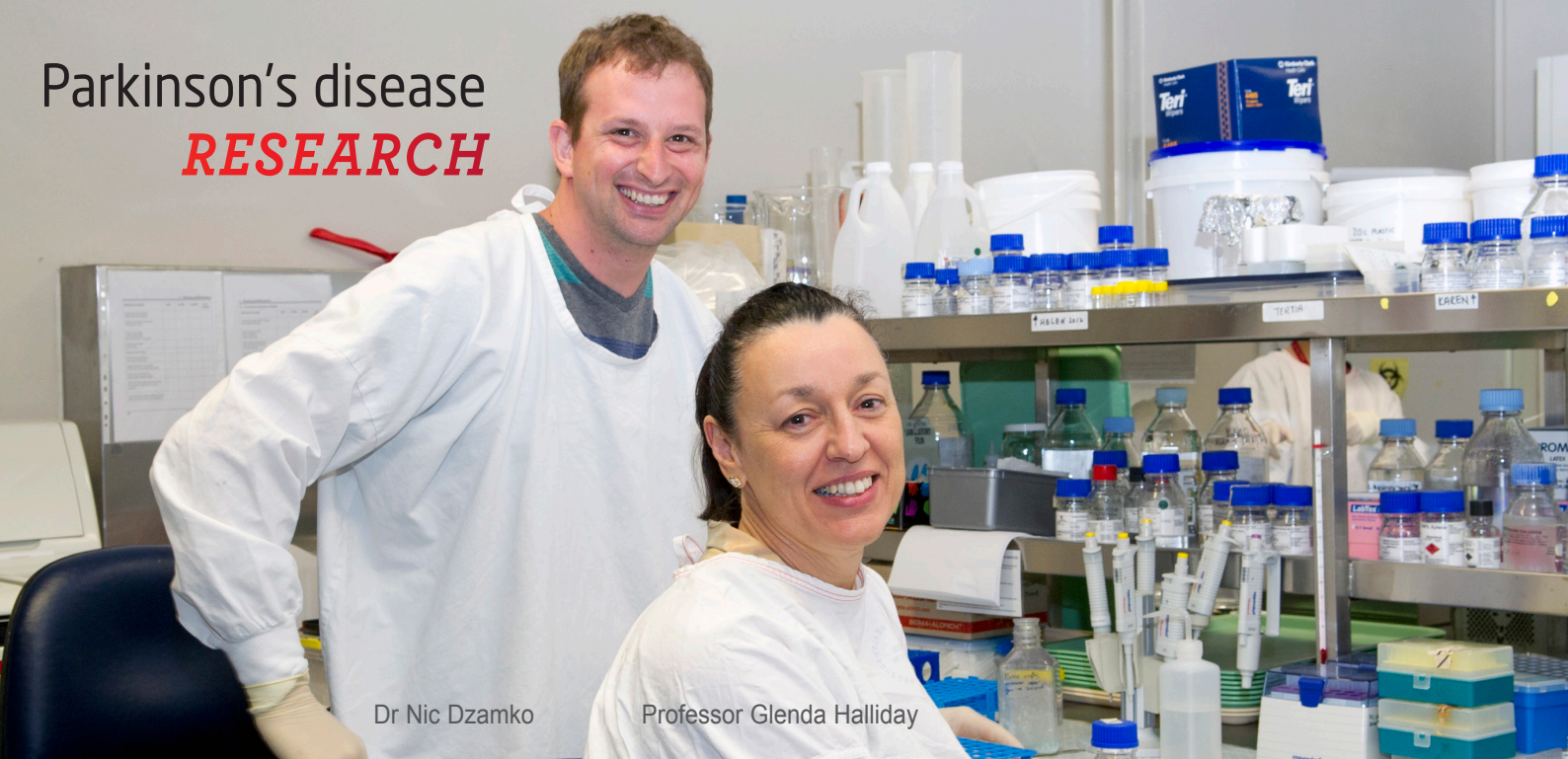


# Parkinson's disease **RESEARCH**



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*NeuRA (Neuroscience Research Australia) is one of the largest independent medical and clinical research institutes in Australia and an international leader in neurological research.*

*Diseases of the brain and nervous system pose the greatest health, economic and social burden of any disease group because they are chronic, debilitating and have no known cures.*

*Medical research is the cornerstone of efforts to advance the health and wellbeing of families and the community. Our dedicated scientists are focussed on transforming their research into significant and practical benefits for all patients.*

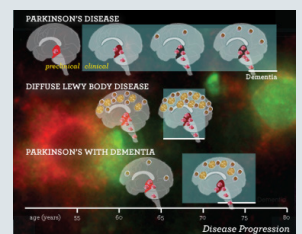
**WHAT WE KNOW ABOUT PARKINSON'S DISEASE** Parkinson's disease affects people differently. It can strike a person early in their 20s and 30s or, later in life, it can be dominated by different clinical problems at different times. In some it progresses very rapidly while in others it progresses very, very slowly. Surprisingly, regardless of these differences, the brain changes that occur in Parkinson's disease are similar. We now know that before symptoms emerge, two changes in the brain are already underway. There is an abnormal accumulation of a normal protein important for nerve cell function, a protein called alpha-synuclein, and a small group of brain cells begins to die - cells that produce dopamine. The symptoms of Parkinson's disease emerge when less than half of these particular dopamine cells are still alive, at a time when alpha-synuclein is found in a small number of cells in many regions of the brain.

The cause, or causes, of Parkinson's disease are not known but we do know that some factors increase the risk of people developing this disorder. Age is the greatest risk factor but both genetic and environmental factors are important. In any person, heritability accounts for around 35-40% of risk with the remaining risk due to environmental factors. The heritability is complex and usually not due to a faulty gene (not an inherited mutation that runs through families). Importantly, prenatal and early life factors do not increase the risk of Parkinson's disease, leaving later lifestyle and environmental exposures as contributing more (factors often shared in families). Men are more at risk than women (suggesting hormones may be involved) and toxic herbicides and pesticides as well as brain infections are implicated.

**ABOUT OUR RESEARCH** We are working to document the biological changes that occur in patients with Parkinson's disease and to determine how genetic and environmental factors contribute to the disease. We are also working to develop tests to predict how fast or slow the disease will progress for an individual, and our biological work is developing new drugs for Parkinson's disease and new methods to determine the effectiveness of these drugs.

**OUR RESEARCH AIMS TO UNDERSTAND** how and why Parkinson's disease affects the brain, and how we can stop it.

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## CURRENT PROJECTS - CELLULAR CHANGES

**WE ARE STUDYING WHAT MAKES ALPHA-SYNUCLEIN ABNORMALLY ACCUMULATE** in Parkinson's disease. This work is investigating what genes are involved as well as the changes that occur to make this protein become abnormal. We have identified certain enzymes that may be involved and are investigating drugs that may stop these changes in laboratory studies. We are collaborating with international colleagues to develop new brain imaging tests to see these changes in life.

**WE ARE ASSESSING WHAT MAKES CERTAIN DOPAMINE CELLS DIE** in Parkinson's disease. This work is investigating how certain proteins, sex hormones and metals interact with the vulnerable dopamine cells to improve our understanding of why these cells are affected by this disorder and how we can improve their survival.

**WE ARE DETERMINING WHICH BRAIN CELLS ARE INVOLVED IN THE DIFFERENT SYMPTOMS** of Parkinson's disease. As different cells in the brain work via different chemical signaling and pathways, this work has the potential to identify new targets for symptom-specific drug therapy. In addition, we are determining if gene variation relates to having particular symptoms in Parkinson's disease, and are developing brain imaging tests so we can monitor future symptom-specific therapies.

## CURRENT PROJECTS - HIGH RISK GENES

**WE ARE STUDYING THE TWO MOST COMMON GENES** associated with Parkinson's disease. This work investigates a gene known as LRRK2 and a gene known as GBA, as common variations in both these genes have been identified as separately increasing the risk of Parkinson's disease. We are determining if the cellular changes in the brains of people with Parkinson's disease are different if there is a mutation in these genes, and also seeing how such gene variations impact on important cell functions.

## CURRENT PROJECTS - ENVIRONMENTAL FACTORS

**WE ARE ASSESSING HOW DIET AND SMOKING IMPACT ON GENES** involved in Parkinson's disease. Tobacco smoking and the intake of common vitamins have been shown to modify genes to make more or less protein. We are investigating how these factors modify relevant genes and the amount of proteins made, as well as identifying if changing these environmental factors has impact on the cell pathways involved in Parkinson's disease.

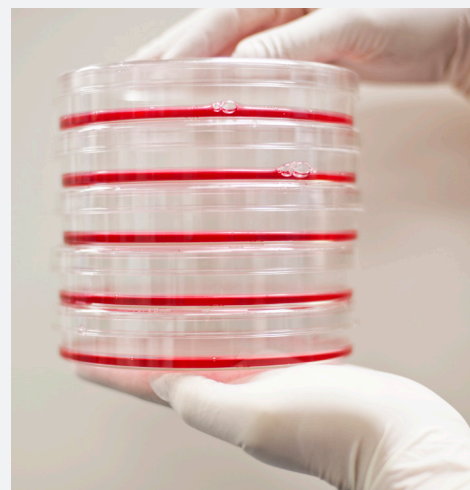
**WE ARE DETERMINING HOW INFECTIONS AND THE IMMUNE SYSTEM ARE INVOLVED** in Parkinson's disease. This work is investigating how the immune system has changed in patients with Parkinson's disease, how using infectious agents can replicate aspects of Parkinson's disease in the laboratory, and what molecules are involved in these changes. Using animal and cell models, we have already identified that LRRK2 is important for immune function and are now verifying this in patients.

## CURRENT PROJECTS - DEVELOPING NEW DRUGS AND TESTS

**WE ARE DEVELOPING METHODS TO PREDICT THE EARLY IDENTIFICATION AND FUTURE COURSE** of Parkinson's disease. We have identified that variations in certain genes relate to how fast the symptoms of Parkinson's disease progress to become disabling. We believe that this information will assist in identifying those most in need of modifying therapies. We have also developed a blood test that identifies dopamine cell loss. We are hoping to develop both tests commercially, as they will certainly contribute to earlier, more accurate and more informative diagnostics.

**WE ARE DEVELOPING AND TESTING NEW DRUGS** for Parkinson's disease. Our researchers have contributed to developing the first new type of drug for Parkinson's disease, LRRK2 inhibitors, and we have also identified other drugs/molecules that impact on the genetic and cellular changes involved in Parkinson's disease. We are also developing methods for monitoring the success of treating these pathways in patients with Parkinson's disease, and are now working with some pharmaceutical companies to develop new LRRK2 therapeutics.

*While we hope you find this brochure useful, it is always important to discuss any questions about Parkinson's disease or its treatment with your doctor or other health care provider.*



Cells being used to test new drugs for Parkinson's disease

## HOW YOUR SUPPORT HELPS

We are able to make significant advances due to the dedication and generosity of countless people who come to NeuRA every day - research participants, families, carers and supporters. Your donation or bequest will play a key role in allowing us to continue to work towards transforming the lives of all Australians through medical breakthroughs. For further information on how you can support our research phone 1300 888 019 or make a secure donation at [neura.edu.au/donate](http://neura.edu.au/donate).



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