Ph.D. Student Works to Stop Spinal Cord Injury-Induced Cell Death in Its Tracks

Summary Angela Davis, and her mentor, Robert Keane, Associate Professor of Physiology and Biophysics, are investigating ways to minimize the damage created by spinal cord injury.

Ph.D student, Angela Davis, and her mentor, Dr. Robert Keane, are using their talents as basic science researchers toward understanding the mechanisms behind spinal cord injury.

While the initial impact of a spinal cord injury does a tremendous amount of damage, it is often what happens afterwards that exacerbates the problem. The trauma causes inflammation that continues to damage the tissue, a process that is referred to as "secondary injury." It is this physiological process that Dr. Keane and Angela Davis are looking at intently.

Cell death after spinal cord injury, called apoptosis, occurs in the weeks to years after the trauma and causes more damage than the initial impact. One of the causes behind this irreversible cell destruction is the activation of cell membrane death receptors following injury. Angela has focused her graduate research on one of these receptors that is known to play a major role in apoptosis, FAS/CD95.

In a healthy central nervous system, FAS/CD95 is expressed at low levels and may have a positive function. However, after spinal cord injury, FAS/CD95 is expressed in a much larger amount and is a key player in the cellular destruction following injury. In order to stop or slow apoptosis, it is necessary to learn where and how FAS/CD95 works.

Angela has determined that in the nervous system FAS/CD95 acts in lipid rafts, dynamic lipid micro-environments on the cell membrane surface believed to be important in regulating intracellular signaling. By bringing together specific sets of proteins, the rafts are thought to facilitate protein-protein interactions and hence to play a role in the activation of signaling cascades. Research has shown that FAS/CD95 activity can be blocked in rats by treating them with an antibody against the molecule that works with FAS/CD95. The antibody stops the interaction and the process of apoptosis. Angela is conducting experiments to determine how this mechanism works within the lipid rafts. If this research could explain what causes apoptosis, perhaps FAS/CD95 could be blocked and preventative measures might be developed to minimize spinal cord injury-induced cell death.

For scientists like Dr. Keane and Angela, the fact that they share an institutional home with the world renowned Miami Project to Cure Paralysis is very appealing. This institute brings together clinical medicine and basic science. Scientists doing relevant work at UM are invited to collaborate with the Miami Project's team.

For example, one of the grants supporting Angela's research is a joint NIH program project grant with the Miami Project. Her work is also supported by a grant from the State of Florida and an NIH training grant.

In addition, the Miami Project to Cure Paralysis offers numerous workshops and seminars and attracts leading researchers from around the globe who present the latest and most exciting research findings in the field. According to Keane, "Having the Miami Project here is a great opportunity and source for looking at injury in the central nervous system. This is a top program for students who are interested in spinal cord injury and quite a few have the opportunity to do rotations and research working with the Miami Project."

Angela has taken advantage of numerous travel opportunities since working in Dr. Keane's lab. She has presented her work at a meeting in San Diego, California. She has also made recruiting trips with members of the faculty. Each year all the students in Dr. Keane's laboratory travel to and participate in the National Neurotrauma Society meeting which will be held in Washington, D.C. this year.

The work that Dr. Keane and Angela are doing is cutting edge and holds a high potential for clinical application. As a graduate student, Angela has been able to work with top thinkers in her field, and to make a contribution in one of the most interesting areas of study in medicine today.

Further Reading

Keane RW, Kraydieh S, Lotocki G, Bethea JR, Krajewski S, Reed JC, Dietrich WD (2001) Apoptotic and anti-apoptotic mechanisms following spinal cord injury. *J. Neuropath. Exp. Neurol.* 60:422-429.

Lotocki G, Alonso OF, Dietrich WD, Keane RW (2004) Tumor necrosis factor 1 and its signaling intermediates are recruited to lipid rafts in the traumatized brain. *J. Neurosci.* 24:11010-11016.

Keane RW, Davis, AR and Dietrich, WD (2005) Inflammatory and apoptotic singaling following spinal cord injury. *J. Neurotrauma* (In Press).

Robert Keane, Ph.D.

"The program in our department is very diverse. We have the opportunity to work with students from other disciplines such as neuroscience, as well as from the M.D./Ph.D. program. The opportunities are here for great students. I strongly believe that our graduate students can match any in the United States."

Angela Davis

"I was interested in physiology, and my first choice was the University of Miami. I've been happy with my decision. The class work was extremely thorough and the department is very supportive. If you're having a problem with an experiment or technique in the lab, you can go to just about anyone in the department for help. I am getting quality training, in an exceptional learning environment."