A new metal detector to study human disease

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Zinc may be a familiar dietary supplement to millions of health-conscious people, but it remains a mystery metal to scientists who study zinc's role in Alzheimer's disease, stroke and other health problems.

They are just beginning to fathom how the body keeps levels of zinc under the precise control that spells the difference between health and disease.

Researchers now have developed a biochemical metal detector to help crack the mystery. It is a biosensor that has yielded the first measurements of the tiny amounts of zinc ordinarily present inside living cells.

The study appears in the current issue of ACS Chemical Biology, the newest of 34 journals published by the American Chemical Society, the world's largest scientific organization.

It was conducted by Rebecca A. Bozym and Richard B. Thompson, Ph.D. of the department of biochemistry and molecular biology, University of Maryland School of Medicine, Baltimore, and Andrea K. Stoddard and Carol A. Fierke, Ph.D. of the Department of Chemistry, University of Michigan, Ann Arbor.

"The question of how much zinc is available in a cell has emerged at the forefront of chemical biology," Amy R. Barrios, Ph.D., of the University of Southern California, Los Angeles, wrote in an accompanying Point of View in ACS Chemical Biology.

Barrios described the new research as “a critical step forward,” and predicted “many more exciting breakthroughs” in measuring levels of metals in human cells.

Just 2-3 grams of zinc (the weight of a penny coin) exist in the entire human body. The metal is a key building block in enzymes and other substances involved in functioning of the nervous system, the immune response, and the reproductive system.

“We believe this new technique can help us understand how zinc is involved in plaque formation in Alzheimer’s disease, how prolonged seizures or stroke kill brain cells, and how the cell normally allocates zinc to different proteins,” said Thompson.

Thompson explained that almost all zinc inside cells is incorporated into proteins, where it plays many vital roles, such as helping to read the genetic code of DNA.

“We know that if there is much zinc in the cell that is not attached to protein or otherwise encapsulated — so-called ‘free zinc’ —the cell is stressed or may be undergoing programmed cell death. This has been observed in animal models of epilepsy and stroke.”

In the past, scientists could only measure the relatively high levels of zinc in sick cells. The new sensing technology can measure very low free zinc concentrations in healthy cells.

The technique uses a special protein molecule that has been re-engineered to report when zinc becomes stuck to it as a change in luminescence that can be seen in the microscope. This protein (originally found in blood cells) is very selective, recognizing tiny levels of free zinc even in the presence of the million-fold higher levels of other metals present in cells, such as calcium or magnesium.

Because proper zinc levels are so important in health and disease, scientists have been seeking ways of measuring zinc inside and outside of cells for more than a decade.

“This is an important discovery,” said Sarah B. Tegen, Ph.D., managing editor of ACS Chemical Biology. “We need to know how the body controls levels of zinc inside cells. Too much zinc can kill nerve cells. With too little, nerve cells will not work properly.

“Now we have a metal detector, technology that can measure tiny amounts of zinc in living cells. Understanding how zinc is stored and released in different cells throughout the body may help us understand some of the nerve damage that occurs during a stroke and other nerve injuries.”

Source: American Chemical Society, by Michael Woods