**CAMBRIDGE UNIVERSITY**

**Type of research carried out**

The majority of the animals used are mice and zebrafish – they make up 97% of all procedures at Cambridge. Where those species are not suitable, they use a small number of other animals, such as xenopus frogs, rats and sheep, as well as non-human primates, namely marmosets and macaques.

**Research carried out**

**Understanding how humans and animals develop and how our immune systems and brains work, for. This knowledge is essential for underpinning our understanding of health and disease for both medical and veterinary purposes.**

Other work is aimed at tackling specific diseases, for example in helping us understand how Parkinson’s disease affects the brain and motor system and how it might be tackled, or in developing new treatments for autoimmune diseases such as type 1 diabetes and multiple sclerosis

**No of procedures carried out**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Species | 2021 | 2020 | 2019 | 2018 | 2017 |
| Mouse | 152,471 | 102,050 | 99,351 | 107,140 | 134,110 |
| Rat | 2,095 | 2,511 | 2,137 | 3,202 | 3,511 |
| Zebra Fish | 42,354 | 71,789 | 12,425 | 30,589 | 18,747 |
| Other fish | 1,496 | 220 | 0 | 0 | 0 |
| Primate | 33 | 41 | 43 | 53 | 39 |
| Sheep | 122 | 84 | 110 | 130 | 62 |
| Guinea-pig | 48 | 0 | 0 | 144 | 74 |
| Other rodents | 78 | 33 | 14 | 21 | 21 |
| Rabbits | 2 | 0 | 0 | 0 | 0 |
| Chicken | 0 | 37 | 20 | 30 | 48 |
| Pigs | 59 | 16 | 0 | 0 | 0 |
| Xenopus | 445 | 438 | 509 | 659 | 1,353 |
| **Total** | **199,203** | **177,219** | **114,640** | **141,640** | **157,970** |

Procedures that are regulated include modifying the genes of a protected animal if this is done for and experimental or other scientific purpose or applied for an educational purpose; for example, breeding mice with genetic alteration is a regulated procedure if the intention is to keep the animals produced beyond two-thirds of the way through their gestation period. This helps explain why the numbers of mice and zebrafish are so high: each offspring born is counted as a procedure.

Moderate and Severe. The table below is a record by species of the numbers of animals assigned to each actual severity classification.

**Non-recovery**

Procedures, which are performed entirely under general anaesthesia from which the animal shall not recover consciousness.

**Mild**

Procedures on animals as a result of which the animals are likely to experience short term mild pain, suffering or distress, as well as procedures with no significant impairment of the wellbeing or general condition of the animals.

Mild procedures include:

* anaesthesia
* non-invasive imaging, like and MRI scan
* short-term social isolation
* taking a blood sample
* superficial non-surgical procedures e.g. ear biopsies in mice and non-surgical implantation of recording devices and minipumps

**Moderate**

Procedures on animals as a result of which the animals are likely to experience short term moderate pain, suffering or distress, or long-lasting mild pain, suffering or distress as well as procedures that are likely to cause moderate impairment of the wellbeing or general condition of the animals.

Moderate procedures include:

* invasive surgery under general anaesthetic e.g. surgical implantation of a catheter into a blood vessel for long term drug delivery
* causing cancer in an animal where the tumour growth impairs normal behaviour
* feeding a modified diet which is deficient in an essential nutrient such that it affects the health of the animal
* exposing the animal to something that they would normally run away from, without enabling them to run away
* the breeding of genetically altered animals where the animals health is affected, e.g. genetic models of diabetes.

**Severe**

Procedures on animals as a result of which the animals are likely to experience severe pain, suffering or distress, or long-lasting moderate pain, suffering or distress as well as procedures, that are likely to cause severe impairment of the wellbeing or general condition of the animals.

* any test where death is the end-point or where deaths are expected and it is not easy to determine when an animal is likely to die, e.g. models of aortic aneurysm
* testing a device that could cause pain/death if it were to fail, e.g. testing devices designed to support patients at risk of heart disease
* inescapable electric shock treatments, e.g. to induce a model of learned helplessness
* breeding animals with genetic disorders that are expected to experience severe and persistent impairment of general condition, for example Huntington’s disease, and muscular dystrophy

**Actual severity:**

The above definitions and examples also provide a good insight into what animals could have experienced when undergoing procedures and so reflect how actual severity is determined.  The only difference is that in the UK the Home Office introduced a further actual severity classification known as sub-threshold.  This classification therefore appears when UK annual returns of procedures are published.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Species andSeverity classifications | No of procedures(2021) | No of procedures(2020) | No of procedures (2018) | No of procedures (2017) |
| **Mice** | **152,471** | **102,050** | **99,351** | **107,140** |
| Non-recovery | 939 | 1,345 | 1,891 | 1,393 |
| Mild | 56,066 | 36,503 | 32,517 | 38,614 |
| Moderate | 24,678 | 11,642 | 13,613 | 15,677 |
| Severe | 2,115 | 1,362 | 1,735 | 1,675 |
| Sub-threshold  | 68,673 | 51,198 | 49,685 | 49,781 |
| **Rats** | **2,095** | **2,511** | **2,137** | **3,202** |
| Non-recovery  | 50 | 68 | 137 | 164 |
| Mild | 440 | 618 | 552 | 859 |
| Moderate | 1,271 | 1,357 | 1,302 | 1,868 |
| Severe | 26 | 9 | 34 | 64 |
| Sub-threshold  | 308 | 459 | 112 | 247 |
| **Rabbits** | **2** | **0** | **0** | **0** |
| Mild | 2 | 0 | 0 | 0 |
| **Zebra fish** | **42,354** | **71,789** | **12,456** | **30,589** |
| Mild | 30,163 | 56,744 | 8,550 | 17,462 |
| Moderate | 10 | 243 | 93 | 2 |
| Severe | 209 | 23 | 26 | 2 |
| Sub-threshold | 11,972 | 14,799 | 3,787 | 13,123 |
| **Other fish** | **1,496** | **220** | **0** | **0** |
| Mild  | 676 | 174 | 0 | 0 |
| Moderate | 210 | 46 | 0 | 0 |
| Severe | 8 | 0 | 0 | 0 |
| Sub-threshold  | 600 | 0 | 0 | 0 |
| Non-recovery  | 2 | 0 | 0 | 0 |
| **Primates** | **33** | **41** | **43** | **53** |
| Mild | 9 | 11 | 19 | 16 |
| Moderate | 21 | 30 | 23 | 37 |
| Severe | 3 | 0 | 1 | 0 |
| **Sheep** | **122** | **84** | **110** | **130** |
| Non-recovery | 0 | 8 | 4 | 5 |
| Mild | 38 | 17 | 11 | 4 |
| Moderate | 65 | 55 | 94 | 119 |
| Severe | 3 | 4 | 1 | 0 |
| Sub-threshold | 16 | 0 | 0 | 2 |
| **Pigs** | **59** | **16** | **0** | **0** |
| Non-recovery | 50 | 13 | 0 | 0 |
| Mild | 6 | 0 | 0 | 0 |
| Moderate | 3 | 3 | 0 | 0 |
| **Guinea-Pigs** | **48** | **0** | **0** | **144** |
| Non-recovery  | 0 | 0 | 0 | 0 |
| Mild | 48 | 0 | 0 | 0 |
| Moderate | 0 | 0 | 0 | 144 |
| Severe | 0 | 0 | 0 | 0 |
| **Other rodents** | **78** | **33** | **14** | **21** |
| Mild | 78 | 33 | 14 | 21 |
| **Domestic fowl** | **0** | **37** | **20** | **30** |
| Mild | 0 | 37 | 20 | 30 |
| **Xenopus** | **445** | **438** | **509** | **659** |
| Mild  | 455 | 438 | 509 | 659 |
| Moderate | 0 | 0 | 0 | 1 |
| **Total** | **199,203** | **177,219** | **114,640** | **141,968** |

**Why do they use chickens?**

Chickens are often used when birds are needed for a physiological study. They have been bred domestically for many years, so a large amount of literature on their physiology is available. They produce hardy embryos, whose development occurs outside the body of the mother. A small portion of the egg shell can be removed and replaced with clear plastic so that development of the chicken can be viewed at all stages. It is also possible to develop chick embryos in culture outside the egg.

Access to the embryo during development means that experiments involving surgical manipulation and chemicals which change the process of development are possible. Since studying the development of mammals is such a difficult process, the insights from these studies often provide useful comparative information.

Since chickens are vertebrates, their developmental processes have a great deal in common with humans, despite the many differences. They have provided valuable insights into the development of the nervous system, showing how cells migrate and differentiate. They have also been used to discover the molecular basis of limb development – a process which is similar in humans and birds - and have helped the understanding of many limb disorders. Chickens are also highly susceptible to infectious diseases, some which also infect humans, such as influenza. By understanding the immune system of the chicken we are able to learn valuable information for prevention of pandemic outbreaks of flu.

**What they study?**

*Breeding disease-resistant chickens*

Chickens are a valuable source of protein rich food, both in their meat and their eggs, in the UK and many other countries worldwide. Just like us, chickens are susceptible to many diseases that have strong effects on their health and welfare. Some of these diseases can also be a threat to human health, like ‘bird flu’ and Campylobacter.

See: **[Food poisoning: the bacteria lurking in your chicken](http://See:%20Food%20poisoning:%20the%20bacteria%20lurking%20in%20your%20chicken)**

*Understanding the immune system*

Cambridge researchers use chickens as a representative non-mammalian vertebrate, to understand more about the evolution of the adaptive immune system in humans. They focus on the major histocompatibility complex (MHC), which encodes molecules with central roles in the immune response. In addition to proposing how the adaptive immune system evolved, they have made contributions to the global poultry industry and to understanding fundamental properties, important for both chickens and humans.

**Why do we use guinea pigs?**

Guinea pigs have biological similarities to humans, which make them useful in many fields of research. They have been used as experimental animals for centuries; hence the term 'guinea pig' for a human experimental subject. Since vitamin C was discovered through research on guinea pigs, they have been important in nutritional research, and were also crucial to the development of: vaccines for diphtheria, TB, replacement heart valves, blood transfusion, kidney dialysis, antibiotics, anticoagulants and asthma medicines.

**What do they study?**

Cambridge researchers are using guinea pigs in work to find potential vaccines against viral diseases including Ebola, Lassa Fever, influenza viruses and Coronaviruses. New and improved vaccines are needed against emerging diseases, as well as against existing infectious diseases where existing vaccines do not offer 100% protection or where protection is only short-lived. The aim is to identify vaccine candidates that will be taken into clinical trials in collaboration with pharmaceutical companies. Animal models can establish that a potential vaccine provides protection against disease before it is trialed in humans. (See also: [H](https://www.cam.ac.uk/research/research-at-cambridge/animal-research/what-types-of-animal-do-we-use/guinea-pigs)[amsters](https://www.cam.ac.uk/research/research-at-cambridge/animal-research/what-types-of-animal-do-we-use/hamsters)).

**Hamsters**

Cambridge researchers are trying to find potential vaccines against viral diseases including Ebola, Lassa Fever, influenza viruses and Coronaviruses. New and improved vaccines are needed against emerging diseases, as well as against existing infectious diseases where existing vaccines do not offer 100% protection or where protection is only short-lived.

A project led by Professor Jonathan Heeney in the Lab of Viral Zoonotics, Department of Veterinary Medicine is looking for potential vaccines against viral diseases including COVID-19. Most of the greatest disease threats to humans come from viruses that naturally infect animals; these are called zoonotic viruses because of their animal origins.The induction of the immune responses is complex, and has never been achieved in cells in a laboratory setting. Hamsters, mice and Guinea pigs are being used as models to provide the complex interactions of a whole body system. Animal models can establish that a potential vaccine is safe and can provide protection against disease before it is trialled in humans.

In August 2020 a vaccine candidate against the group of Bat Coronaviruses that caused SARS and COVID-19, which arose from this work, [received £1.9 million from UK government for clinical trials](https://www.cam.ac.uk/research/news/cambridge-developed-sars-cov-2-vaccine-receives-ps19million-from-uk-government-for-clinical-trial) in the UK. (See also: [Guinea pigs](https://www.cam.ac.uk/research/research-at-cambridge/animal-research/what-types-of-animal-do-we-use/guinea-pigs)).

See also: [Cambridge research team working towards vaccine against COVID-19.](https://www.cam.ac.uk/research/news/cambridge-research-team-working-towards-vaccine-against-covid-19)

**Why do we use mice?**

Over eight out of ten animals used in research at Cambridge are mice. Their short life span and fast reproductive rate make it possible to investigate biological processes in many areas, at all stages of the life cycle.

The mouse makes an excellent model for human disease because the organisation of their DNA and their gene expression is similar to humans, with ninety-eight percent of human genes having a comparable gene in the mouse. They have similar reproductive and nervous systems to humans, and suffer from many of the same diseases such as obesity, cancer and diabetes.

It is possible to manipulate the DNA of mice either through cross-breeding or using techniques that ‘knock out’ certain genes, or edit their genes using recently-developed CRISPR-Cas techniques. This enables us to study novel genes of interest in the specific areas of the body without the need for generating new GM mice, which will dramatically reduce the number of animals needed to perform research.  Manipulating their genes can lead the mice to develop other diseases that do not naturally affect them. As a result research on mice has helped the understanding of both human physiology and the causes of disease.

**What do they study?**

*Understanding abnormalities in embryo development*

Our researchers have used mice to model aneuploidy, where some cells in the embryo contain an abnormal number of chromosomes. Normally, each cell in the human embryo should contain 23 pairs of chromosomes, but some can carry multiple copies of chromosomes, which can lead to developmental disorders. For example, children born with three copies of chromosome 21 will develop Down’s syndrome.

Pregnant mothers – particularly older mothers, whose offspring are at greatest risk of developing such disorders – are offered tests to predict the likelihood of genetic abnormalities. Until very recently, little was understood about the fate of embryos containing abnormal cells and about the fate of these abnormal cells within the developing embryos.

Our researchers developed a mouse model of aneuploidy by mixing 8-cell stage mouse embryos in which the cells were normal with embryos in which the cells were abnormal and showed that the embryo has an amazing ability to correct itself. This means that even when early indications suggest a child might have a birth defect because there are some abnormal cells in its embryonic body, this isn’t necessarily the case.

See also: **[Early-stage embryos with abnormalities may still develop into healthy babies](https://www.cam.ac.uk/research/news/early-stage-embryos-with-abnormalities-may-still-develop-into-healthy-babies)**

*Finding a treatment for heart disease*

In 2020, Cambridge researchers trying to turn off a gene that allows cancers to spread made a surprising U-turn. By making the gene overactive and functional in the hearts of mice, they triggered heart cell regeneration.Since adult hearts cannot usually repair themselves once damaged, harnessing the power of this gene represents major progress towards the first curative treatment for heart disease.

See also*:* **[Switching on a key cancer gene could provide first curative treatment for heart disease](https://www.cam.ac.uk/research/news/switching-on-a-key-cancer-gene-could-provide-first-curative-treatment-for-heart-disease)**

*Finding a vaccine against COVID-19*

**Why do we use naked mole-rats?**

Naked mole-rats live in large underground colonies of approximately 80 animals, which are dominated by a single breeding female, the queen; this social system is highly unusual in mammals but is similar to that commonly observed in bees and termites. Unlike queen bees and termites that use pheromones to control colony behaviour, a naked mole-rat queen uses aggression, being the physically dominant animal in a colony.

Over the last decade further physiological peculiarities of naked mole-rat physiology have come to light:

* Extreme longevity – naked mole-rats live until 30 years of age, whereas the longevity of similarly sized mice is two to three years; moreover, naked mole-rats display sustained good health into old age and unlike most mammals do not display an increased incidence of death with ageing
* Cancer resistance – naked mole-rats have an exceptional resistance to cancer
* Insensitivity to acid as a noxious stimulus – naked mole-rats respond normally to mechanical and thermal stimuli, but fail to perceive acid as noxious
* Hypoxia resistance – naked mole-rat brain tissue can withstand sustained periods of hypoxia (low oxygen levels) and even anoxia (no oxygen).

Learn more in this film, produced by *[Understanding Animal Research](http://www.understandinganimalresearch.org.uk/)*.

**Why do we use non-human primates?**

Monkeys and apes are our closest relatives in the animal kingdom, and because of their high cognitive abilities and complex social behaviour, biomedical research using these animals requires additional justification and high welfare standards.

Due to the high degree of genetic, anatomical and physiological conservation, non-human primates can be the best models for understanding human biological processes. They may be used to understand normal or abnormal structure and function or determine the efficacy of treatments where no other suitable animal models exist. Their use has led to a number of valuable medicines and treatments.

Whilst genetic similarity to humans is high in non-human primates, it is also high in less developed species; for instance, we share 96% of our DNA with mice, 70% with fruit flies, and indeed 50% with crops such as bananas. In different species the same gene may be expressed in different ways or interact in different ways with other genes. Having genes in common may help with comparing and understanding some biological processes but is of limited relevance with respect to assessing welfare, social needs etc.

Despite their close relatedness, research with non-human primates is not widespread and is only undertaken when other mammals are clearly inadequate. They are used to study brain disorders such as Parkinson’s disease and obsessive compulsive disorder. The brain is an incredibly complex organ, and while we can study some brain function in tissue culture, computer models and rodents, the study of advanced behaviour (both normal and abnormal) requires a human-like brain. Our only option is therefore to study these processes in non-human primates, such as marmosets and rhesus macaques.

The majority of non-human primates used in biomedical research are either marmosets or rhesus macaques.

What do we study?

We use primates to study a limited number of potentially serious conditions that affect the health of many millions of people in the UK alone. Ultimately, this will aid the development of new treatments to transform the lives of those affected by these conditions. In all cases, we only use animals where absolutely necessary and where, for ethical and practical reasons, it is not possible to carry out the research in humans.

We use non-human primates – marmosets and macaques – to study how advanced behaviour is controlled by the brain.

*Mental health research*

Our marmoset work provides a fundamental understanding of the processes behind the symptoms of psychiatric disorders including depression, obsessive compulsive disorder and anxiety. The current range of potential treatments for many of these psychiatric disorders is relatively restricted and their success rates are limited and highly variable. Basic research is essential to identify new treatments by analysing the cellular activity and chemical processes within regions of the brain that control those complex behaviours impaired in psychiatric disorders.

Brain manipulations often involve the permanent implantation of tiny metal tubes known as cannulas that permit direct delivery of drugs into specific brain regions in awake marmosets. Once implanted, the cannulas do not bother the animals. This allows researchers to determine the causal effects on behaviour of temporary alterations in the chemical function of these regions. The drug infusion procedure only takes a few minutes while marmosets are held gently by a handler very familiar with them. The drug effects are only temporary.

See: **[Marmoset study finds single brain region linking depression and anxiety, heart disease, and people's sensitivity to treatment.](https://www.cam.ac.uk/research/news/single-brain-region-links-depression-anxiety-heart-disease)**

*Understanding reward and risk*

Our macaque research is aimed at underpinning our knowledge of how the brain functions in healthy individuals and how malfunctions can have potentially serious health implications. In particular, the work concerns how we use information about reward and risk for making crucial decisions and has relevance to issues as widespread as obesity, drug addiction, schizophrenia and Parkinson’s disease. A better understanding of how reward and risk affect our decisions could lead to significant health benefits in the long term.

*Image: Marmoset*

**Other birds**

What species of birds do we use?

Our researchers study social and physical cognition in corvids (members of the crow family, which includes jackdaws, rooks and jays), from studies of alliance formation and post-conflict behaviours in rooks, and food-sharing in jackdaws, to tests of what jays and rooks understand about tools. Corvids are surprisingly intelligent birds and as such may be able to help us understand human behaviours.

What do we study?

Professor Nicky Clayton (Department of Psychology) has carried out pioneering research into the thinking power of corvids. Her observations have revealed these crows to be extremely clever. In Aesop’s Fables, the wise old crow drops pebbles into a pitcher of water to raise the level and allow her to drink. Clayton’s work has revealed that in real-life crows can, if they need to, use pebbles in just this way.

Corvids, including jays, cache food so that they can retrieve it later. They know who’s watching them and they also show the ability to plan ahead. Perhaps even more remarkably, corvids share their food. Male corvids even demonstrate an ability to understand what foods females prefer and will bring their mates tasty titbits.

*See also:*

**[Jays: the birds that can talk like humans](https://www.cam.ac.uk/research/features/jays-the-birds-that-can-talk-like-humans)**

**[It's a kind of magic](https://www.cam.ac.uk/stories/akindofmagic)**

**Pigs**

Organ transplantation is a life-saving treatment for organ failure in humans, but there is a growing disparity between the number of patients in need of a transplant and the number of suitable donor organs available. When an organ is donated for transplantation, it can spend several hours outside the body without a blood or oxygen supply. This can cause damage that may make it unsuitable for transplantation.

In 2020 a project led by Mr Kourosh Saeb-Parsy in the Department of Surgery began using pigs to better understand the cellular mechanisms underlying this damage and to test promising treatments. Previous work has been carried out in mice, but pigs are much more like humans in size and complexity. The pig model will also be used to test the safety and efficacy of new treatments before clinical trials in humans. Through this work it is hoped that more suitable organs will be available for human transplantation in the future.

**Why do we use rats?**

The laboratory rat has made invaluable contributions to cardiovascular medicine, neural regeneration, wound healing, diabetes, transplantation, behavioural studies and space motion sickness research. Rats have also been widely used to test drug efficacy and safety. Improved models in all these areas of research should result from our new knowledge of the rat genome.

Almost all disease-linked human genes have counterparts in the rat. Pinpointing these should help researchers to develop rat genetic models of human disease.

Rats are often used to study behaviour in psychology experiments. Their brains are larger than mice, and the animals are less timid and more intelligent. Although rats do not ‘think’ like humans, some of their brain structure resembles the more primitive elements of human brains, and hence they can be used to model some human behaviours.

**What do we study?**

*Cocaine addiction*
Rats are helping us understand why some people are more likely to become addicted to cocaine and why they can find it so difficult to overcome their addiction. Estimates suggest that for the year 2010-11, there were [just short of 300,000 opiate and crack cocaine users in England alone](http://www.drugwise.org.uk/how-many-people-are-addicted/).

Using rats, researchers showed that addiction manifests itself differently in different individuals and that, for some, compulsive cocaine-seeking behaviour continues despite adverse circumstances. Drug addiction had largely been regarded as the end point of a progressive loss of control over drug seeking resulting from a failure of part of the brain – the prefrontal cortex – that deals with decision making. However, our researchers were able to show that long term exposure to drugs also alters an area of the brain called the basolateral amygdala, which is associated with the link between a stimulus and an emotion.

In fact, using their rat model, our researchers have now identified a completely new path in the brain that links impulses with habits. This brain circuit links the basolateral amygdala indirectly with the dorsolateral striatum, which is the neural locus of habits.

See also: **[Highway to addiction: how drugs and alcohol can hijack your brain](https://www.cam.ac.uk/research/features/highway-to-addiction-how-drugs-and-alcohol-can-hijack-your-brain)**

*Understanding atherosclerosis*

Atherosclerosis is a severe disease of the arteries, responsible for heart attack and stroke. The disease is initiated by accumulation of fatty deposits in the artery wall. In 2019, Cambridge scientists were involved in research that identified the mechanism behind hardening of the arteries, and, using rats, found a generic medication normally used to treat acne could be an effective treatment for the condition.

See also: **[Cause of hardening of the arteries - and potential treatment - identified](https://www.cam.ac.uk/research/news/cause-of-hardening-of-the-arteries-and-potential-treatment-identified)**

*Image: Rat taking part in test of 'checking behaviour', a key trait in OCD*

**Why do we use sheep?**

Sheep are large mammals that have many similarities to humans in terms of physiology and suffer from many diseases which affect humans.  Because they have been used in farming for many decades, we know a significant amount about their care, handling and welfare that we are able to bring into the research field. They also have a shorter gestation period than us yet give birth to young of a similar weight to human babies, making them an ideal species for studying development and genetics. Sheep also live much longer than mammals such as mice and rats, enabling us to study diseases that affect humans in their adult lives, including neurodegenerative diseases such as Huntington’s disease.

They are also used extensively in veterinary research, studies of digestion in ruminants, and research on the impact of farming on the environment.

**What do we study?**

*Development in the womb*
We use sheep to help us understand the effects on an individual’s health in later life of poor oxygenation during development in the womb. We know that babies of low birth-weight are at a greater risk of developing diabetes and high blood pressure in later life, and have a greater chance of dying early from a heart attack or stroke as a consequence. Our researchers are investigating how and why this occurs, by looking at fetal development and early newborn life in a range of animals, from mice through to sheep. The ultimate goal of the research is to improve identification of individuals at risk of life-shortening conditions as a result of their early life environment and to offer potential therapeutic interventions to reduce this risk. This will have implications for both humans and veterinary medicine.

*Neurodegenerative disorders*
Sheep’s brains are much larger than those of rodents, similar in size to the brain of a rhesus macaque, and with the complex folds that are seen in primate brains. Crucially, their brains also have basal ganglia similar to ours – this is the area deep in the brain that, along with the cerebral cortex, is responsible for important functions such as the control of movement and ‘executive functions’ such as decision-making, learning and habit formation. It’s this that makes sheep a useful model for studying brain diseases such as Huntington’s disease and Batten disease that affect the basal ganglia and cerebral cortex.

See: **[High doses of ketamine can temporarily switch off the brain, say researchers.](https://www.cam.ac.uk/research/news/high-doses-of-ketamine-can-temporarily-switch-off-the-brain-say-researchers)**

Batten disease is extremely rare, and only a handful of infants or children are diagnosed each year in the UK. It is a genetic disease caused when a child carries two copies of an aberrant gene – one copy from each parent. But it is also extremely serious – symptoms include progressive blindness, severe seizures and the loss of language, swallowing and motor skills. Death at a young age is inevitable and there is no cure. Although Batten disease affects humans, it also occurs naturally in sheep.

Our researchers have used Batten disease sheep to validate behavioural tests which will now be used to investigate Huntington’s disease, a more common, but equally devastating disease. Unlike those with Batten disease, people – and sheep – with Huntington’s do not begin showing signs of disease until adulthood. We have good mouse models for studying Huntington’s disease, but mice are short-lived animals, whereas sheep can live to at least 12 years.

See also: **[Counting on sheep](https://www.cam.ac.uk/research/features/counting-on-sheep)**

**Why do we use xenopus frogs?**

The xenopus – known more commonly as the African clawed frog – is one of the most studied of all amphibians. The frog can be bred and maintained easily in the laboratory, where they can live for more than 30 years. In its lifetime, a female xenopus can produce as many as 30,000 eggs, depending on the particular species; it can lay thousands of eggs each year.

The frog is genetically surprisingly similar to humans, which means that scientists can model human disease in this amphibian and replace the use of higher sentient species.

Unlike humans and other mammals, the xenopus’s offspring grow outside of the body. Although the eggs are initially opaque, within a couple of days they become transparent, enabling researchers to see how the tadpole grows at all stages of development.

**What do we study?**

*Can we obtain heart or brain cells from skin or blood cells?*
Professor Sir John Gurdon was awarded the Nobel Prize in Physiology or Medicine 2012 for his work, carried out using xenopus, which showed that it is possible to take a nucleus from another cell (in this case, a tadpole cell), insert it into a frog egg cell and fertilise the egg, and that this would then grow into a healthy offspring – the principle that was later used by researchers to clone Dolly the Sheep from an adult cell.

Now, Professor Gurdon is continuing his work to find ways of obtaining embryo cells from the cells of an adult. The eventual aim is to provide replacement cells of all kinds starting from easily obtainable cells of an adult individual, for example to obtain spare heart or brain cells from skin or blood cells. The important point is that the replacement cells need to be from the same individual, to avoid problems of rejection and hence the need for immunosuppression. His team is trying to identify the molecules and mechanisms by which eggs can reverse the process of specialisation, so as to derive embryo cells from adult skin cells.

*Image:[Xenopus laevis (Brian Gratwicke)](https://www.flickr.com/photos/briangratwicke/8326790426/)*

**Why do we use zebrafish?**

The zebrafish has many features that make it an excellent animal model for studying development in vertebrates. The embryos develop externally to the mother and are transparent, so they can be easily viewed and manipulated. Compared to frogs the organisation of the zebrafish embryo is simple, and they develop more quickly. Zebrafish grow to maturity and are able to breed within two to three months. They also produce large numbers of offspring – a female zebrafish can lay up to 200 eggs a week.

Like the mouse, the zebrafish is suitable for genetic analysis, and is a valuable animal for creating genetic models of human diseases. Although the zebrafish genome is only half the length of the human genome, the genetic structure is remarkably similar. Many genes responsible for human diseases often have equivalents in the zebrafish. The use of zebrafish allows us to use a less sentient animal in research.

It is easy to produce mutations in zebrafish, and screening programmes have been developed to find mutations that affect particular biological systems, such as the development of the nervous system.

*Information adapted from [AnimalResearch.info](http://www.animalresearch.info/)*

**What do we study?**

*Neurodegenerative diseases*
Huntington’s disease is a neurodegenerative disease that causes difficulties with behaviour, feeding and communication, and abnormal movements, getting progressively worse and leading to premature death. There is no cure and treatments relieve only some symptoms.

The disease is caused by a defective gene which encodes huntingtin, which is toxic to cells in its mutant form. Professor David Rubinsztein is using zebrafish to model the disease, and in particular to see whether it is possible to stimulate a process known as autophagy (‘self-eating’). In this research the mechanism where cells ‘eat’ defective material, including mutant huntingtin, is being investigated as a means to alleviate the disease.

*Tuberculosis*
Professor Lalita Ramakrishan uses zebrafish to study tuberculosis (TB). The disease affects millions of people worldwide and without treatment, many of these will die. TB is on the increase worldwide, with the emergence, too, of multi-drug resistant strains. We tend to associate human TB with the lungs, but in fact it can affect almost all of our organs.

Fish are affected by a close relative of the human TB bacterium. Understanding how TB works in fish, and how to prevent it and treat it in fish, will take us a step closer to solving a major health problem in humans.

See also: **[Even without lungs, zebrafish help us study TB](https://www.cam.ac.uk/research/features/even-without-lungs-zebrafish-help-us-study-tb)**