Understanding ANIMAL RESEARCH

February 2012

ANIMAL RESEARCH SNAPSHOTS
Insights and Benefits

Good animal welfare means good science. The scientific community welcomes better regulation* which should reduce meaningless red tape, protect animal welfare and allow important research to continue.

These snapshots of research – some familiar, some less so – show some of the insights and benefits for both humans and animals which could not be achieved without the use of living animals.

Stem cell hope for blindness

Stem cell treatments have come a long way since the first pluripotent cells were isolated from mouse embryos in 1981. Grafts of stem cells, first tested in animal models, have been used to treat damage to various parts of the eye, including damaged corneas and macular degeneration in the retina.

Model Katie Piper, who went blind in her left eye after an acid attack in 2008, recently underwent a corneal stem cell graft and regained her sight.

Successful grafts of human embryonic stem cells into the retinas of rats and mice with macular degeneration have allowed scientists to move on to human trials. The early results from a small number of patients provide hope that this could become a routine procedure. For those who have been successfully treated, the techniques are life-changing.

Mice and melanoma

Yervoy (Ipilimumab) is a cancer drug that has dramatically prolonged the lives of a small number of patients with advanced metastatic melanoma since it was licensed for use in 2011. It was basic research on the mouse immune system function which led scientists to this exciting treatment.

Traditional cancer treatments like chemotherapy attack the cancer itself. *Yervoy* works in a more complex way, interacting with the immune system so that the patient's own cells are able to attack and destroy the cancer.

In 1995, scientists discovered that tumours in CTLA-4 knockout mice were completely destroyed by the T-cells in their immune systems. By developing a monoclonal antibody which interacted with the CTLA-4 molecule, they were able to treat cancers in normal mice and later in humans.

The treatment seems to work only in 10–15% of patients, but those who do respond exhibit dramatic responses.

Deep Brain Stimulation

A chance clinical observation in the early 1980s related to drug abuse led to the creation of a clinical model of Parkinson's disease in the monkey. With this model scientists made rapid progress to identify the brain circuit that becomes dysfunctional in Parkinson's, and reveal a target for treatment.

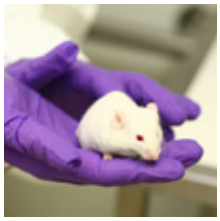
Within four years, the idea of Deep Brain Stimulation (DBS) to treat the condition had been born. Fifteen years after its approval for treatment of patients with Parkinson's disease, it has transformed the lives of an estimated 200,000 patients world-wide.

The monkey research identified a brain structure known as the subthalamic nucleus (STN) as the best possible target for DBS. Continuous stimulation delivered by a wire inserted into the STN, driven by a battery stimulator implanted under the collarbone, blocks the abnormal nerve signals that cause tremor and other Parkinson's symptoms.

This target would not have been discovered through research in patients.

DBS shows promise to treat other movement disorders including dystonia, much rarer than Parkinson's but affecting children. Doctors have been testing DBS to relieve chronic pain and severe depression and to regulate blood pressure.

Recent reports suggest it may reverse memory loss in Alzheimer's disease, and treat Tourette's syndrome and obsessive compulsive disorder.



* For more information about the scientific community's reaction to the EU Directive 2010/63/EU, go to: www.UnderstandingAnimalResearch.org.uk/new_EUDirective

Videos and high resolution images of research animals are available from our online photolibrary at http://www.understandinganimalresearch.org.uk/resources/

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The endangered red squirrel

The risk of extinction to the UK red squirrel is possibly the most emotive conservation issue in Britain today. Red squirrels have died out in areas invaded by grey squirrels from North America.

Until recently, it was thought that this was simply due to competition for resources. However, a few small whole-animal studies have shown that a parapoxvirus (squirrel pox) has partly caused the red squirrel's decline.

Scientists infected a small number of red and grey squirrels with the virus serum, with controls receiving distilled water. The red squirrels showed disease symptoms and were put down to avoid suffering. The grey squirrels, however, were immune.

Later studies built on this finding, to prove that grey squirrels carrying the pox virus were a factor in red squirrels' decline. Using a small number of animals to gain this understanding has been crucial in conservation efforts that, it is hoped, could save the entire red squirrel species.

Zebrafish mending hearts

The zebrafish, which can mend its own heart muscle, is providing clues to heart failure. Heart failure affects 750,000 people in the UK. This condition of the heart muscle, often caused by a heart attack, is a leading cause of disability.

Zebrafish are important in biomedical science because they are semi-transparent and have a fully functioning simple heart and circulatory system. If part of their heart is removed, they can grow it back in a matter of weeks.

Researchers recently identified a molecule that tells certain stem cells in the zebrafish embryo whether to become either heart muscle or blood vessel cells. This molecule – called Fibroblast growth factor (Fgf) – may be the evolutionary switch that triggered four-chambered human hearts, from the two-chambered 'tube' in fish.

The hope is that the Fgf switch can prompt stem cells to create brand new heart muscle in people with heart defects or who have suffered a heart attack. In the lab, the research will help the production of stem cells for use in heart repair.

Pharming medicines from milk and eggs

Complex proteins are very difficult, or impossible, to produce using cell-based systems. That's why scientists have begun to produce protein treatments using GM animals.

A human antithrombin protein made by genetically modified goats in their milk was licensed for use in 2006. *Atryn* is used during surgery for patients with a congenital blood clotting disorder who are prone to life-threatening blood clots. One GM goat can produce the same amount of antithrombin in one year as 90,000 blood donations.

Similar therapeutic proteins in development include human α-1 antitrypsin for hereditary emphysema and cystic fibrosis, blood clotting factors for haemophiliacs, and monoclonal antibodies.

Paracox vaccine for poultry

The result of 30 years of research in chickens, first in the USA and then in the UK, was the *Paracox* vaccine which protects chickens against the disease coccidiosis.

Coccidial infection was costing the UK poultry industry around £40 million a year, and global costs were estimated to be hundreds of millions. The parasites developed resistance to drugs added to poultry feed. Vaccination has reduced reliance on such additives to control coccidiosis.

Coccidiosis is caused by the single-celled parasite *Eimeria*, which lives and reproduces in the cells lining the bird's intestine. The vaccine protects virtually all the highly valuable chickens kept for breeding purposes and a newer version of the vaccine protects chickens kept for meat.

Around 1 billion doses of the vaccine are now sold annually in more than 30 countries.

Skipping muscular dystrophy

Duchenne muscular dystrophy (DMD) is an inherited muscle wasting disease affecting young boys. About 100 boys with Duchenne muscular dystrophy are born in the UK each year. At around the age of 10, sufferers are likely to need a wheelchair. However, with high standards of medical care and support, many young men with the condition live into their 30s.

The disease is caused by mutations in the very large dystrophin gene, which contains 79 exons or coding regions. A new type of gene treatment called "exon skipping" involves small pieces of antisense DNA (molecular patches) which mask an exon where there is a mistake or mutation.

Various exon skipping drugs have been developed using mice with a form of DMD. These treatments are currently at different stages of testing in animal and human trials. Completed human trials show "proof of principle" of the treatment, which is safe and mirrors results found in dystrophic mice.

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