Imperial College London

ANIMAL RESEARCH

Annual Report 2017–18

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FOREWORD

Animal research at Imperial

It gives me great pleasure to introduce the 2017–18 Animal Research Annual Report. This is the fourth such report we have published and looking back over the previous three reports, it is pleasing to see how far we have come over the past few years.

The Report this year contains articles celebrating the science that our research involving animals facilitates. It also once again celebrates the excellence that exists within our community of technicians and researchers by showcasing the winners of the 2017–18 Provost's Awards for Excellence in Animal Research. My sincere congratulations go to all this year's winners. Celebrating excellence in this way not only recognises the essential contributions to advancing the College's mission made by many people, but the prize awards also enable our colleagues to showcase their work to a wider audience – an essential part of our commitment under the Concordat on Openness on Animal Research.

In some ways writing the introduction to the Report this year is a bittersweet experience, as this is my last *Animal Research Annual Report* as Establishment Licence Holder. On page 8 I talk about the journey I embarked on when I took over the role of Establishment Licence Holder in 2014. I want to use this opportunity, however, to convey my heartfelt thanks to all the colleagues I have worked with during my time at Imperial. We are fortunate to have a large number of outstanding professional staff supporting animal research at Imperial, and getting to know many of those people closely has been immensely rewarding. Thank you to all of you for your hard work and commitment.

Thank you also to those academic colleagues who dedicate a significant amount of their valuable time to supporting animal research at Imperial, either through communicating their work to a wide audience, or by serving on the various committees which make up our governance and management structure.

In terms of developments in the past year, we are delighted to be celebrating the re-opening of our South Kensington Central Biomedical Services facility. The project has been an immensely complicated one, and the fact that it has been completed on time and on budget is testament to the way that our community has worked together – our academic, technical and estates colleagues deserve a lot of credit.

Last year I thanked Professor Maggie Dallman for her service as Chair of our Central Animal Welfare and Ethical Review Body (AWERB). One year on, Professor Sian Harding has made an outstanding start as our new Chair, overseeing the work of this vital committee with her customary rigour and diligence.

Overall, I look back on my period as Establishment Licence Holder with great fondness. With refurbished facilities, a renewed focus on the application of the 3Rs, and a highly capable leadership team, I am confident that I leave animal research at Imperial in a strong place. I am sure that there is more that we can do – and we must never be complacent – but I have no doubt that over the coming years we will go on to reach new heights, and to achieve our stated aim in 2014 of being 'best in class'.

Professor James Stirling

Provost and Establishment Licence Holder
May 2018

DISCOVERIES

Recent findings from animal research

Xenon gas may mitigate blast-induced brain injury

Researchers from the Department of Surgery and Cancer have used xenon gas for the first time to try to reduce the impact of traumatic brain injuries (TBI) caused by blasts such as those in conflict zones and terror attacks.

Blast TBI (bTBI) is one of the most common injuries experienced by soldiers in recent conflicts and has been dubbed a 'signature injury' of the wars in Iraq and Afghanistan. Unlike blunt force trauma, which are often localised to one area of the brain, blast injuries create a shockwave that affects the whole brain and causes widespread damage.

Previously, Dr Robert Dickinson and colleagues have shown that xenon gas has helped to limit brain damage and improve long term neurological outcomes in mice that had suffered blunt force brain injury. Now, the same research group has found that xenon gas can also limit blast-induced brain injury from developing in mouse brain tissue exposed to a blast shockwave.

Xenon reaches the brain within a few minutes after inhalation, so if these preliminary results translate to humans, it could become a viable treatment option after blasts occur.

Mini robotic labs for testing fly behaviour

Fruit flies are commonly used in neuroscience studies because of their surprising similarities to humans. However, studying flies often requires expensive bespoke equipment that can only examine a small number of flies at once.

Researchers from the Department of Life Sciences led by PhD student Quentin Geissman have invented a cheap and easy-to-use machine for the rapid study of flies. The device, called an ethoscope, combines a small Raspberry Pi computer with a camera and can be made with 3D printed components, LEGO bricks and even folded card.

Studies on fly activity usually involve researchers looking at recorded video and manually recording each fly's movements. Ethoscopes can do this automatically, with many flies at once, saving researchers time. The device can also be customised to manipulate the behaviour of the fly, allowing researchers to study their responses in a range of different scenarios.

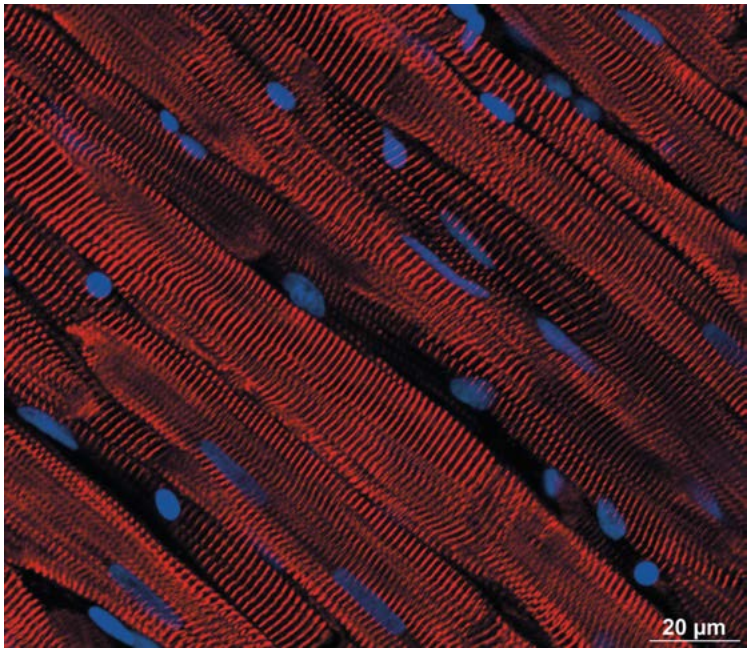
Ultra-thin tissue samples could help researchers to treat heart disease

A new method for preparing ultra-thin slices of heart tissue in the lab could help scientists to study how cells behave inside a beating heart.

Traditional methods for studying conditions affecting the heart have either used living animal models, which can be too complex to observe the heart in detail, or heart cells kept alive in the lab, which may provide an oversimplified view of the whole organ. A reliable intermediate model that can be easily studied in the lab, but without losing the complexity of the heart, has so far been out of reach.

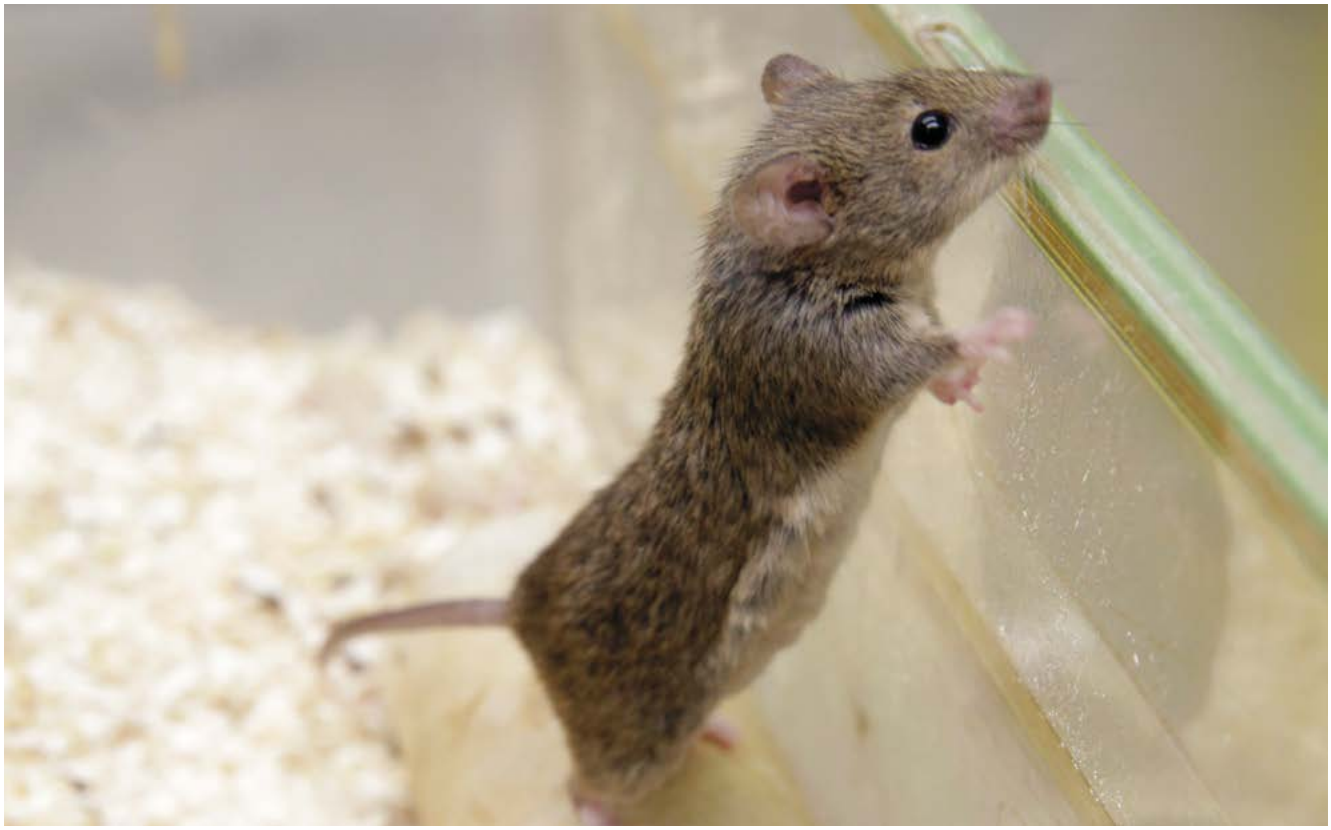
A team from the National Heart and Lung Institute has perfected an alternative method that can be used to prepare samples of heart tissue from small animals such as rodents, as well as larger animals and humans. Their new approach takes the structure of the heart into account, which is made up of sheets of muscle fibres, like a deck of cards. By ensuring that these sheets align, the heart tissue can be sliced without cutting through the muscle fibres.

This new refined method, which keeps more of the cells alive, could help to accelerate the development of new drugs and treatments by providing a more accurate experimental model of the heart.



Left: PhD student Michael Madekurozwa working in the Ocular Biomechanics laboratory in the Department of Bioengineering. Researchers in the laboratory have developed a mouse model of glaucoma that mimics the hallmarks of human steroid-induced glaucoma.

Right: The new method for preparing ultra-thin tissue samples perfected by researchers at the National Heart and Lung Institute enables high quality imaging of heart cells.



Human antibodies from Dengue patients effectively treat Zika infection in mice

Scientists have discovered that antibodies taken from patients infected with Dengue virus are effective in treating Zika infection in rodents.

The team, led by researchers at Imperial and Washington University in St Louis, USA, found that giving Zika-infected mice the antibodies was enough to treat the early stages of infection, and even protected unborn pups in pregnant animals.

According to the researchers, if the findings can be replicated in humans, the discovery could potentially lead to a single therapy to protect against both viral threats.

In trials, animals infected with Zika were treated with the antibodies in the first five days of infection and monitored for 21 days. Researchers found that treatment with antibodies reduced deaths and weight loss in the rodents when compared to a control group and that overall, the treatment was able to reduce the damage caused by the virus.

Signalling protein found to drive heart scarring and organ failure

Researchers in the National Heart and Lung Institute have discovered that a protein called interleukin 11 (IL-11) plays a key role in the scarring process, which in turn can cause heart, kidney and liver failure.

The research, published in the journal *Nature*, also found that inhibiting IL-11 could prevent the build-up of excess connective tissue in the hearts and kidneys of mice, a process called fibrosis. Interleukins are proteins involved in relaying signals between cells. They are known to help regulate cell growth, differentiation, and movement and are particularly important in immune responses, inflammation and fibrosis.

By developing drugs capable of blocking IL-11, the team hopes to be able to reduce the damage caused by a heart attack and prevent the onset of devastating heart failure.

Scientists link new genetic variants to osteoporosis in largest ever study

Researchers have identified 153 new genetic variants linked to bone mineral density, and have highlighted GPC6 as a new gene involved in osteoporosis.

The results, published in *Nature Genetics*, could be used to define osteoporosis risk and identify new targets for future drug development.

As part of the study, researchers analysed data from 140,000 individuals in the UK Biobank, a large repository of clinical data and biological samples from 500,000 participants across the UK.

In a key part of the study, co-authors Professor Graham Williams and Professor Duncan Bassett from the Department of Medicine also identified abnormal bone mass and strength in genetically modified mice, in which the GPC6 gene was deleted.

This work was performed as part of their Wellcome Trust-funded Origins of Bone and Cartilage Disease (OBCD) Strategic Award in collaboration with the Wellcome Trust's Sanger Institute and International Mouse Phenotyping Consortium (IMPC).

Genetic mutations that cause sickle cells identified in deer

A team of researchers led by Dr Tobias Warnecke from the Institute of Clinical Sciences have found that the sickle cell trait in deer took a different evolutionary path to that in humans. Although in its early stages, this research provides potential for a new model to study the effects of sickling in humans, such as resistance to malaria.

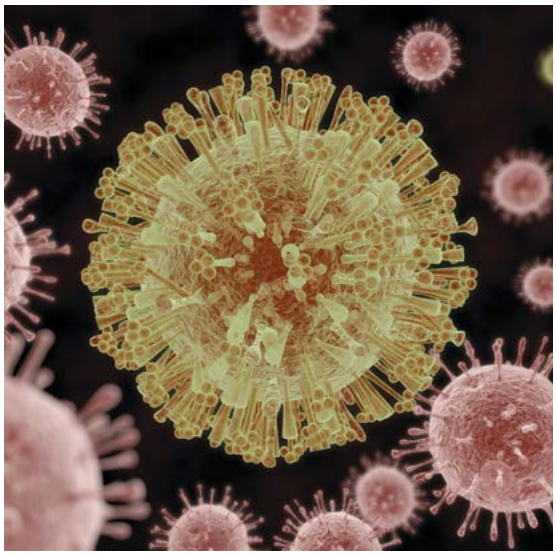
In humans, sickled red blood cells (RBCs) can become stuck and build up in blood vessels, causing severe pain and damage to organs. However, deer with sickle cells do not suffer from these debilitating symptoms.

The researchers found that in deer species with sickled cells, three of the 146 amino acids that form beta globin – the blood protein linked to sickle cells – differ from those found in deer that do not sickle. In humans with sickled cells, the change in cell shape is caused by a different mutation affecting another part of the gene. However, although the genetic architecture of sickling is different between humans and deer, both species produce RBCs of the same shape.

Dr Warnecke said: "If it turns out that sickling in deer also happens because it protects against malaria, then we may be able to start thinking of deer as a model to help us understand the link."

> "If sickling in deer also happens because it protects against malaria, we may be able to start thinking of deer as a model to help us understand the link."
>
> – Dr Tobias Warnecke, Institute of Clinical Sciences

An artist's impression of the Zika virus. Researchers have found that human antibodies from Dengue patients can treat Zika infection in mice.



The Imperial research communications team regularly publishes news stories about the impact of the College's research with animals. Visit **www.imperial.ac.uk/news** to read the latest stories or search 'animal research' on the site.

PROVOST'S AWARDS

for Excellence in Animal Research: **2017–18 winners**

The Provost's Awards for Excellence in Animal Research recognise best practice and acknowledge staff who have made advances in the 3Rs, shown openness in communicating about animal research, or demonstrated outstanding collaboration between research and Central Biomedical Services (CBS) staff. Winners receive £1,000 which can be used to cover costs associated with the presentation of the award-winning work to a wider audience.

Professor Esther Rodriguez-Villegas, Department of Electrical and Electronic Engineering

Application of the 3Rs, researchers

Professor Esther Rodriguez-Villegas, Chair of Low Power Electronics

Department of Electrical and Electronic Engineering

Professor Rodriguez-Villegas receives the Provost's Award for the pioneering research that has led to the development of TaiNi, a wireless brain monitoring system that has the potential to revolutionise the field of neurophysiological research, whilst at the same time significantly improving animals' welfare. The technical difficulties surpassed by Professor Rodriguez-Villegas to create TaiNi, the world's smallest and lightest neural monitoring system, is a prime example of her expertise, creativity and leadership, as well as her vision and commitment in improving animal research. Her work is an excellent example of the application of the 3Rs with the potential to transform science, drug development and animal welfare, and offers significant 3Rs benefits.

Application of the 3Rs, CBS staff

Mr Anthony Iglesias, CBS Facility Manager

Mr Gareth Wild, Animal Technician

Mr Iglesias and Mr Wild receive the Provost's Award for researching and testing a new long lasting, non-toxic marker pen specifically for use with laboratory animals. By restraining an animal very lightly, the pen can be applied to the fur anywhere on their body, allowing the handler to follow a simple guide to identify animals individually. A trial involving sentinel mice has shown that the marks made by the pen last for over ten weeks without the need for re-application. This refinement work will allow individual identification of animals as soon as they begin to grow fur, while the non-invasive application method means that no pain is involved. The new pen also means that animals can be identified and tracked at an early age without regular restraint – reducing the risk of disturbance to the dam and litter.

Team award

Miss Hannah Jones,
Animal technician

Mr Phil Rawson,
Senior Technician and Named Animal Care and Welfare Officer

Dr Lindsay Benson,
Named Veterinary Surgeon

Dr Richard Jabbour,
BHF Clinical Research Fellow

Professor Sian Harding,
Professor of Cardiac Pharmacology

This team receives the Provost's Award for their development of a rabbit model to test stem cell patch grafting onto injured hearts. The rabbit myocardial infarction model was successfully established and implemented at Imperial in September 2017 thanks to the exceptional team work between researchers and CBS staff. Dr Richard Jabbour, a cardiologist, learned the complex myocardial infarction model after spending time with experts at the University of Glasgow. The staff at Imperial, in particular Miss Jones, Dr Benson and Mr Rawson, used their expertise to advise Dr Jabbour on both periprocedural and post-operative care. Since initiation, several refinements have been implemented which have improved the existing Glasgow model. The team work highlighted in this application is an exemplary illustration of how research should be carried out at Imperial.

Communications award

From Imperial College London:

Dr Rebecca Holloway,
School Partnership Coordinator (Secondary)

Dr Annalisa Alexander,
Head of Outreach and Widening Participation

The CBS Team at South Kensington

From Understanding Animal Research:

Mr John Meredith,
Head of Education and Outreach

Ms Liz Danner,
Education Officer

From Westminster Academy:

Ms Holly Youlden

Ms Paula Bull

Mr Harry Gilloway

Ms Julia Dwyer

This team receives the Provost's Award for their innovative and novel approach to communicating animal research developed in collaboration with Imperial's Outreach team, CBS and the membership organisation, Understanding Animal Research (UAR). Students from Westminster Academy took part in a carefully coordinated outreach event in the Wohl Reach Out Lab at Imperial consisting of a pre-visit by UAR to their school to gauge their understanding and feelings about using animals in research, followed by a full-day visit to the College. The students participated in a lab activity using daphnia and had a tour of the animal facility, where they learned about the work that goes on there. They also had the chance to handle some of the animals and to speak to a wide range of staff. The collaboration between CBS, the Outreach team and UAR was a fantastic opportunity and has opened doors for future collaborative events and projects, which more schools are keen to be involved in.

AN UNEXPECTED JOURNEY

Professor James Stirling joined Imperial as Provost in 2013. Within a year of joining he took over as Imperial's Establishment License Holder (ELH), a legally required post which oversees animal research at the College and ensures regulatory compliance. As he prepares for retirement, Professor Stirling explains how he became ELH and how animal research at Imperial has changed during that time.

When I became Imperial's first Provost I had a long and varied list of jobs to work on. But with a background in physics and mathematics, I had absolutely no idea that animal research was an issue that I would become so involved in during my time here.

My arrival was preceded in April 2013 by a headline-grabbing infiltration of the College's animal facilities by animal rights activists. This event triggered a series of investigations, including one by the Home Office.

By the summer of 2014, this investigation was reaching its conclusion and Home Office officials made contact with Imperial. As it happened I was away on holiday that week when I received a phone call asking me to report to the then Minister, Norman Lamb, on the following Monday just after I was due to arrive back in London.

The upshot of the meeting was that Imperial had to install a new ELH, one who would remain under close scrutiny by the Home Office while the College dealt with the issues that the infiltration had raised. And that's how I found myself holding the post, having never been near an animal in my professional career. I took the role extremely seriously and made a huge effort to familiarise myself with the subject, including taking part in the basic training for scientists who plan to use animals in research.

There are a set of formal responsibilities for an ELH but, for me, there was so much more to the job. I was working towards a new culture for animal care

> “I am convinced that better use and care of animals in research leads to better science.”
>
> – Professor James Stirling, Provost and Establishment License Holder

at Imperial; not only to be ‘just’ compliant with the regulations but to go further and aim to become ‘best in class’. This was a message that resonated with colleagues in the animal research community. Being Provost as well as ELH also meant I was in a position to make things happen, such as approving new staff appointments and financial investments to refurbish our facilities (see page 10).

Following its own internal and independent investigations, the College had already created its Action Plan for World Class Animal Research and my job was to see that plan enacted. One thing quickly became apparent: that despite the incredibly challenging circumstances, the commitment of the people on the front line was never in question. We have an outstanding team of animal technologists and vets led by Mandy Thorpe, who brings almost 40 years of experience of working with animals here at Imperial.

By the end of 2014 we had made good progress against the Action Plan with a reformed ethical and welfare review process, then being expertly led by Professor Maggie Dallman, a new governance structure and stronger links between different parts of the animal research community.

But there was still one outstanding issue. The Action Plan called for a Director of Bioservices, a new senior post to oversee animal care and our animal research strategy. After an extensive search for an external candidate we finally realised that the person we needed was already at Imperial. Professor Marina Botto, a well-respected medical researcher, took up the post in the summer of 2015 and her impact has been swift, profound and sustained.

Imperial has always been committed to the principles of the 3Rs – reduction, refinement and replacement. The 3Rs advisory group, with Professor Richard Reynolds as chair, has strengthened this work and now recognises best practice by animal technologists and scientists with a set of annual awards.

The College was one of the first signatories to the UK Concordat on Openness in Animal Research in 2014, and since that time has twice been recognised by Understanding Animal Research for its communications and public engagement work. The Home Office also recognised progress at Imperial when it issued us with what in effect was a ‘clean bill of health’ in 2016. We have always maintained good relations with our Home Office Inspectors and we recently hosted a visit by new Home Office senior staff where Imperial was shown as an example of good practice in the sector.

Imperial is a big and complicated organisation and I know that we are not perfect. There is always the risk that an individual will let us down, often unintentionally, but I will not defend poor practice and we are constantly monitoring for any work with animals that is not up to the high standards we have set ourselves.

The College’s mission is to carry out world class research and teaching for the benefit of society, and animal research is key to that aim. And I am convinced that better use and care of animals in research leads to better science, improved healthcare and other societal benefits.

Being ELH has been a challenge but I am immensely proud of the progress we’ve made thanks to the hard work and dedication of the many people involved. Together, I think we have achieved a very solid platform for accomplishing our aims. I would like to thank the whole animal research community and I wish them the very best for the future.

SOUTH KENSINGTON FACILITY REFURBISHMENT

The makeover of the twenty-year old Central Biomedical Services (CBS) facility at South Kensington has efficiency and flexibility at its heart.

In summer 2018, the CBS facility at the South Kensington Campus will reopen following a year-long refurbishment. The project has been carefully planned to meet the needs of researchers and technicians working with animals at South Kensington, creating flexible workspaces and improving the efficiency of day to day processes. As the builders put the finishing touches to the facility, CBS Deputy Director and Site Manager, Wendy Steel, explains what's changed.

"The facility is over 20 years old. It had been in need of refurbishment for a few years, so we're very happy that the College decided to invest in it," says Wendy. "The main problem we had was that some of the machinery was reaching the end of its lifespan. The air handling unit – which is really important to maintain the environment for the animals – was old and parts needed replacing. To remain compliant with the Home Office's guidelines, we had to refurbish the facility, otherwise we would eventually have had to close it."

During the works, the animals were moved to alternative facilities on the Hammersmith and St Mary's campuses, although some remained at South Kensington. "There's a lot of work on site that couldn't be moved to either Hammersmith or St Mary's," explains Wendy. "We have around 700 cages still on the South Kensington Campus, so we've still been quite busy while the main unit has been closed."

The refurbishment has enabled the CBS team to rethink the space and the experience of the staff and animals who spend time in the facility. Access routes throughout the facility have been replanned to improve efficiency. Larger changing areas and meeting spaces for staff have been created. Even the colour scheme and the lighting has been updated to better support the well-being of animals and the staff working with them. However, one of the most radical changes has been the installation of three new machines which will automate the majority of work involved in cleaning animals' cages and water bottles.

The new machines divide the cleaning area in two, creating a 'clean' and 'dirty' side. Used cages and water bottles come in on the dirty side where they are emptied, cleaned and refilled, before they emerge on the clean side ready to use.

The cage handling machine – which the team expects will be able to handle up to 3,000 cages each week – is equipped with a robotic arm that can pick cages up and scrape soiled bedding into a waste bin. All of the waste that goes into the bin is macerated and then extracted by vacuum, where it is directly transferred to a clinical waste compound outside the building. The empty cages are then transferred to a rack washer for cleaning, before moving to the clean side of the facility to be refilled with bedding or sterilised.

Used water bottles are brought into the cleaning area on crates, ready to be loaded onto the bottle washing machine's conveyor belt. The machine automatically removes the bottles' caps, before they are emptied, washed and rinsed. The bottles then move through the machine to the clean side of the

Right: The new cage cleaning machine automatically empties bedding from used cages.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A new secure suite within the facility will be used for research of infectious diseases.

room where they are filled with fresh, sterilised water. New clean caps are put back on to the bottles inside the machine and they come out at the other end of the machine in crates ready for use.

The refurbished cleaning area will bring huge benefits to the CBS team working in the facility, as Wendy explains, "Although previously a machine was used to wash the cages, each one had to scraped by hand to remove soiled bedding and the waste material was removed from the facility manually. The new automated system improves manual handling and makes things more hygienic."

> "The new automated system improves manual handling and makes things more hygienic."
>
> – Wendy Steel,
> CBS Deputy Director and Site Manager

New animal holding areas and procedure suites, fitted with state-of-the-art equipment, have been created as part of the works, and the facility now also includes an area where animals who have been used in research elsewhere on the South Kensington Campus can be kept separately from other animals already housed in the facility. This area includes a holding and procedure suite, as well a room where equipment can be sterilised using vaporised hydrogen peroxide before it enters the main unit.

The facility's improved flexibility also means that the CBS team can reduce the number of animal research operations at South Kensington that are housed outside the facility. Wendy explains, "Some of the specialised equipment, such as that used by the Department of Bioengineering, has to be kept outside CBS – we can't bring it in here. So there'll always be a need to have some animals outside CBS at South Kensington. But with the refurbishment, we've been able to reduce that as much as we can.

"There are some operations that were housed outside just because we didn't have the room, but because now we have a more flexible space, we'll be able to bring some of that work in. This is better for everyone: better for the animals and better for the people working with them. From a 3Rs perspective, we definitely see that as a refinement."

Top and middle: Surgical suites in the facility have been fitted with new state-of-the-art equipment, including a height adjustable perfusion table that can be used during the preparation of animals for surgery and in their recovery.

Bottom: New LED lighting in animal holding areas can recreate dawn and dusk light levels. Red lighting has also been installed for out of hours work to avoid disturbance to sleeping animals.

An animal technologist handles a guinea pig.

LOOKING INTO BONE MARROW

Intravital microscopy using live mice has led to ground-breaking discoveries in the study of haematopoiesis and leukaemia. By developing the technique, Dr Cristina Lo Celso and her team have been able to reduce the number of animals they use.

It's easy to see why a young researcher might be drawn to working with stem cells, the body's resource for producing and repairing tissues and organs. With an apparently limitless ability to divide, these amazing cells both replenish themselves and have the potential to become specialised in tissues such as blood, muscle or the brain.

"Since my undergraduate studies I've always been fascinated by stem cells," says Dr Cristina Lo Celso, a reader in the Department of Life Sciences. "I always had the feeling that they have incredible potential in terms of therapeutic approaches."

Those undergraduate studies took place at the University of Turin, in Italy, before she came to the UK for a PhD in biochemistry at Cancer Research UK's London Research Institute. After that, she moved to Harvard University in the USA. By then she had switched her research interest from skin to haematopoietic stem cells, the stem cells in bone marrow that produce blood.

In addition to studying the way these stem cells function, she started to work on leukaemia, a disease that disrupts healthy blood production. "You have to know your enemy," she says. "If you want to learn how healthy stem cells lose out to leukaemia, then you have to understand what it is that allows leukaemia to win."

Intravital microscopy

It was during her time at Harvard that, together with physicists at the university, she developed the technique that has underpinned her research ever since. "We were able to build a microscope that would allow us to see inside the bones of live mice, and within the bone marrow to see haematopoietic stem cells in their own environment," she says. "The first time we saw real haematopoietic stem cells in their own real place, doing their real job, that was quite amazing."

The method, called intravital microscopy, combines two different techniques. First of all two-photon microscopy makes it possible to see bone tissue, and so locate the cavity within it containing bone marrow. Then, within that cavity, confocal microscopy can pick out fluorescent proteins that have been engineered into the mice.

"If we use different fluorescent proteins to label leukaemia cells and components of the bone marrow, then we can look at the interaction of the leukaemia cells with different cell types at the same time, in real time and over time."

The mice are under anaesthetic throughout the procedure and recover afterwards. "One of the powerful things about this technique is that we can look at the mice for a couple of hours, put them back in their cages, and then return to them one or two days later and see how the leukaemia has grown and how healthy haematopoiesis has been responding to it. This is particularly important when we want to assess the effect of treatments."

Cells on the move

Dr Lo Celso moved to Imperial's Department of Life Sciences in 2009 and her 'bone marrow dynamics' group has continued to develop intravital microscopy for the study of haematopoiesis and leukaemia. One of their most dramatic discoveries has been that the vast majority of leukaemia cells move about within the bone marrow.

"This is something that we would have never known unless we had looked at them directly and followed them over time in live mice," she explains. "It completely changed the way we think of leukaemia and the way we approach it."

It had been thought that leukaemia might spread through the body by taking advantage of blood vessels, or perhaps that it relied on interactions with a particular kind of cell for its development. Dr Lo Celso's work showed, however, that the cancer cells move more freely in bone marrow and have a wide range of interactions. Now the challenge is to learn more about this behaviour.

"We want to understand why these leukaemia cells run and, if we stop them from running, can we gain some advantage on them, for example making them more sensitive to chemotherapy."

Fortunately there is a lot of research on cell migration to draw on. "We know that a lot of genes are involved in cell migration, and we have an idea of which ones are expressed in our cells. Now it is a matter of figuring out exactly what their role is and how we can target them, ideally just in the leukaemia cells and not in healthy cells."

Dr Cristina Lo Celso,
Department of Life Sciences

Refining the model

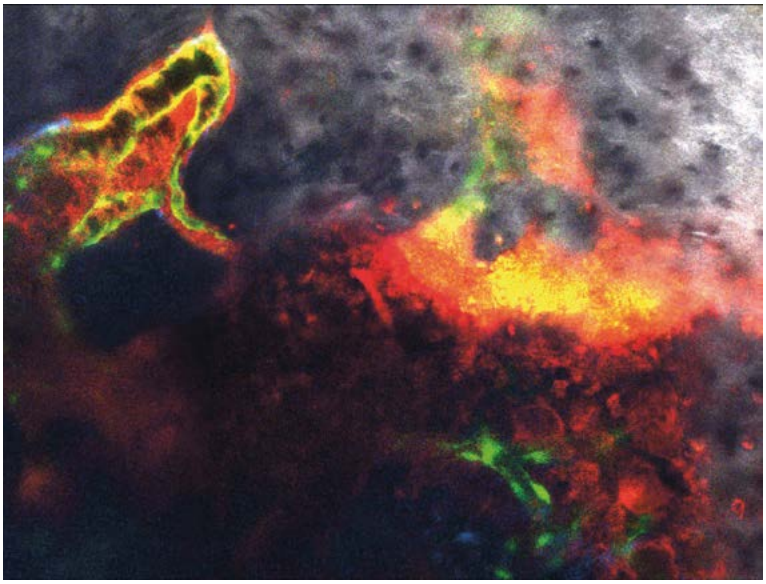
Working with live animals remains essential to pursuing this line of research. “Bone marrow is very complex and we cannot, yet, reproduce it *in vitro*. Instead, by looking *in vivo*, we are able to understand a lot about this tissue,” Dr Lo Celso says. “But I’m fairly optimistic that, in the future, we will be able to replace animals and do a lot of experiments *in vitro*.”

Mice are chosen because their haematopoietic system is very close to the human one, and genetically modified mice allow researchers to test the role of specific genes. “We can use what we find with the mice to start thinking about clinical applications and translation of our findings to people.”

Several refinements have been made to the procedure over the years that Dr Lo Celso has been using it. “For example, we anaesthetise the mice in a much more controlled way now, so that they recover a lot better, and the way we do the surgery has also been improved.”

This surgery involves exposing an area of bone so that an image can be taken with the minimum of intervening tissue. The best place to do this is the skull, since there is no muscle. It is relatively easy to lift a small piece of skin to get to the bone beneath, then close it after the images have been taken. However this creates scar tissue which, while small, can still obscure further microscopy and may be a little uncomfortable for the mouse.

“So we have optimised this technique, making a little imaging window that we put on top [of the skull], with some gel and a plaster, and the mice don’t scar,” says Dr Lo Celso. “That is better for the mouse, and also better for the research because we can go back and easily see our cells again.”



A microscopy image of leukaemia cells, shown in red, distributed throughout the bone marrow cavity. The green areas show endothelial cells delimiting blood vessels, and blue areas highlight bone making cells, called osteoblasts. The grey areas show collagen, one of the main components of bone and which encase the bone marrow.

> “I’m fairly optimistic that in the future, we will be able to replace animals and do a lot of experiments *in vitro*”
>
> – Dr Cristina Lo Celso, Department of Life Sciences

Reduction and replacement

The number of animals going through the procedure has been reduced with the introduction of more powerful microscopes, which allow the simultaneous imaging of more fluorescent proteins. Where previously a different transgenic mouse would be needed for each kind of cell to be observed, now the transgenic lines can be crossed together and multiple cell types observed in a single animal.

Meanwhile mathematical models have been used to generate specific hypotheses that can be tested *in vivo*, rather than pursuing broader lines of enquiry with the animal models. "Of course, we still have to do some experiments, but we end up doing fewer experiments that we would otherwise," Dr Lo Celso says.

She also sees a broader trend in her area of research towards more sophisticated animal procedures. "Animal work remains necessary, but we can reduce the number of procedures as we understand more and more, both about the physiology of the animals, and also the subjects that we are studying."

For example, 10 or 20 years ago a cancer study might conclude rather crudely with the death or the survival of the animal. "We don't do that anymore, because we understand how the disease progresses and we don't have to take it all the way until the mouse is really suffering. There are signs that we can use [as end points] and specific phenotypes we can see in the disease cells that are in the mice."

In addition, the evolving regulation of animal procedures across Europe has strengthened the position of researchers. "Everything is more controlled, is discussed more, and is a lot more open. Everybody can see that we are doing things in the best possible way."

Meanwhile her own work is getting closer to the point where it will be tested in cancer patients. "We are coming up with very interesting drug candidates, and we have already tested on murine leukaemias some drugs that are approved for use in humans, but for other conditions. Some of them seem promising."

A clinical trial might be possible in the next two to five years, funding permitting. "Of course we have to do a little bit more work, but the word 'trial' is starting to be mentioned when I discuss science with the people in my group. And that's incredibly exciting."

TURNING PEOPLE INSIDE OUT

By producing cells outside the body, researchers from Imperial's Faculty of Medicine have been able to replace animal procedures while delivering better scientific results.

Researchers are often limited in the work they can do with humans by how hard it is to reach certain organs. The brain and the heart are challenging to work on, and tissues deep in the lungs or intestine are almost impossible to reach in living subjects. This is one reason they turn to animal models. At Imperial, however, several groups are building tissues outside the body, making them easier to study. This often produces better scientific results, while reducing or replacing animal procedures.

Several of these approaches involve using stem cells, the cells responsible for building or repairing tissues in the body. Some of these stem cells, known as pluripotent stem cells, can take on a wide range of specialised functions, depending on the signals they get from the body.

Researchers are now able to produce pluripotent stem cells from ordinary body cells, such as skin cells, tooth pulp or blood cells. They can then reprogramme them and grow them in cell culture 'lines' that develop into the tissues they want to examine.

From the heart

Professor Sian Harding and her group at the National Heart and Lung Institute have used this technique to produce cardiomyocytes, the cells in the heart responsible for the organ's rhythmic beating. And just like heart muscle, these cells pulse spontaneously when cultured in a dish. "After about ten days they start to produce this beating effect," says Professor Harding.

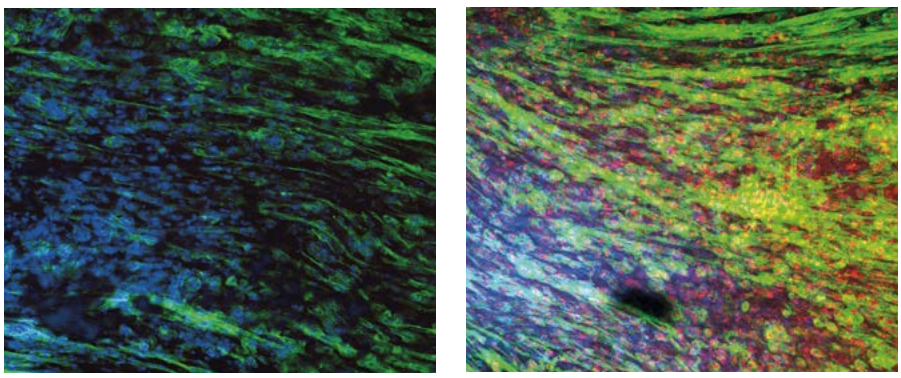
The cells can also be made into heart tissue, and when a small strip is attached to two silicon posts, it pulls rhythmically at the supports, essentially working out. Measuring these contractions, or looking at fluctuations in calcium within the tissue culture, can be used to answer a range of research questions.

The advantage is not only that this heart tissue is human, but if the stem cells are produced from patients with heart conditions, these appear in the cultured tissue as well. "If people have the mutations that cause poor contraction or rhythm disturbances, in many cases we've been able to show that you can see these conditions either in the cells or in the engineered heart tissue," explains Professor Harding.

"You can then investigate that mutation, in a human background, without having to produce transgenic mice. With new gene editing technology you can put the mutation into a normal line or take it out of that line, and so you can understand what is happening in the background and what is happening due to the mutation. And you can test drugs on it."

The method can also be used as a more general screen to see if drugs for other conditions have an adverse affect on the heart. This is often the case if they affect the hERG channel, a structure that contributes to the electrical activity of the heart and helps coordinate beating.

"A lot of drugs are thrown out of development because they have hERG channel activity, and you can see the electrical potentials changing in the cardiomyocytes," says Professor Harding.



Microscopy images of engineered human heart tissue used for toxicity testing. Here, human-induced pluripotent stem cell cardiomyocytes are shown in green. The red staining in the image on the right indicates cell death after treatment with a chemotherapeutic agent.

Mr Tankut Guney,
National Heart and Lung Institute

> “Imaging in humans was not developed as a means of reducing animal experimentation, but it is a very nice side effect.”
>
> – Dr David Owen, Department of Medicine

A response to dementia

Dr David Owen in the Department of Medicine is also working with material developed from pluripotent stem cells, to study the role of the immune system in dementias such as Alzheimer’s disease.

“The immune system in the brain is probably not the underlying cause of these diseases, but it may be making things a lot worse,” he explains. For example, it may become less effective at cleaning up the damage caused by dementia, or start to damage the brain as the dementia progresses.

Investigating this in the living human brain is practically impossible, and animals often provide poor models. For example, stimulating the immune response in a mouse’s brain will increase production of translocator protein (TSPO), the molecule Dr Owen is studying, while levels fall when the human brain is stimulated.

So he and his colleagues took pluripotent stem cells, derived from human skin, and turned them into cells that resemble microglia, which are responsible for the immune response in the brain. “That enables us to study human cells, and get around all the problems of species differences.”

As new information about the immune response emerges from these human microglia-like cells, it can be followed up in other human settings. One option is to look for the same phenomena in macrophages, the immune cells in the blood, with experiments involving volunteers or patients.

Another is to cross-check the findings with post-mortem samples, such as those held in the Multiple Sclerosis and Parkinson’s Tissue Bank at Imperial, or to run brain imaging experiments on patients. “You make a discovery in a cell line, but to see whether or not it is relevant you need to look directly at the brain,” says Dr Owen.

He is particularly keen on imaging, for its scientific potential and as a way of avoiding animal procedures. “Imaging in humans was not developed as a means of reducing animal experimentation, but it is a very nice side effect.”

Dr David Owen examines a brain sample from the Multiple Sclerosis and Parkinson’s Tissue Bank.

Professor Irene Miguel-Aliaga uses organoids derived from mice to explore how the intestine adapts to challenges like changing diet and pregnancy.

Out of the lungs

The difficulty in creating accurate animal models of the human immune response is also behind the work of Mr Tankut Guney, currently completing a PhD in the National Heart and Lung Institute. He is interested in lung diseases, such as asthma and chronic obstructive pulmonary disease (COPD), in which immune response plays an important role.

"We don't have very representative animal models for the lung," he explains. "The mouse immune system is different from that in humans, and the way lung repair happens in mice is also completely different, which is why they don't get asthma or COPD." Underlining these differences, drugs developed with animal models often fail when they reach clinical trials.

So Mr Guney has been working with organoids, small three-dimensional replicas of lung tissue derived from human cells. Rather than using pluripotent stem cells, he starts with the progenitor cells whose role is to repair the inner surface of the lung in case of damage.

Grown outside the body on a basement membrane, these progenitor cells independently form spheres, which in turn develop a cavity or lumen in the centre. "On the outside of the sphere you have an undifferentiated stem cell population that regenerates the inside, and inside you have functional cells, such as mucus producing cells or cells with beating cilia," Mr Guney says.

Working on these organoids not only gets around the differences between humans and other animals, but allows research on individuals with different medical histories. For instance, Mr Guney is currently comparing responses to cigarette smoke in organoids drawn from people who have never smoked and those who have COPD.

This promises to increase knowledge about the factors that lead to COPD and help identify potential treatments. "It may not give us the complete answer, but it will give a good indication of where to go, without having to use a lot of mice in the process and then risk a high percentage of those treatments failing in clinical trials."

Building small guts

While most effective when using human tissues to replace animals, the notion of building tissues outside the body can also help reduce the use of animals. Professor Irene Miguel-Aliaga, of the Institute of Clinical Sciences, is doing this in her work on how the intestine adapts to challenges such as changing diet or pregnancy.

"There is increasing evidence that these intestinal adaptations are key to maintaining our normal physiology," she says. "It is also increasingly recognised that, when they fail, they contribute to obesity and diabetes."

Complementary *in vivo* and *in vitro* approaches have been developed to explore how these adaptations take place. "We first characterise them in fruit flies (which have complex and adaptable intestines too) and then explore their broad relevance in intestinal organoids derived from mice. These are miniature versions of the mouse gut which you can grow – and genetically manipulate – on a dish."

Rather than embryonic stem cells, these organoids are produced from stem cells dissociated from the adult mouse's small intestine. But only a small number of animals are involved.

"You can derive many organoids from one single mouse and you can maintain them on a dish for months, even years," says Professor Miguel-Aliaga. "This reduces the need for continuously breeding mice and also reduces the overall number of mice involved."

She is enthusiastic about the potential for taking this approach further. "Organoid technology is in its early days and the more we can learn about the organoids themselves, the easier it will be to determine whether certain genes affect their structure and/or physiology."

CHASING INFLUENZA

Refining models used in animal research can produce better results and improve animal welfare. By reflecting how flu is picked up in daily life in their studies, Professor Wendy Barclay and her team have been able to gather better data on its transmission.

Ferrets catch, carry and pass on the influenza virus in the same way as humans. This makes them the gold standard for studying the disease. Work led by Professor Wendy Barclay, in the Department of Medicine, has fine-tuned the way this uncommon laboratory animal is used, reducing the number of ferrets involved, improving the experience for those that remain, while generating ever more relevant scientific results.

Influenza is a moving target when it comes to devising effective vaccines. There are three broad types of flu virus, labelled A, B and C, with type A further divided into subtypes based on the proteins that appear on the surface of the virus. The subtypes currently dominant in seasonal flu are H1N1 and H3N2 (the focus of Professor Barclay's work).

The virus evolves very quickly, which means that a vaccine based on one year's outbreak of seasonal flu may not be effective the following year. "By the time we get ready to give it to people and protect them, the virus has already mutated onwards," says Professor Barclay, describing the process known as antigenic drift.

This rapid evolution also lies behind pandemic flu, which happens when virus strains in other species, particularly birds, change in such a way that they start infecting humans. "These pandemics are very unpredictable. Out of the thousands of different animal viruses that are in nature, we don't know which ones will achieve the right combination of mutations to transform them into pandemic viruses that affect humans."

A tough case

Discovering more about how the flu virus evolves, and how it is transmitted, would lead to more effective vaccines and perhaps other strategies to lessen the impact of the disease. But it is not an easy virus to study, since it does not naturally infect the most common research animals. Mice and guinea pigs can be adapted so that they become infected, but even then they get different symptoms from humans, or no symptoms at all.

Ferrets, on the other hand, have a respiratory tract that is much closer to humans. They are naturally susceptible to human strains of flu, but – just like humans – not to bird flus. Once infected they fall sick and show clinical signs that are similar to human flu. And the virus can pass from one animal to another in close proximity.

This makes them the perfect model for both basic and applied research on influenza. "We can study the virus as it evolves in the animal, and then look at it passing from one animal to the next. This allows us to think about things like bottlenecks at the point of transmission," says Professor Barclay. In other words, however much a virus evolves in one host, its ability to spread these changes will depend on how well it passes from one person or animal to the next. "We can also use the ferret as a model, for example, to test new vaccines, new drugs and new interventions."

Realism in research

One way in which this research has been refined by Professor Barclay's group is to make procedures for testing the effectiveness of a drug or vaccine as natural as possible.

"To show protection what you would normally do is to immunise your animals, or give them some sort of drug, and then challenge them with a fairly large dose of virus, maybe in quite a large volume, and that is likely to make the animal quite sick," she explains.

However that is not what happens when a person picks up a flu virus in daily life. "The actual dose we receive is quite small and the route is through the airway, in a droplet." So this is how Professor Barclay's group works, with smaller doses of the virus and transmission through the air between animals in the same or adjacent cages.

The data gathered is better, because it is closer to the real situation, and it causes less stress to the animal. "The animals are not getting severely ill," she explains. "We can detect that they are infected and see some mild clinical signs, but overall the model is much milder than a traditional challenge might be."

Handled with care

There have also been refinements to the way the ferrets are monitored to see if they have become infected. Conventionally that would be done with a nasal swab or a nasal wash while the ferret is anaesthetised, but repeating this procedure for daily monitoring would lead to a harmful build up of anaesthetic.

So, working closely with the College's Central Biomedical Services (CBS) staff, a new procedure has been devised in which two people, and sometimes three, hold the animals and apply a nasal wash without anaesthetic. The ferrets are used to this kind of contact, having been handled regularly from the moment they arrive in the animal unit, and during the procedure they are rewarded with pleasant-tasting treats.

"That is a refinement to the procedure which enables us to avoid the over-use of anaesthetic, which is detrimental to the animals," says Professor Barclay. "The animals have had frequent handling, so they are not fazed by this approach."

Colleagues from CBS were instrumental in developing this new method. "We worked very closely with them on how to perform the nasal washing procedure without anaesthetics, how to hold the animals and get them, basically, to sneeze into a little pot. So now we do this quite differently from many other places around the world."

And while ferrets sometimes have the reputation of being feisty, aggressive animals, Professor Barclay has found that by selecting the smaller, more placid females there is little problem in working with them.

Professor Barclay has developed a breath sampling device that uses a cell culture to show when a ferret is exhaling infectious virus.

> "Our current experiments are aimed towards understanding why the virus weaves and turns in the way it does, in a whole, transmitting animal."
>
> – Professor Wendy Barclay, Department of Medicine

The ferrets are handled regularly and are used to contact.

Looking forward, Professor Barclay hopes to be able to work with genetically modified ferrets.

Reduction and replacement

Collaboration between Professor Barclay's team and CBS has also permitted a reduction in the number of animals used, and their replacement has also been possible. The team are investigating when an infected ferret is able to transmit the virus. One way of doing this is to introduce uninfected ferrets into the cage of an animal known to have the virus, but to get a precise result over the course of an infection would mean using a large number of these 'sentinel' animals.

So Professor Barclay and her colleagues devised a breath sampling device that uses a cell culture to show when the ferret is exhaling infectious virus. "And what we find is a really narrow time window two days after infection when virus is coming out in the breath of the animal," she says. "Then there are days either side when there is nothing in the air."

While a ferret is still needed as the virus host, the other animals have been replaced. "To have done that experiment with animals as sentinels, instead of cell culture dishes, would have taken about 30 animals per experiment," says Professor Barclay. "We no longer need to use those animals now." This approach will make it possible to examine contagiousness under different conditions in a whole range of viruses, with minimal involvement of animals.

Looking forward

The potential exists to get even more information out of these kinds of experiments, for instance by looking at how ferrets which have been infected with the flu virus respond to a second exposure. Again this mirrors the human situation, where people are exposed to the virus multiple times over their lives.

"The idea is that we will re-infect or re-challenge them with viruses, and then sequence the virus as it then evolves in those partially immune animals. That will be much more like what happens in a real scenario, with flu evolving within humans," Professor Barclay says.

"Our current experiments are aimed towards understanding why the virus weaves and turns in the way it does, in a whole, transmitting animal," she goes on. "In that situation, where you are working in an animal, the virus is subject to a whole number of different evolutionary pressures, which we hope will help us to predict in the future the way that the virus is going to evolve."

Another possibility is to extend the work beyond the present focus on the H3N2 subtype of influenza. "With flu you can never be sure that your answers with one type or subtype are going to be the same as the others. If we are successful in doing it this way, we may well branch out and see how other flu viruses compare, and ask if they are all evolving in the same way, at the same rates, and do they all experience the same bottlenecks."

And looking forward to the next 10 or 20 years, Professor Barclay hopes to be able to work with genetically modified ferrets, in the same way as mice are used in other research. "Then we could test the role of host genes in the outcome of infection."

The obstacle is not the difficulty of such genetic manipulation, but simply that ferrets are such uncommon laboratory animals that no-one has yet invested the time and money in developing appropriate transgenic techniques. "We are not really expert in that, but we are keeping a close eye on other people who are, because it would have a massive impact on our work."

THE 3RS

For Dr Anna Napolitano, who joined Imperial in 2017 as CBS Quality Assurance and 3Rs Programme Manager, no two days are the same. With responsibilities including training and education, policy and welfare and communicating about animal research, Anna's work demonstrates the depth of Imperial's commitment to reducing, refining and replacing animals in research.

Anna's role is dedicated to enhancing the culture of care at Imperial, and supporting students and staff to apply the 3Rs principles of replacement, refinement and reduction in their work with animals.

With a background in research and experience of working with animals in the lab, Anna has a good understanding of the issues and concerns researchers often face when they work with animals. Anna joined Imperial after completing a post-doc on infection immunology at the Francis Crick Institute, where she studied the early immune response to the Toxoplasma Gondii parasite in mice.

Her career began as a researcher at Federico II University in Naples, Italy, where she used mice models in gene therapy research, and further developed her expertise using animal models during her PhD in Milan. Despite a passion for lab work, Anna's love for talking about science and helping people to improve their scientific knowledge took her down a different path – still surrounded by science, but this time, away from the bench.

Six months in at Imperial, Anna has already made a big impact. She's a part of the committee that oversees compliance with animal care policies, guidelines and legislation, and sits on the College's 3Rs advisory group, which explores new and effective ways to reduce, refine and replace the use of animals in research at Imperial.

"My role is heavily focused on the 3Rs," she explains. "I have lots of ideas for developing new opportunities for people to engage with animal research and getting researchers to think about how they can apply the 3Rs approach in their everyday work. The College has made a lot of investment in training and new facilities, and has been really proactive in improving its 3Rs approach."

This investment in training has led to the development of a new suite of training programmes for staff and students at Imperial, including the first 3Rs course for researchers, which was held in November 2017.

Created with external partners, these training programmes aim to broaden the awareness that staff have about research with animals at Imperial and elsewhere in the sector, and strengthen their understanding of the tools and resources available to support research practice involving animals.

Earlier this year, Anna delivered a new course for animal technicians in collaboration with the RSPCA. "The feedback we've had on this course has been really good," says Anna. "The technicians really appreciated having more information about the 3Rs, as well as seeing that there is someone in the College that they can talk with about using the 3Rs, and about animal welfare and animal research."

These courses will become part of the core training for staff, and could even lead to professional accreditation. Anna is also hosting a number of smaller workshops for staff that bring together scientists and technicians working on the same subject or with the same animals to discuss and share ideas on best practice and the 3Rs in animal research.

Improving communication about animal research at Imperial is something that Anna sees as crucial to encourage greater engagement with the 3Rs at the College.

"It's good to see how Imperial communicates its animal research," she says. "Historically, there has been some reticence about talking about research with animals, and often you can't find people on the Imperial website easily if they work with animals. It's difficult to find my contact details, even though I should be someone who's easy to find.

"However, the College is committed to increasing transparency through good communication and I hope that by developing our communications further, we can continue to improve."

As part of this development, Anna has turned her attention to the College's webpages on animal research. She's produced new case studies and resources for the College's website to show how and why animals are used, and added more information about her role to encourage greater openness around animal research.

She's also supported researchers in new public engagement activities, including a live 'Ask Me Anything' session about animal welfare on Reddit with Professor Richard Reynolds (see page 32) and has plans for a series of 'Ask Me Anything' sessions with other Imperial academics who work with animals. Anna has been involved in organising animal research activities for the Imperial Festival too, including a space for researchers in the CBS stand at the Festival to help visitors understand the link between the research results and the animals they have been obtained from.

WORKING FOR ANIMAL HEALTH

Lindsay and Alasdair are familiar faces to researchers working with animals at Imperial. As the College's Named Veterinary Surgeons, they are closely involved in the process for beginning any scientific procedures involving animals, and they make daily rounds of the facilities where work with animals takes place.

"We try to be as visible as possible," says Lindsay. "We try to get into the unit every day, so if half the day is taken up with meetings, we will aim to go and see a researcher in the other half."

Under the Animals (Scientific Procedures) Act, a Named Veterinary Surgeon is required to provide advice on the health, welfare and treatment of animals. "Our main job is to look after their general health and then to help refine the scientific procedures that researchers undertake to cause the least distress and harm possible to the animals," Lindsay explains.

At Imperial this role is contracted out to Red Kite Veterinary Consultants. Its vets specialise in research animals and also provide training for researchers who want to work with animals.

In an average week around a third of Lindsay's time is taken up with paperwork, such as helping prepare research proposals for submission to the Animal Welfare and Ethical Review Body (AWERB). "We review every project licence proposal or application, and discuss with animal care staff how those proposals can be managed on the ground," she says.

"We consider things like the training and competence of the scientists doing the procedures, and the facilities and equipment that we have. Then we follow that proposal through to the AWERB, where a larger body of people will consider it both from the scientific and the welfare perspective."

Each day also includes routine inspections of the areas where animals are kept. "We walk around, and talk to the Named Animal Care Welfare Officer and the technicians who are responsible for the day-to-day care of the animals. We also come across researchers doing procedures, observe them and identify if refinements or improvements are needed. We will then conduct further training if required."

The animals are also screened on a regular basis, to make sure that they are healthy in a general sense but also to maintain the high health status of the whole population. "We also visit the suppliers of our animals, to make sure they are keeping animals in a way that we find acceptable," Lindsay says.

The detailed planning involved in each piece of animal research means that most of the adverse health effects are foreseen and procedures are in place to deal with them. Even so, the vets may still find themselves confronted with animals that are not well.

"If the animal is in extreme distress and that cannot be ameliorated, then the animal is killed immediately to relieve its suffering," Lindsay says. "The Animals (Scientific Procedures) Act is really clear on that. There are no heroic treatment programmes, such as you might employ with a much loved pet. Our priority is to limit the suffering that the animal undergoes."

If the problem is more minor, then a discussion takes place with the researcher involved about whether or not it is a result of the scientific study. If it is, the project licence will cover the steps to be taken. If not, then they consider if treatment will interfere with the scientific results.

"If the prognosis is good and we can treat it easily, then we go ahead and treat the condition, with the researcher's permission," Lindsay says. If the researcher thinks the treatment will interfere with the results, then the animals are usually killed to prevent further distress.

While both Lindsay and Alasdair belong to an external consultancy, they work closely with the College's researchers. "We try to cultivate a positive relationship, and make them understand that we are here to refine their procedures, and hopefully to improve the quality of their scientific data."

The work is also rewarding from the vets' point of view, thanks to its strong focus on animal welfare. "If we can help the researchers refine their procedures and improve their competence, it feels that we make a really big difference to the animals."

COMMUNICATING

Telling stories of animal research

This year, Imperial has continued to find new ways to engage the public with stories about animal research and its impact, while maintaining its commitment to communicating openly about research using animals.

In February 2018, Professor Richard Reynolds, Professor of Cellular Neurobiology and Chair of the College's 3Rs Advisory Group, hosted Imperial's first animal research 'Ask Me Anything' session on the social news platform, Reddit. In the live two-hour session, Professor Reynolds answered questions submitted by Reddit users on a range of topics related to his work on multiple sclerosis (MS) and the role played by animals in research. Speaking after the session, he said: "I enjoyed the chance to interact with a wide community and to talk about my passion for MS research and animal welfare."

The session was well received by the Reddit community and helped to spread the principle of 'good animal welfare for good science'. In line with Imperial's involvement in the Concordat on Openness on Animal Research, the College plans to host more 'Ask Me Anything' sessions with researchers who contribute to the dissemination and improvement of animal research according to the 3Rs principles.

> "I enjoyed the chance to interact with a wide community and to talk about my passion for MS research and animal welfare."
>
> – Professor Richard Reynolds, Department of Medicine

During Professor Richard Reynolds's Reddit 'Ask Me Anything' session, users submitted 25 questions on topics ranging from stem cell therapies for MS to the hurdles he faces in his research. Here's a selection of the questions he received:

"How is responsibility for animal welfare shared across personnel in the lab?"

"Can we replace the use of animals in such tests? And how much of the data obtained from the use of animals does not match the reality when you go to human trial and testing?"

"Why are rats the most effective models for MS? How do you implement the 3Rs into your research?"

"The current mouse model that I know of for MS is mice with experimental autoimmune encephalomyelitis (EAE). Are you working with a different model? How are you improving on the current models?"

"What are the most significant hurdles that hinder MS research?"

"Have you stumbled across any possible causes to MS that perhaps hadn't been, or have yet to be, fully considered?"

Visit **redd.it/80vvt5** to find Professor Reynolds's answers to these questions and read others submitted to the 'Ask Me Anything' session.

Members of the CBS team talking to visitors at the Imperial Festival.

CBS at the Imperial Festival

In April, the Central Biomedical Services (CBS) team joined the exhibitors at the Imperial Festival for the third year running. Festival visitors had the opportunity to meet scientists working with animals and find out how animals are used as part of different research projects.

Members of the public were also able take a guided virtual reality tour of the South Kensington CBS facility with Google Expedition and a CBS volunteer. By explaining the work that goes on in each room of the facility, visitors learned about the advanced technologies used by Imperial to provide the highest possible welfare standards for the animals housed in the facility. They were even able to learn how CBS staff perform health checks on the animals in their care with the help of a toy rabbit.

Enhancing communication

Alongside these outreach activities, the College also focused on developing the animal research website pages to improve their visibility and make information about animal research easier to find. Throughout the year, the College has reported on research projects that involve animal studies in news stories and press releases, and has been clear about where, how and why animals have been used.

To keep up to date on animal research at Imperial, including the latest news on research projects and discoveries, awards and resources for researchers and technicians, visit: **www.imperial.ac.uk/research-and-innovation/about-imperial-research/research-integrity/animal-research**

The Concordat on Openness on Animal Research

By signing the Concordat on Openness on Animal Research, Imperial has made the following commitments:

Commitment 1

We will be clear about when, how and why we use animals in research

Commitment 2

We will enhance our communications with the media and the public about our research using animals

Commitment 3

We will be proactive in providing opportunities for the public to find out about research using animals

Commitment 4

We will report on progress annually and share our experiences

Writers: Ian Mundell, Kerry Noble

Design, editorial and photography:
Communications and Public Affairs, Imperial College London

Additional images: page 5 (Zika virus), AuntSpray/Shutterstock; page 21, Mica Jenkins and Tom Owen; page 34, Anthony Iglesias

www.imperial.ac.uk/animal-research