CASE STUDY

Detecting the tiny peptide that could transform Alzheimer's disease diagnosis

Preventing the gradual cognitive decline associated with Alzheimer's disease is at the heart of research efforts to find new treatments. The team at Neuro-Bio, an Oxfordshire-based biotech led by Baroness Susan Greenfield, aims to not just treat this early memory loss, but want to halt cognitive decline up to 20 years before symptoms first appear. To drive their drug development efforts, the University of Oxford spinout won a 12-week residency programme at the Rosalind Franklin Institute, through a competition designed specifically for SMEs with technical challenges that Franklin expertise and technologies can solve.

With a therapeutic focus on neurodegenerative disease, Neuro-Bio's work centres around their discovery of a novel peptide in the brain called T14, a potential driver of neurodegeneration and cognitive decline in adults. Unlike plaques and amyloids commonly linked with Alzheimer's onset, T14 begins accumulating in cerebrospinal fluid years before early symptoms first emerge, so has potential as a biomarker for the disease. Neuro-Bio's early studies in mice show that simply blocking T14 with the right compound can halt memory loss.

Using T14 to signal danger ahead, and targeting it with an effective drug, could prevent cognitive decline for many Alzheimer's patients globally. Like a canary in the coal mine, creating a simple and effective way to detect this biomarker in people as they age could be a game changer. This is where the Franklin's expertise comes in.

"We image and study brains to look at their chemical makeup, so this peptide is the perfect target for us – it's the right size and the right type of molecule and we have a whole host of ways to detect it," says Dr Dan McGill, Liquid Chromatography-Mass Spectrometry (LC-MS) Lead for the Franklin's Biological Mass Spectrometry theme. "When Neuro-Bio came to us, we started talking about using mass spectrometry, which is a gold standard forensics technique, to develop something uniquely suited to detecting and quantifying T14. While research like this is outside what we would normally do, the SME Competition's seed funding means we can work with a company like Neuro-Bio to translate our work into something that could deliver real benefits to patients."

Throughout the residency, Neuro-Bio and Franklin researchers successfully used the Franklin's LC-MS technology to both detect the presence of T14 in

> Taking our pilot study forwards with a huge translational leap like this is only something we can do with the right expertise and the right equipment. As a small spin-out company, we're very proud to have this collaboration with the Franklin.
>
> Dr Garcia-Rates

samples and start developing methods to quantify the volume of peptide in each one. This is crucial information to help understand how T14 levels correspond with the different stages of Alzheimer's.

Rather than using lumbar puncture to collect cerebrospinal fluid, which is a painful and invasive procedure for patients, their approach was to look for T14 in spit samples, since some biomarkers from the brain can find their way into saliva. Collected over many years from hundreds of patients with Alzheimer's disease, saliva samples were obtained through a partnership with the University of Edinburgh and the European Alzheimer's Disease Consortium.

"If we're going to progress this research into clinical trials, we need a simple way to tell us exactly how much T14 is in a patient's sample, so they can be referred and treated with a drug to prevent cognitive decline," says Dr Sara Garcia-Rates, Chief Scientific Officer at Neuro-Bio. "The lightbulb moment for us was detecting the T14 biomarker for the first time in a saliva sample. Crucially, we could also see it at a very low level, showing this test is really quite sensitive."

The residency format has brought benefits to both sides, combining the right mix of people together under one roof. Dr Felicia Green, Interim Theme Lead of the Franklin's Biological Mass Spectrometry Theme explains: "Having someone from Neuro-Bio physically located in our labs has helped us to discuss our techniques and their limitations and to better understand how both groups can benefit from the project. For our team, seeing how our work to identify and quantify proteins can be applied is proof-of-principle that our research has clear translational value with end goals."

Armed with an effective technique to detect and quantify T14 in saliva, Neuro-Bio will be able to determine who might be eligible for a drug trial of their early Alzheimer's therapeutic. They now hope to see this enter clinical trials within the next two years.

"Being able to detect this biomarker proves it's the earliest warning sign of Alzheimer's disease so far, and for us, that's very exciting," says Dr Garcia-Rates. "Taking our pilot study forwards with a huge translational leap like this is only something we can do with the right expertise and the right equipment. As a small spin-out company, we're very proud to have this collaboration with the Franklin. The project validates our test and opens new avenues for moving our approach into a clinical setting."