Progression of Lou Gehrig's disease explained

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Researchers in Uruguay and Oregon have discovered a previously unknown type of neural cell that appears to be closely linked to the progression of amytrophic lateral sclerosis, or Lou Gehrig's disease, that they believe will provide an important new approach to therapies.

There is now no treatment for this disease, which causes progressive death of motor neurons, serious debility, paralysis and ultimately death within a few years.

Even a way to slow its progression would be hugely important, scientists say.

The findings were reported today in Proceedings of the National Academy of Sciences, by researchers from the Pasteur Institute of Montevideo, Clemente Estable Institute and the Linus Pauling Institute at Oregon State University.

The scientists discovered a type of "astrocyte" cell that displays atypical behavior and causes motor neuron death. They are referring to them as aberrant astrocyte, or AbA cells. Astrocyte cells are very common in the brain, and usually help provide metabolic support and protection to neurons. But they can sometimes also become toxic and cause the death of neuron cells.

The researchers now have markers to identify the AbA cell, and found them adjacent to dying motor neuron cells in the spinal cord of

laboratory animals with ALS.

The newly-identified AbA cells are selectively toxic to motor neurons, the researchers reported in the study, and 10 times more toxic than any other astrocyte cell known to exist. That level of toxicity is unprecedented, they said.

"We believe these aberrant astrocyte cells are helping drive the progression of ALS," said Joe Beckman, an OSU professor of biochemistry and principal investigator in the Linus Pauling Institute who has been working on amyotrophic lateral sclerosis for more than 15 years.

"These cells are a new target to aim at, a basis for therapies for this disease," Beckman said. "It should allow us to rapidly screen existing or new drugs to identify ones that could kill the AbA cells, which are easy to culture in the laboratory. This is very exciting."

Of considerable interest, the researchers said, is that these AbA cells share some of the same characteristics as cells that cause glioblastoma, a serious brain cancer. The AbA cells divide unusually fast, though not as fast as a cancer cell, and don't respond to the ordinary biological mechanisms that help control cell division. The scientists said they "appear as a new subclass of astrocytes" with an unusual affinity for killing motor neurons.

The aberrant astrocyte cells were initially discovered by Pablo Diaz-Amarilla, a doctoral student in Uruguay, who tried to develop some cell cultures of astrocyte cells from an adult rodent dying of ALS. That should not have worked – researchers for decades have been unable to propagate laboratory cultures of astrocyte cells from adult animals. But Diaz-Amarilla, with the direction of Luis Barbeito, director of the Pasteur Institute of Montevideo, persisted in this attempt and found a

new type of cell that rapidly propagates.

"Our colleagues in Uruguay kept trying something that conventional wisdom said could not be done, an experiment that no one thought would work," Beckman said. "And they succeeded. We now have laboratory cultures of the specific types of cells that we think are causing the spread of ALS, and new markers to identify them when we find them. This is very important."

Other scientists have recently demonstrated in laboratory experiments that transplant of astrocyte cells into the spinal cord of a healthy animal will give it ALS.

Slowing or stopping the progression of ALS would be a critical first step on the road to understanding its exact causes and working towards a cure, the researchers said. At any given time, about 30,000 Americans have this disease.

Provided by Oregon State University