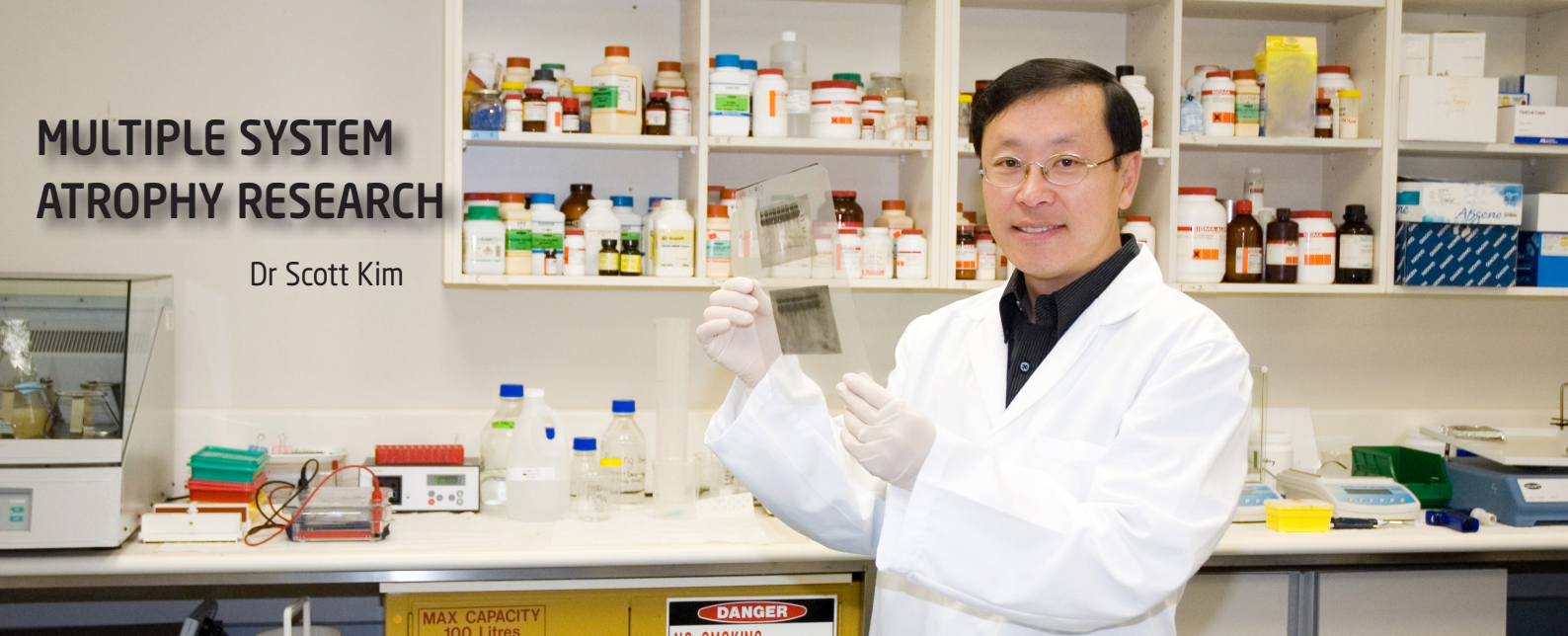


# MULTIPLE SYSTEM ATROPHY RESEARCH

Dr Scott Kim



*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.*

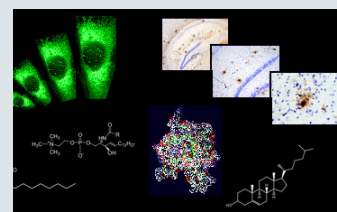
**WHAT WE KNOW ABOUT MULTIPLE SYSTEM ATROPHY** Multiple system atrophy (MSA) is a rapidly progressive brain disorder. It affects multiple systems in the body, impacting on blood pressure, heart rate and bladder function, as well as movement and coordination. Initial signs of MSA include a loss of balance, slowness in initiating movement, and genito-urinary problems. Approximately 1 in 5 people with MSA will suffer a fall in their first year of having the disease. MSA affects men and women equally, and its onset typically occurs in the late fifties.

The clinical features of MSA overlap with those of Parkinson's disease, and for this reason, early cases of MSA are often misdiagnosed as Parkinson's disease. We now know that the feature that definitively identifies MSA pathology is the buildup of a protein called alpha-synuclein in oligodendrocytes, the support cells of the brain. These cells are responsible for producing myelin, which is the specialised membrane that encases the nerve fibres in the brain. The alpha-synuclein protein buildups in the brain of people with MSA mean that the oligodendrocytes cannot properly make myelin, and without myelin the neurons will degenerate and eventually die.

The cause of MSA is unknown, no specific risk factors have been identified, and there is no cure or effective treatment. Furthermore, there is very little public awareness of or research into MSA. In fact, the current MSA research at NeuRA is the first NHMRC-funded research into MSA in Australia. Therefore, it is urgent that more research is directed towards understanding and finding a cure for this important yet poorly understood disease.

**ABOUT OUR RESEARCH** Our aim is to define the pathological pathway that leads to MSA and to identify molecular targets for potential treatment strategies for MSA. Our early research has been instrumental in determining the sequence of pathological events in MSA, which is now recognised as myelin dysregulation (abnormal protein redistributions in oligodendrocytes), followed by demyelination and then neurodegeneration and loss of neurons.

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## GENETIC CHANGES IN THE BRAINS OF PEOPLE WITH MSA

## MSA AND CHANGES IN ENERGY REGULATION INSIDE CELLS

## MAKING THE LINK BETWEEN CAUSE AND EFFECT

*While we hope you find this information sheet useful, it is always important to discuss any questions about multiple system atrophy or its treatment with your doctor or other health care provider.*

## CURRENT PROJECTS

**WE HAVE RECENTLY SHOWN THAT** a protein called ABCA8 is associated with early events in MSA pathology. ABCA8 stimulates the production of a fat molecule called sphingomyelin, which is a key component of myelin. We now want to know how the abnormal expression of ABCA8 is associated with the disease process. We plan to measure the levels of ABCA8, alpha-synuclein and other proteins in post-mortem brains from people with MSA, focusing on specific brain regions that are known to be affected by the disease. This study will facilitate a detailed understanding of the role that ABCA8 plays in regulating pathological events in MSA.

**OLIGODENDROCYTES NEED SUFFICIENT ENERGY** to be able to produce enough myelin. COQ2 is a gene related to energy production in cells and also to the production of sphingomyelin. Recently, it has been thought that changes in the COQ2 gene increase the risk for MSA; however, very little is known about levels of expression of this gene, or of the associated energy molecule ATP, in the brain of people with MSA. To establish whether COQ2 activity is indeed a contributing factor in the pathology of MSA, we will measure levels of COQ2 gene and protein in multiple regions of the brain of people with MSA. We will also measure how much of the energy molecule ATP is made. This will help us determine the mechanism of how any deficits in the COQ2 gene contribute to the MSA disease process.

**IT IS POSSIBLE THAT BOOSTING THE FUNCTION** of COQ2 might combat the disease process of MSA. We will test whether treatment with coenzyme Q10, the product of the COQ2 gene, prevents or reduces alpha-synuclein aggregation in the brain, the dominant pathological hallmark of MSA. Using a cell model of MSA, we will measure the effects of different doses of coenzyme Q10 on alpha-synuclein production and aggregation. We expect that coenzyme Q10 treatment will prevent or reduce alpha-synuclein aggregation in oligodendrocytes by ameliorating the levels of ATP and of other molecules known to be involved in MSA pathogenesis. If this approach is successful, we will begin initial therapeutic treatment studies using animal models of MSA.



Special staining of sections of MSA brain to detect pathological changes associated with the disease

07/14

## 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).