Imperial College London

ANIMAL RESEARCH REPORT

2020–21

CONTENTS

Cover: A young mouse in a breeding room for genetically altered mice.

Above: Marina Botto in the animal research labs at our Hammersmith Campus.

FOREWORD

Animal Research at Imperial

I am delighted to introduce the 2020–21 Animal Research Report. This is the fifth 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 unprecedented events of 2020 have shown the value of science in helping us tackle the emergence of a new disease. Research has helped us anticipate the course of the COVID-19 pandemic and its impact, and discover the vaccines, treatments and protective measures needed to achieve a global recovery.

Imperial has played a vital part in this research and many of our efforts have been recognised internationally. In this report, you will discover the role that animal studies played in some of our COVID-19 research. You will also find out how, despite the restrictions imposed during national lockdowns, our animal care staff supported this vital research while maintaining the highest standards of animal welfare.

During the first lockdown when the majority of UK workers remained at home, the animal technicians and vets from the Central Biomedical Services (CBS) team continued to come into work, along with some CBS support staff. Doing so not only involved establishing and following COVID-safe procedures, such as rotas and shifts, but sometimes also adapting their personal lives. For example, some chose to temporarily live on campus to avoid public transport or keep apart from shielding family members. I want to take this opportunity to thank all CBS staff for their hard work and the sacrifices they made.

Their work meant vital research could continue in 2020, including research on COVID-19. In the following pages, you can read about a study using ferrets and hamsters to understand how virus spike proteins enable disease transmission, researchers using mouse models to investigate the immune response to coronavirus in the lungs, and animal research helping the development of RNA vaccines for COVID-19.

As we look ahead to the coming months and years, we know that there will be lasting impacts from the pandemic. A key concern is the dramatic drop in research funding from medical charities, which together pay for around half of all publicly funded medical research in the UK. The Association of Medical Research Charities predicts a £310 million shortfall in research spend as a result. We do not yet know how this will affect the discoveries our scientists are making in fields such as cancer, heart disease and diabetes.

Nonetheless, there will also be opportunities, such as continued growth in vaccine research, and opportunities for collaborations with industry and start-up companies that can utilise our world-class specialist facilities and services.

> **“You will find out how, despite the restrictions imposed during national lockdowns, our animal care staff supported this vital research while maintaining the highest standards of animal welfare.”**
>
> – Professor Ian Walmsley FRS

These prospects will be boosted by our new research facility due to open in summer 2022 at the MRC London Institute of Medical Sciences on our Hammersmith Campus. This will bring researchers with a range of expertise together into one collaborative space, and our CBS staff will provide the operational support to underpin the work of this facility. The Incubator and Enterprise hubs based at our new campus in White City provide extra opportunities for research organisations to collaborate with Imperial and to benefit from our expertise in animal research.

The efforts of CBS and research staff working with animals over the last 12 months, and in preceding years, mean we are well-positioned to forge these new relationships within the research sector. And so I look forward to another year of progress and success in science and animal research at Imperial.

Professor Ian Walmsley FRS
Provost and Establishment License Holder,
May 2021

DISCOVERIES

Recent findings from animal research

Gene therapy shows potential for treating childhood brain disorder

Researchers in the Department of Brain Sciences have developed a gene therapy with potential for treating a debilitating childhood neurological condition called CDKL5 deficiency disorder. The condition affects the developing brain, and its symptoms can include severe epilepsy and autism.

The team developed a treatment that aims to introduce a functional version of the CDKL5 gene into brain cells. They used a modified virus that crosses the blood-brain barrier to deliver working copies of the gene to see if it could restore some of the function lost in the condition.

In a proof-of-concept study, juvenile mice that lacked functioning CDKL5, and displayed many of the characteristics found in people with CDKL5 deficiency disorder, had some of their impaired brain functions restored with a single treatment of the gene therapy. The research team is now keen to see if the therapy could be further developed and taken to clinical trials.

Left: Mice and other rodents have been used in animal research for many years.

Right: Juvenile mice with their mother in paper nesting, in a breeding room for genetically altered mice.

Bacteria-fighting cells in the airways raise infection risk from viruses

Having more bacteria-fighting immune cells in the nose and throat may explain why some people are more likely to be infected by respiratory syncytial virus (RSV), according to recent research from the National Heart and Lung Institute. RSV causes symptoms of a common cold, but for infants and the elderly it can lead to hospitalisation.

Researchers found that human volunteers who succumbed to RSV infection had higher levels of white blood cells called neutrophils in their airways. The team recreated high levels of neutrophils in the noses of mice. They found the virus was better able to infect the mice, causing worse symptoms and making them more likely to transmit the virus.

The findings could help researchers predict who is more at risk of infection and could lead to preventative treatments to protect against RSV and other viruses, including influenza and coronaviruses.

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Precise mapping shows how brain injuries inflict long-term damage

Researchers have shown how forces acting on the brain during traumatic injury are linked to damage seen years later. Traumatic brain injury (TBI) results from a sudden impact or jolt to the head, such as during a road traffic accident or bomb blast, or during sports like rugby and American football.

A cross-disciplinary team including Imperial medical researchers and engineers built a computer model to predict the location of long-term damage following TBI and tested the model in rats. They found that the effect of shear stresses on the brain's white matter helped predict the location of long-term damage. Shear stresses push two parts of an object, in this case the brain, in different directions.

Now that the computational model has been validated in real rat brains, it can address a range of research questions – for example to predict the severity of brain injuries and help design more effective helmets for a range of sports and other activities.

Dragonflies perform upside down backflips to right themselves

High-speed cameras and computer-generated imagery (CGI) technology have revealed the inbuilt righting mechanisms used by dragonflies when they are thrown off balance.

Researchers from the Department of Bioengineering dressed 20 common darter dragonflies with tiny magnets and motion tracking dots like those used to create CGI. They then magnetically attached each dragonfly to a platform either rightside-up or upside-down with some variations in tilt, before releasing the insects into a freefall. The motion tracking dots were captured by high-speed cameras for 3D reconstruction.

The researchers found that dragonflies most frequently perform upside down backflips, known as 'pitching', to right themselves from upside down positions in the air. The findings add to current knowledge of how insects fly and keep stable in the air. They could also help to inspire new designs in small aerial vehicles like drones, which can be useful for search-and-rescue attempts and building inspection.

Tumours illuminated brightly and precisely with new nanoprobe

Nanoprobes are tiny optical probes that light up when they attach to tumours, allowing doctors to detect the location, shape and size of cancers in the body. Now, scientists have developed new nanoprobes, named bioharmonophores, that emit light with a new type of glowing technology known as second harmonic generation.

The researchers, from the Department of Bioengineering, modified bioharmonophores to target cancer cells and tested them in zebrafish embryos. They found that bioharmonophores highlighted tumours more brightly and for longer periods than existing nanoprobes. They also attached precisely to tumour cells but not healthy cells, making them more precise in detecting the edges of tumours.

The bioharmonophores now need to be tested in mammals to see how well the findings translate beyond zebrafish. The researchers are also looking into how bioharmonophores could be used to guide cancer surgery and how they could generate light at different frequencies to help kill tumour cells.

Analysis of how bacteria attack could help predict infections

Bacteria, such as *E. coli* and *Salmonella*, use miniature molecular syringes to inject chaos-inducing agents, called effectors, into cells in our guts. These effectors take control of our cells, overwhelming their defences and allowing an infection to take hold.

A team of researchers co-led by life scientists at Imperial studied mice infected with the mouse version of *E. coli*, called *Citrobacter rodentium*, which injects 31 effectors. They were able to remove different effectors when infecting mice with the bacteria, tracking how successful each infection was. The team collected data on more than 100 different combinations of the 31 effectors and they used this to build an artificial intelligence algorithm that could predict the outcomes of infection with *Citrobacter rodentium*.

The study revealed how effectors work together as a network, allowing bacteria to colonise their hosts even if some effectors are removed. It also showed how the host's immune system can bypass the obstacles the effectors create, triggering immune responses. These insights could help predict infection outcomes and lead to new treatments.

Genetic modification aims to stop mosquitoes spreading malaria

Malaria is caused by the parasite *Plasmodium*, which certain species of mosquito carry in their guts. A team from the Department of Life Sciences have genetically modified *Anopheles gambiae* mosquitoes so that after they have consumed blood, they produce antimicrobial molecules that target the *Plasmodium* parasite and impair its development.

The researchers bred the mosquitoes to ensure they were able to reproduce and remain healthy. They also tested how well the malaria parasite developed in the mosquitoes' guts. The ultimate aim is to alter the mosquitoes' gut genes to make them spread antimalarial genes to the next generation.

Worldwide in 2019, there were an estimated 229 million cases of malaria and 409,000 deaths, most of which were young children in sub-Saharan Africa. Mosquitoes are increasingly becoming resistant to pesticides, and the *Plasmodium* parasite is becoming increasingly resistant to antimalarial drugs, so researchers say there is an urgent need for new ways to fight the disease.

DNA testing helps researchers keep tabs on elusive dormice

The hazel dormouse is classified as vulnerable to extinction in the UK due to habitat loss. It is a nocturnal mouse species which spends most of its time hidden among foliage, making it difficult to study and monitor in the wild.

Researchers from the Department of Life Sciences have been developing a new way of keeping tabs on this elusive species. The scientists used nest tubes that offer a sheltered environment to attract dormice. Inside the tubes, the researchers leave strips of paper that catch any urine the animals leave behind. Urine can be detected by UV light and then checked for tiny amounts of dormouse DNA left behind.

The technique has been tested at the British Wildlife Centre and proved quicker and more accurate than conventional methods. As a result, it could play a role in improving the conservation prospects for dormice and other threatened species.

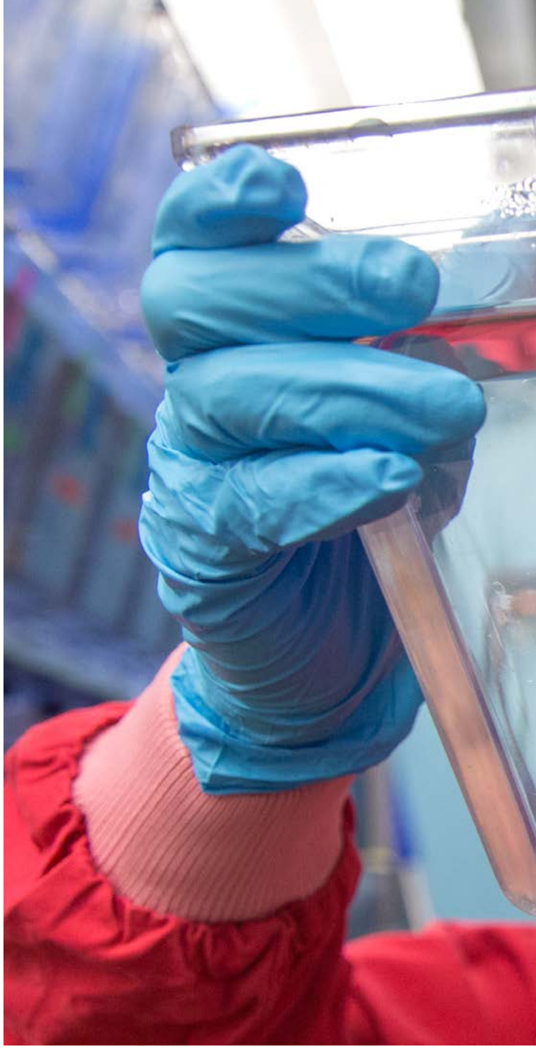
Above left: A dragonfly is here wearing the world's lightest high bandwidth neural telemetry backpack for study in a dragonfly flight arena.

Left: Hazel dormouse in the wild.

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



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.

2020–21 WINNERS

Application of the 3Rs, Researchers

Mr Alex Ainscough, PhD Student, National Heart and Lung Institute

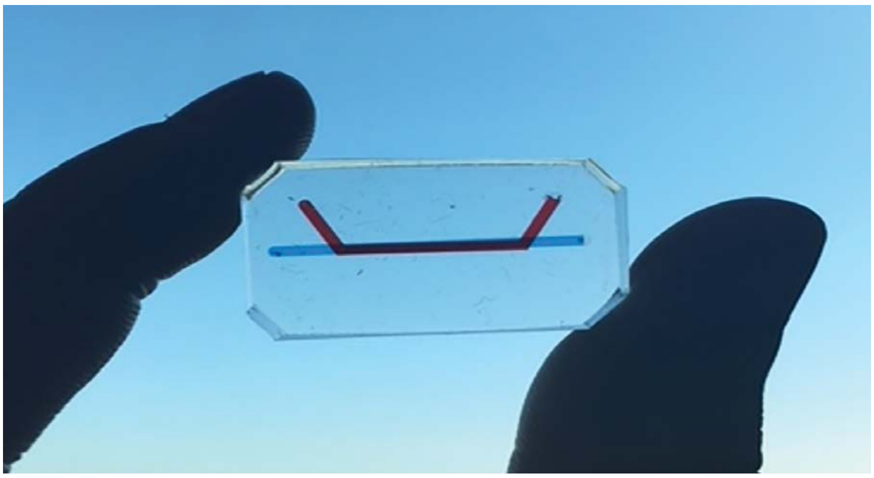
Alex received the Provost's Award for the generation of an organ-on-a-chip model of a pulmonary artery, as a model to study Pulmonary Arterial Hypertension (PAH). PAH is an incurable and severe disease of the pulmonary arteries and animal models are used to observe its effects in the body. However, no single animal model of PAH can reproduce exactly what happens in humans with PAH and researchers have to use multiple animal models to obtain meaningful insights into the causes and effects of the disease.

Alex's organ-on-a-chip could enable scientists to recreate key elements of normally functioning blood vessels and induce the kinds of functional responses associated with PAH. This should particularly help researchers to understand how the disease alters the normal functioning of the blood vessels.

Moreover, data shows that the model of PAH within the pulmonary artery-on-a-chip created is a viable alternative to animal experimentation for PAH and potentially other pulmonary diseases. This novel system potentially reduces the number of compounds that may need to be tested on animals at a later date, which should reduce avoidable, unnecessary animal suffering.

Above: Research with zebrafish at our South Kensington Campus.

Below: Actual image of the optically transparent pulmonary artery-on-a-chip device. Micro-scale channels are illustrated in red and blue and indicate where cells are cultured to recreate the structure of the innermost layers of a small lung blood vessel.



Application of the 3Rs, Researchers

Dr Jacob Broughton-Venner, Research Associate, Department of Bioengineering

Jacob received the Provost's Award for setting up a novel non-ionising ultrasound imaging and image processing system, to produce images in unprecedented detail of the structure and flow of animals' smallest blood vessels, called microcirculation. This work is the first to non-invasively image the intestinal villi, which are tiny, finger-like projections made up of cells that line the entire length of the small intestine.

Using Jacob's system, scientists can obtain metrics, such as the length of villi, without animals needing to be culled. Not only can this novel protocol measure these metrics non-invasively but it can also directly measure how blood passes through the internal villi and at what velocity – metrics never considered in the literature. Jacob estimates that using the new protocol to look at the small intestine could reduce the number of animals needed by six-to-tenfold.

Furthermore, although this work has concentrated on the small intestine, the technology and protocol are now being expanded to other organs, namely the liver, pancreas, terminal ileum and large intestine, which will widen the uses for it and increase the reduction in animal numbers. The use of non-invasive imaging to investigate blood flow also represents a refinement of current practices such as intravital microscopy, which involves imaging live animal cells through an imaging window that is implanted into the animal tissue during a special surgery.

Application of the 3Rs, CBS staff

The Central Biomedical Services team

For 2021 the CBS staff category was dedicated to all CBS staff to commend their dedication to both the welfare of animals and the vital science carried out at Imperial. The commitment and dedication that CBS staff have demonstrated during the COVID-19 pandemic, under the exceptional circumstances they have faced since early 2020, is an example for many. Therefore for this year, the 3Rs Advisory Group Committee, which selects the winners, have decided to give the Provost's Award to every member of staff in CBS.

“The commitment and dedication that CBS staff have demonstrated during the COVID-19 pandemic, under the exceptional circumstances they have faced since early 2020, is an example for many.”

Public Engagement award

Ms Julia Nagonska, animal technician;

Ms Amy Wathen, Named Training and Competency Officer

This team receives the Provost's Award for setting an excellent example for others and enabling the public to learn more about animal research and what it means to work in an animal facility. In 2020, the CBS department began producing a series of podcasts to hear directly from animal research workers about their experiences during the pandemic and how these have affected their everyday lives and jobs. Julia and Amy were the interviewees for the first two episodes.

The commission praised the passion with which Julia and Amy participated in the project, giving the public the chance to learn firsthand what it means to work in the animal research industry, and how the pandemic has affected them.

Their commitment towards openness, and the innovative use of a podcast, should open the door for future similar initiatives. The project was welcomed with enthusiasm from the Imperial community and was also commended by UAR and NC3Rs as an excellent example of openness in animal research.

Team award

Dr Andrea Pollard, Research Associate, Division of Diabetes, Endocrinology and Metabolism

Dr Davide Komla-Ebri, Research Associate, Department of Metabolism, Digestion and Reproduction

Dr Alasdair Gallie, Named Veterinary Surgeon

This team receives the Provost's Award for their work on refining how the drug Tamoxifen is administered in their animal research. Andrea and Davide are using Tamoxifen as part of their work investigating the role of the thyroid hormone in osteoarthritis and fracture repair. Their work involves overexpressing the DIO3 enzyme in animals that have undergone surgery, to induce osteoarthritis or create a stabilised fracture.

Mice receive regular doses of tamoxifen for up to 12 weeks post-surgery to maintain recombination in target cells during injury repair. Oral delivery of Tamoxifen in a mouse's diet or drinking water can have unpredictable results, as it tastes bitter and this can result in animals becoming dehydrated, receiving a variable dose and phenotype outcomes. This means large numbers of mice are needed to conduct these kinds of experiments.

With the help and support of Dr Gallie, the team has investigated approaches to refine how Tamoxifen is administered and the dose of Tamoxifen required to achieve optimal recombination yet minimise adverse effects. The team's work has contributed to College-wide guidance for scientists using Tamoxifen in their work. Moreover, the results from this study will be published to provide evidence-based recommendations to the wider scientific community.

Top: Amy Wathen, Named Training and Competency Officer

Far left: Dr Davide Komla-Ebri, Research Associate, Department of Metabolism, Digestion and Reproduction

Left: Professor James Stirling opening the new Animal Research labs

2018–19 WINNERS

Application of the 3Rs, Researchers

Dr Anna Blakney, Postdoctoral Research Fellow

For her pioneering use of human skin explants for the development of RNA vaccine formulations.

Application of the 3Rs, CBS staff

Anthony Iglesias, CBS Facility Manager; Philip Rawson, Senior Technician; David MacDonald, Animal Technician

For the introduction of a new caging system to avoid single housing of rats.

Team award

Dr Elina Akalestou, Research Associate; Dr Alasdair Gallie, Named Veterinary Surgeon; Dr Livia Lopez Noriega, Research Associate; Dr Isabelle Leclerc, Reader in Diabetic Medicine

For their work to optimise a newly-approved severe protocol focusing on a type of gastrointestinal surgery, known as bariatric surgery.

Public Engagement award

Andrew Youngson, News and Digital Content Editor, and Dr Anna Napolitano, CBS Quality Assurance and 3Rs Programme Manager

For using the Reddit – Ask Me Anything platform for a series of Q&As with Imperial researchers, talking about the use of animals in research and its welfare implications.

2019–20 WINNERS

Application of the 3Rs, Researchers

Aldara Martin-Alonso, PhD student
For her work on refining a surgical technique in mice that allows unprecedented insights into the function of the vagus nerve.

Application of the 3Rs, CBS staff

Dr Nicoleta Baxan, Manager and MRI Physicist, Biological Imaging Centre

For her vital role in the Biological imaging Centre (BIC) in ensuring the successful implementation of the 3Rs into all projects.

Team award

Yateen Patel, PhD student; Anna Roberts, PhD student; Dr Alasdair Gallie, Named Veterinary Surgeon; Philip Rawson, Senior Technician

For their work developing glucose clamping in the conscious, unrestrained mouse.

Public Engagement award

Dr Anna Napolitano, CBS Communications Quality Assurance and 3Rs Programme Manager

For her significant commitment to enhancing communication with wider audiences about the role of animal research, and improving communication between the research community and the public.

Top: Dr Anna Napolitano, CBS Communications Quality Assurance and 3Rs Programme Manager

Right: Dr Anna Blakney, Postdoctoral Research Fellow

Far right: Andrew Youngson, News and Digital Content Editor

WORKING TOGETHER TO DEFEAT COVID-19

Since the beginning of the pandemic, researchers across Imperial have been working overtime to understand the SARS-CoV-2 virus and to develop treatments for COVID-19, the disease it causes. Animal research has been crucial to this effort, from testing candidate vaccines to revealing how and why the virus has such a devastating effect on our health.

The challenge of developing a vaccine against SARS-CoV-2 was taken up early on in the pandemic by Professor Robin Shattock, from the Department of Medicine. His group was already developing a novel vaccine platform for use against diseases such as Ebola, Lassa fever and rabies, which could be adapted for the new virus. The platform works by delivering strands of genetic code, called RNA, to cells in the body, where they produce a protein usually found on the surface of the virus in question. This protein is recognised by the body's immune system as foreign, priming the system to react if it later encounters the virus.

The novelty in Robin's approach is that the RNA works by making many copies of itself within the body's cells. The result is that only a small amount of this self-amplifying RNA is required to produce an effective immune response, which should ultimately make it cheaper and easier to produce vaccines in large quantities.

Having selected the SARS-CoV-2 spike protein as a suitable basis for the vaccine, it was relatively simple to cut and paste the necessary genetic sequence into a version of the vaccine platform designed for Ebola. The RNA produced in this way must then be wrapped in a tiny droplet of fat, which helps deliver it to the target cells in the body. Formulating this droplet so that it works effectively is not so simple, and animal research is required to see that an immune response is indeed being produced.

Left: Professor Robin Shattock speaking with Research Assistant Hadijatou Sallah at our St Mary's Campus during the development of the COVID-19 vaccine.

"Ours are the simplest and mildest of animal experiments," explains Dr Paul McKay, who worked on the project. "We inject the animals twice, and take blood to see if there is an immune response. Then, the animals are culled to harvest the spleen and other organs to examine the immune response in detail."

As much preparatory work as possible is done in cell culture, to reduce the number of animals used, but it is impossible to simulate the complexity of the body's immune system in a dish. "There is no replacement for an intact immune response in an animal."

A range of animals was used in this work, beginning with the lowest vertebrate species possible. "We did the initial assessment in mice, and saw that the vaccine worked extremely well," Paul says. This was followed by studies in rats, to assess the toxicology of the vaccine in preparation for a human clinical trial.

Smaller studies were also done in hamsters, ferrets, rabbits, guinea pigs, pigs and monkeys, either to answer specific questions about the vaccine or to see if additional data could be gathered. As always, animals were only used when a question could not be answered in any other way, and the type of animal used was considered carefully. The work with monkeys, which did not take place in Imperial's animal houses, was a challenge study to see if the vaccine gave them practical protection when they were exposed to SARS-CoV-2. Such studies could not, at that time, be carried out with people, and the other animal models were not close enough to humans to produce a meaningful result. Once animal trials had been completed successfully, the researchers were able to move forward with stage I and II clinical trials in humans.

> **"We did the initial assessment in mice, and saw that the vaccine worked extremely well."**
>
> – Dr Paul McKay, Faculty of Medicine, Department of Infectious Disease

While the Imperial vaccine produced an encouraging immune response, others using more established technologies were further along in their development, and a number of effective vaccines began to be rolled out globally. So Professor Shattock's group has moved on to explore whether the Imperial vaccine can be adapted for use against new variants of SARS-CoV-2. "This research will enable us to develop, perhaps, a vaccine booster that is effective against several of the variants," says Dr McKay. And since the formulation for delivering the vaccine will remain the same, the initial animal studies will not need to be repeated.

What the group has learned in the last year will also have benefits beyond the present pandemic, given the technology's potential for use in vaccines against many other diseases. "We've developed a lot of knowledge and knowhow around the self-amplifying RNA vaccine platform, which otherwise might have taken us five to ten years to accomplish. It has really accelerated our research."

Tracking virus transmission

In parallel with efforts to develop a vaccine, researchers at Imperial have also been investigating how the SARS-CoV-2 virus is spreading. This was just a small sideways step for Professor Wendy Barclay and her group, who had been asking similar questions about pandemic influenza when SARS-CoV-2 emerged. "We've been trying to understand how pandemics arise, with a particular focus on transmission between individuals. Transmission is key to sustaining outbreaks," says Wendy, who is the Head of the Department of Infectious Disease.

Part of her group's previous research had involved studying how the flu virus passes between ferrets. While relatively unusual as a laboratory animal, ferrets are a good model for studying flu because they are infected by the virus and develop symptoms in a similar way to people, whereas mice and rats do not. When the COVID-19 pandemic set in, Wendy decided to find out if her ferrets were also a good model for the transmission of SARS-CoV-2.

This could be done relatively quickly because the influenza procedures put on hold were already at the right biosafety level for working with SARS-CoV-2. The main technical challenge involved the way the samples collected from the ferrets were analysed. "We were working with a new virus, which grows in different cells and has different characteristics, and we needed to make sure that everything lined up."

The group decided to focus on a particular sequence – a furin cleavage site – in the SARS-CoV-2 spike protein, the part of the virus that helps it infect lung cells. "This sequence rang so many bells for us," Wendy explains. A furin cleavage site features in some highly dangerous bird flus, yet it is not present in SARS-CoV-1, which caused more easily controlled disease outbreaks in 2003. "So, we wanted to test the role of the furin cleavage site in infection and transmission in the animal model."

"This research will enable us to develop, perhaps, a vaccine booster that is effective against several of the variants."

– Dr Paul McKay, Faculty of Medicine, Department of Infectious Disease

Right: Dr Paul McKay examines a sample in a laboratory at the St Mary's Campus.

Far right: Ferrets are inquisitive and sociable animals and though used commonly in animal research were found to not be the best models for SARS-CoV-2 research as they do not become ill when infected.

This was done by comparing a circulating strain of SARS-CoV-2 and a variant that lacked the furin cleavage site. Ferrets could be infected with both kinds of virus, but the version without the furin cleavage site proved much less transmissible. Only low levels were breathed out by infected animals, and healthy ferrets housed alongside did not become infected. With the circulating virus, exhaled levels were high and neighbouring animals fell ill.

Together with cell culture studies and observations of variants in the human population, this work suggested that the furin cleavage site is indeed crucial for transmission. Knowing this helps scientists assess the risks posed by new variants of the virus as they emerge. “When we look through the thousands of sequences that are being reported, if we see one that has an optimised furin cleavage site then that is a clear warning signal.”

While the ferrets proved to be a good way of testing the transmission of SARS-CoV-2, they are not the best model for further research, because they do not become ill when infected with the virus. So Wendy’s group has now switched to golden hamsters. “They get quite sick, and are a much better model of the moderate to severe end of the COVID spectrum in people.”

Switching to hamsters has meant adapting the group’s research methods, but also updating licenses, carrying out new safety assessments, and building appropriate facilities for the new work. “A whole team of people has helped and advised us, allowing us to scale up quickly,” Wendy says. “Everyone has pulled together. That has been a real moment of pride for all of us.”

Meanwhile the approach to the 3Rs developed for the ferrets has been carried over to the hamsters. This includes keeping infection levels to a minimum, so that the animals do not suffer severe symptoms unnecessarily, and adapting nasal washing techniques that allow virus levels to be assessed without distressing the animals.

But new approaches are also being developed, such as a method for studying SARS-CoV-2 in the lungs that does not involve killing and dissecting the animals. This makes use of genetically modified versions of the virus that give off light, which can be detected in live animals using sensitive imaging systems.

“That means we will be able to watch the virus move, over time, between the upper and lower respiratory tracts, in the same animal,” Wendy says. This will reveal where the virus is when the animals become sick, and when transmission begins. “That will tell us a huge amount. It also means that we use many fewer animals to see where the virus is within the body.”

“Ferrets could be infected with both kinds of virus, but the version without the furin cleavage site proved much less transmissible.”

Explaining the severity of infection

Just what happens when SARS-CoV-2 reaches the lungs is a question that Dr Cecilia Johansson turned to when the pandemic broke out – a question she was able to investigate using mice. Cecilia is no stranger to respiratory viruses, having worked for many years on respiratory syncytial virus (RSV) and influenza, in particular studying the immune responses they generate in the lower airways. "It was obviously very interesting to ask the same questions about the new SARS-CoV-2 virus," says Cecilia, from the National Heart and Lung Institute.

These questions are almost impossible to answer by studying people, and not just because it is hard to sample human lung tissue. "We are interested in the early events and how inflammation is initiated. That happens a long time before someone arrives in hospital with signs of the disease." Animal models make it possible to follow the disease from the very first moments of infection.

The first challenge for Cecilia was that the mice she usually works with are not susceptible to the circulating strains of SARS-CoV-2. Various approaches are now being tried to create a useful model, either by genetically modifying the mice to make their cells appear more human, or by modifying the virus so that it targets the mice more effectively. The important point is not so much that the mice should have the same symptoms as people, as the same kind of immune response when the virus arrives in the lungs.

"In a lot of cases, including COVID-19, the virus infection is cleared from the lungs, and what we suffer from is an uncontrolled immune response, which causes a lot of damage," Cecilia explains. "So, in the mouse models we want to see the same kind of immune response, with the same mediators produced and the same cells coming in, so that we can find out where this regulation of the immune response goes wrong."

> **"Having good animal models, which we have completely characterised, can be really useful to drive the basic understanding of the disease and work on therapeutic targets."**
>
> – Dr Cecilia Johansson, Reader in Respiratory Immunology, National Heart and Lung Institute

Once a mouse model has been validated as a good representation of what is happening in humans, more in-depth characterisation of the immune response and lung damage can begin, using the techniques she and her colleagues have developed for other viruses. One of these involves taking thin slices from the lungs of the mice, which can then be used to answer a range of different questions, maximising the data gathered from each animal. “We are developing that method in parallel with the model validation work, in order to use fewer mice.”

The main aim of this research work is to increase our basic understanding of how SARS-CoV-2 operates. “The big question in my field is: why do some people get really sick, and in the case of SARS-CoV-2 even die, while other people are asymptomatic and don’t even notice that they have the same infection. So, what is driving the severity of the disease?”

Revealing this mechanism will help improve assessments of individual susceptibility to the disease, and suggest targets for new treatments. And the animal models themselves will be tremendously important in other research. “Having good animal models, which we have completely characterised, can be really useful to drive the basic understanding of the disease and work on therapeutic targets.”

Looking back on the past year, Cecilia saw a unity of purpose in this work on COVID-19, not just among the researchers at Imperial, but also the administrators, the technicians who care for the animals, and other support staff. “This disease has had an impact on everyone, and everyone wants to contribute.” ■

Top left: Dr Cecilia Johansson in the lab with Dr Patricia Ogger.

Top right: Dr Cecilia Johansson looking at infected cells at the microscope.

SHINING A LIGHT ON OBESITY

Researchers studying obesity are increasingly looking to the brain in order to understand how the condition develops and what can be done to treat it. This is possible thanks to innovative techniques that allow precise groups of brain cells to be activated in mice, so that scientists can observe the effects on their eating behaviour.

Obesity is a global health problem, affecting some 2 billion people worldwide. In the UK approximately 60% of the adult population and 20% of 4–5-year-olds are overweight. "With obesity comes all the comorbidities, such as cardiovascular disease, type-2 diabetes and cancer," explains Dr Elaine Irvine, a senior investigator at the MRC London Institute of Medical Sciences. Alongside the toll these illnesses take on a personal level, treating them also costs the NHS upward of £5 billion a year.

Initial efforts to understand obesity focused on processes such as hunger and appetite. When you need food, the gut releases hormones that travel through the blood to the hypothalamus region of the brain, activating particular neurons that create an urge to eat. When digestion is well underway, different hormones signal to the brain that eating can stop. But this is only part of the story, and researchers such as Elaine have begun to ask how other areas of the brain might be involved.

"We are looking at top-down control from higher brain centres, and how these centres link into the hypothalamus and cause increases in feeding," she explains. "For instance, when you are feeling emotional maybe you choose high-calorie foods. We want to know if particular neuronal pathways are involved in the reward system behind that choice."

These pathways might be directly involved in how someone perceives food, or associated with how behaviour is learned. "Currently we are looking at an area of the brain that is heavily involved in memory formation, and the links into it from other systems, such as the smell and taste sensors. And we want to see if we can manipulate those pathways and see a change in feeding behaviour."

For example, it might be possible to reduce appetite by switching off a particular set of brain cells so that food does not taste as good. The researchers are also exploring whether tolerance builds up to high-fat diets, just as it does with certain narcotics, so that the brain demands more eating to get the same level of reward.

Left: To ensure an enriched environment for mice, they are provided with cardboard tubes and shredded paper.

Untangling this interaction of the brain, the senses, the digestive system and behaviour can only be studied in living animals. "It is such a complex process," says Elaine. "You need all these systems to be in place and working together to understand it."

The methods that make it possible to turn on or off distinct populations of brain cells are relatively new. One, called chemogenetics, uses viruses to genetically alter specific sets of neurons within a brain area so that only they can be activated by a designer drug injected into the blood stream. This procedure is usually carried out with mice, and allows for these particular neurons to be activated for several hours.

A related method, called optogenetics, allows researchers to have more temporal control over the neurons being activated. In this case, the viruses genetically alter brain cells so that they produce light-sensitive proteins called opsins. These then act as switches, allowing the cells to be turned on and off with light pulses delivered with fibreoptic filaments inserted into the brain. "Once you have targeted that specific neuronal population, you can then activate the neurons in that specific brain area and precisely link that particular set of neurons to changes in feeding, using a regular diet or high-fat diet."

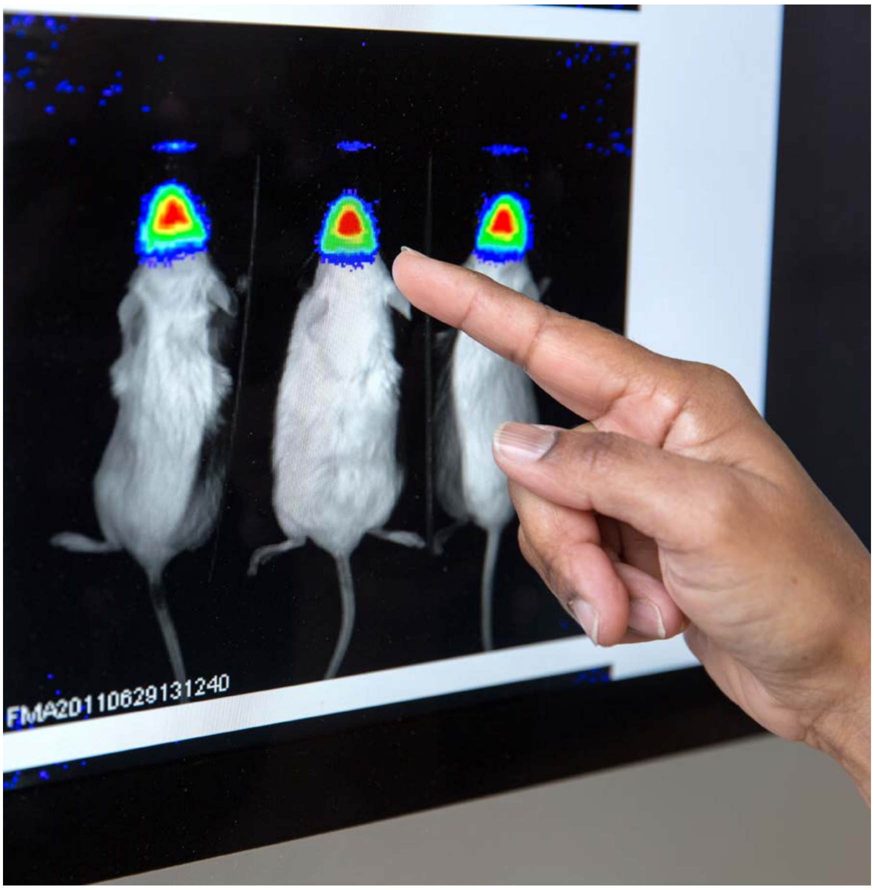
When it comes to feeding behaviour, mice are a good match with humans. "We like to eat fatty foods and have 'bad' things, and rodents are exactly the same," Elaine says. Meanwhile, the neuronal and biochemical systems that control mouse behaviour are broadly similar to those found in humans. "You can't see that in lower organisms, which is another reason we have to use mice."

Care is taken to minimise the number of mice used in this work, both in the breeding stages when genetic modifications needed to direct the viruses are put in place, and during the experimental procedures. For example, when using optogenetics the feeding studies can be repeated using the same mice, once stimulating their brains with the laser light, then with the light turned off. Randomise the order in which this happens, and the mice act as their own controls. "Using this crossover design can reduce the number of mice used by half."

During the procedures, the mice are left undisturbed as much as possible. "Normally, when you do a feeding study, someone has to go in and weigh the food and weigh the mouse, and that can mean quite a lot of disruption," Elaine says. "So, we have an automated feeding system, where the food is on a weighing scale and measurements are recorded directly onto a computer. That means we can just start the experiment and leave the mice without disturbance, which is a lot better for the mice."

Similarly, efforts are made to keep the mice in groups as much as possible when they are not being observed in a feeding study. "They don't like to be on their own, and so we try to limit the time that they are singly housed to as short a time as possible." This is important for the welfare of the mice,

> **When a human or an animal is obese, the activities of the neurons will change and the system will be different. If we are going to treat obesity, we will need to know what the system is like in the obese patient.”**
>
> – Dr Elaine Irvine, senior investigator, MRC London Institute of Medical Sciences



Left: Mice being weighed in an Imperial animal research facility.

Right: Imaging of mice aids Imperial researchers in their research.

and also for the broader context of their feeding behaviour. “You might get an alteration in feeding, but along with that an alteration in anxiety and stress. So, are the animals not eating because they are stressed, or stressed because they are not eating? It is important to understand that balance.”

The technicians looking after the animals are particularly important in this respect, and Elaine is keen to involve them in the research as much as possible. For the past few years – until interrupted by the pandemic – she has run a monthly seminar series in which researchers present their projects to staff in Central Biomedical Services.

At the moment, Elaine’s research is concerned with identifying the pathways that control feeding behaviour in normal mice. Once these are established, the next step could be to look for differences in mice with a predisposition to obesity. “You can imagine that when a human or an animal is obese, the activities of the neurons will change and the system will be different. If we are going to treat obesity, we will need to know what the system is like in the obese patient.”

Just what that treatment will look like is hard to say at present. The research so far suggests that it will have to target not only specific populations of neurons, but also specific locations in the brain. That will be difficult to achieve with a drug that simply mimics a particular neurotransmitter, for example. “In one area of the brain it might inhibit feeding, while in another it might stimulate feeding, so it is all very complex.”

Optogenetics provides that spatial and temporal precision, but will be challenging to convert from an experimental method into a therapy. The types of viruses used to introduce the light-sensitive proteins are already used in human gene therapy, but the targeting presently relies on genetic markers that are bred into the mice, an approach not possible in humans. Also the viruses need to be injected directly into the brain during a neurosurgical procedure. On top of that, inserting an optical fibre into the brain is also very invasive, although alternative approaches are being tested. For example, more sensitive protein switches are being designed that are activated by different light that can penetrate tissue better, and could therefore be activated by simply shining light through the skull.

“I think the technology will progress, and there is a chance that it could be used, but it’s certainly not there yet,” Elaine concedes. But she does think that targeting the brain is a valid approach to obesity, given the lack of effective treatments, other than bariatric surgery to restrict stomach volume. “All the peripheral hormones go up to the brain to tell you to eat, or to stop eating, so there has to be some kind of intervention involving the brain,” she concludes. ■

OPENING A WINDOW INTO THE CIRCULATION

Researchers at the National Heart and Lung Institute have found more efficient ways to study tissues and cells. As a result, we can learn more about cardiovascular health whilst using fewer animals.

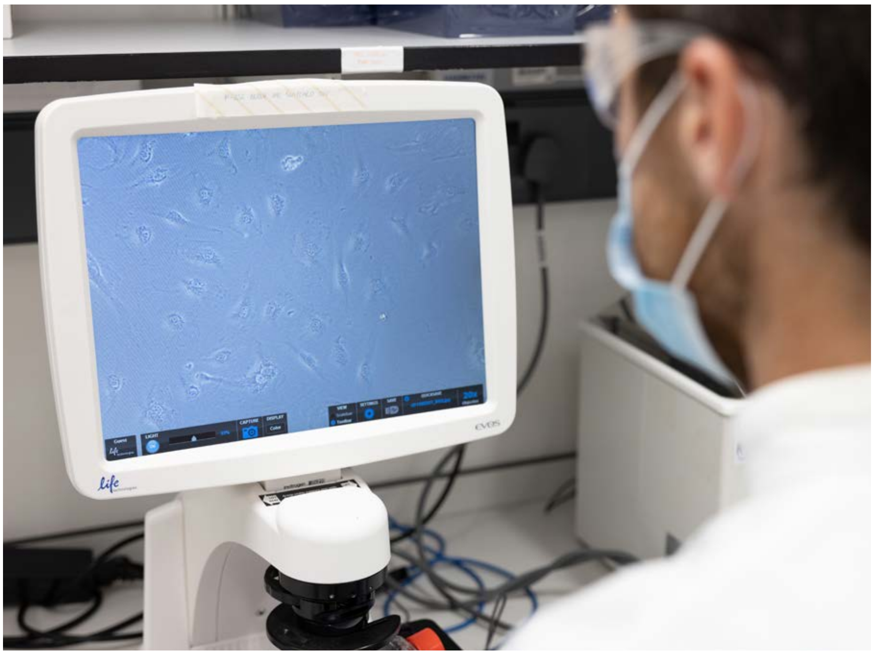
When scientists set out to investigate a complex health issue, no single approach will deliver all the answers. “We always look for the best way to test each individual research question,” says Dr Nick Kirkby, from the Cardio-Respiratory Interface section at Imperial’s National Heart and Lung Institute. “That might mean very simple studies with cultured cells, or using many types of cultured cells together, or animal models, or small clinical studies with patients.”

Each line of enquiry will deliver different, complementary information, which together builds into a better understanding of the question. In this case, the goal is to understand how blood vessels function in healthy and unhealthy bodies, and how drugs can control those processes. “What we want is to create a window into the circulation,” says Dr Blerina Ahmetaj-Shala, a colleague working in the same area.

The challenge when studying blood vessels is that they are complex structures, made up of different types of cells and tissues. These interact together, and with the tissues that the vessels supply with blood. If you break these structures down in order to study them, or take the blood vessels out of context, then you risk not getting the whole picture. A common thread in Nick and Blerina’s work is that they are looking for ways to preserve this natural complexity as much as possible.

Nick’s research focuses on drugs like aspirin and ibuprofen. “People take aspirin to protect against heart disease. It’s a very good drug, but some people taking aspirin still have heart attacks and strokes, so we think there is potential to improve it. Then with ibuprofen-like drugs, which people take for painful conditions such as arthritis, the problem is that they can actually cause heart attacks and strokes in some people. We would like to solve those problems.”

Whole animal studies can provide the big picture, for instance how a particular drug affects blood pressure and other cardiovascular indicators, but they are also time-consuming and can involve a lot of animals, which is not ethically desirable. In addition, this approach does not reveal in detail how blood vessels are behaving to control these effects.



Far left: Dr Nick Kirkby in discussion with Research Associate Maria Lopes at our South Kensington Campus.

Left: Dr Kirby looking at a blood vessels slice under a microscope.

While it has long been possible to study large blood vessels, which are easily accessible, they do not tell us everything about the finer points of vascular behaviour. "They are essentially hosepipes that take the blood around the body. We've learnt a lot from studying them but they are quite different from the much smaller blood vessels that are inside your tissues and organs," Nick explains. "These small vessels are really important in controlling your blood pressure and your cardiovascular risk and there is still a lot we don't know about them."

So he and his colleagues came up with a compromise method, in which fine slices are taken from tissues and kept alive in a petri dish. "We can observe the small blood vessels within each slice, while they are still influenced by all the other components of that tissue. We can look at each slice under a microscope and watch the blood vessels contract and relax as we add different substances."

Lots of slices can be taken from each organ to profile different drug responses, and several organs can be studied from the same animal. "This is a stepping stone that allows us to retain the complexity of a whole-animal system, while getting much more information and using fewer animals," says Nick. "We can also use the technique to study human tissues biopsies and so avoid the need to use animals altogether."

Efforts are also made to get even more information from each piece of tissue, using 'omic' technologies, where hundreds or thousands of molecules can be measured in the blood vessels at the same time. "Even if you start the study with a very specific question, using these approaches we can often make completely unexpected discoveries, which is really exciting. And by getting so much information at the same time we add extra value to the animal studies that we do."

This work mainly involves mice and human tissue, although sometimes rats or spare tissue from pigs collected as a by-product of other research or food production are studied. "Wherever animals are used for research, it is our obligation to make sure we use as few as possible, and do it with as little impact on their welfare as possible."

This tissue slicing method has been used to examine the adverse effects of ibuprofen-like drugs in different tissues. "We found that they have a very negative effect on the blood vessels in the kidney," Nick says. "People don't necessarily think of the kidney as part of the cardiovascular system, but it is really important in controlling cardiovascular health."

His group is now pursuing this lead with other basic science studies, as well as through clinical studies. "We have samples from a big clinical trial of people taking ibuprofen-like drugs, and we want to see if changes in kidney function markers in the blood predict whether or not the person is likely to go on to have a heart attack."

"This is a stepping stone that allows us to retain the complexity of a whole-animal system, while getting much more information and using fewer animals."

– Dr Nick Kirkby, Faculty of Medicine, National Heart and Lung Institute

Right: Dr Nick Kirkby works in his lab.

Far right: Mice being studied at our South Kensington Campus.

This research may also result in better treatments. “Ultimately we hope we can develop a new drug, or say that a particular drug combination lowers a patient’s risk of heart attack.”

Blerina is approaching the question of blood vessel complexity from the other side, with research into how studies of cells from blood vessels cultured in the laboratory can be improved. The tissue that lines blood vessels, called the endothelium, can be grown under laboratory conditions, but these cell cultures change over time and so may not function in a dish the same way that they do in the body. This also removes them from the smooth muscle cells that they would normally be attached to in a blood vessel in the body.

Her approach involves isolating progenitor cells from the human blood stream, which can then be grown into endothelial and smooth muscle cells. Cultures of these cells are fresh, and therefore behave as they do in the human body. More importantly, they can be combined so that the interactions present in the body between the two kinds of cells are also present in the dish. “We’ve created a model where we can layer both of the cell types together,” she says. “When we add different drugs to that model, the cells respond in a similar way to what is expected in the body.”

Since the progenitor cells can be isolated from simple blood samples they can be studied from different people and patient groups. “If we know that endothelial or smooth muscle cells are affected by certain diseases, like pulmonary hypertension, then we can isolate these cells from patients who have these diseases, compare them to healthy patients, look for differences and then test potential drugs that are available and see which works best.”

Another possible application that Blerina is using these cells to investigate is diabetes. “Cardiovascular issues are a big problem for patients with diabetes, with 80% of diabetic patients dying from cardiovascular complications. So, we want to isolate these cells from diabetic patients to understand what goes wrong in the blood vessels of these people and how we could reverse or prevent that.”

In addition to answering questions about diseases in general, this approach could make treatments much more personal. Once a blood vessel model has been created for a specific patient it can be stored for future use, to test new treatments as they are developed. “If you give me a blood sample, I can grow your endothelial cells and your smooth muscle cells, then use them together in a personalised medicine approach to see which drugs your cells respond to best before you start taking them.”

In the long term, this technology could also make it possible to build three-dimensional blood vessels, which could be transplanted into patients to replaced damaged blood vessels. “This will not be easy, however, and will require help from engineers and a range of other researchers.”

The relationship between this research with cell cultures and the research with animals is not simply that one can replace the other. Instead, there is an exchange of information, with each approach capable of influencing the other. “There are many diseases where we are not sure of the mechanism, so by getting cells from people who have these diseases we can learn more about these mechanisms, and then use animal models to test potential treatments and therapies that target them,” says Blerina.

And unless you know which factors are involved in a biological process, you cannot begin to make a cell culture model. This is where an animal study may hold the key. “Once you realise that a pathology or a drug response is driven by interactions between, say, endothelial cells, smooth muscle cells and white blood cells, then you can address that with human cells in a dish, and you no longer have to use animals,” Nick says.

Dr Huai-Ti Lin here sets up the dragonfly flight arena. This allows detailed dissection of aerial prey interception strategies and general visual guidance. Dr Lin chooses to work with insects both in the lab and in the field.


of Aeroelasticity in Dragonfly Wings

THE CENTRAL BIOMEDICAL SERVICES' RESPONSE TO COVID-19

During the COVID-19 pandemic, the dedication and hard work of CBS staff enabled animal research to continue, even during periods of lockdown.

In 2020, the global pandemic changed how many people worked, but for others, a working routine had to be maintained.

As soon as the Government announced the beginning of lockdown early in 2020, the management team for Imperial's Central Biomedical Services (CBS) introduced several changes across the facilities. Whilst those who could work from home continued to do so, most staff had to come onto campus despite the risks, in order to ensure that the animals in Imperial's facilities would continue to be well cared for.

From an animal welfare point of view, it is vital to maintain husbandry protocols at all times, whatever happens in the outside world. Even in a pandemic, animals need to be fed and watered, their housing needs to be maintained, and their health closely monitored. It is also crucial to keep the animal research facilities operating as potentially lifesaving research is being carried out there.

Exceptional measures for exceptional circumstances

With ensuring the safety and wellbeing of staff and animals as their top priority, the CBS management team implemented several measures. To maintain social distancing, staff had to follow a new rota system, changing their working hours and the number of days they were going into work each week.

Some of the new measures potentially left staff feeling more isolated. They had to take shorter breaks to bring their finishing time forward, and contact during break times was minimised by taking their breaks in shifts. Staff were also given the option of moving to temporary accommodation closer to campus to minimise the risk of spreading the virus to vulnerable family members. The everyday job for an animal technician is usually characterised by periods of working alone whilst caring for the animals, so the mental wellbeing of staff was a concern.

"Some of the biggest challenges we had to face were ensuring that there were enough staff, and also ensuring they were coping well and in a good place to provide a good service," says Alex Stepney, manager of the breeding unit on the Hammersmith Campus. Senior managers offered support to help staff cope, as well as ensuring a Mental Health First Aider was available 24/7 and that staff knew how to access general College mental health support. Despite the personal and professional challenges, Alex felt that staff adapted well to the new measures. "I was really impressed by how everyone dealt with all the changes. We have coped amazingly! I am very proud of what we have managed to achieve in such tiring circumstances," continues Alex.

However, the pandemic was also an occasion for learning and improvement, with staff able to take up more training when the animal houses were less busy. Reece Williams, an advanced technician at Hammersmith Campus, says: "I believe that everyone was able to use and learn skills they had felt they didn't need. As fewer researchers were allowed in during this time, staff were able to step up and had the opportunity to train in techniques that we would not normally have time for. It has brought confidence to all staff that they are needed, trusted, and overall appreciated. We can continue to use these skills in the future to keep everyone safe and improve the workflow."

Left: Dr Joy Nagawesi working in a laboratory at our St Mary's Campus.

Supporting new COVID-19 science

Many scientists at Imperial swiftly turned their attention to investigating the SARS-CoV-2 coronavirus once the pandemic hit, exploring everything from the nature of infection to possible vaccine development (see pages 13–17). Many of these new projects involved animals and so the CBS team needed to respond quickly to requests to set up new research studies and ensure that the appropriate steps and resources were in place. Staff managed to support this important scientific work and at the same time make sure that everyone factored the 3Rs – reduction, replacement and refinement – into planning for these new research studies. "The department has learnt things as they progressed. For everybody it has been a new, unexpected and stressful situation but we didn't stop working, even for one day," says Justyna Glegola, Named Training and Competence Officer.

During the pandemic the animal care staff at Imperial have demonstrated their dedication to animal welfare and the 3Rs, and their close working relationship with the research community. Robert Floyd, Director of CBS, says: "The pandemic showed us how adaptable, resourceful and committed we are and also how quickly we can respond to a situation that has the potential to disrupt our operations. We have learnt new ways to communicate, adopted new technologies and are able to be a more efficient and flexible workforce. Operations and standards have been maintained due to the commitment of our people." ■

> **"It has brought confidence to all staff that they are needed, trusted, and overall appreciated."**
>
> – Reece Williams, Technician, Hammersmith Campus

Right: During the pandemic, the welfare of animals was maintained by dedicated CBS staff.

THE 3RS

The college's 3Rs advisory group explores new and effective ways to reduce, refine and replace the use of animals in research at Imperial.

In 2019, Professor Richard Reynolds stepped down as chair of the College's advisory group on reduction, refinement and replacement (3Rs) of animals in research. The new co-chairs, Dr Tristan Rodriguez and Dr Bryn Owen, are building on the group's achievements with the creation of a new 3Rs Hub at Imperial.

"There has been a huge cultural shift in animal research at Imperial, and Richard Reynolds has played an important role in promoting the 3Rs and making them central to College policy," says Tristan. "Both Bryn and I believe there is an opportunity now to build on the work of the advisory group and take it a step further."

Tristan is Reader in Cell and Developmental Biology at the National Heart and Lung Institute at Imperial. He is also a longstanding member and current deputy chair of the local Animal Welfare Ethical Review Body (AWERB). He says his time with the AWERB committee spent looking through project licence applications has given him a strong sense of where further improvements could be made.

Bryn's work focuses on female fertility and reproduction. He studied for his PhD at Imperial then moved to the US for five years before returning to the Department of Metabolism, Digestion and Reproduction in 2015 as a junior group leader. He says: "When you're studying fertility, you need to have happy healthy mice, or they're not fertile. All my studies have included some elements of refinement, at least, to ensure the animals I work with behave normally."

Left: Animal technologist Helen Goyal holds a rabbit, which is used to help train technologists and researchers on how to handle animals.

As co-chairs, their major accomplishment so far has been the creation of the 3Rs Hub. This builds on the remit of the advisory group and promotes Imperial's trajectory as a world leader in the 3Rs. With its own budget, the Hub has three key aims: to expand 3Rs research through better links to 3Rs funders, such as NC3Rs and UKRI; to improve and develop the College's existing 3Rs training for CBS staff and researchers; and to boost the visibility of 3Rs work within and beyond Imperial, particularly encouraging researchers to share resources, such as tissue samples, to minimise the number of animals used.

Tristan explains: "Through training and seminars, we want to improve awareness of experimental design and reporting of animal studies. We want to get researchers to be more proactive when they're planning experiments, for example by using proper statistical design to help reduce and refine the use of animals at Imperial.

"Most importantly, we need to improve reporting. Reporting of animal research in literature is not good enough in general. This is a key way of avoiding people repeating experiments, which leads to a lot of animal waste." Tristan says that papers published in research journals seldom provide the basic characteristics about the animals used.

For example, detailing how many animals of each sex were used is important since female animals may respond differently as a result of fluctuating hormone levels.

Bryn says: "The key role of the advisory group has been to advise AWERB and the wider College, but with the Hub we can reach out to more researchers and have more influence. Everyone is aware of the 3Rs now, but we need the technical training and support so that everyone can put this into practice."

He adds: "Since returning to Imperial, I've seen a huge culture change at Imperial. I genuinely feel that CBS staff and researchers are working well together and that's improved animal welfare." ■

"I've seen a huge culture change at Imperial. I genuinely feel that CBS staff and researchers are working well together and that's improved animal welfare."

– Dr Bryn Owen, Faculty of Medicine, Department of Metabolism, Digestion and Reproduction

LEADERS IN COMMUNICATIONS

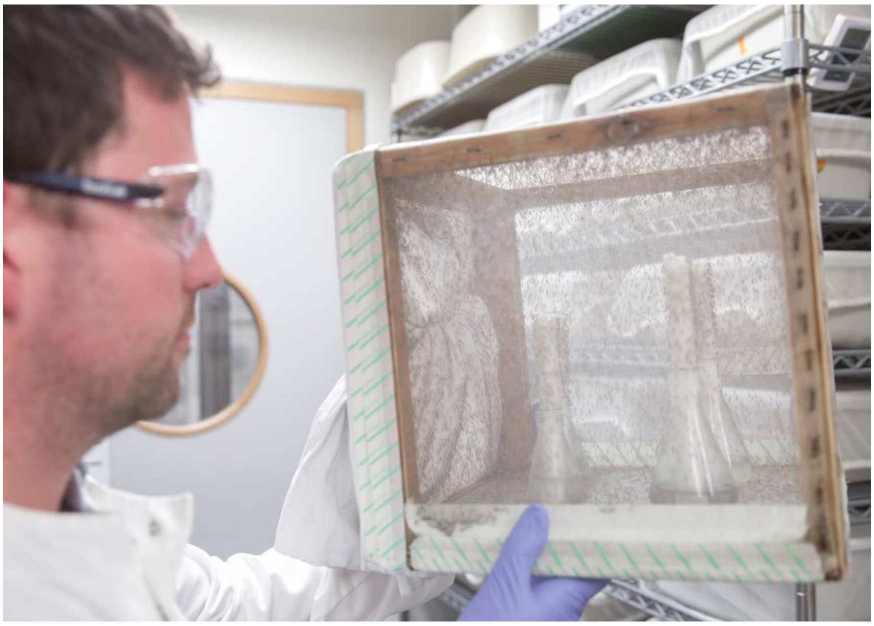
Imperial has continued to find new ways to engage the public with stories about animal research and its impact, whilst maintaining its commitment to communicating openly about research using animals.

The College is a signatory member of the Concordat on Openness on Animal Research, meaning that along with 120 other organisations, it has made the following commitments:

- We will be clear about when, how and why we use animals in research
- We will enhance our communications with the media and the public about our research using animals
- We will be proactive in providing opportunities for the public to find out about research using animals
- We will report on progress annually and share our experiences

In 2019 Imperial was granted the status of Leader in Openness from the Concordat on Openness on Animal Research in the UK, which guides how animal research is communicated.

The College went through a thorough assessment process involving a public panel, a peer review process and a public review. This independent assessment found that Imperial commits considerable resources and energy towards following best practice, embedding openness within the organisation and making the aims of the Concordat a reality. Robert Floyd, Director of Central Biomedical Services, said: "The award is a further demonstration of Imperial's commitment to following best practice and to be open about the use of animals in research both within the College and with the general public. Congratulations to all the people who have made it possible."



Animal researchers take to social media

Imperial's Communications and Public Affairs Division shares stories about Imperial's animal research through various channels, such as press releases and news stories. In recent years it has also been using the social media platform Reddit to give members of the public the chance to talk to animal researchers directly. Reddit's Ask Me Anything interviews allow people to submit questions and have them answered in real-time.

Since 2018, Communications and CBS have organised five Reddit sessions, with scientists talking about everything from how work with zebrafish is helping us understand more about inflammatory diseases, to how animal research is helping in the fight against MS (multiple sclerosis). Thousands of Reddit users have given positive votes for these sessions and posted questions and comments.

Imperial has also published more than 50 stories featuring animal research on the College's online news pages over the last two years. The stories highlight examples of where research involving animals is leading to scientific advances – everything from helping nerves to repair after spinal injuries to understanding the effect of pesticides on developing baby bee brains. You can read more of this news on pages 5–7 and at **www.imperial.ac.uk/news/animal-research**

Left: Cages of adult Anopheles stephensi mosquitoes used at the Baum Laboratory to aid the study of malaria.

> The award is a further demonstration of Imperial's commitment to following best practice and to be open about the use of animals in research both within the College and with the general public."
>
> – Robert Floyd, Director, Central Biomedical Services

Communicating about the use of animals and COVID-19

The contribution of CBS and animal research at Imperial to the fight against COVID-19 has been in the public spotlight since the pandemic began.

In July 2020, documentary makers filmed inside the St Mary's facility for a film covering the work being undertaken at College to develop a vaccine for COVID-19.

The same month, Imperial's website published a long story, featuring five CBS staff, on how Imperial's animal research facilities have fared during the pandemic. The Director of CBS, Robert Floyd, also featured in the College's 'Imperial People' series discussing how CBS had continued to operate, allowing ongoing research to continue and new essential COVID-19 research to start.

One of the 2020 Reddit Ask Me Anything sessions allowed college researchers to discuss their ongoing work creating a COVID-19 vaccine with the public. This Q&A was well-received, with over 13,000 upvotes and many questions regarding animals' use in COVID-19 vaccine research and how this related to human trials.

In 2020 Imperial's animal research department also produced a podcast series to hear from animal research workers about their experiences during the pandemic and how it has affected their jobs. ■

Right: Bees, such as these at Silwood Park, were used to understand the effect of pesticides on developing baby bee brains.

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

Design, editorial and photography:
Communications Division,
Imperial College London

www.imperial.ac.uk/animal-research