Agilent case study: Empowering researchers

Iron Man

Agilent Aids Research into How Essential Elements Can Become Killers

Iron, like oxygen, is essential to life. But too much can be deadly. Too much and you could end up with a neurodegenerative disease like Parkinson's.

Scientists have long known that Parkinson's patients have abnormally high concentrations of iron in their brains, and Dominic Hare wants to look at that more closely.

But that's just the beginning.

Hare, who runs the Atomic Pathology Laboratory at the Florey Institute in Melbourne, is working to measure—and actually visualize—the level of iron and other essential elements in biopsies, surgical resections, and other tissue samples. To that end, he and his team are using a combination of laser ablation ICP-MS technology from Agilent and special software they have developed in-house.

The end game? Figure out how the various elements in a given sample interact and, ultimately, determine where things begin to go wrong.

"Knowing that everything a cell does in its life starts as a chemical reaction," Hare says, "we can assume that disease starts as a chemical reaction as well."

Iron is of particular interest because it facilitates so much of what our bodies do—and has been implicated in a number of diseases for that very reason.

"An iron atom isn't a sentient being. It doesn't understand if it's doing a good thing or a bad thing. So the cell has to be very careful to regulate what iron is doing," Hare says. "Humans and every other species on earth have evolved complex mechanisms to keep iron under wraps and make sure it's doing what it's supposed to be doing, but when that regulatory mechanism breaks down, you can have really catastrophic events."

Again, consider Parkinson's disease, where a particular type of iron-rich brain cells that contain dopamine slowly degenerate. The body can't produce dopamine without using iron, but the two are metaphorically combustible and must be carefully regulated.

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"We believe that unwanted reactions between iron and dopamine, while they may not be the very first thing to go wrong in Parkinson's disease, are something we can actually directly target and eventually stop," Hare says. "I've begun working with Professor David Devos and his team at the University of Lille Nord de France. They're in the middle of a clinical trial with a drug, deferiprone, to reduce the iron level in the brain. This drug has been around for decades, but Professor Devos' team were the first to have the idea that it might be able to stop what may be the first chemical reaction that is causing the death of neurons in Parkinson's disease."

Originally trained as an analytical chemist, Hare now leads a multidisciplinary team and collaborates with an even more diverse group of scientists at the Florey Institute. He recently received a prestigious Career Development Fellowship through Australia's National Health and Medical Research Center.

Over the past ten years, he has acted as a sort of evangelist for laser ablation ICP-MS, a technology most often used in mining, manufacturing, and environmental testing.

"Just because something was designed for a specific application doesn't mean that's the only application it can do, and there is a lot that ICP-MS can do that doesn't involve just looking at metals," Hare says. "One of our biggest challenges has been convincing people who work in different spaces of medical research that this technology is essential for them. Often, because people have never heard of a technique, they don't know how it can open new doors in their own research."

He points out that the technology can detect all 28 essential biological elements, as well as environmental toxins such as heavy metals.

"We are now looking at what we think is the next big advance in laser ablation ICP-MS imaging. Rather than looking at just one element and how that compares to a control case, we've been developing ways of applying chemometrics, advanced pattern recognition, and machine learning with the idea of looking at the entire elemental content within the tissue," Hare says. "We know that in any living organism things don't happen in isolation. There are always upstream and downstream effects. We're looking at how we can actually visualize the relationship of not, say, two elements to each other but maybe 8 or 15 or 20—however many that we can objectively show are involved in the process."

And this process isn't restricting Hare to Parkinson's disease research. He and his team are also using archived samples from the Victorian Cancer BioBank (and other archives around the world) to build a highly detailed record of what they call the "elemental signatures of disease."

"All matter is made up of a very precise ratio of elements. What makes up a tumor, the actual chemical components, exist in a very precise ratio of, say, calcium to phosphorus to zinc to copper to bromine," Hare says. "What we're trying to do is produce hyperspectral images where we are using all of these different elements to precisely classify the tumor."

Their research may even lead to discoveries about whether the level of a particular element makes the tumor resistant to a particular treatment such as radiology, for example.

Hare believes that the knowledge that comes from such basic research could form the foundation for more precisely targeted treatments in the future—thanks to a technology invented for a completely different purpose.

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