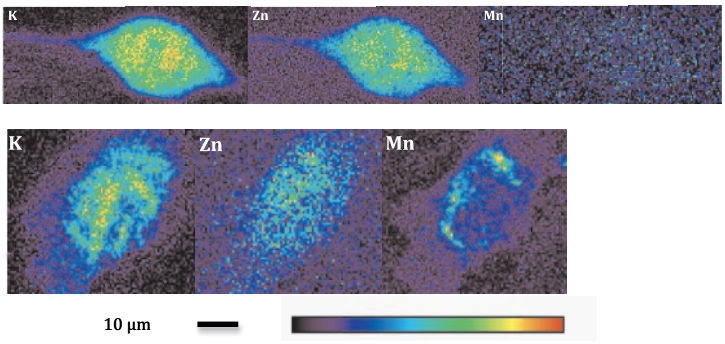
X-tending the Frontiers of Medical Science

Australian researchers are hot on the trail of new clues that could help identify the cause of Parkinson's disease in some patients.



Synchrotron X-ray images of manganese and other metal ions inside neural cells could help to reveal the metabolic defects behind Parkinson's disease.

Parkinson's disease is a debilitating and degenerative neurological disorder that affects as many as 50 000 Australians. Symptoms include uncontrollable shaking, muscle rigidity and slowness of movement. Sufferers are typically aged 50–75, with the youngest in their 30s. Most forms of Parkinson's do not have a clear genetic link, but some less common forms do.

Although the cause of Parkinson's is not known, a group of Australian researchers led by Antony Cooper from the Garvan Institute of Medical Research in Sydney appears to have found an important clue.

Some types of Parkinsonism are linked to a dysfunctional form of the recently-identified *PARK9* gene. The function of the *PARK9* protein is unknown, but its similarity to other proteins suggests that it is involved in pumping specific cations such as iron, zinc and manganese across internal cell membranes into important cell compartments (organelles).

Collaborating with American researchers, Antony's group discovered that yeast has a similar gene (*YPK9*), and that yeast cells lacking *YPK9* are sensitive to manganese.

"Knowing that excessive manganese exposure can sometimes cause Parkinsonism in humans, we wondered if *PARK9* patients who lack the protein might be unable to transport manganese where it needs to go inside their neurons," Antony says. "This could then lead to highly localised manganese imbalances that stop neurons working properly.

"We're now trying to find out exactly how *PARK9* deficiencies result in Parkinsonism. Identifying that mechanism could provide useful insights into how other sufferers get the disease."

Garvan Institute PhD student Brian Chan and Jade Aitkin and PhD student Joonsup Lee from the University of Sydney recently brought some samples to the Australian Synchrotron to find out precisely where manganese and other metal ions are located inside the cells and whether there is a difference between *PARK9* patients and healthy controls. They used the Synchrotron's X-ray fluorescence microprobe beamline to obtain the first ever maps of elemental distribution and concentration in human olfactory cells from patients with the *PARK9* mutation.

The X-ray fluorescence microprobe offers resolution down to 0.1 µm and can detect much lower concentrations of elements than other techniques such as proton-induced X-ray emission (PIXE). To put that in perspective, a typical human cell is about 10 µm across, while human hair varies from 20–180 µm thick.

Finding a link between Parkinson's disease and the distribution of manganese or other metal ions within neural cells would help to speed up international efforts to better understand this devastating disease and perhaps even lead to a potential treatment. Manganese might also prove useful as a diagnostic aid to help identify people at greater risk of developing the disease.

Preliminary results suggest that cells from *PARK9* patients contain more manganese than the control cells. Further research is underway.

A New Breast Cancer Test

Another futuristic application of synchrotron X-rays is a non-invasive breast cancer test based on an Australian discovery that scalp hair from breast cancer patients shows a unique diffraction pattern when examined by small angle X-ray scattering (SAXS). The test is being commercialised by Sydney-based medical research company Fermiscan Holdings Ltd using the Australian Synchrotron.

A large-scale Australian clinical trial completed in 2008 found that the test had an accuracy of 77% compared with mammography and tissue biopsy. Its accuracy increases when dyed and permed hair samples are eliminated.

Breast cancer affects one in eight Australian women and is the most common invasive cancer diagnosed in females worldwide.

The new test could be particularly useful for screening women under 50, whose breast tissue can be too dense for mammography. The technique may also have potential as a diagnostic tool for other diseases.

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