

Regenerative Medicine

If an octopus loses an arm, the tentacle will grow back, or “regenerate.” Today, researchers at Houston Methodist Research Institute are discovering regenerative treatments to bring patients new hope for healing.

The ideas sound like the stuff of a science fiction movie:

- A hydrogel that can be injected into an injured spine to regenerate bone tissue, similar to the way a salamander grows a new tail or a starfish grows a new arm.
- The use of “nano-scaffolds” – imagine Russian nesting dolls made up of tiny nanoparticles, one inside the other – to allow the reconstruction and recovery of nerve connections from the spinal cord to urological functions.
- A computerized exoskeleton that allows paraplegics to stand up and walk while directing the computer with their brain waves.

It is the Neuroregenerative Medicine Program and the Regenerative Medicine Program at Houston Methodist Research Institute. And the time frame is not centuries in the future, but now, or very soon.

In 2013, The Cullen Trust for Health Care awarded \$3 million to establish the Regenerative Medicine Program. Two years earlier, in 2011, Houston Methodist was awarded a \$500,000 challenge grant from The Brown Foundation toward the launch of the Neuroregenerative Medicine Research Program. In 2013, the Cullen Foundation and The Institute for Rehabilitation and Research (TIRR) Foundation, through Mission Connect, awarded grants totaling \$695,000



Dr. Tasciotti IS OPTIMISTIC ABOUT THE TIME IT WILL TAKE FOR NANO-MEDICINE TREATMENTS TO PROGRESS FROM THE BENCH TO THE BEDSIDE.

for a robotics research collaboration between the University of Houston and Houston Methodist Research Institute. (See the story on page 39.)

“Houston Methodist is at the forefront of the burgeoning field of regenerative medicine,” says Dr. Cullen Geiselman, board chair with The Cullen Trust for Health Care. “Regenerative medicine holds great promise for new

therapies and treatments for a host of diseases and conditions, and we look forward to the pioneering work underway by these brilliant researchers as they tap into the ability of cells and tissues to heal and defend themselves. This research represents the future of medicine.”

“A number of things have made a start on these projects possible,” says Dr. Robert Grossman, Professor of

Neurosurgery and Robert G. Grossman Chair in Neurosurgery. “First and foremost, we appreciate the tremendous generosity of The Brown Foundation, The Cullen Trust for Health Care, TIRR Foundation and numerous others who have provided funding for this leading-

edge research. We are truly grateful for their vision and investment to make this work a reality.”

Dr. Grossman says the timing is right for other reasons as well.

“The tremendous growth of computer programming, with the miniaturization of electronics, and the development of molecular biology allow us to have a much better understanding of the structure and chemistry of the nervous system.” The Neuroregenerative Medicine Program links three complementary components: spinal cord injury and other neurological disorders; urological (bladder and kidney) dysfunction; and biomaterials engineering and stem cell technology. Dr. Grossman is joined by colleagues Dr. Timothy Boone, Chair of the Department of Urology at Houston Methodist,



Dr. Boone SAYS THAT “THE BEST FORMS OF REPAIR ARE INHERENT TO YOUR OWN BODY.”

and Dr. Ennio Tasciotti, Associate Member, Houston Methodist Research Institute and Co-Chair, Department of Nanomedicine.

“Neuroregeneration implies that there is some damage or injury to the nervous system that needs to be repaired,” says Dr. Boone. “The best forms of repair are inherent to your own body.” Many things stand in the way of that normal repair mechanism, Dr. Boone says. It’s particularly difficult in the nervous system, because the cells are less apt to regenerate centrally than they are peripherally.

“Regenerative medicine is trying to understand the natural processes and

the barriers to natural recovery, and based on those two factors, figure out a way to facilitate the natural repair by dealing with the barriers,” he explains.

The program’s specific focus involves the use of nanotechnology – nanoparticles are, in effect, a bridge between bulk materials and molecular structures – for spinal cord repair and bladder reconstruction after a spinal cord injury (SCI). It is difficult to overstate the trauma that follows an injury to the spinal cord. SCI often results in the loss of everyday neurological functions, causing varying degrees of motor, sensory, bowel, bladder and sexual dysfunction.



Dr. Grossman CREATED AN ANATOMICAL ATLAS OF THE HUMAN SPINAL CORD, HELPING SURGEONS WITH NEUROREGENERATIVE THERAPY.

The adjustment to this stark new reality brings with it a barrage of physical and emotional challenges.

Among Dr. Grossman's top priorities has been the creation of an anatomical atlas of the human spinal cord. The atlas is currently being prepared for publication, but it is available to surgeons who are engaged in human clinical trials for neuroregenerative therapy.

"I think it will be a major step forward in clinical trials involving the injection of stem cells into the spinal cord," he says. "You have to have an atlas to know the exact position of where to inject, and how deep you should go.

"For example, we now know that Parkinson's Disease can be treated with deep brain stimulation," Dr. Grossman

says. "That discovery was made possible by an atlas of the human brain created in Germany. Until now, we have not had a similar atlas for the spinal cord."

Dr. Tasciotti, in whose spinal technology lab the clinical trials are taking place, says he is optimistic about the time it will take for nanomedicine treatments to progress from the bench to the bedside.

"Nanomedicine is the application of nanotechnology to the biomedical arena, to problems that we couldn't find solutions for with current techniques, whether they are pharmacological or surgical," Dr. Tasciotti says.

"Nanomedicine offers a lot of Holy Grails, from the magic silver bullet that attacks the cancer cell and spares the other tissues, to a lot of other fields,"

he says. "In this case, with regenerative medicine, the big advantage of nano is that we can create materials that are closer to the actual architecture and structure of the tissues that we want to regenerate."

Dr. Tasciotti points to a clinical trial in which bone tissue was successfully regenerated in rats. Another revolutionary research project involved bone regeneration in a sheep's leg. By implanting a polymeric scaffold reinforcement in the injured leg, researchers averted amputation and the sheep was running and walking normally within weeks.

"Ten years ago, we would have been talking about science fiction," he says. "With the right team and the right resources, we can solve these problems."

REX

In 2007, Dr. Eugene Alford, a respected surgeon at Houston Methodist, was clearing brush on his family's ranch in Bellville, Texas, when a dead tree fell on him, resulting in a severe spinal cord injury. After months of intensive therapy, he eventually recovered well enough to use a wheelchair and resume his surgical practice, but his legs were permanently paralyzed.

Five years later, Dr. Alford walked into a room full of doctors and scientists at the Houston Methodist Research Institute. He is still paralyzed from the waist down, but he is able to stand upright and move with the help of Rex, a robotic exoskeleton that relies on an external brainwave/machine interface.

In other words, Dr. Alford thinks about moving, and Rex moves.

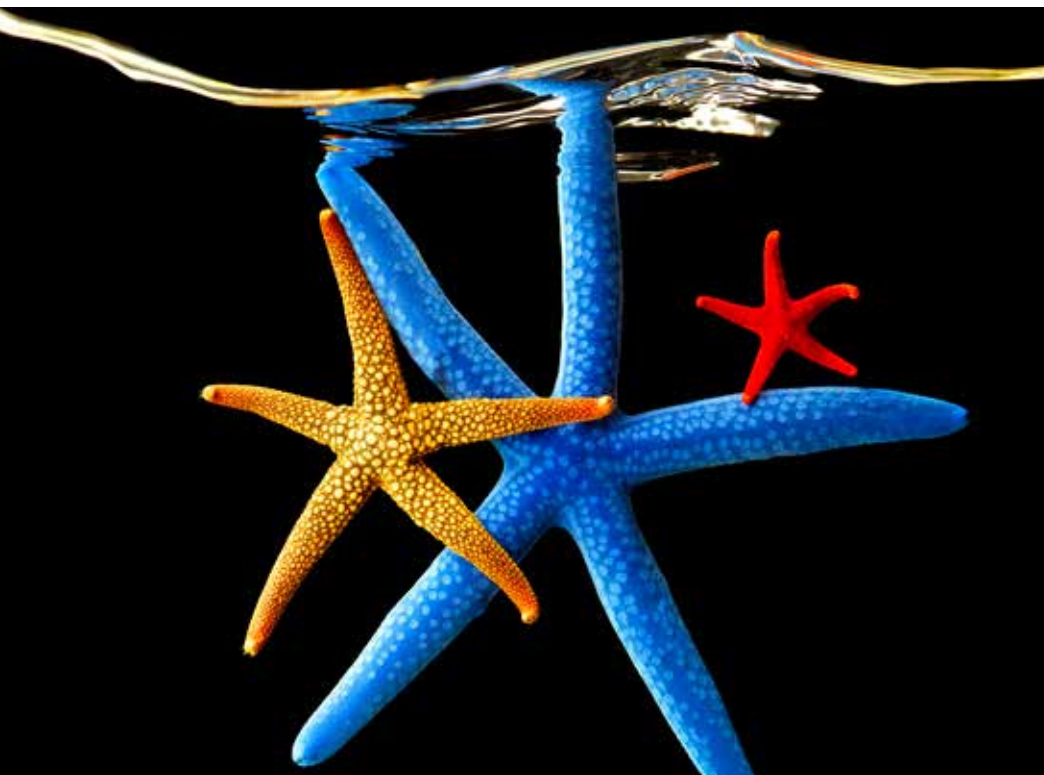
Rex is the result of a partnership between Houston Methodist Research Institute's Neuroregenerative Medicine Research Program, under the direction of Dr. Robert Grossman, and University of Houston computer engineering professor

Jose Contreras-Vidal, Ph.D. It takes its name from its manufacturer, Rex Bionics of New Zealand.

"Dr. Contreras is leaps and bounds ahead of what they are doing in surgery," says Dr. Alford.

Houston Methodist recently purchased the latest version, nicknamed NeuroRex, with the support of a grant from The TIRR Foundation. "This version has integrated circuitry that makes it possible to communicate with our brain-machine interface (BMI) system based on a high-density scalp electroencephalogram (EEG)," says Dr. Contreras.

"Facilitating research that will improve and restore neurological functions in individuals with spinal cord and brain injuries is what TIRR Foundation's neurotrauma research program, Mission Connect, is all about," says TIRR executive director Cynthia Adkins. "When you see a person who is completely wheelchair dependent stand and walk, assisted only by the Rex, it is wonderful!"



OUR DEEPEST THANKS TO THE LEAD CONTRIBUTORS TO THESE PROGRAMS

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Starfish can regrow limbs. For humanity, regenerative medicine is the 'next evolution of medical treatments:'