SHORT CV

Name: Keith E. Tansey, MD, PhD

Position Title: Senior Scientist, Methodist Rehabilitation Center; Professor, Neurosurgery/Neurobiology, University of Mississippi Medical Center; Physician, Spinal Cord Injury Clinic, Jackson VA Medical Center

A. Personal Statement

My research could be characterized as "restorative neurology in spinal cord injury (SCI)" and is focused on neural plasticity and functional recovery following injury. I am especially interested in understanding the underlying mechanisms of this neural plasticity and how it could be augmented to bring about greater recovery.

In our animal lab, we are studying changes in an intersegmental spinal reflex following SCI. The cutaneus trunci muscle (CTM) reflex produces a skin "shrug" in response to pinch on a rat's back and is mediated by a three neuron circuit: C and A-delta pain afferents in lumbar and thoracic segmental dorsal cutaneous nerves (DCNs), ascending propriospinal interneurons, and the CTM motoneuron pool at the cervico-thoracic junction. Activation of these DCNs also generates a blood pressure response via the autonomic nervous system. Using this reflex, we are now asking specific questions about anatomical and physiological plasticity in a neural circuit simple enough to determine cause and effect. We have found that the pain afferents of this reflex can generate "hypereflexia" and "dysautonomia" after SCI making it an approachable neural circuit in which to study how some aspects of neuropathic pain and autonomic dysreflexia develop after SCI. Our current work is showing that this physiological plasticity is paralleled by pain afferent central projections anatomical plasticity. Most recently, we have been able to modify both the physiological and anatomical plasticity seen in the CTM reflex away from the injury site by modifying microglia activation there, resolving nociceptive hypereflexia.

In our human research, we are studying the neural plasticity underlying the recovery of locomotion in SCI and the effect locomotor training and other clinical therapeutic interventions has on that process. For this work we have combined the technologies of electrophysiology, imaging and robotics. We have used fMRI to demonstrate that locomotor training, which improves the recovery of over-ground stepping, also generates supraspinal plasticity, especially in the cerebellum. We are now using electrophysiology to investigate the nature of spinal circuit plasticity in our subjects by studying muscle activation patterns and spinal reflex modulation during stepping. We have learned that soleus H-reflex modulation during gait changes over the course of locomotor training and is related to the final over ground gait speed subjects obtain. We are now studying the progression of this recovery across multiple lower extremity muscles using posterior root motor reflexes (PRMRs). We are also using the robotic gait orthosis, the Lokomat, to relate mechanical measures of stepping to the neural plasticity we find and to characterize how these mechanical signals perturbations are handled by the recovering neural circuitry for stepping. We have begun to study how we can augment motor output during stepping in SCI subjects using tonic transcutaneous spinal cord stimulation (tSCS) and peripheral nerve stimulation. Early work is showing that the neurophysiology and mechanics of stepping and of spasticity can be positively impacted with tSCS in a stimulation frequency dependent manner and by peripheral nerve stimulation depending on when during the gait cycle that neuromodulation is supplied. We are starting to extend our studies of motor control after cervical spinal cord injury to the upper extremities using the Armeo robotic orthosis to parallel our lower extremity studies in the Lokomat.

I also contribute to the field of spinal cord injury medicine/rehabilitation through service and leadership. In addition to caring for spinal cord injury patients in the Veterans Administration system, I am currently the President Elect of the American Spinal Injury Association and I served on the board of the American Society of Neurorehabilitation. I work with several committees and consortia on clinical trials and on research tools in spinal cord injury. Finally, I just co-edited a book from Springer, "Neurological Aspects of Spinal Cord Injury".

B. Positions and Honors

C. Positions

2008-2016	Attending Physician, Spinal Cord Injury Clinic, Atlanta VA Medical Center, Atlanta, GA
2013-2016	Associate Professor, Departments of Neurology and Physiology, Emory University School of Medicine, Atlanta, GA
2016-present	Senior Scientist, Center for Neuroscience and Neurological Recovery and NeuroRobotics Lab, Methodist Rehabilitation Center
2016-present	Professor, Departments of Neurosurgery and Neurobiology and Anatomical Sciences, Neurotrauma Center, Neuro Institute, University of Mississippi Medical Center

2016-present Physician, Spinal Cord Injury Medicine and Research Services,
G.V. (Sonny) Montgomery Veterans Administration Medical Center

Honors/Appointments

2014 - 2016 Data Safety Monitoring Board, Neuralstem Inc.
2014 - now International SCI Data Set Committee, International Spinal Cord Society (ISCoS)
2015 - 2016 Trans NIH Rehabilitation Research Coordinating Committee, NIH
2015 - 2017 President Elect, American Spinal Injury Association (ASIA)
2015 "Celebration of Faculty Excellence" Award, Emory University School of Medicine
2017 - now Data Safety Monitoring Board, WISE trial (Walking Intervention for SCI with Exoskeletons)
2017 - now Medical Monitor, Neuralstem Inc.
2017 "President's Research Initiative" Award, American Association of Neuromuscular and Electrodiagnostic Medicine
2017 - 2019 President, American Spinal Injury Association

Board Certifications

2000 Neurology, American Board of Psychiatry and Neurology
2005 Spinal Cord Injury Medicine, American Board of Physical Medicine and Rehabilitation
2012 Neural Repair and Rehabilitation, United Council for Neurological Subspecialties

D. **Contribution to Science** - full Tansey citation list at:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1Var-TbygrikF/bibliograpahy/49250056/public/?sort=date&direction=descending

1. Neural plasticity in locomotor recovery in human spinal cord injury - For this work we have combined the technologies of electrophysiology, imaging and robotics. We have used fMRI to demonstrate that locomotor training, which improves the recovery of over-ground stepping, also generates supraspinal plasticity, especially in the cerebellum. We are now using electrophysiology to investigate the nature of spinal circuit plasticity in our subjects by studying muscle activation patterns and spinal reflex function during stepping. We have also begun to study how we can augment motor output during stepping in SCI subjects using tonic transcutaneous spinal cord stimulation (tSCS). That work is showing that the neurophysiology and mechanics of stepping and of spasticity can be positively impacted with tSCS in a stimulation frequency dependent manner.

1. Winchester, P., McColl, R., Querry, R., Foreman, N., Mosby, J., Tansey, K., and Williamson, J., Changes in Supraspinal Activation Patterns following Robotic Locomotor Therapy in Subjects with Motor Incomplete Spinal Cord Injury. *Neurorehabilitation and Neural Repair* 19:313-324, 2005
2. Querry, R., Pacheco, F., Annaswamy, T., Goetz, L., Winchester, P. and Tansey, K.E., Synchronous stimulation and monitoring of the H-reflex during robotic body weight ambulation in subjects with spinal cord injury, *J. Rehab. Res. & Dev.* 45:175-186, 2008
3. Minsassian, K., Hofstoetter, U., Tansey, K., and Mayr, W., Neuromodulation of lower limb motor control in restorative neurology, *Clin Neuro and Neurosurg* 114:489-497, 2012
4. Hofstoetter, U., McKay, B., Tansey, K., Mayr, W., Kern, H., and Minassian, K., Modification of spasticity by transcutaneous spinal cord stimulation in incomplete spinal cord injured individuals, *J Spinal Cord Med* 37:202-211, 2014
5. Minassian, K., Hofstoetter, U.S., Danner, S.M., Mayr, W., Bruce, J.A., McKay, W.B., and Tansey, K.E., Spinal rhythm generation by step-induced feedback and transcutaneous posterior root stimulation in complete spinal cord injured individuals, *Neurorehabilitation and Neural Repair 30:233-243,* 2016

2. Neural plasticity in basic science models of spinal cord injury - In a variety of basic science models, we have explored neural plasticity in the form of astrocyte biology, gene expression, motoneuron properties, synaptic plasticity, and axon regeneration. We are currently working in a model neural circuit, the nociceptive intersegmental cutaneus trunci muscle (CTM) reflex. Not only can we study nociceptive biology, activation of the afferents in this reflex generates cardiovascular responses via the autonomic nervous system. We are finding that the pain afferents of this reflex can generate "hypereflexia" and "dysautonomia" after SCI and this physiological plasticity is paralleled by anatomical plasticity in these pain afferents' central projections.

1. Faulkner, J.R., Hermann, J.E., Woo, M.J., Tansey, K.E., Doan, N.B., and Sofroniew, M.V., Reactive astrocytes protect tissue and preserve function after spinal cord injury. *J. Neurosci.* 24:2143-2155, 2004.
2. Petruska, J.C., Ichiyama, R.M., Crown, E.D., Tansey, K.E., Roy, R.R., Edgerton, V.R., and Mendell,

L.M., Changes in Motoneuron Properties and Synaptic Inputs Related to Step Training Following Spinal Cord Transection in Rats *J. Neuroscience* 27:4460-71, 2007

3. Tansey, K.E., Seifert, J.L., Botterman, B.R., Delgado, M.R., and Romero, M.I., Peripheral Nerve Repair through Multi-luminal Biosynthetic Implants, *Ann Biomed Eng* 2011
4. Lee, H.J, White, J.M., Chung, J., and Tansey, K.E., Peripheral and central anatomical organization of cutaneous afferent subtypes in a rat nociceptive intersegmental spinal reflex*, J Comp Neurol* 15:2216-2234, 2017

3. Advances in clinical research and care in spinal cord injury - Through work in clinical networks, societal committees and personal efforts, I have contributed to advancing the standard of care and of clinical research in the field of spinal cord injury medicine.

1. Tansey, K.E., Profiling Motor Control in Spinal Cord Injury: Moving towards Individualized Therapy and Evidence-based Care Progression, *J Spinal Cord Med* 35:305-309, 2012
2. Kirshblum, C.S., Biering-Sorensen, F., Betz, R., Burns, S., Donovan, W., Graves, D.E., Johansen, M., Jones, L., Mulcahey, M.J., Rodriguez, G.M., Schmidt-Read, M., Steeves, J.D., Tansey, K., and Waring, W., International Standards for Neurological Classification of Spinal Cord Injury: Cases with classification challenges, *J Spinal Cord Med* 37:120-127, 2014
3. Biering-Sorenson, F., Alai, S., Anderson, K., Charlifue, S., Chen, Y., DeVivo, M., Flanders, A., Jones, L., Kleitman, N., Lans, A., Noonan, V.K., Odenkirchen, J., Steeves, J., Tansey, K., Widerstrom-Noga, and Jakeman, L.B., Common Data Elements for Spinal Cord Injury Clinical Research: A National Institutes for Neurological Disorders and Stroke Project, *Spinal Cord 53:265-277,* 2015
4. Marino, R.J., Schmidt-Read, M., Kirshblum, S.C., Dyson-Hudson, T.A., Tansey, K.E., Morse, L.R., and Graves, D.E., Reliability and validity of S3 pressure sensation as an alternative to deep anal pressure in neurological classification of persons with spinal cord injury, *Archives of PM&R 97:1642-1646*, 2016
5. Frontera WR, Bean JF, Damiano D, Ehrlich-Jones L, Fried-Oken M, Jette A, Jung R, Lieber RL, Malec JF, Mueller MJ, Ottenbacher KJ, Tansey KE, Thompson A., Rehabilitation Research at the National Institutes of Health *Neurorehabil and Neural Repai, 31:304-314,* 2017

E. Research Support

Ongoing Research Support

Completed Research Support (selected)

Project #: 297076 PI: Malu Tansey Funding Agency: Neilsen Foundation
Grant Title: "XPro1595 to inhibit soluble TNF and modulate inflammation in spinal cord injury"
Grant Dates: 7/1/14-2/28/17 (NCE) Role: Co-Investigator

Project #: 1IO1RX000417-01A1 PI: Keith Tansey Funding Agency: VA RR&D
Grant Title: "Human Spinal Circuit Plasticity with Locomotor Training in SCI"
Grant Dates: 10/1/12 – 9/31/16 (NCE) Role: Principal Investigator

Project #: 284874 PI: Keith Tansey Funding Agency: Neilsen Foundation
Grant Title: "Pain induced dysautonomia in SCI: neural plasticity and intervention"
Grant Dates: 2/1/14-1/31/16 Role: Principle Investigator