Research shows regenerative benefit of MultiStem after spinal cord injury

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Case Western Reserve University School of Medicine and Athersys, Inc. announced a joint scientific study on spinal cord injury will be published today in the January issue of the *Journal of Neuroscience*. The study, by leading researchers from the Department of Neurosciences at the School of Medicine and scientists at Athersys, presents data supporting the potential therapeutic benefit of Athersys' MultiStem program for spinal cord injury. Researchers observed that administration of Multipotent Adult Progenitor Cells (MAPC) following spinal cord injury in rodent models prevented the retraction of neurons, a process referred to as "axonal dieback," reduced inflammation in the region of injury, and also promoted the regrowth of neurons.

According to the Christopher & Dana Reeve Foundation, there are currently more than 1,200,000 people in the United States living with spinal cord injury, and approximately 12,000 to 20,000 new cases occur each year. Most patients that suffer spinal cord injury are between the ages of 15 and 35. The long term cost of spinal cord damage is estimated to range from $500,000 to more than $3 million per patient, depending on the severity of the injury.

"This study demonstrates for the first time that an adult stem cell is capable of modifying multiple aspects of the wound response following a spinal cord injury, concurrently altering the inflammatory response to mitigate secondary injury in the central nervous system and increasing the regenerative potential of the damaged neurons themselves. Certain adult adherent stem cells are known to have immunomodulatory

capabilities, but their potential to inhibit this detrimental inflammation-related process in spinal cord injury had not been investigated until now," said Jerry Silver, PhD, Professor in the Department of Neurosciences at Case Western Reserve School of Medicine. "Using preclinical models of spinal cord injury, we found that MAPC can both dynamically regulate macrophages, which cause inflammatory damage, and stimulate neuron growth simultaneously. Our results demonstrate that MAPC convey meaningful therapeutic benefits after spinal cord injury and provide specific evidence that these adult stem cells can exert both positive immunomodulatory and neurotrophic influences."

The study, "Multipotent Adult Progenitor Cells Prevent Macrophage-Mediated Axonal Dieback and Promote Regrowth after Spinal Cord Injury" demonstrates how the administration of MAPC potently affects immune cells responding to the initial injury in a number of ways. First, MAPC significantly decrease the release of a harmful protein called MMP-9 (matrix metalloproteinase-9), made by certain cells of the immune system known as macrophages, that is known to induce axonal dieback. MAPC also induce a shift in macrophages from an M1, or "classical activated" pro-inflammatory state, to an M2, or "alternatively activated" anti-inflammatory state. In addition to these effects on macrophages, MAPC promote sensory neurite outgrowth beyond the site of the injury, induce sprouting, and further enable axons to overcome the negative effects of macrophages as well as inhibitory molecules in their environment by increasing their intrinsic growth capacity.

"These results are consistent with effects we see in other neurological injury models, and provide further validation of MultiStem as an emerging stem cell therapy with broad potential for the treatment of a variety of conditions, including the often-devastating and seemingly irreversible after-effects of spinal cord injury ," said Gil Van Bokkelen, PhD, Chairman and Chief Executive Officer of Athersys. "Although significant research remains before we can apply these methods in

human therapy, we view these results as very exciting, and we look forward to further exploring the clinical utility of MultiStem across a range of neurological indications."

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Provided by Case Western Reserve University