



## Integra LifeSciences Supports Study On Spinal Cord Injuries

PLAINSBORO, N.J., April 2, 2004 (PRIMEZONE) -- Integra LifeSciences Holdings Corporation (NASDAQ:IART) today announced its participation in a study published last month in the European Journal of Neuroscience. The study concluded that infusing a naturally occurring anti-scarring agent called decorin into the damaged spinal cords of rats suppresses key molecules that block nerve regeneration after spinal cord injury. Integra LifeSciences supported the study through grants and the donation of the genetically engineered form of human decorin utilized in the study.

The scientists at Integra LifeSciences and Baylor College of Medicine (BCM) who authored the paper demonstrated the ability of decorin to suppress inflammation and scar formation in spinal cord injuries. Glial scar tissue that forms as a result of spinal cord injury not only presents a physical barrier to nerve regeneration but also contains molecules called chondroitin sulfate proteoglycans that are inhibitory to nerve fiber growth. Pro-inflammatory transforming growth factors are released in spinal cord injuries. These molecules are known to promote scar tissue formation and their action is inhibited by decorin. The successful suppression of scarring achieved by the application of decorin directly into spinal cord lesions opens the door to possible therapies for spinal cord injury that could result in functional recovery.

"The progress made in this research program to date is the result of a series of successful academic and industrial collaborations," said Simon Archibald, Vice President, Clinical Affairs at Integra LifeSciences and a co-author on the paper. "The decorin technology is the result of pioneering discoveries made by scientists at The Burnham Institute and is covered by a series of US patents (5,726,149, 5,583,103, 6,509,314, 6,046,162, 6,436,900, 6,277,812, and 6,316,258 licensed exclusively by Integra LifeSciences from The Burnham Institute; 5,958,411 licensed exclusively by Integra LifeSciences from Cambridge Antibody Technologies; and 5,997,895 and 5,510,328 assigned to Integra LifeSciences). The collaboration with Stephen Davies and his group at Baylor has further elaborated the biology of spinal cord injury as well as demonstrated the effectiveness of decorin infusion as a new approach by which adverse tissue reactions to traumatic injury may be controlled in the spinal cord. This is a major advance in the spinal injury field, however, these results are 'proof of principal' and much has yet to be accomplished before the possibility of clinical application."

"Scar tissue that develops at sites of injury stops regeneration of connections in the adult central nervous system," said Dr. Stephen Davies, lead author on the study and an assistant professor of neurosurgery and neurosciences at BCM. "Infusion of decorin into spinal cord injuries prevents the formation of proteoglycan rich scar tissue and suppresses inflammation."

Researchers in the study infused decorin directly into the injury site in rats with a mini-pump system, which used silica cannulas 160 microns in diameter. Using a laser scanning microscope and protein chemistry to analyze tissue samples, Davies and co-workers were able to show that decorin infusion reduced inflammation, scar formation and the levels of some proteoglycans by 80-95 percent allowing nerve fibers (called axons) to grow across spinal cord injuries in just 4 days.

"We have found a promising new approach to control inflammation and scar formation in damaged spinal cord tissue, which will be an important part of future strategies to encourage axon regeneration and recovery after spinal cord injury," Davies said.

Integra LifeSciences licensed the genetically engineered form of human decorin that was used in the study from The Burnham Institute and it was produced transgenically in collaboration with scientists at GTC Biotherapeutics, Inc. (NASDAQ:GTCB).

"We are pleased to have contributed to this effort," said Harry Meade, Senior Vice President of Research and Development, GTC Biotherapeutics. "Decorin was a challenge to produce in tissue culture. However, we were able to produce decorin in the milk of transgenic mice, further establishing the milk system as a viable option for another hard to express protein. More importantly, the high levels of protein produced by this system facilitated purification of sufficient quantities of decorin to allow these experiments to be performed."

The work was also supported by TIRR (The Institute for Rehabilitation and Research) Foundation's Mission Connect, a consortium of scientists working to reverse the consequences of spinal cord and brain injuries.

CONTACT: Integra LifeSciences Holdings Corporation  
John B. Henneman, III  
Executive Vice President  
Chief Administrative Officer  
(609) 936-2481  
jhenneman@Integra-LS.com  
or  
Maria Platsis

Director of Corporate Development  
and Investor Relations  
(609) 936-2333  
mplatsis@Integra-LS.com