Breakthrough Provides New Tool for Degenerative Disease Studies

by Bend Weekly News Sources

CORVALLIS, Ore. â€“ Scientists in the Linus Pauling Institute at Oregon State University have discovered a new technique to let them watch, visualize and precisely measure a key oxidant in animal cells, an important breakthrough that could dramatically speed research on everything from Lou Gehrigâ€™s Disease to heart disease, hypertension, diabetes and aging.

The findings are being published online this week in Proceedings of the National Academy of Sciences, a professional journal. They could open the door to major advances on some of the worldâ€™s most significant degenerative diseases, researchers say.

The OSU scientists, in collaboration with Molecular Probes-Invitrogen of Eugene, Ore., found a chemical process to directly see and visualize â€œsuperoxideâ€• in actual cells. This oxidant, which was first discovered 80 years ago, plays a key role in both normal biological processes and â€“ when it accumulates to excess â€“ the destruction or death of cells and various disease processes.

â€œIn the past, our techniques for measuring or understanding superoxide were like blindly hitting a box with a hammer and waiting for a reaction,â€• said Joseph Beckman, a professor of biochemistry and director of the OSU Environmental Health Sciences Center. â€œNow we can really see and measure, in real time, whatâ€™s going on in a cell as we perform various experiments.â€•

In research on amyotrophic lateral sclerosis, or Lou Gehrigâ€™s Disease, which is one of his labâ€™s areas of emphasis, Beckman said they have used the new technique to learn as much in the past three months about the basic cell processes as they did in the previous 15 years. Hundreds of experiments can now rapidly be done that previously would have taken much longer or been impossible.

â€œThis will enable labs all over the world to significantly speed up their work on the basic causes and processes of many diseases, including ALS, arthritis, diabetes, Parkinsonâ€™s disease, Alzheimerâ€™s disease, heart disease and others,â€• Beckman said. â€œAnd it should be especially useful in studying aging, particularly the theory that one cause of aging is mitochondrial decay.â€•

The process of oxidation in the body, researchers say, is one thatâ€™s fundamental to life but also prone to problems. Oxygen in the cells can be reduced to a molecule called superoxide, which is part of normal immune system processes and may also have other functions â€“ it was first named by OSU alumnus Linus Pauling in 1934.

â€œOxygen is actually one of the more toxic molecules in the environment,â€• Beckman said. â€œBreathing 100 percent pure oxygen will destroy your lungs in about three days because it increases the formation of superoxide.â€•

Superoxide is efficiently removed by an enzyme, superoxide dismutase. Antioxidants in food, such as vitamin C and E, are also part of this process. And in healthy animals, including humans, this delicate balancing act can work well and cause few problems. But sometimes the process breaks down and excess levels of superoxide begin to accumulate and lead to a wide variety of degenerative diseases.

Prior to this, there was no direct and accurate way to measure superoxide or its origin from the two places that produce it, the cellâ€™s cytosol or mitochondria. Now there is.

With the new system developed at OSU, researchers can use a fluorescent microscope, a fairly standard laboratory tool, to actually see levels of superoxide and observe changes as experiments are performed with living cells.

â€œIf we poison the mitochondria, using something like the pesticides that have been implicated in Parkinsonâ€™s disease, we can actually see superoxide levels begin to rapidly rise,â€• Beckman said. â€œYou get a similar reaction if a growth factor is added thatâ€™s implicated in the development of Lou Gehrigâ€™s Disease.â€•

The data available from this new technology, Beckman said, are so profound that for some time many in the science community didnâ€™t believe it was possible.

â€œThis will become a critical tool in learning how superoxide works in a cell,â€• he said. â€œIâ€™ve been studying this for more than 10 years and never thought we would have such a clear and accurate picture of whatâ€™s going on inside a living cell.â€•

In their research on ALS, for instance, OSU scientists have used the new system to actually see cells eating

themselves alive and dying from excess superoxide production. A new compound is in phase one clinical trials that appears to inhibit this process and may ultimately provide a therapy for the disease.

Oxidative stress resulting from mitochondrial dysfunction has already been implicated in neurodegeneration, aging, diabetes and cancer, the researchers said in their report. The new findings could rapidly speed research in all of those fields, they said.

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About the Linus Pauling Institute: The Linus Pauling Institute at OSU is a world leader in the study of micronutrients and their role in promoting optimum health or preventing and treating disease. Major areas of research include heart disease, cancer, aging and neurodegenerative disease.

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