

Taking a Look Inside a 'flu Research Laboratory

Emily Brown

Although almost all of us have at some stage suffered from the 'flu, most know relatively little about the virus that causes it and of the ongoing research that is investigating it.

Like all viruses, the influenza ('flu) virus grows by infecting a host, taking over cells in the host's body and turning them into factories that produce more virus particles. The disease is much more severe than the common cold and usually consists of an unpleasant week in bed suffering from a fever, muscular aches and pains, headaches, a sore throat and a cough. However, in the most severe cases, 'flu can be fatal. There are three types of the virus—A, B and C—of which influenza A presents the greatest threat, as it can infect many different species and cause severe disease. 'Flu remains a major uncontrolled disease; every year it causes seasonal epidemics which affect three to five million, and kill 250,000 to 500,000 people globally [1]. Influenza A has caused pandemics three times in the last century due to major genetic changes in the virus. These pandemics spread on a global scale and kill millions of people—the Spanish 'flu pandemic of 1918 is estimated to have caused between 30 and 50 million deaths. At present, there is concern about a new 'bird flu' pandemic developing if the avian H5N1 strain (an influenza A subtype) adapts to cause disease in humans. Thus, continued research into influenza is vital to try to control this virus and prevent the suffering it causes.

The University of Cambridge has seven research groups studying different aspects of the influenza virus. I spent some time asking members of the Digard group about their work on the influenza A virus. The group, which has eight members, is within the Division of Virology, Department of Pathology and the laboratory is on the Addenbrookes site...

Courtesy of Paul Digard



Dr Paul Digard, as the head of the group, could you give an overview of your lab's work – the general research interests and aims of the work? Also, how may the work potentially impact on society and aid in controlling 'flu?

My lab studies the molecular and cellular biology of how influenza A virus replicates; we're interested in the 'nuts and bolts' of how the virus turns an infected cell into a factory for new viruses. On one hand the virus can be viewed as being very simple—a tiny genome of only 14,000 nucleotides that only encodes 10–11 proteins—so one might think it would be relatively easy to understand. On the other hand, because it has so few proteins of its own, it subverts a myriad of normal cellular processes to its own ends, and this means that to fully understand the virus, we have to also understand how the host cell works. This

makes things more than complicated enough to keep me and many other researchers round the world busy for many years to come!

As for how this work can potentially aid in controlling 'flu—the better you understand something, the easier it is to predict how to successfully interfere with it. As an example (not work from my own lab), the Tamiflu/Relenza type of 'flu drugs were developed through a rational process



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based on knowing the function of the viral NA protein, and how it performs that function. Nothing my own lab has done is so far advanced through the process, but we're involved in a couple of collaborations with pharmaceutical companies studying the mechanism of action of potential anti-influenza drugs.

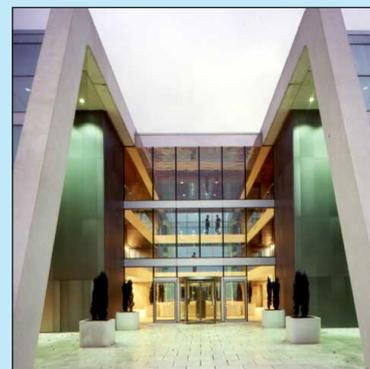
Over the years, how have advances in technology and innovation aided 'flu research?

Viruses have been isolated and defined as such for a little over a century now. Influenza A was one of the first animal viruses to be isolated, in 1904. This virus is still available in laboratories now. But, now think about how the virus has been kept for all these years... Freezers were largely unavailable until the 1940s or later. Freeze drying to preserve 'flu wasn't worked out until the 1940s. Growth of animal cells in the laboratory (tissue culture) wasn't available until the 1950s... These first influenza isolates had instead to be kept alive in the laboratory by serial passage from animal to animal—very inconvenient, and also forcing the virus to change and adapt to its new host. So, really basic advances in technology such as refrigeration make a huge difference to how we work! To give another, more 'cutting edge' example, the biggest single change I've seen to how we study 'flu during my career is

Cambridge Science Park

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Cambridge Science Park was established in 1970 by Trinity College for technology transfer, in which research is converted into commercial applications. Since then, it has become a hub for science and technology-related businesses, housing more than a hundred companies in sectors ranging from biomedical technology to energy industries. The Park's strong links to Cambridge University and ready access to venture capital funds has helped to attract brand names such as Cambridge Consultants. Today, the Park continues to build its partnership between industry and academia. In 2003, the Centre of Molecular Materials for Photonics and Electronics was set up in collaboration with the University's Department of Engineering. Cambridge Science Park has also attracted multinational companies, such as Toshiba Research Europe Ltd, who set up their first overseas R&D laboratory here, to focus on speech and computer vision technology. To cope with the needs of more and larger tenants, the Park has developed the adjacent land owned by Trinity Hall. Its latest building, 101 Cambridge, has just secured its first tenant, Royal Philips Electronics, which will specialise in wireless communications and patient monitoring systems. ■



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Jinyue Liu is a second year studying Biological Natural Sciences at Gonville & Caius College.



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Reference:
[1] www.cambridge-science-park.com

the development of 'reverse genetics'. This has made it much easier to introduce deliberate mutations into the influenza virus, which is very important in testing hypotheses about how viral proteins function.



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Ed Hutchinson is a 4th year Wellcome Trust PhD student working in the Digard group. Ed, could you give an overview of the research you are doing, what the aims are and how the work may potentially impact on society and aid in controlling 'flu?

I'm looking at how influenza packages all of its genes into new viruses. This is a poorly understood process, but it's something the virus has to do every time it reproduces—as such, it is potentially something we could interfere with to control an infection. Influenza assembles its genes in an unusual way which allows different strains of the virus to breed with each other, producing the novel strains that can cause pandemics. Studying genome packaging is therefore likely to help us predict which new versions of the virus are likely to be produced in the run-up to a pandemic.

In your opinion, how real is the risk of a pandemic and do you think we are prepared for one?

I'm not involved in outbreak monitoring, but I think the risk is still high—the trouble is, if something stays risky for a long time but never quite arrives, the press lose interest. A recent government report identified pandemic influenza as the most serious threat facing Britain today (considering both impact and likelihood)—a greater risk to the country than terrorism [2]. The country is taking some steps to prepare, but a major outbreak would have effects on infrastructure that go far beyond the direct problems caused by a lot of people getting seriously ill and dying: a pandemic will be very difficult to deal with no matter how prepared we are.

Does your lab collaborate with any other 'flu labs in Cambridge itself or throughout the UK?

We certainly do. Cambridge has one of the highest concentrations of basic science groups specialising in influenza in the world, covering everything from molecular biology to the complex mathematical modelling used in updating the 'flu vaccine. We have good working relationships with groups within the university and also those at nearby UK institutions—as well as direct collaborations, we also meet regularly to present work in progress and have informal discussions. It's one of the things that makes Cambridge such a stimulating and productive place to study the influenza virus. ■

Emily Brown is a third year studying Biological Natural Sciences at Christ's College.

References:

- [1] World Health Organisation, Influenza Fact Sheet, <http://www.who.int/mediacentre/factsheets/fs211/en/>
[2] Government: Flu poses greater risk than terrorism, The Guardian, 8th August, 2008, <http://www.guardian.co.uk/politics/2008/aug/08/health.terrorism>