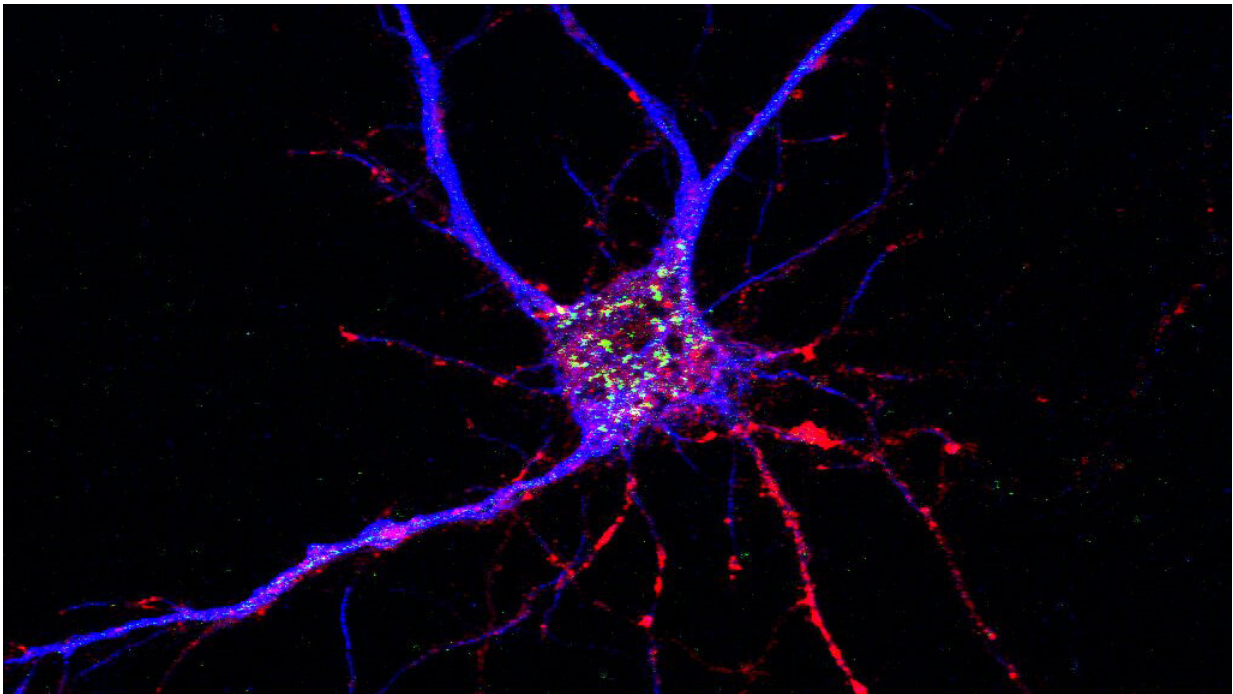


Drug target for Alzheimer's disease has dual action

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Credit: Queensland Brain Institute

Researchers have discovered a potential drug target for Alzheimer's disease—an enzyme which has effects on both the immune and nervous systems.

Dr. Ramón Martínez-Mármol and Professor Frédéric A. Meunier from the Queensland Brain Institute Clem Jones Centre for Ageing Dementia

Research found that targeting one [enzyme](#) could combat the disease on two fronts.

"In [nerve cells](#), the enzyme dPI3K produces a toxic peptide which accumulates into plaques in the [brain](#) of Alzheimer's disease patients, causing havoc," Dr. Martínez-Mármol said.

"Our study shows that the enzyme is also involved in the secretion of one of the most important signaling proteins involved in inflammation.

"Most treatments focus on only one aspect of the disease; we want to change this point of view and focus on developing therapies that touch different aspects of the disease, like the combined approaches used to treat cancer.

"Alzheimer's is a complex disease that involves more than nerve [cells](#), so let's try to develop drugs that will work on both the brain and the immune system."

To confirm they had identified a potential [drug](#) target, Dr. Martínez-Mármol knocked out the enzyme in mice with Alzheimer's disease and found the levels of plaques in the brain and the inflammatory response were all back to normal.

"We were surprised to find that having none of the enzyme in their system, the offspring of this cross didn't have Alzheimer's disease at all—the mice were completely normal with intact memory," Dr. Martínez-Mármol said.

"These offspring still produced toxic peptides but for some reason they did not accumulate into plaques; we found no plaques in the brains of these animals and no inflammatory response at all."

After confirming dPI3K as a potential target for Alzheimer's disease, Dr. Martínez-Mármol tested drugs that affect it.

"We found a drug targeting this enzyme had already been used to treat leukemia—we used it to treat cells taken from mice with the disease and found that the movement of the toxic peptide inside the cells reduced," he said.

"The challenge of treating Alzheimer's disease in mice or people rather than isolated cells is that any treatment has to cross the blood-brain barrier.

"We are now keen to collaborate with other researchers to work out how to solve the issue of transporting the drug across the blood-brain barrier."

The study was published in *Journal of Neuroscience*.

More information: Ramón Martínez-Mármol et al. p110δ PI 3-kinase inhibition perturbs APP and TNF α trafficking, reduces plaque burden, dampens neuroinflammation and prevents cognitive decline in an Alzheimer's disease mouse model, *The Journal of Neuroscience* (2019). DOI: [10.1523/JNEUROSCI.0674-19.2019](https://doi.org/10.1523/JNEUROSCI.0674-19.2019)

Provided by Queensland Brain Institute

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