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Parkinson's: Beyond the Bench Newsletter (Issue 1)

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DOI:
10.20933/100001521

Publication date:
2026

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Document Version
Publisher's PDF, also known as Version of record

Link to publication in Discovery Research Portal

Citation for published version (APA):
Flitton, C., Francis, R., Patrick, S. (Ed.), Alessi, D. (Ed.), Sammler, E. (Ed.), Howden, A. (Ed.), & Dundee Research Interest Group (2026, Aug). Parkinson's: Beyond the Bench Newsletter (Issue 1). University of Dundee. https://doi.org/10.20933/100001521

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Parkinson's: Beyond The Bench

Issue #1 // August 2026 // LRRK2

MRC Protein Phosphorylation and Ubiquitylation Unit

University of Dundee

Welcome to our newsletter on Parkinson's Disease (PD) Research! Every month we will be bringing you an article focusing on different PD related topics. Expect to see an explanation of the biology behind each month's research focus, a deep dive into one of the techniques used, and answers to some of the questions you have about our work! This month's focus is a hot topic here at Dundee - the protein Leucine rich repeat kinase 2, also known as **LRRK2** (we pronounce it like lark-2), who we'll get to know a bit better in this issue!

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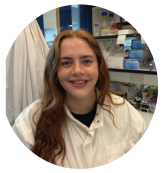
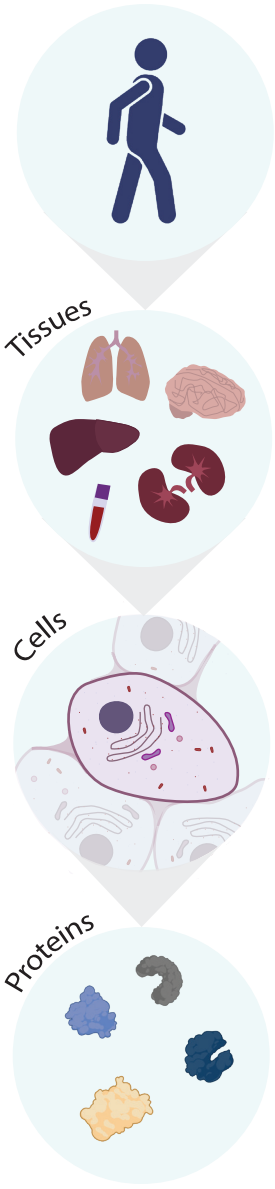


At the beginning of July, over 150 scientists from around the world met in Dundee for the Biennial LRRK2 conference, organised in part by Esther Sammler, to present and discuss their research on LRRK2, a protein that has been linked to Parkinson's. Many people from the MRC PPU in Dundee work on LRRK2 and were able to present their work, but why is this protein special and why is research on it so important?



Background Biology:

What do we mean by a 'Protein'?

All the organs and tissues in our bodies are made up of cells, and these cells contain proteins. All proteins have jobs in our cells and they keep our bodies going by working together and carrying these jobs out. Proteins make things happen - they can bring about changes on a big scale in our bodies by bringing about little changes in our cells.

There are lots of different jobs for proteins, including structural roles or by sending messages around the body, but the protein type we will focus on is enzymes:

Enzymes are proteins that make chemical reactions happen faster, so that the cell has everything it needs to respond to a situation. A lot of this is done by turning **other** proteins on or off in response to being in different biological situations. One type of protein that does this is called a **kinase**, which puts a chemical tag onto specific proteins to switch them on or off. This chemical tag is called **phosphorylation**.

Tissues
What organs are made up of; groups of similar cells that work together to carry out a specific function

Cell
The basic structural unit of all living things, like a brick in a house that also has to make everything we need to survive

Protein
A biological building block that carries out most of the work in cells by performing a specific function, e.g. sending messages

Kinase
A type of protein that phosphorylates other proteins, usually to turn them off or on

Phosphorylation
A small chemical tag that can be put on proteins to alter their function

LRRK2 is a kinase - so how does this relate to PD?

LRRK2 in focus

LRRK2 is a kinase that is responsible for switching on a group of proteins called Rab-GTPases (what we usually just call 'Rabs'). We're still trying to figure out exactly what jobs these proteins have and how they do them.

Some people with PD have dysfunctional LRRK2. LRRK2 is too active, it's a bit like a traffic light stuck on green – it's going to cause a pile-up. Too many of the proteins that it controls are turned on, which interferes with the jobs that they are supposed to do.

A lot of the research into LRRK2 looks at what the consequences of this 'pile up' are in our cells and how this can lead to Parkinson's Disease. In the brain, LRRK2 may interfere with mechanisms that keep our neurons safe, but LRRK2 has jobs all over the body that we are still trying to understand. For example, there are also high levels of LRRK2 in the kidneys and the lungs, so groups such as Dario Alessi's are trying to understand what this may do.

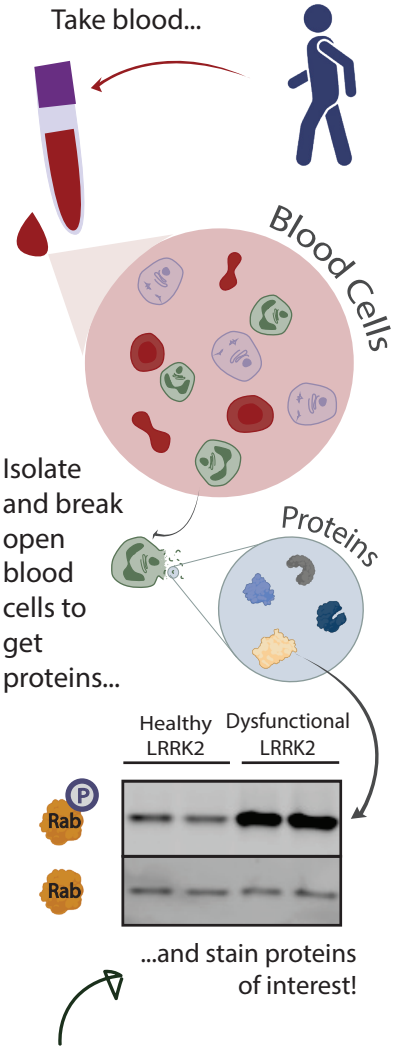
TECHNICAL SPOTLIGHT:
WESTERN BLOTTING

One of the ways we can study a specific protein is by doing a western blot. We use a gel to separate out the proteins by size, a little bit like a sieve. Imagine dropping a golf ball and a tennis ball in jelly - the golf ball is smaller, so faces less resistance and travels further. The same is true for proteins: the big proteins get stuck at the top and the smaller proteins easily flow through to the bottom of the gel.

We can then stain proteins that we are specifically interested in and use this stain to measure how much is in our sample – people with Parkinson's may have too much or too little of one of these proteins.

We also use this technique to see how much LRRK2 is activated. We do this by measuring the levels of unphosphorylated vs phosphorylated Rabs.

This is Nur Rashidova, a research technician, running a Western blot. She has been at the PPU for nearly 3 years and is about to start a PhD in Constance Alabert's lab. Outside of the lab, Nur enjoys judo and jiu-jitsu!



This is what a finished western blot looks like (This is one that Chloe ran). This is how we tell how active LRRK2 is: by looking at the phosphorylation on one of the proteins it controls – Rab10

Thank you for reading our first issue of Parkinson's: Beyond the Bench! Huge thanks to Jo, Andy, & Sarah from the DRIG steering committee for their input, and if you have any questions or topics you would like us to focus on then please get in touch at the form below, or feel free to email us!
https://forms.gle/tJHu1BSnW3gYGefU6