Blaine Roberts is looking for ways to detect diseases such as Alzheimer’s and Parkinson’s long before symptoms emerge.

“What’s interesting about any of these neurodegenerative diseases is that they begin a long time before you have symptoms,” Roberts says. “In Alzheimer’s, for example, the buildup of the amyloid—the material that is the hallmark of the disease—begins at least 15 years, if not more like 20 years, before any symptoms show up.”

Roberts, a researcher at the Florey Institute of Neuroscience and Mental Health and the Cooperative Research Centre for Mental Health in Melbourne, Australia, notes that, as with cancer, the earlier you can detect the disease, the better the outcome is likely to be. This should apply to neurodegenerative disease as well.

“Amyloids can be detected with a PET scan, but you can’t just go out and give a PET scan to anyone over the age of 65,” he says. “That’s way too expensive.”

So Roberts is using cutting-edge technology from Agilent to search for biomarkers that would show up in a far less expensive test.

“One aspect of my research is trying to develop a blood-based test so you could take a measurement of the proteins that are in there, and then determine if the buildup of amyloid is occurring in your brain. The benefit there is you could do more targeted and perfected clinical trials and hopefully find a therapy quickly,” he says.

Indeed, Roberts and his team in the Neuroproteomics and Metalloproteomics Lab have already found three proteins whose presence in a blood sample could indicate whether the Alzheimer’s process has begun—before there’s any sign of cognitive impairment. This matches what we are looking for: a way to detect the pathological process before clinical symptoms are noticeable.

Roberts is excited about the possibilities of a blood-based test.

“You could do a test just like you would when screening for cholesterol, for example. If the test was positive for high amyloid markers, a PET scan could be conducted to validate the presence of amyloid in your brain,” he says. “Once a therapy is available, it would be like, ‘OK, here’s your amyloid-lowering compound.’ That’s the vision of how we would use that type of a blood test. We have three markers we’re working with, and we’ve made really good progress.”
Equipped with high-performance liquid chromatographs and a range of mass spectrometers from Agilent, Roberts’ lab is on the cutting edge of a new discipline: metalloproteomics.

“We’re one of the few labs in the world that has the ability to do both metal analysis and the protein analysis in the same room,” he says.

Roberts makes good use of those capabilities in his study of motor neuron disease (often called Lou Gehrig’s disease), which can be caused by a mutation to an abundant copper- and zinc-containing protein.

“A major focus of my research recently has been studying the metal status of that protein,” he says. “We’ve actually been able to describe a mechanism for how this protein has worked in the disease and a possible treatment.”

Using technology from Agilent, along with new techniques of his own, Roberts noted that the protein wasn’t getting its full complement of essential metals.

“What that means is the protein isn’t functional, and actually seems to gain a function that is abnormal, so it functions in a bad way,” he says. “However, with the treatment we developed, we were able to deliver metal to it and restore it to its full metal state—the way it is meant to be, with its full complement of copper and its full complement of zinc.”

What Roberts observed then surprised him: With treatment, the test animals had more of the mutant protein, but they lived longer.

“Ordinarily, the greater the concentration of the protein the more severe the disease is,” he explains. “But here we were expressing more of the protein but the animals got better—the reason being that the protein now had its full complement of metals.”

In short, the key to treating the dysfunction was restoring the protein to a fully functional state. Without the ability to measure both the metal cofactors and the protein we would not have been able to make the connection so rapidly.

The treatment is now in clinical trials, by a local biotech company.