

PARKINSON'S^{UK} CHANGE ATTITUDES. FIND A CURE. JOIN US.

PROGRESS

The research magazine of Parkinson's UK
Issue 10: winter 2012

Why we're joining the
genetic revolution

CONTENTS

Welcome.....	3
From Dr Kieran Breen, Director of Research and Innovation	
Parkinson's and the genetic revolution.....	4
How genetic discoveries are accelerating the search for a cure	
Project grants.....	9
We've awarded five new project grants worth almost £1 million	
Career Development Award.....	14
We talk to Dr Lydia Alvarez about her new approach to gene therapy	
Innovation grants.....	16
Three new innovation grants exploring bold new ideas in Parkinson's research	
Research results.....	19
We share some new and important findings from Parkinson's UK projects	
Monument Discovery project – update.....	24
An update from our largest ever research project	
Bringing supporters and researchers together.....	26
Research supporter Will Waites tells us about his work at the Nottingham Branch	
Taking part in research.....	28
Brian Russell-Taylor shares his experiences of taking part in research	
Parkinson's UK Brain Bank.....	30
A donation story with a difference	
A gift in your Will.....	33
Your legacy – a cure for Parkinson's	
Your feedback needed.....	34
Help us make Progress magazine even better	



Front cover image
Human chromosome 1 (scanning electron microscope)

WELCOME

Hello and welcome to the winter 2012 issue of Progress – Parkinson's UK's research magazine.

In 2011 we awarded 26 new grants to researchers in the UK who are working hard to help us find a cure and improve life for everyone living with Parkinson's. This issue is packed with the latest news from these projects, including recently awarded grants and exciting results from ongoing and completed projects.

One of the most exciting areas of Parkinson's research at the moment is genetics. So, in this issue, our feature article 'Parkinson's and the genetic revolution' takes you on a journey through the latest breakthroughs and how understanding the role genes play is moving us closer to a cure for Parkinson's.

I'd also like to highlight the articles towards the end of the magazine (pages 26-33), which show the vital role people affected by Parkinson's can play in our research. Without our dedicated research supporters raising much needed funds, pledging their brains for research and taking part in studies, the research we do just wouldn't be possible.

We're committed to involving people living with Parkinson's in everything we do. And with that in mind, we're asking you to help us improve Progress magazine.

We'd like to know what you think about Progress and what you want to see in the magazine in future. So please take the time to either complete our quick online survey at parkinsons.org.uk/progressfeedback or fill in the short form on the back page of the magazine and post it in to us.

I hope you really enjoy the magazine, and we look forward to receiving your feedback.

All the very best,



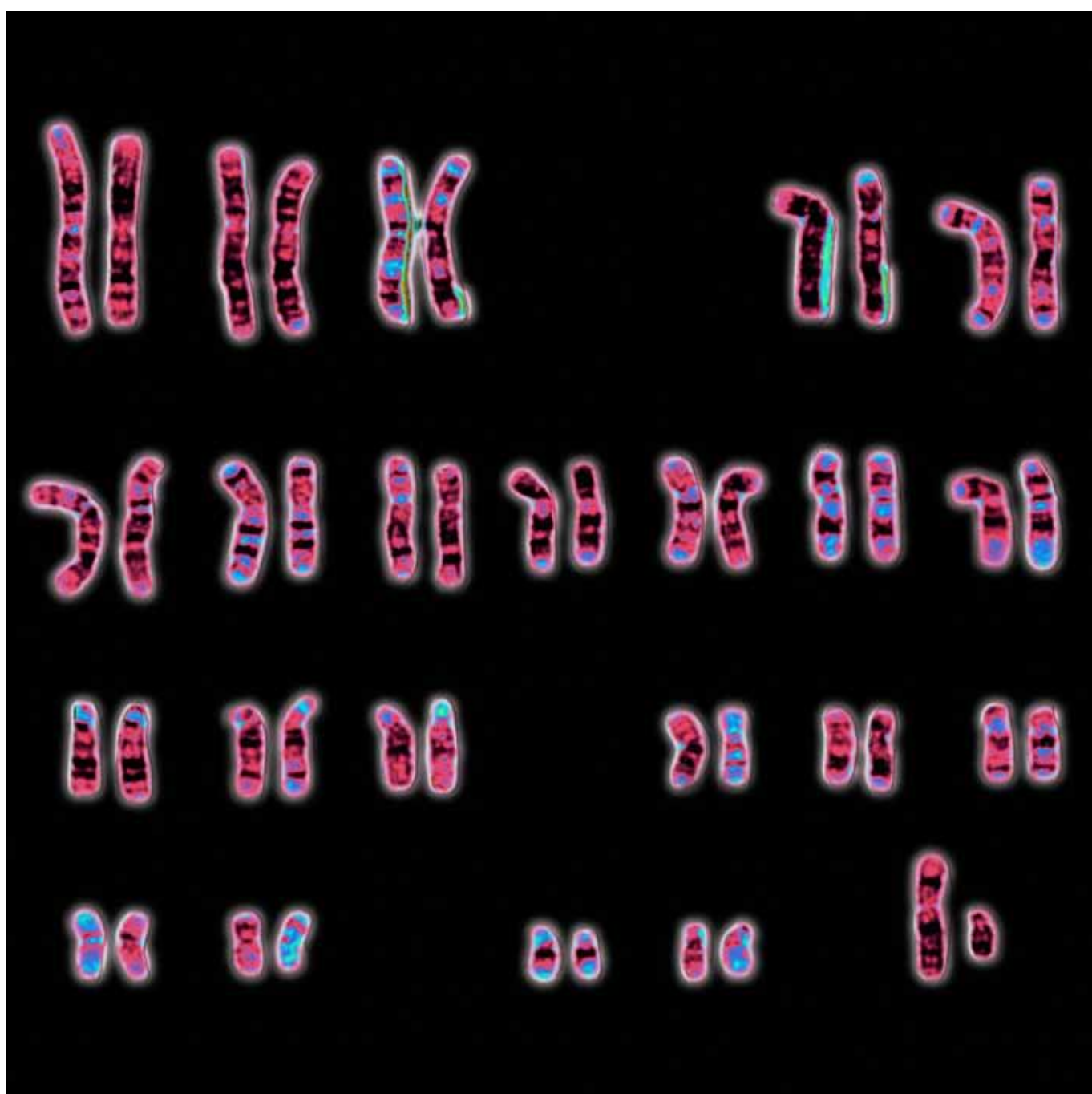
Dr Kieran Breen
Director of Research and Innovation



Kieran

PARKINSON'S AND THE GENETIC REVOLUTION

The field of genetics has exploded since 2003. This is when the complete human genome – the DNA sequence of more than three billion letters containing all the genes that make us who we are – was mapped for the first time. Now, advances in technology mean that scientists are learning more about our genes and what they do inside our bodies at record pace.



Above: Normal set of 23 human chromosomes that contain all our genes

These discoveries are helping us to understand more about complex conditions, such as Parkinson's. Research is also allowing us to develop new drugs that can directly target the genes that play a part in the condition.

Only 15 years ago, genetics weren't considered to play a part in the development of Parkinson's. So the progress in this area of research has been astonishing.

What's in a gene?

A gene is a short segment of DNA that provides our cells with the instructions for making a protein. Humans have around 23,000 genes, and these contain the blueprint for creating all the proteins required to produce the cells, tissues and organs that make up our bodies.

We all have our own unique mixture of genes, that we inherit from our parents. And this is what makes us all different. These natural variations affect everything from our personality to our height, as well as our susceptibility to different illnesses.

Some illnesses are directly caused by changes in specific genes. A good example is cystic fibrosis. This condition is caused by a single faulty gene that controls the movement of salt in the body. This single tiny genetic change causes internal organs to get clogged up with sticky mucus – making it difficult for people with the condition to breathe and digest food.

But conditions that are caused by faulty genes alone are pretty unusual. Most conditions, such as Parkinson's, are not usually caused by changes in a single gene.

We are now beginning to understand how genes work as part of a complex mixture of factors, including things in our environment and lifestyle to cause Parkinson's.

The first genetic clues to Parkinson's

Our understanding of Parkinson's changed forever in 1997 when researchers at the National Institutes of Health in the USA discovered that changes in a gene called alpha-synuclein could cause Parkinson's.

“
Our understanding of
Parkinson's changed
forever in 1997... ”

They found alpha-synuclein by studying an Italian family with a strong pattern of hereditary Parkinson's, stretching back many generations. Inheriting just one faulty copy of the alpha-synuclein gene is enough to cause the condition.

This particular faulty gene is very rare, but this research showed, for the first time, that genes could play a part in Parkinson's.

Hot on the heels of this first genetic clue to Parkinson's, Japanese researchers identified a second gene in 1998. They found that people who inherit two faulty copies of a gene called 'Parkin' – one from each parent – develop a very rare early-onset form of Parkinson's.

Our researchers discover two new genes

The hunt was on for more important genetic factors. In 2004 Parkinson's UK-funded researchers at University College London, uncovered two new genes that cause hereditary forms of Parkinson's.



“Our research team were first to identify the PINK1 gene that causes a rare form of inherited Parkinson's,” comments Professor Nick Wood who led the studies. “And shortly afterwards we, along with colleagues

from the USA, uncovered another important Parkinson's gene called LRRK2.

“Relatively few people with Parkinson's have these specific gene changes. But studying these genes and the effects on nerve cells is adding tremendously to our knowledge and directing the way we think about designing novel therapies.” ▶

From genes to treatments

We now know that Parkinson's is directly caused by rare inherited genes for a very small number of people.

These faulty genes are extremely rare, but studying them is already helping us understand more about how the nerve cells affected in Parkinson's work and how things go wrong. They also provide scientists with important clues for developing new treatments.

In 2009, Parkinson's UK-funded researchers at the University of Sheffield identified a major lead for new treatments for Parkinson's.



Lead researcher Dr Alex Whitworth explains:

“We were studying how two genes known to cause rare inherited forms of Parkinson's (the PINK1 and Parkin genes) affect nerve cells in the brains of fruit flies.

“Fruit flies with either of these mutations have damaged dopamine-producing nerve cells and problems with mobility similar to Parkinson's.

“But we found that giving the fruit flies a drug called Rapamycin – usually used to prevent the rejection of transplanted organs – could protect the flies against the effects of mutations in both the PINK1 and Parkin genes.”

Crucially, this study identified a key pathway inside nerve cells that can be stimulated to protect the cells affected in Parkinson's.

“It's early days yet, and there's a great deal of work to be done before we will know if these findings can be applied to all forms of Parkinson's.

“But the discovery of this pathway reveals the exciting potential that genes hold for understanding Parkinson's and developing drugs that could slow or even stop the progressive loss of nerve cells in the brain.

Dr Alex Whitworth, lead researcher at the University of Sheffield.

Common genes with subtle effects

The first human genome sequence in 2003 cost \$3billion and took an international consortium of geneticists a decade to complete.

Now, just over a decade later, a full genome sequence costs just a fraction of that. Combined with the use of more powerful computers, this

means that researchers are no longer restricted to studying the genetics of rare inherited forms of Parkinson's in isolated families. They can now study the genetics of Parkinson's on a global scale to spot more common risk factors.

In 2011, results from the largest and most comprehensive genetics studies of Parkinson's were published. These studies were huge, involving researchers from the US and across Europe, and including teams funded by Parkinson's UK.

The researchers compared genes from more than 12,000 people with Parkinson's and 21,000 people without the condition. They discovered a whole host of common genetic changes that can slightly increase the risk of developing Parkinson's, including 10 common genes that seem to play a part in its development. But people who have one of these genes are only slightly more likely to develop the condition.



Dr Michelle Gardner, now our Research Development Manager, was a member of the University College London team who were involved in the study.

“
But the discovery of this pathway reveals the exciting potential that genes hold for understanding Parkinson's and developing drugs that could slow or even stop the progressive loss of nerve cells in the brain.”

Michelle explains:

“These new studies take our understanding of the genetics of Parkinson’s to the next level.

“The new genes we’ve found are much more common, but they do not cause the condition directly. This means that the people who have them are only slightly more likely to develop Parkinson’s than those who don’t – perhaps by 1–2% at the most.

“But understanding how these more subtle genetic variations increase people’s risk of developing Parkinson’s will help us build a much more complete picture of the condition. Piecing them together will help us understand why nerve cells die, and hopefully, lead to new and better treatments in the future.”

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These new studies take
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the next level.”

Towards personalised treatments

The holy grail of treatment for any illness is a treatment regime that tackles the root cause of the condition in each individual person. And Parkinson’s is no different.

No two people with Parkinson’s are the same. The symptoms a person may have, the response to medication and how quickly the condition develops will differ from one person to the next.

But genetic research could one day help doctors to choose treatments based on a person’s individual genetic make-up.



Dr Kieran Breen, Director of Research and Innovation at Parkinson’s UK, comments:

“Personalised treatments for Parkinson’s are still some way off. But in 2011, researchers in the USA found the first evidence that the

genetic makeup of a person with Parkinson’s may determine how well they respond to specific treatments.

Research has previously shown that people who drink coffee regularly may be less likely to get Parkinson’s. But this study revealed that it’s actually only people who carry a particular version of a gene called GRIN2A that experience the protective effects of coffee.

“And in 2011 we awarded Dr Thomas Foltynie at the Institute of Neurology in London an innovation grant worth £14,845 to investigate how genetics affect people with Parkinson’s risk of developing uncontrollable movements known as dyskinesia.

“Studies like these, along with more targeted treatments, may one day make it possible for specialists to choose drugs for their patients based on their own unique genetic make-up – an exciting prospect.” ▶



Above: Multiple DNA samples are loaded onto a gel to separate out the fragments and create a DNA fingerprint

Genetic research and the future

Research over the last 15 years has revolutionised our understanding of Parkinson's and the role genes play in the development of the condition. But we still have a lot to learn. There are probably still important genes to discover, we also need to work out what all the different genes do and how they work together inside the nerve cells.

And Parkinson's UK is leading the way. Our researchers have uncovered key genes involved in Parkinson's. And now we're working on understanding what these genes do to guide the development of new targeted treatments that would transform the lives of people with Parkinson's.

In 2010 we awarded Dr Patrick Lewis at University College London a Career Development Award worth £250,000 over three years. His project aims to find out more about one of the key genes identified by Parkinson's UK researchers at UCL in 2004 – LRRK2:

“

I believe this is the most exciting time to be involved in Parkinson's research that there's ever been.

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“The genetic discoveries we've made have already completely changed the research field. They're giving scientists like me so much more to work with and so many new avenues to explore.

“Figuring out how genes like LRRK2 work and how we can change their activity will guide the development of drugs that actually tackle the root causes of nerve cell death – and hopefully one day make Parkinson's a thing of the past.”

References

Polymeropoulos M et al (1997) 'Mutation in the alpha-synuclein gene identified in families with Parkinson's disease' *Science*; 276:2045.

Kitada T et al (1998) 'Mutations in the parkin gene cause autosomal recessive juvenile parkinsonism' *Nature*; 392:605.

Valente E et al (2004) 'Hereditary early-onset Parkinson's disease caused by mutations in PINK1' *Science*; 304:1158.

Paisán-Ruiz C et al (2004) 'Cloning of the gene containing mutations that cause PARK8-linked Parkinson's disease' *Neuron*; 44:595.

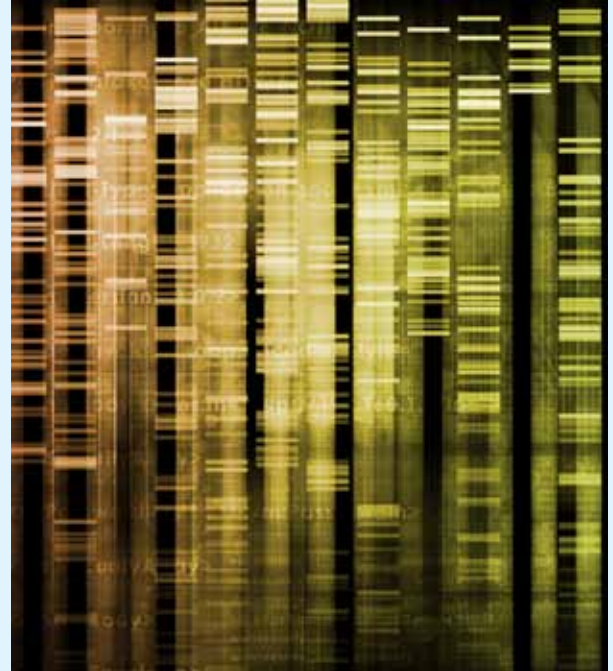
Tain L et al (2009) 'Rapamycin activation of 4E-BP prevents parkinsonian dopaminergic neuron loss' *Nat Neurosci*; 12:1129.

International Parkinson Disease Genomics Consortium (2011) 'Imputation of sequence variants for identification of genetic risks for Parkinson's disease: a meta-analysis of genome-wide association studies' *The Lancet*; 377:641.

Hamza T et al (2011) 'Genome-wide gene-environment study identifies glutamate receptor gene GRIN2A as a Parkinson's disease modifier gene via interaction with coffee' *PLoS Genet*; 7:e1002237.

What about genetic testing?

At the moment, genetic tests for Parkinson's are not available on the NHS. This is because the inherited genes that directly cause Parkinson's are so rare.



Above: DNA fingerprint

The genetics of Parkinson's are incredibly complex. Researchers have found lots of different changes in many different genes that are linked to the development of the condition. Some of these changes (which are very rare) can cause Parkinson's directly. But the families that are affected by these changes will usually already be aware, because they will have several family members that have the condition.

For the vast majority of people with Parkinson's, their genetic make-up has probably only played a very minor role in the development of their condition. Very large studies comparing the genes of thousands of people with and without Parkinson's have found subtle genetic variations that increase a person's susceptibility to developing Parkinson's very slightly. But they don't cause the condition.

For most people, Parkinson's is probably caused by complex mixture of factors including lifestyle, environment, ageing and possibly a genetic susceptibility.

PROJECT GRANTS

Project grants tackle the major research challenges in Parkinson's. Five new projects worth almost £1 million in total are just getting underway. These groundbreaking studies aim to get right to the heart of Parkinson's.

Studying the potential of nicotine to treat Parkinson's

Some studies have found that smokers are slightly less likely to get Parkinson's than non-smokers – could this be down to nicotine?



This is what Dr Stephanie Cragg at Oxford University is investigating with her new two-year project grant of £142,451.

Stephanie's previous work has

shown that nicotine may boost the production of dopamine – the chemical that is lacking in the brains of people with Parkinson's. Now she plans to explore whether nicotine and other nicotine-like substances have potential as new treatments for Parkinson's.

People with Parkinson's don't have enough dopamine, because some of the nerve cells in their brain that make it have died. Current treatments can help to manage the symptoms of Parkinson's, but they cannot stop, slow or prevent the death of dopamine-producing nerve cells inside the brain.

Dr Cragg's team have found that, in a typical healthy brain, nicotine can boost the amount of dopamine that nerve cells produce. But we don't yet know

whether it would have the same effect in the brain of someone with Parkinson's.

Because smoking seems to reduce the risk of developing Parkinson's, nicotine may also have exciting potential in the development of treatments that protect the dopamine-producing nerve cells from damage. By protecting these cells, such treatments could therefore slow the development of Parkinson's.

“Our studies show that nicotine receptors play a crucial role in controlling how much dopamine is released from nerve cells.”

“Dopamine-producing nerve cells have several different types of nicotine ‘receptor’ – proteins on the surface of the cell,” says Stephanie. “These detect and respond to nicotine in the brain.”

“Our studies show that nicotine receptors play a crucial role in controlling how much dopamine is released from nerve cells. In

this project, we'll study mice lacking a particular nicotine receptor called alpha5. We believe that alpha5 plays an important role in dopamine release.

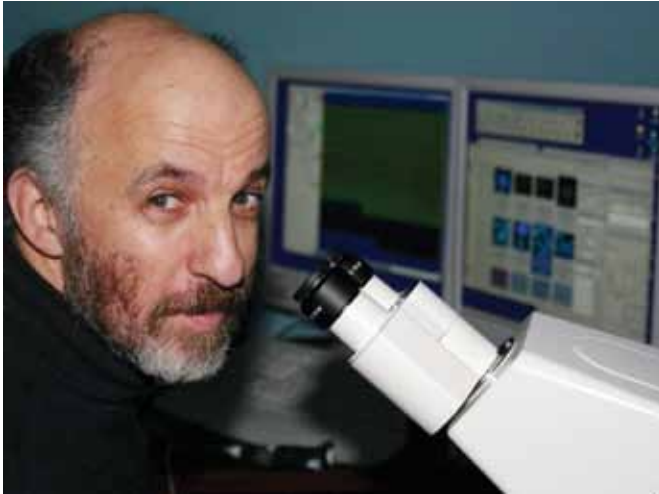
“I hope this project will help to identify which nicotine receptors can boost dopamine function in the brain and how they do this. This work could lead to new drug treatments that target the vital nicotine receptors, treating the symptoms and slowing the development of Parkinson's.”

Smoking may slightly reduce the risk of developing Parkinson's, but its most significant side effects are an increased risk of cancer, cardiovascular disease and chronic lung conditions, such as chronic obstructive pulmonary disease, so it won't become a treatment for Parkinson's.



Can a diabetes drug also help people with Parkinson's?

Recently, a group of drugs used to treat type 2 diabetes, called thiazolidinediones (TZDs), have shown exciting potential to protect against nerve cell death. They also seem to boost the number of mitochondria inside cells. Mitochondria are the energy-producing 'batteries' inside cells that become damaged in Parkinson's.



We've given Professor Michael Duchen from the University of London a grant of £106,835 over two years to explore whether TZDs could be used to slow down the progression of, or even prevent, Parkinson's.

Mitochondria are often described as cellular batteries. They produce the energy that powers our cells. If they become damaged, cells may struggle to function and eventually die.

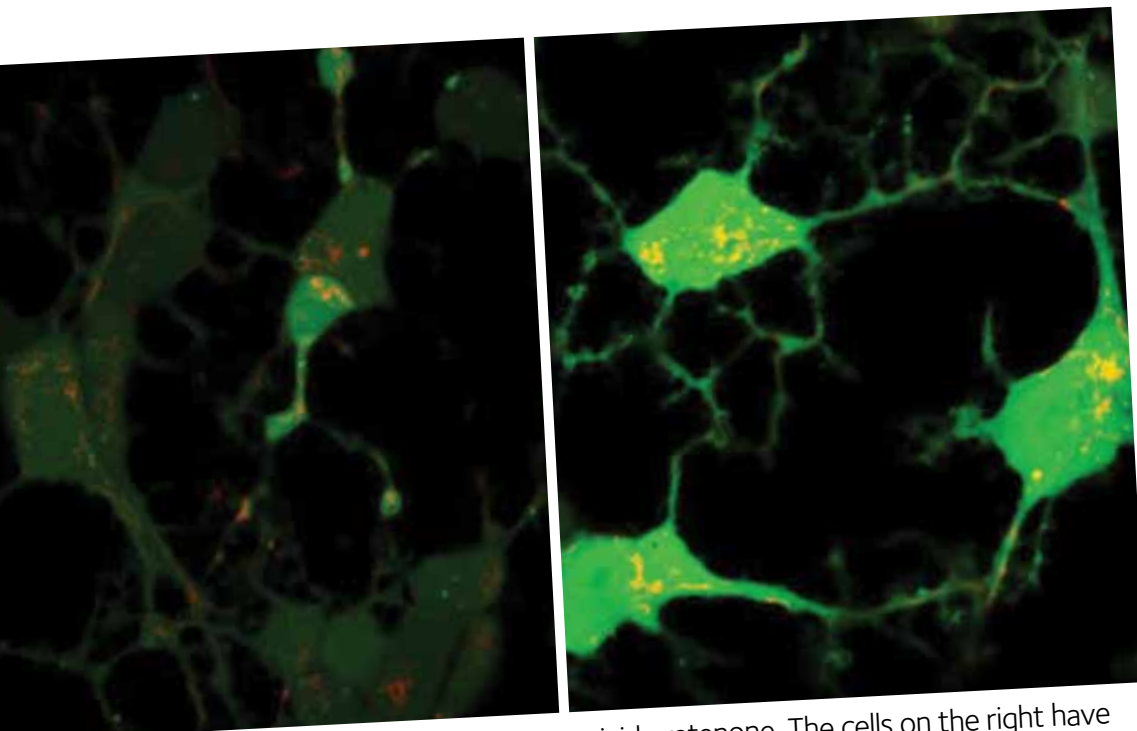
Crucially, damaged mitochondria are found inside the affected nerve cells in Parkinson's. Current research now points to a small cluster of proteins inside the mitochondria, known as 'complex I', which may be the key to nerve cell death in Parkinson's.

"People who work with pesticides are known to be slightly more likely to develop Parkinson's," says Michael. "Now we think this is because chemicals in the pesticides damage the vital complex I proteins inside the mitochondria of dopamine-producing nerve cells.

"With this project we plan to further investigate these mitochondrial problems and test whether they can be reversed by TZDs.

"We've already grown nerve cells in the lab and treated them with a pesticide called rotenone. Next, we'll examine in detail how the mitochondria are damaged and whether TZDs can reverse or repair the damage.

"If we find that TZDs have potential for Parkinson's, this could lead to the development of new treatments that can actually prevent the nerve cells from dying. And because TZDs are already used to treat type 2 diabetes, it may not be long until they can be tested in people with Parkinson's."



Above: Nerve cells exposed to the pesticide rotenone. The cells on the right have been protected from damage by TZDs

Improving how we replace the nerve cells lost in Parkinson's

Cell transplants have great potential as a future cure for Parkinson's, but there are still many challenges to overcome before this can become a reality.



One of the key difficulties is making sure that transplanted cells can survive and work properly once inside the brains of people with Parkinson's. This has proved tricky to do in animal studies.

We've given Professor Anne Rosser at Cardiff University a three-year project grant of £184,787 to explore better ways to support transplanted nerve cells and help them survive inside the brains of people with Parkinson's.

In Parkinson's, nerve cells in a part of the brain called the substantia nigra stop producing a chemical called dopamine and start to die.

Transplants offer the opportunity to replace the dead nerve cells with new, healthy cells.

In the 1990s, scientists took dopamine-producing nerve cells from developing foetal brains and transplanted them into the brains of people with Parkinson's.

The results were mixed, but some patients showed remarkable improvements. However, the lack of a regular supply of foetal tissue makes this type of therapy impractical.

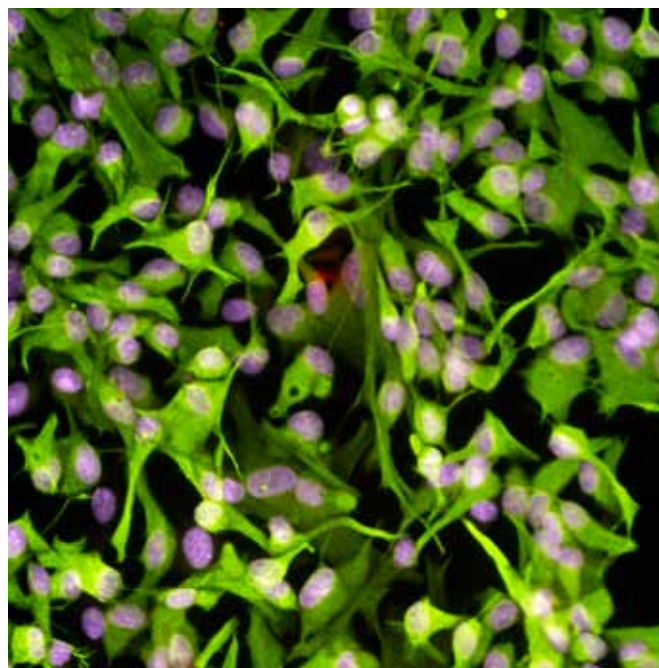
Stem cells have the potential to become any cell type in the body, including dopamine-producing nerve cells in the brain. Stem cells grown from embryos or adult tissues are now the main hope for people with Parkinson's. But so far, studies in animals show that stem cells that have transformed into dopamine-producing nerve cells don't survive or perform as well as dopamine-producing nerve cells taken from foetal brains.

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If I'm right about astrocytes, the hope is that my study will bring stem cell transplants a step closer to becoming a treatment for people with Parkinson's.”

Professor Anne Rosser believes that the key to successful transplants may be special star-shaped cells, called astrocytes.

“Astrocytes are found throughout the brain,” she says. “They surround the nerve cells, act as a support, and help the nerve cells to work and survive.”

Below: Astrocyte – fluorescence light micrograph of astrocyte cells in the human brain



“There are many more astrocytes inside the developing foetal brain than in stem cell transplants. Also, there are lots of different types of astrocytes in the brain but we don't know which ones are needed to help transplanted cells to work properly.”

“We will look at how astrocytes and dopamine-producing nerve cells interact in a rat model of Parkinson's. We will study what happens to foetal cell transplants if the astrocytes are removed and whether adding astrocytes can 'rescue' stem cell transplants.”

“If I'm right about astrocytes, the hope is that my study will bring stem cell transplants a step closer to becoming a treatment for people with Parkinson's.”

What's the link between Gaucher's disease and Parkinson's?

People who have a condition called Gaucher's disease are more likely to develop Parkinson's. While we don't understand why this happens, genetics seems to play key role.



Professor Anthony Schapira at the Institute of Neurology in London has a three-year grant of £333,229 from us to find the connection between the two conditions.

Gaucher's disease is a serious condition caused by changes in a gene called the GBA gene. It's an 'autosomal recessive condition'. This means that for a child to be affected they must inherit a copy of the abnormal gene, from each parent.

Doctors treating people with Gaucher's disease noticed that people with the condition and their families seemed to be at greater risk of Parkinson's. This led to studies which in 2008 found mutations in the GBA gene as the most common genetic risk factor for Parkinson's.

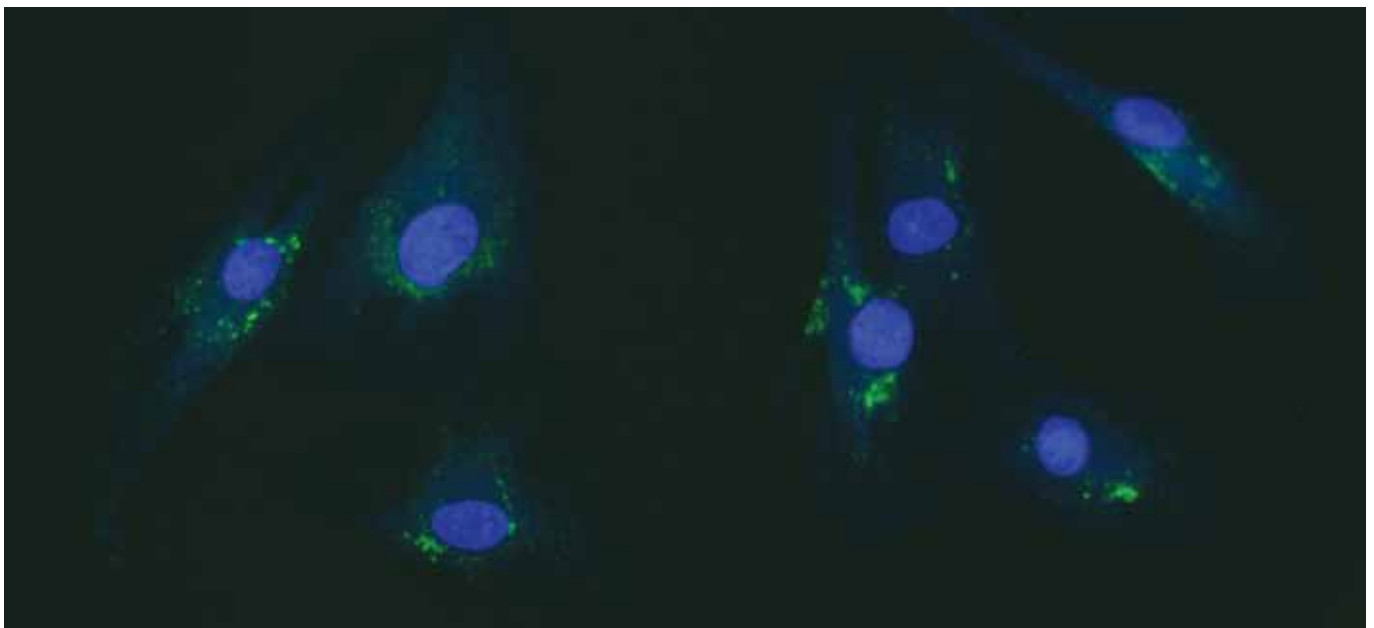
“Our research has already shown that blocking GBA in the nerve cells affected in Parkinson's stops the mitochondria from working properly.”

While changes in this gene increase the risk of Parkinson's they do not cause the condition. In fact, most people with Gaucher's disease still don't develop Parkinson's.

So clearly other factors are important in deciding who goes on to develop Parkinson's. Anthony believes that problems keeping the proteins inside our nerve cells healthy may be the key:

“The GBA gene plays an important role in making and recycling proteins, including the proteins inside the mitochondria – the cell's tiny energy-producing batteries. And our research has already shown that blocking GBA in the nerve cells affected in Parkinson's stops the mitochondria from working properly.”

“Now in this project we plan to use post-mortem mouse and human brain tissue to explore how changes in the GBA gene affect the dopamine-producing nerve cells lost in Parkinson's. It will hopefully, provide important clues for developing treatments that could slow, stop or even prevent the nerve cells dying.”



Above: Skin cells from people with Parkinson's who have mutation in the GBA gene. The GBA protein is highlighted in green. Picture courtesy of Dr Alisdair McNeill

Linking alpha-synuclein to Parkinson's

Alpha-synuclein may be a key to Parkinson's. It's a protein that builds up and forms sticky clumps. These clog up the dopamine-producing nerve cells that are affected in people with the condition.



We've given Professor Maria Grazia Spillantini at Cambridge University £127,997 for her two-year project to study, in more detail, alpha-synuclein and how it behaves.

Changes in the gene that makes the alpha-synuclein protein cause some very rare, inherited forms of Parkinson's. But alpha-synuclein is also a key component of Lewy bodies, the clumps of proteins seen inside the nerve cells affected in the condition. This means that alpha-synuclein is probably important in most forms of Parkinson's.

Some research, including previous work by Maria Grazia, suggests that these sticky protein clumps may interfere with the release of dopamine from nerve cells.

"The formation of Lewy bodies in the nerve cells seems to be a gradual process," says Maria Grazia. "First, a few proteins come together to form a small bundle. These bundles join together to form sticky strands. The alpha-synuclein strands stop the nerve cells working properly. These eventually form the large spherical Lewy bodies that are the hallmark of Parkinson's."

Maria Grazia's team has already developed a genetic mouse model of Parkinson's with an altered alpha-synuclein protein.

In this project, they will use their mouse model, alongside post-mortem brain tissue from people with Parkinson's, to see which form of alpha-synuclein causes problems inside nerve cells. Is it the small bundles, or the sticky strands?

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Our study will tell us more about how alpha-synuclein builds up inside the nerve cells affected in Parkinson's.

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"Ultimately, we hope this will lead to treatments that can prevent the build up of alpha-synuclein, and bring us closer to a cure for Parkinson's," says Maria Grazia.

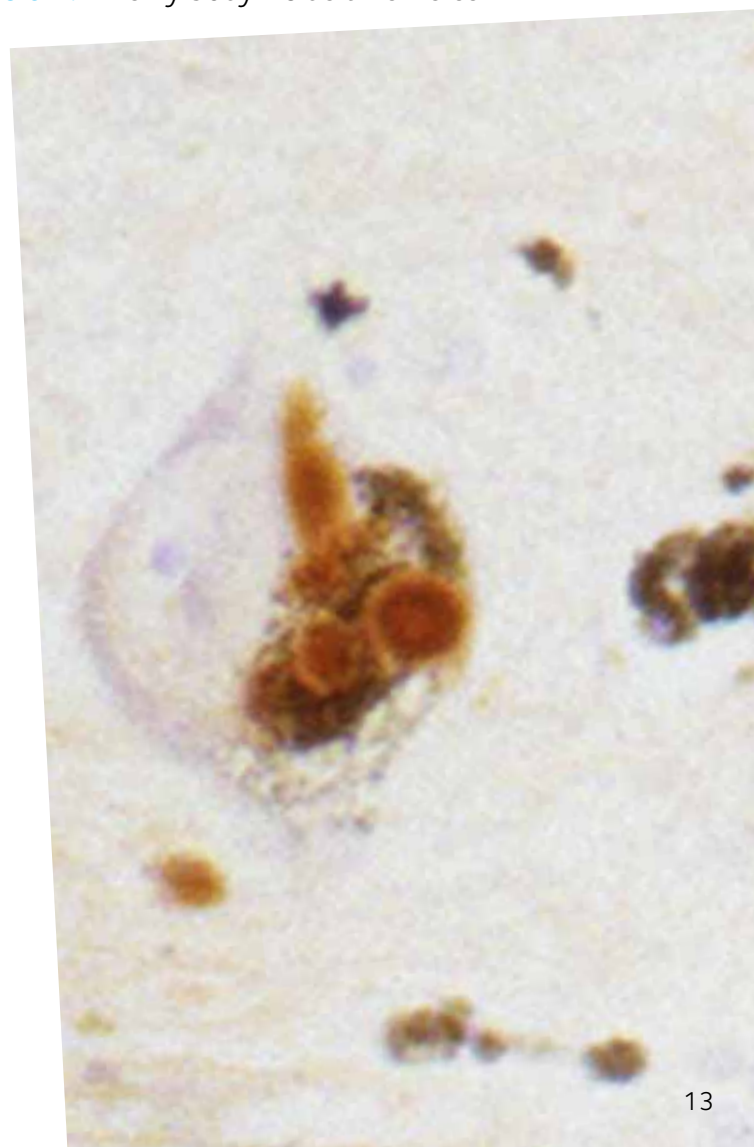
Is alpha-synuclein the key to Parkinson's?

People who inherit an altered version of the alpha-synuclein gene have an increased risk of developing Parkinson's.

The alpha-synuclein protein is also a key component of Lewy bodies – the sticky protein clumps found inside the nerve cells that die in Parkinson's.

This makes alpha-synuclein a prime target for researchers studying Parkinson's, and we've invested almost £1 million in projects to understand and tackle this problem protein.

Below: A Lewy body inside a nerve cell





CAREER DEVELOPMENT AWARD:

A new gene-therapy approach to treating Parkinson's

Dr Lydia Alvarez is a postdoctoral fellow at University College London. We've awarded Lydia a Career Development Award worth £248,629 to explore her exciting new ideas for gene therapy.

We've been talking to Lydia about what inspired her interest in Parkinson's research, and her plans for her three-year project.

Why did you decide on a career in Parkinson's research?

Parkinson's is one of the most common neurodegenerative disorders but, in most cases, the cause remains unknown and there are no treatments to halt the progression of the condition.

After my PhD I decided to focus on Parkinson's to, hopefully, contribute to a better understanding of the causes, and to design and develop new and better therapies.

What breakthroughs have you seen in Parkinson's research since you started working in the area?

I think the most important advance in Parkinson's research in recent years has been the discovery of the genetic factors involved in the condition. This has really advanced our understanding of what goes wrong inside the nerve cells in the brain that die and will eventually lead to much better treatments.

More recently, the discovery that we can create stem cells from adult skin cells – so called induced pluripotent stem (iPS) cells – was very exciting. This means we can now create new nerve cells from people with Parkinson's to study closely in the lab, which will be an incredibly useful tool for developing and testing new treatments for the condition.

Another major breakthrough, in my opinion, has been the discovery that alpha-synuclein – a sticky protein that clogs up nerve cells affected in Parkinson’s – seems to spread through the brain in a very particular pattern. Understanding this spread and how to prevent it happening may be the key to treatments that can slow or stop Parkinson’s in its tracks.

What’s been the most exciting Parkinson’s research you’ve been a part of so far?

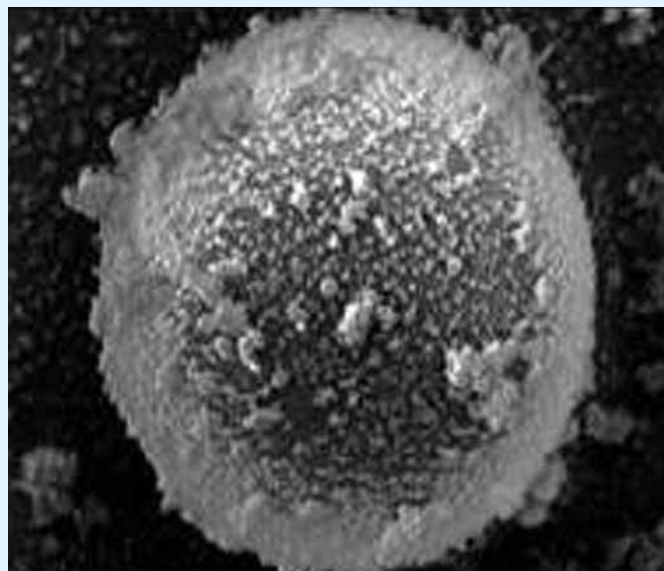
I’m most proud of my work investigating how cells handle alpha-synuclein. Our research team found that certain proteins responsible for removing excess alpha-synuclein from cells are much lower than normal in the Parkinson’s brain.

This really gave me the idea for my Parkinson’s UK-funded project. In this new study I hope to develop a new gene therapy that can boost the activity of these vital proteins and decrease the levels of damaging alpha-synuclein inside the nerve cells. But I hope the most exciting research of my career is still to come!

So what’s your new Parkinson’s UK-funded Career Development Award all about?

I’m interested in developing new and better ways to deliver Parkinson’s treatments to the brain. And in my new Parkinson’s UK-funded project I will explore the potential of using ‘exosomes’ for the widespread delivery of gene therapy to the brain.

Below: An exosome – small packages that cells use to send proteins and information to other cells



Exosomes are small packages that cells use to send proteins and information to other cells. I hope to develop ways to hijack the brain’s natural exosome delivery system to transport treatments, like gene therapy, to areas of the brain that are affected by Parkinson’s.

In particular, I will use this system to try to decrease the levels of the alpha-synuclein protein, which is thought to play a major part in nerve cell death.

There are already several gene therapy trials for Parkinson’s underway at the moment – how is your approach, using exosomes, different or better?

All the current gene therapy trials for Parkinson’s use disabled viruses to deliver the genes to the target nerve cells.

These kinds of gene therapies are given by a surgical injection into the brain. But because the body has an immune reaction and tries to fight off the virus, this severely limits the number of repeat injections and makes long-term therapy difficult.

Our gene therapy will use exosomes that have been modified to have a specific molecule on their surface that means they get sent to the brain. Our exosomes could then be injected directly into the body without the need for an injection into the brain.

And because exosomes are produced naturally by the body, they could be tailored to work for each person. This would avoid an immune response and would be much better for long-term treatment.

What do you hope your project will achieve?

It’s still incredibly early days but I hope that we’re able to develop a gene therapy that can lower alpha-synuclein levels in the brain. A treatment that could do that may be able to really slow the progress of Parkinson’s, or even stop it in its tracks.

I’m also hopeful that the exosome delivery system we’re developing will provide a useful way to deliver other types of gene therapy into the brain to treat people with Parkinson’s.

INNOVATION GRANTS

Our innovation grants offer researchers up to £35,000 for projects lasting no longer than 12 months. These projects explore bold new ideas that could lead to exciting breakthroughs in the causes, treatment and cure of Parkinson's.

What makes dopamine-producing nerve cells vulnerable in Parkinson's?

People with Parkinson's don't have enough of a chemical called dopamine because some nerve cells that produce the chemical in their brain have died. But, we don't understand what it is about these dopamine-producing nerve cells – among all the hundreds of millions of cells in the brain – that makes them so susceptible to damage in Parkinson's.



In this 12-month project, Professor Paul Bolam and his team at the University of Oxford, will use their innovation grant of £34,866 to work out what makes dopamine-producing nerve cells vulnerable.

This will hopefully lead to developing treatments that can rescue and protect these precious cells.

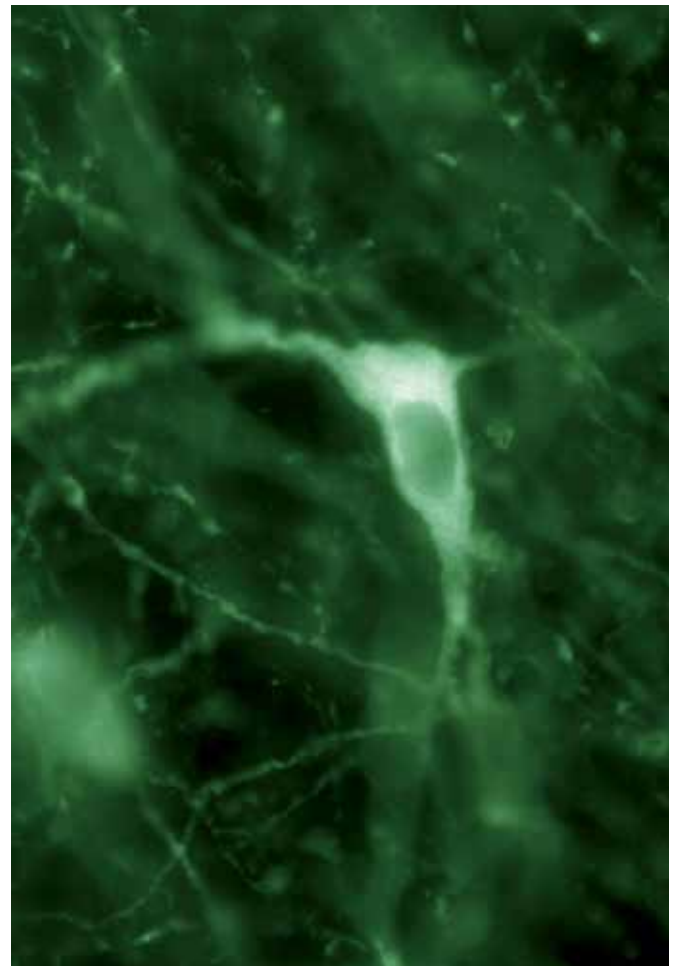
“We already have evidence to suggest that dopamine-producing nerve cells are bigger, work harder and are more complex than other types of nerve cells in the brain,” says Paul.

“This puts the cells under huge pressure as they need to produce massive amounts of energy to keep working at this level. This may make them vulnerable if they are put under any extra stress and unable to produce enough energy to meet their needs.”

With this innovation grant Paul, and his colleague, Dr Eleftheria Pissadaki, will firstly use computer models to compare different types of dopamine nerve cells – to work out what could make the cells so vulnerable.

Secondly, they will modify the dopamine-producing nerve cells of rats to reduce their energy demands, and test whether this helps the cells cope better with stressful events that would usually lead to cell death.

Below: A dopamine-producing nerve cell



Understanding why these dopamine producing nerve cells die in Parkinson's is a major first step in working out how we can protect these precious cells. This could lead to the development of new treatments and therapies that can slow, stop or even reverse Parkinson's – something no current treatments can do.

Does the drug apomorphine help treat dementia in Parkinson's?

Many people with Parkinson's develop problems with thinking and memory at some stage. As their condition progresses, some people with Parkinson's will be diagnosed with dementia. There are drugs that can help manage the thinking and memory problems experienced, but they are not always effective and they cannot slow or prevent the development of dementia.



Professor David Burn and his team at Newcastle University will use their six-month innovation grant of £29,318 to investigate whether apomorphine – a drug already used by many people with Parkinson's –

has affect on dementia symptoms.

“Apomorphine has been used in the UK for many years to help people with Parkinson's manage their movement problems,” says David. “But our research will look at the drug from a completely new angle.

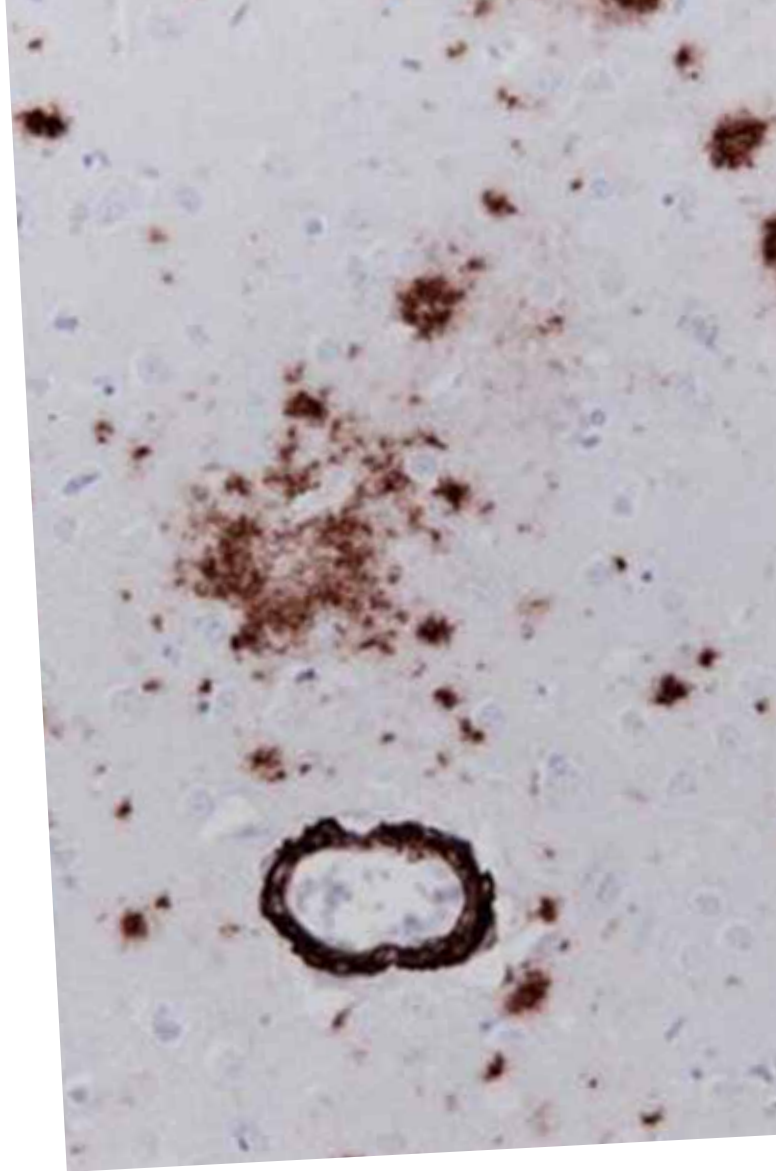
“At the moment, we don't know why some people with Parkinson's develop problems with thinking and memory and others don't.

“But some researchers believe that the build-up of a protein called amyloid in the brain – which is also found in the brains of people with Alzheimer's – may be responsible. And there is some evidence that apomorphine may help to prevent the build-up of the amyloid protein.”

This research could lead to apomorphine being used as a treatment to slow or prevent the development of thinking and memory problems in people with Parkinson's.

In this collaborative project, David and his team will work with Professors Andrew Lees and Tamas Revesz, who are both based at University College London.

“
At the moment, we don't know why some people with Parkinson's develop problems with thinking and memory and others don't.”



Above: Post-mortem brain tissue showing amyloid protein in brown

By comparing donated brain tissue from people with Parkinson's who experienced thinking or memory problems with those who didn't, they hope to see if the build-up of amyloid protein in certain brain areas is linked to dementia.

They will then look for amyloid protein inside the brains of people who took apomorphine for their Parkinson's. This should help establish whether apomorphine can prevent or reduce the build-up of amyloid protein and therefore whether it has potential as a dementia treatment for people with Parkinson's.

Using mobile phones to tackle speech problems in Parkinson's

Speech problems affect around 70% of people with Parkinson's. This can make everyday things much more difficult, and can have a profound impact on your quality of life. Speech therapy can help, but speech therapists have limited time and resources.



Dr Roger Eglin at the University of Portsmouth has been given an innovation grant of £35,000. His 12-month project aims to develop a mobile phone application that could help people with Parkinson's improve their speech.

"Many people with Parkinson's already have and use mobile phones, making them a low-cost, simple and effective way for helping people improve their own speech," says Roger. "We've developed a basic mobile phone application to improve speech, but it needs to be improved and tailored for people with Parkinson's. We will be testing our application with people with Parkinson's at every stage of development to make sure it is effective and easy to use."

The team includes Peter Nolan, Julia Johnson and Lee Prior and they will be collaborating with Professor Ray Chaudhuri at King's College Hospital.

They aim to develop two key functions to help people improve their speech:

- A 'feedback-meter' to show people how loud their current speech is compared to background noise, and help them raise their voices to be heard properly
- A 'voice-training' function to encourage people to speak more loudly, which can make their voice easier to understand.



Above: Julia Johnson holds a mobile phone showing the team's new speech therapy application

How speech problems can affect people with Parkinson's

"I was diagnosed just one year ago and one of my first and worst symptoms was slurred and garbled speech.

"I form a sentence in my mind perfectly and articulately. But by the time it is made vocal much is lost. In fact I find myself using few words as possible. This leaves people confused as to what I am trying to communicate to them. I often get the impression that people think that I am somewhat demented.

"I have completed the Lee Silverman Voice Training and while I have more control of volume, clarity seems to be getting worse. My speech tends to freeze up for no apparent reason or in no particular situation. Background noise can lead to confusion too. For example, when ordering in a restaurant I often resort to pointing to the menu."

Trumble a person from our online forum

Read more about what people with Parkinson's are sharing about speech problems on our online forum: parkinsons.org.uk/forum

RESEARCH RESULTS

We currently support around ninety vital research projects up and down the UK – which in total add up to more than £15million. We carefully track the progress of every project we fund, and we've got some new and important results to share.

Real-life problem solving in people with Parkinson's

We all experience unexpected challenges and problems on a daily basis – people with Parkinson's perhaps more than most. Some problems are easily dealt with, but others can be much more difficult to resolve.

People with Parkinson's can also experience thinking problems, and this could affect their ability to deal with these everyday challenges. But until now, problem solving had only been measured using standard 'paper and pencil' or computerised tests, which have very little to do with real-life.



In 2008, we awarded Professor Richard Brown at the Institute of Psychiatry in London £70,171 to investigate how well people with Parkinson's deal with real-life problems.

Depression affects many people with Parkinson's. And Richard wanted to find out if people with Parkinson's can become stuck in a 'vicious circle' involving poor problem solving, stress and mood.

The research team measured how well a group of people with Parkinson's with and without depression solved real-life problems – particularly problems involving other people. They also asked questions to find out the sort of things might affect people's problem solving – including their ability to think clearly and how they felt at the time.

Richard tells Progress more about the study:

"Dealing with day-to-day problems is important, especially in Parkinson's, which can pose many extra challenges.

"If these get too much, people can sometimes react by getting depressed, and unresolved problems can cause anxiety and worry.

"The good news is that people with Parkinson's without depression had no difficulties suggesting effective solutions to the real-life problems that we put to them.

"However, the group with depression did less well, and the solutions they suggested were not as likely to be effective in solving the problems. But this wasn't directly related to how depressed the person was. More important was their performance on other tests that measured how clearly they could think.

"Having shown that thinking difficulties can affect how people deal with real-life problems, it means there are steps people with Parkinson's can take to help themselves.

“
Dealing with day-to-day problems is important, especially in Parkinson's, which can pose many extra challenges.”

“Problem solving is a skill that can be learned like any other. And there are plenty of books and information on the internet that can provide some valuable tips.

”
“For many people, a few simple problem solving strategies will be enough to help them cope more easily with potentially stressful everyday problems.”

Richard is planning to publish his findings in a scientific journal, and to apply for further funding.



Our scientists grow nerve cells from skin cells

Stem cells are like blank cells that can turn into any type of cell in the body. And by exposing them to the right conditions, scientists can turn them into dopamine-producing nerve cells – the type of cells lost in Parkinson’s.

Studying these cells will help researchers to understand what causes nerve cells to die in Parkinson’s. And crucially, these cells could one day be used to replace the cells that have been lost.

Stem cells derived from embryos have been the most extensively studied so far. But they come with ethical issues and aren’t a genetic match for people living with Parkinson’s. Induced pluripotent stem cells, or iPS cells, are a new type of stem cell

created from adult skin cells. Researchers can now transform adult skin cells into cells that have all the potential of stem cells.

Parkinson's UK-funded scientists at the University of Edinburgh have grown nerve cells from a person with one of the most rapidly progressing inherited forms of Parkinson's. Dr Tilo Kunath, who has a Career Development Merit Award, is leading the research, made possible by a three-year grant of £367,116 awarded in 2010. We talked to Tilo about his research.

What inspired you to study this area of Parkinson's research?

Being able to make nerve cells from people with inherited Parkinson's simply by taking a skin sample has provided an incredible opportunity. For the first time we can study human nerve cells that are genetically destined to get Parkinson's.

People with this form of Parkinson's have twice as many copies of the gene that produces a key protein – alpha-synuclein – compared with the general population. Although this form of the condition is rare, the alpha-synuclein protein is a central player in nearly all Parkinson's cases. So understanding how it affects nerve cells is relevant to all Parkinson's research.

What were your goals for the project?

The major goal of the project was to make iPS cells from people that are genetically destined to get Parkinson's. We'll be able to use these cells to study how the condition starts and progresses. And we can also use them as a tool to test drugs that could slow or halt the process.

What have you found so far?

We've made iPS cells from a person with a rare, inherited form of Parkinson's and a relative without the condition. We've turned these stem cells into

dopamine-producing nerve cells and confirmed that the Parkinson's cells are making double the amount of alpha-synuclein you'd expect in a normal cell. This is crucial as it means these cells mimic, the cause of Parkinson's in the person they came from.

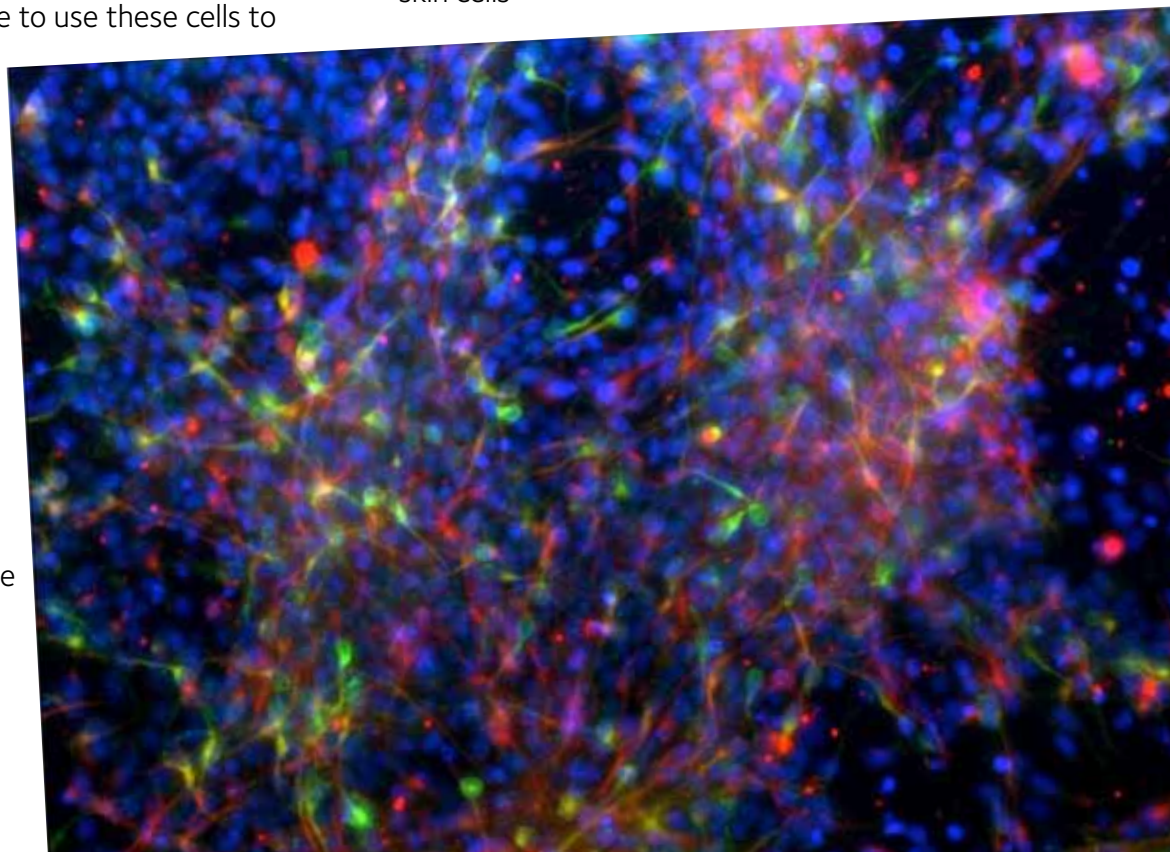
What are the next steps?

We want to compare the Parkinson's nerve cells to the nerve cells generated from a relative without the condition, so the cells are as closely matched as possible. We'll examine the cells for clumps of alpha-synuclein. And we'll test whether the Parkinson's nerve cells are more sensitive to chemicals that can specifically damage the equivalent cells in the brain.

How will this research help people with Parkinson's?

Our iPS cells will be used by us and our collaborators at University College London to investigate how alpha-synuclein damages nerve cells. And because the cells are very similar to those that die in Parkinson's, we'll be able to use them to test drugs that could prevent or reduce the harmful effects. Any drugs that show potential will be candidates for animal studies, which could lead to clinical trials in the future.

Below: Dopamine-producing cells made from skin cells



Preventing dyskinesia after nerve cell replacement therapy

Early clinical trials have shown that foetal cell transplants have great potential for improving the symptoms of Parkinson's. But some people who had the transplants developed uncontrollable movements known as dyskinesia.

This side effect is a major hurdle preventing cell transplants for Parkinson's moving forward. So understanding what causes it is essential for the future development of this treatment.



We awarded Professor Steve Dunnett at Cardiff University a five-year grant of £148,192 in 2006 to investigate how cell transplants may lead to dyskinesia in an animal model.

Steve's project is now complete, and he explains the main findings and the next steps to Progress:

"We looked at a number of factors we thought might be involved in the development of dyskinesia following cell transplants.

"We found the age of cells being transplanted did not influence how likely our animals were to develop dyskinesia. But there may be a relationship with the length of time the cells are stored before transplantation.

"Now we're investigating whether inflammation in the brain contributes to the development of dyskinesia.

"Foetal cell transplants given to people with Parkinson's are made up of tissue from five to six different fetuses. We want to mimic this approach in our animal model to see if a mixture of tissues could cause an immune reaction that affects how the transplant works.

"Our research is helping to shape the development of cell transplants for Parkinson's.

"We've contributed to, and continue to be involved in the TRANSEURO clinical study, the first new patient trial of foetal transplants for Parkinson's in more than a decade."

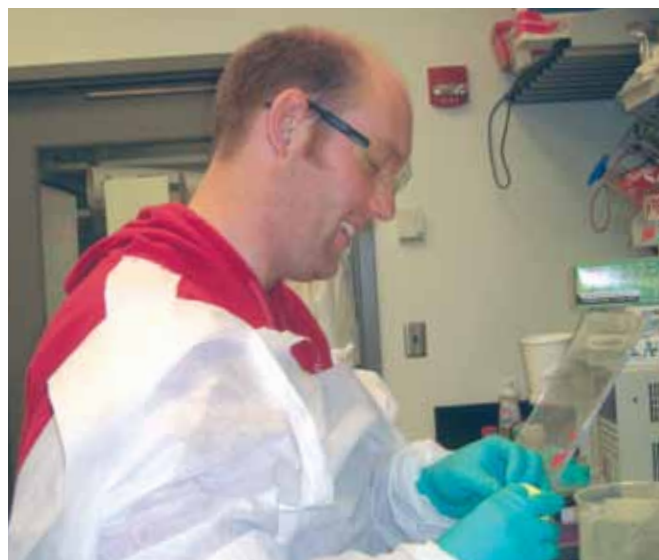
How similar are nerve cells made from embryonic stem cells to nerve cells in the brain?

Researchers now have the ability to turn stem cells into nerve cells. But how useful these cells prove to be may depend on how closely they match those found naturally in the brain.

In 2010, we awarded Dr Patrick Lewis at the Institute of Neurology in London and Professor Siddharthan Chandran at the University of Edinburgh an innovation grant of £30,593 to investigate how similar nerve cells made from stem cells are to nerve cells in the brain.

One way to compare different types of cells is to look at their RNA. RNA is the substance cells use to convert genes into proteins. All cells contain the same genes, but different cells use their genes in different ways and each cell type has its own RNA 'fingerprint'.

Patrick and his team compared RNA from dopamine-producing nerve cells derived from embryonic stem cells to, samples taken from the part of the human brain affected in Parkinson's. They used cutting-edge technology to look at the levels of RNA from around 30,000 genes.



Patrick explains the potential of this work to Progress:

“Our work has generated detailed information about the relative levels of RNA in the different types of cells tested. And we’re making the data freely available to researchers around the world on internet databases.

“This project has opened the door for further research investigating how closely nerve cells made from stem cells match those found in the brain.

“This will shape the future of stem cells, both as a research tool and as a potential treatment for Parkinson’s.”

Our researchers find a key protein, moving Parkinson’s treatments a step closer

New research at the University of Oxford that is part-funded by Parkinson’s UK has identified a key protein called Nedd4 that may lead to the development of potential new treatments for Parkinson’s.



In 2009, we gave Dr George Tofaris an innovation grant of £15,000. Now, in collaboration with researchers at Harvard Medical School in the USA, George has found that boosting the activity of Nedd4 could prevent the

build-up of another protein called alpha-synuclein.

Tackling alpha-synuclein

Alpha-synuclein forms the sticky clumps, known as Lewy bodies, found inside the Parkinson’s brain. And changes in the alpha-synuclein gene have been linked to some rare inherited forms of the condition.

Scientists believe that the build up of alpha-synuclein may play a major role in causing nerve cells to stop working and die. This discovery offers an exciting

new target for developing treatments that could help nerve cells remove alpha-synuclein.

What the team did

The researchers found that Nedd4 interacts with alpha-synuclein inside cells. They then showed that reducing the activity of Nedd4 causes alpha-synuclein to build up.

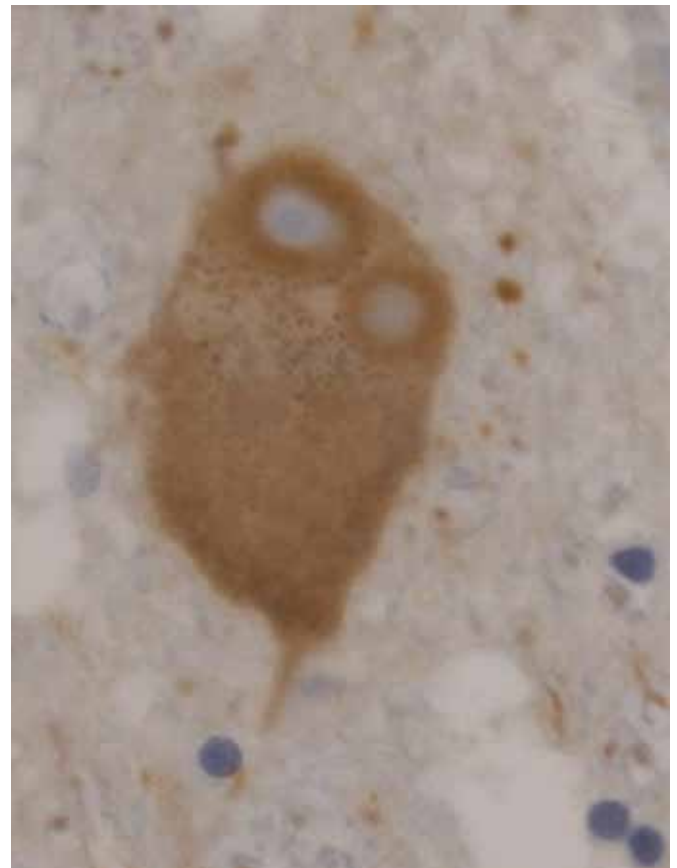
George explains:

“We found that Nedd4 plays a vital part in targeting alpha-synuclein for recycling. By this we mean it helps clean up and remove damaging material from the affected nerve cells.

“Boosting the activity of Nedd4 inside the nerve cells affected in Parkinson’s could lead to new treatments that can slow or stop the progression of the condition.

“Our results are very promising, but we need to confirm our findings in an animal model before we can be sure that Nedd4 is a suitable target for developing new drugs.”

Below: Nerve cell showing Nedd4 stained brown and Lewy bodies in blue



MONUMENT DISCOVERY PROJECT – UPDATE

The Monument Discovery Project is Parkinson's UK's largest ever research study. In 2009 we awarded a team in Oxford £5million over five years to crack the code of Parkinson's and bring us closer to a cure.

The Monument Discovery Project ultimately aims to accelerate a cure for Parkinson's by addressing three major challenges facing Parkinson's research.



Dr Richard Wade-Martins is head of the Laboratory of Molecular Neurodegeneration at the University of Oxford and is leading the Monument Discovery Project:

“When we were awarded the Monument Discovery Project we knew we had a tremendous opportunity to do something very special for Parkinson's research.

“Our vision is that what we're building in Oxford will be a centre for excellence in Parkinson's research for many years to come. And I believe that the discoveries we are making will accelerate our progress towards a cure.

“In our first year we set up a new world-class centre for Parkinson's research – the Oxford Parkinson's Disease Centre – to nurture,

encourage and support collaborative research into the condition. And the team are already making excellent progress on the three central themes of the project as we all work towards a cure for Parkinson's.”

Theme one: Diagnosing Parkinson's earlier – before symptoms develop

Diagnosing Parkinson's can be a long and difficult process. New tests to identify Parkinson's as early as possible would give us the opportunity to protect or rescue the dying nerve cells.

Dr Michele Hu is leading the first theme of the Monument Discovery Project which is looking for the earliest signs of Parkinson's in people with and without the condition:

“We are now recruiting people through ten different hospital sites across the Thames Valley.

“In the first year we've recruited almost 400 people with early-stage Parkinson's and more than 70 people without the condition as a comparison group.

“We collect in-depth information about people's health and medical history. Each person visits the clinic for a series of tests, including assessments of their symptoms, a blood test and a smell test. We're also using state-of-the-art brain scans in some volunteers to look for early changes in brain function.

“
When we were awarded the Monument Discovery Award we knew we had a tremendous opportunity to do something very special for Parkinson's research.”

“We are already finding some interesting changes that will hopefully lead to tests to diagnose Parkinson’s at an earlier stage. This, coupled with treatments that can tackle the root problems, would provide the best chance of protecting the remaining nerve cells and slowing or stopping Parkinson’s.”

Theme two: Understanding what happens inside the nerve cells that die

Research has uncovered many changes inside nerve cells that may be involved in their death. But we still don’t know enough about how or why it happens.

Theme two of the Monument Discovery Project is led by geneticist Professor Chris Ponting. He’s leading a team of researchers who are investigating how rare faulty genes affect the nerve cells that are lost in Parkinson’s.

“We have used cutting-edge techniques to grow dopamine-producing nerve cells from skin cells taken from people with Parkinson’s.

“We now have a selection of nerve cells that we can study at close-quarters in the laboratory – including some grown from people with rare genetic forms of Parkinson’s and from people without the condition.

“Pinpointing what goes wrong inside the nerve cells affected in Parkinson’s will provide vital new clues for treatments. And these nerve cells will also be a tremendously useful tool for screening new drugs that may have the potential to slow or stop the progression of the condition.”

Theme three: Better animal models that truly reflect Parkinson’s

Parkinson’s is a progressive condition that develops over time. It’s vital that we study the whole brain and body as well as investigating what happens in individual nerve cells. And to be able to look at the gradual development of the condition in animals as they age.

Professor Paul Bolam and Dr Pete Magill jointly lead this third strand of the project:

“Current animal models mimic some of the symptoms of Parkinson’s but they don’t recreate the changes that happen in the human brain.

“We’ve produced several new and unique mouse and rat models of Parkinson’s, that we’re now breeding in the laboratory. As they age we will study them closely to look for the first signs of any movement problems.

“Studying these models will give us crucial information about how Parkinson’s starts, develops and spreads inside the ageing brain.

“We can then use our new models to test treatments that could protect the remaining nerve cells or even reverse the development of Parkinson’s.”



BRINGING SUPPORTERS AND RESEARCHERS TOGETHER

Our Research Support Network brings together Parkinson's UK members, local groups, supporters, staff and researchers, all driven to help find a cure and better treatments for Parkinson's.

Will Waites is a research supporter and member of the Nottingham Branch. Will takes a keen interest in local projects and recently arranged for Professor Chris Moody, who leads a Parkinson's UK funded project at Nottingham University, to give a talk. The Nottingham Branch hosted the event, and invited members of local groups across the East Midlands to join them.



We talked to Richard about supporting our research:

How long have you been involved with Parkinson's UK?

I've been volunteering with Parkinson's UK for about seven years. In that time I've been on the committee of the Nottingham Branch, reviewed grant applications, and even travelled to Brussels to talk to members of the European Parliament about the importance of Parkinson's research.

When did you first get interested in Parkinson's research?

Before I retired I was a Professor of Food Microbiology at the University of Nottingham, so I've always been interested in research generally. With hindsight, I think I've had Parkinson's since 1985, when I was asked to leave a food tasting panel as I'd lost my sense of smell. But it was when I was diagnosed seven years ago that I really became interested in Parkinson's research.

What do you enjoy about being a research supporter?

I find it really rewarding travelling around the UK and visiting different research projects. My professional background means that I'm only an expert on one aspect of research, so I have learnt a lot, and I enjoy hearing the questions from people with other backgrounds.

How did Professor Moody's visit to the Nottingham Branch come about?

When the Nottingham Branch received a legacy last year, we decided to donate £20,000 to funding Professor Moody's work at the University of Nottingham. Altogether, Professor Moody is receiving funds of £120,000 from Parkinson's UK over two years and he kindly agreed to come along and tell us how the money is being spent.

What's Professor Moody's project about?

People with Parkinson's don't have enough of a chemical called dopamine because some nerve cells in their brain have died. Professor Moody explained that although we don't really know how or why the

nerve cells die, certain proteins may be involved because they are folded wrongly. Folding is controlled by important proteins called 'chaperones'.

Professor Moody is interested in one particular chaperone called HSP90. More HSP90 than normal has been found in the brains of people with Parkinson's. And blocking HSP90 from working in animal models of Parkinson's seems to protect the dopamine-producing nerve cells.

Professor Moody and his team are trying to develop new molecules that can stop HSP90 working. He hopes that they could lead to new drug therapies for Parkinson's.

Did your branch enjoy the talk?

We invited all the local groups and people came from across the East Midlands including Long Eaton, Derby, Lincoln, Newark and Nottingham. In total we had more than seventy people come along to hear Professor Moody, which was brilliant.

Professor Moody gave an excellent presentation. He described really clearly how the money from our legacy would be used in his research. He also explained the process for developing a new drug – and why it can take up to 20 years for a new drug to go from being a twinkle in the researcher's eye to becoming a successful treatment.

There were lots of questions from the audience which showed how interested everyone was. And Professor Moody has promised to come back next year and update us on his progress, so we're watching this space!

Professor Moody said:

“

As my research is lab-based, I don't often get the chance to meet people directly affected by Parkinson's. It's inspiring to meet people who could one day benefit from the work I'm doing. I was particularly encouraged by the level of interest in my project and the wide range of interesting questions the members had for me.

”

Bridget

Join the Research Support Network

Our Research Support Network brings together people driven to help find a cure and better treatments for Parkinson's. Through our network, anyone can get involved in research and raise funds and awareness for Parkinson's research.

Our network is free to join, so if you have an interest in research and would like to support our groundbreaking work, join us.

When you've signed up to the network we'll keep you updated by email with the latest opportunities to support research.

To find out more or to sign up as a research supporter, contact Emily Hughes, Research Support Network Manager, on **020 7963 9376** or rsn@parkinsons.org.uk

TAKING PART IN RESEARCH

People with Parkinson's can play an important role in research. Research helps us learn more about the condition, find the best possible drugs and explore new hopes for a cure.

Brian Russell-Taylor from Hampshire was diagnosed with Parkinson's in 2003. He took part in a Parkinson's UK-funded research study at Southampton University.

Below: Brian with his wife Janice



The aim of the study was to find out if non-invasive brain stimulation can improve mobility for people with Parkinson's.

Transcranial direct current stimulation, or tDCS, is a new technique for stimulating nerve cells in the brain. Preliminary results suggest that tDCS may help people with Parkinson's to move better. It's done using electrodes placed on the scalp, so it's painless and non-invasive.

How did you find out about the study?

I'd enjoyed taking part in a previous study with the same team about walking and turning. So they

contacted me to see if I'd like to be involved in this new project. I found out about the first study when my wife attended a talk at my local branch and came home and told me about it.

What motivated you to take part?

I wanted to help towards finding a cure for Parkinson's, because that's what we all want at the end of the day. I also wanted to find out if the stimulation would help increase my range of movement. Taking part in a study doesn't take up much time and both times I've been involved they have been really interesting experiences – certainly worth missing a couple of rounds of golf for!

What was the process of joining the study?

Jo from the team visited me at home. We sat down for about an hour and ran through everything. She asked me lots of questions including how long I'd had Parkinson's, and how I felt now. Then she told me about the study and what I would be doing, and it all sounded really exciting! A few days later she rang me up and said 'you're in'.

How much information were you given?

They gave me plenty of information beforehand, which I could read through and discuss with my wife. They were happy to answer all my questions and reassured me that everything was perfectly safe. Because as soon as you think of electricity going round your brain you think, blimey, is it dangerous? But they really took all the fear out of it.

What did taking part involve?

I went to the lab four times in total, twice in the morning and twice in the afternoon, for about an hour and a half each time. I had to wear a special cap on my head with leads going out the back, and run through four activities involving different kinds of movement. After each session, the researchers asked me whether I thought the electrical stimulation was on or off – but I really couldn't tell.

What did you get out of taking part?

I enjoyed taking part, and the researchers made me feel at ease and very welcome. It was fascinating to see them at work and a privilege to be involved in cutting-edge science. They're going to let me know the outcome of the study, which I think is really important. Even if no new treatment comes out of it, I'm pleased that I was part of moving the research forward.

What would be your advice to someone else who wanted to take part?

I think the most important thing is that people know what they're getting into. And the only way to do that is to talk to the people doing the research. Listen carefully and read all the information provided thoroughly. It's also good to discuss it with other people, including your family or your Parkinson's nurse if you can. But also be open and see where it takes you.

Take part in a study

Here are just a few of the projects currently happening in the UK that are looking for people affected by Parkinson's to take part.

The Monument Discovery Project

The researchers are studying people recently diagnosed with Parkinson's to develop better ways to diagnose the condition. The study is running across ten hospitals in the Thames Valley region. You may be eligible to take part if you have been diagnosed with Parkinson's in the last three years or have a brother or sister with the condition.

Joanna Glennon
01865 234 892
joanna.glennon@nhs.net

Representing action in Parkinson's

This study is investigating how people with and without Parkinson's react to different objects and movements in their environment, and how well they can communicate. The researchers are looking for people with and without Parkinson's who live in the Greater Manchester area and are aged between 50 and 75.

Dr Ellen Poliakoff
0161 275 7333
ellen.poliakoff@manchester.ac.uk

Non-motor symptoms in early Parkinson's

This international study, led by Professor K Ray Chaudhuri, is investigating the non-motor symptoms of the condition – such as sleep problems, fatigue, pain and depression. The researchers are looking for 1,000 people diagnosed with Parkinson's for five years or less at hospitals in London, Kent, Norwich, Yeovil, Harrogate, Lincoln and Grantham.

Ms Alex Rizos
020 3299 7153
a.rizos@nhs.net

Why do people with Parkinson's have trouble swallowing?

This Parkinson's UK-funded study is investigating how and why swallowing problems develop in people with Parkinson's. The researchers are looking for people with Parkinson's in the North West who take levodopa medication and have problems with swallowing to take part in the study.

Dr Emilia Michou
0161 206 1510
emilia.michou@manchester.ac.uk

More opportunities to get involved

Full details for these studies and many more are available on our website: parkinsons.org.uk/researchstudies

Our list is provided for information only and should not be treated as advice or a recommendation to participate in any of the studies. We encourage anyone who's interested in taking part in a study to consult their specialist or Parkinson's nurse.

THE PARKINSON'S UK BRAIN BANK

The Parkinson's UK Brain Bank is the UK's largest brain bank dedicated to Parkinson's.

The Brain Bank collects tissue from people with and without the condition and provides this tissue to researchers in the UK and around the world who are working towards a cure for Parkinson's.

Last year the Brain Bank team successfully collected 70 brains – that's more than one a week.

Unfortunately sometimes the team is unable to collect tissue from donors.

Celia Chappell's father 'Don Davies' had Parkinson's and wished to donate his brain. He passed away in hospital on 20 March 2010.

Sadly Don's tissue could not be collected despite the best efforts of Celia and her family, the hospital nursing staff, and the Parkinson's UK Brain Bank team.

Celia explains a bit more about what happened:

When my father went into hospital he had already decided that he wanted to donate his brain. We even discussed it with the doctors looking after him in the week before he passed away.

But despite these conversations and him being in hospital for four weeks when he died, we couldn't get anyone to sign the death certificate.

This delay meant his tissue could not be collected within the crucial 48-hour window, beyond which tissue can no longer be used for research.

Asking questions

It's difficult to explain the distress and frustration of not being able to fulfil my father's wishes.

We wanted to know why such a simple thing – signing a death certificate – was too big a hurdle for the hospital. So to get some answers we wrote to the hospital. We also wrote to other local hospitals and MPs – to highlight the problems we experienced.

Here's an extract from our first letter: 'Our father had this one chance to help the research into this disease and help future sufferers and, as his family, we feel totally let down by your lack of organisation

'Will you please respond to our concerns that no one else will have their wishes ignored and that a doctor is always on hand to sign the death certificate in similar circumstances?'

Gaining momentum

To our surprise, the first person we heard from was Andrew Smith MP, Chair of an NHS-related All-Party Parliamentary Group, who wrote to my father's hospital himself.

Below: Don Davies (centre) with his grandchildren



Thanks to his support we swiftly received a letter from the hospital acknowledging our complaint with the promise to respond fully in 25–40 working days.

Six months and many reminders later, we eventually heard from their Deputy CEO. But instead of accepting responsibility for the problems, they blamed the Brain Bank, claiming they had not contacted the hospital mortuary staff.

Gathering evidence

Determined not to be beaten, we wrote to Dr Kieran Breen, Director of Research and Innovation at Parkinson's UK.

Kieran helped us find evidence to prove that staff at the Brain Bank had not only been in touch, but even had the on-call mortician's mobile and home telephone numbers so he could be contacted immediately once the death certificate was signed.

Armed with this knowledge, we wrote again to the hospital.

Making a difference

At last, on 1 July 2011, 13 months after our first letter, we received a full reply from the Macmillan

Consultant Nurse Practitioner at my father's hospital, this time admitting total responsibility for the problems that prevented his donation to the Parkinson's UK Brain Bank.

But most importantly, they are making vital changes to their internal systems and staff training to help make sure tissue donations happen more smoothly in future.

We're very lucky to have had the unwavering support of our MP, Paul Burstow, throughout and he has written to NHS South West London asking hospitals across the region to adopt similar systems.

It has been a long and difficult struggle but this experience has reinforced our family's determination to donate tissue and organs in the future.

We hope that our persistence will lead to lasting changes that mean other families will not go through what we did, and help make sure that precious tissue needed for research is not wasted unnecessarily.

Dr David Dexter, Scientific Director of the Parkinson's UK Brain Bank



"We're on call 24 hours a day, 365 days a year. But, because tissue must be collected within 48 hours after death to be suitable for research, delays sometimes mean we cannot collect tissue from donors in time.

"Delays can be unavoidable – for instance if a post-mortem is required to determine cause of death. But sometimes we are frustratingly prevented from collecting tissue because we can't get a signed death certificate or because there are no post-mortem staff available to remove the tissue – a particular problem at weekends.

"We're working hard alongside other medical research charities, as part of the UK Brain Banking Network, to raise awareness of the importance of brain donation and to educate health-professionals.

"The hard work and determination of Celia and her family will help make other tissue donations possible in the future."

What can prevent a donation taking place?

- Referral to a coroner or a post-mortem to establish the cause of death.
- Medical conditions affecting the brain, such as infection or cancer.
- Lack of a death certificate or suitable hospital mortuary facilities.
- Brain Bank informed too late to collect tissue.

Top tips for donors and their families

There are a number of things you can do to improve your chances of a successful donation:

- Discuss your wish to donate with your family, friends and the healthcare professionals looking after you.
- Always carry your Brain Bank donor card with you.
- Contact the Parkinson's UK Brain Bank as soon as possible. You don't have to wait until the donor has died. If someone is likely to die in the coming few days, contact us and we can make preparations to make sure things go smoothly when the time comes.



To find out more about the Parkinson's UK Brain Bank or to request an information pack, visit parkinsons.org.uk/brainbank or call **020 7594 9732**.

A GIFT IN YOUR WILL

Your legacy – a cure for Parkinson's.

In 2011, we received an amazing gift from Agnes McConnell from Lanark in Scotland.

Miss McConnell left us £250,000 in her Will in memory of her mother Mary who had Parkinson's with the hope that it will help make a difference in funding research to find better treatments and speed up progress to find a cure.

Miss McConnell was keen for her gift to be invested in Parkinson's research so she could help people living with Parkinson's today and in the future. So we've been working with Miss McConnell's nephew, Ian to choose specific research projects for her gift to support.

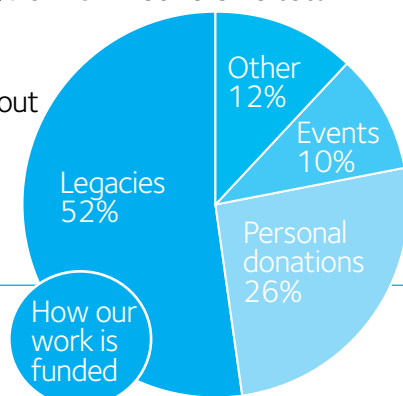
The three projects that Miss McConnell's gift will fund are:

- Professor Philip Robinson at the University of Leeds: Targeting the parkin protein to develop new and better treatments – worth £154,988
- Professor David Burn at Newcastle University: Does the drug apomorphine have 'anti-dementia' effects? – worth £29,318
- Dr Maeve Caldwell at the University of Bristol: CDFN and MANF – a protective pair for Parkinson's? – worth £34,999

We rely on gifts in Wills

A combination of large and many smaller legacy gifts make up 50% of Parkinson's UK's total annual income.

Quite simply, without these gifts, half of what we do as a charity would not be possible!



How our work is funded



Adenike

How to include a gift in your will

18 out of 20 people feel they have something to leave behind to charity. Large or small, your gift could help us find a cure and help ensure we are here for everyone affected by Parkinson's. Including a legacy to Parkinson's UK is straight forward. Simply instruct your solicitor of our name, address and registered charity registration number.

Parkinson's UK
215 Vauxhall Bridge Road
London
SW1V 1EJ

Charity registration in England and Wales
No. 258197 and in Scotland No. SC037554

To request our free guide to making or updating your Will, or for more information, call **020 7963 9344**, email legacies@parkinsons.org.uk or visit parkinsons.org.uk/legacy

Your gift could one day help us find a cure.

YOUR FEEDBACK NEEDED

Help us make Progress even better by completing our online survey at parkinsons.org.uk/progressfeedback or returning this form.

1. Are you (please tick the relevant box):

Someone with Parkinson's A carer or partner A friend/family member
Healthcare professional Researcher Other

2. How **interesting** did you find this issue of Progress?

Very Somewhat Neutral Not interesting

3. How **easy to read** did you find this issue of Progress?

Very Somewhat Neutral Not easy to read

4. What do you enjoy reading about? (please tick all that apply)

New research projects	<input type="checkbox"/>	Research results and progress	<input type="checkbox"/>
Interviews with scientists	<input type="checkbox"/>	People with Parkinson's	<input type="checkbox"/>
Opportunities to take part	<input type="checkbox"/>	The Parkinson's UK Brain Bank	<input type="checkbox"/>
International research news	<input type="checkbox"/>		

Other:.....

5. What topics would you like covered in future issues of Progress?

.....

6. How would you improve Progress?

.....

7. Do you have any other comments about Progress?

.....

Cut out this form and return to
Parkinson's UK Research team
215 Vauxhall Bridge Road
London
SW1V 1EJ

CONTACTS

Parkinson's UK

215 Vauxhall Bridge Road, London SW1V 1EJ

020 7931 8080

hello@parkinsons.org.uk

parkinsons.org.uk

Helpline

0808 800 0303 (freephone*)

18001 0808 800 0303 (Text relay for text phone users)

hello@parkinsons.org.uk

The helpline is open Monday to Friday 9am–8pm,

Saturday 10–2pm

*calls are free from UK landlines and most mobile networks

Regional and country teams

For details of our regional and country teams, visit

parkinsons.org.uk/regionalteams or call our helpline.

Information and support workers

For details of your local Parkinson's UK information and support worker visit parkinsons.org.uk/isw or call our helpline.

Parkinson's UK local groups

For details of your nearest group visit

parkinsons.org.uk/localgroups or call our helpline.

Research and Innovation team

You can find out more about our research by visiting

parkinsons.org.uk/research or by getting in touch with us at:

research@parkinsons.org.uk or by calling 020 7963 9326

Progress is produced by the Parkinson's UK Research and Innovation team in collaboration with the Resources and Diversity team.

Dr Lubna Arif-Schmidt

Research Liaison Manager

Claire Bale (Editor)

Senior Research Communications Officer

Michelle Bendix

Research Grants Officer

Dr Kieran Breen

Director of Research and Innovation

Michael Eversham

Design Manager

Karen Foord

Research Liaison Coordinator

Dr Michelle Gardner

Research Development Manager

Bunia Gorelick

Research Grants Manager

Charlotte Jackson

Editorial Manager

Emily Hughes

Research Support Network Manager

Dr Katie Le Blond

Research Communications Officer

Dr Senel Mehmet

Research Communications Manager

Stacey Storey

Research Coordinator

To contact us:

research@parkinsons.org.uk

parkinsons.org.uk/research

Research and Innovation team

Parkinson's UK

215 Vauxhall Bridge Road

London SW1V 1EJ

020 7963 9326

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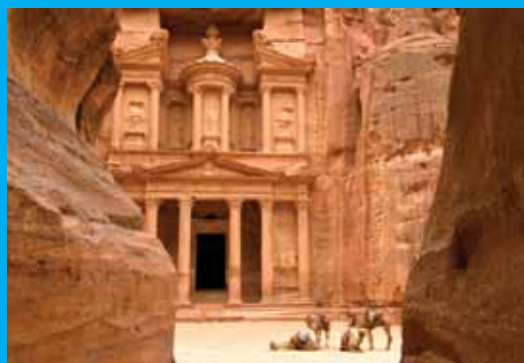


TREK PERU

21-30 September 2012

Experience the magic of the Andes

Trek at heights of up to 4,600m to reach Machu Picchu, one of the most enigmatic sites in the world.



TREK JORDAN

13-21 October 2012

Explore the ancient world

Your challenge is to trek 100km through spectacular desert and jagged mountains, to the ancient city of Petra.



CYCLE VIETNAM TO CAMBODIA

14-25 November 2012

Discover the tropical beauty of Asia

Cycle 500km through bustling city markets and beautiful rural landscapes, to the stunning temple of Angkor Wat.

Come to our information day!

If you would like to find out more about any of these challenges, please come along to our information day on Saturday 11 February. The day will take place at our London office, from 1pm-4pm.

Please get in touch to join us or receive more information about our challenges.

020 7932 1328

events@parkinsons.org.uk

parkinsons.org.uk/overseasadventures

PARKINSON'S^{UK} CHANGE ATTITUDES. FIND A CURE. JOIN US.