with Professor Robin Weiss and his team, were the first in the world to prove that it was possible for cancer to be transmissible in this way, rather than via another agent such as a virus. Subsequently other examples were found elsewhere, including a disease which causes facial tumours in Australia's Tasmanian Devil.

"Usually cancers are different in different hosts but in this case the cancers in different dogs were quite similar in appearance and genetic composition, even across different continents."

The discovery has opened up two distinct lines of research. When this cancer is treated with a drug called vincristine it has the effect of making the cancer visible to the immune system, which then kills it.

The other potential treatment path has huge implications particularly for transplant patients. "This cancer crosses the barriers which would usually stop it moving from one individual to another. It simply bypasses the normal immune response – the same response that means we have to give transplant patients immunosuppressant drugs for life to prevent organ rejection.

"Yet when we give the drug, some kind of switch is turned on, and the cancer becomes visible. What makes that switch and how can we harness this phenomenon to help transplant and cancer patients?"

Prof Fassati is greatly looking forward to the collaborative opportunities created by the move to the Pears Building later this year. "It will bring me in close collaboration with HIV clinicians and also one of the best groups of HIV patients in the country – they are so willing to participate in studies and the biobank of samples is fantastic."

HIV RESEARCH

a patient's view

GRAEME LONG

When Graeme Long was told he had HIV infection in 2004, it came out of the blue. "It was just one in a number of tests and I assumed it would be negative. It was a massive shock. I was totally unprepared."

Although the hysteria caused by a dramatic government campaign in the late 1980s had calmed down a little, there was still a huge amount of stigma attached to the diagnosis. "I knew little about the condition. It was very scary."

But he remembers a comment made by his consultant, Margaret Johnson, the Royal Free Hospital's (RFH) HIV professor. "She said 'Don't stop paying into your pension - you'll need it.' It was really reassuring."

Openness leads to support

He knew he would be open about his status and almost immediately told his family and friends, who were a great support. "I even wrote a piece for my workplace intranet to help break down the stigma. I've seen people at work struggle to come to terms with the illness and it can end up affecting their performance. There's so much that can be done to support people but if they're not able to be open, they must feel very alone."

When he was diagnosed, Graeme's CD4 count – a marker for how well the immune system is functioning – was extremely low and the level of HIV in his blood very high. "But I didn't feel particularly ill. I started the drugs straight away and luckily for me the drug regimes had advanced to a point where the virus could be controlled."

"I had some problems initially – nausea, night sweats, palpitations and neuropathy in my fingers and toes – but by trying a few different combinations we found one that suited me."

Since then, as well as continuing to be open about his condition, Graeme has become deeply involved in both research and patient advocacy. "At one point Margaret Johnson asked me if I'd be interested in taking part in a drugs trial, initially for a year and then for two. As well as helping future patients, it meant that I had closer monitoring and faster access to clinicians if necessary."

"The research team was fantastic, accommodating my need to have blood tests early in the morning so they didn't interfere with work."

He was then asked to talk to a group of doctors about his experiences as a patient. "I was delighted to help



because it seemed to me that the clinicians were often focused very much on the science and sometimes didn't see what patients needed – for example, information in plain English.

"Patients need one side of A4 with the trial's purpose, how it will affect them, what's expected of them and what they can expect from the researchers. Another important aspect is feeding back to the patient the outcomes of the trial – it makes them feel valued and useful."

He has now been asked to work with the National Institute for Health Research as a patient research ambassador, and to co-chair a patient research forum for the Ian Charleson Day Centre at the RFH. "I'm very interested in looking at how we can better promote research to patients. The drug companies could do more on this – most people don't realise how much money they put into research."

He sometimes finds it hard to believe how far he has come since the day he was diagnosed. "I'm probably fitter than my husband. I stopped smoking five years ago, I do an hour's brisk walking every day and I eat healthily."

Research for future generations

"HIV hasn't actually impacted significantly on my general health. I had pneumonia shortly after I was diagnosed and was in hospital overnight but since then I've been well. And for me the drug regime isn't onerous – I take one tablet a day and they're talking about offering an injection every three-to-six months instead."

"Things have come on so much. That's why it's so important, for me, to carry on being involved in research. What went before made it easier for me and I'd like to make it easier for future generations."

There's one development that worries him. "There's a risk that people, especially younger people, may think that it doesn't matter if they get HIV – they just have to take a pill. If you're in a stable situation where you can adhere to the drug regime and look after yourself, it definitely helps to minimise the impact, but it's still essential that you take it, and for life."

"For people who are homeless, have mental health issues or addictions, it's much harder to achieve that stability. If my circumstances changed, it would be a very different matter coping with this disease."