BIOGRAPHICAL SKETCH

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NAME: **Mu, Liancai**

eRA COMMONS USER NAME (credential, e.g., agency login): **LIANCAIMU**

POSITION TITLE: **Senior Scientist**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
China Medical University, Shenyang, China	**M.D.**	**07/1973**	**Medicine**
China Medical University, Shenyang, China	**M.S.**	**09/1981**	**Otolaryngology**
China Medical University, Shenyang, China	**Ph.D.**	**09/1993**	**Otolaryngology**

A. Personal Statement

The goal of the proposed work is to investigate nerve and muscle pathology of the human tongue and larynx in Parkinson's disease, a neurological disease that causes impaired swallowing, speech and voice in most patients. We expect that our research will elucidate mechanisms involved in these disorders. As an independent PI since 1996, my continuous NIH funding including one R03 and five R01s (1996-2021) on the neuroanatomy and neuropathology of the human upper airway structures, including the larynx, pharynx, soft palate and tongue for more than two decades demonstrates that I have the expertise, leadership, training, and motivation necessary to successfully carry out the proposed work. This demonstrated record of successful and productive research projects spans 30 years of research experience in neuroanatomy, electrophysiology, neurobiology, and neuropathology of the human upper airway structures and resulted in published more than 65 peer-reviewed articles. At an early stage of my research career, I served as a major co-investigator and was closely involved in NIH-funded 3 R01's projects (PI: Dr. Ira Sanders) that focused on investigating neuroanatomy and neuromuscular compartments within the human laryngeal and tongue muscles (1991-2003). I have also characterized the neuromuscular specializations of the human pharynx and soft palate as well as one R01 (2007-2012) to treat muscle paralysis using our recently developed novel microsurgical technique called "nerve-muscle-endplate band grafting (NMEG)". More recently, I modified the NMEG technique and this research is funded by two DOD grants (2014-2018; 2020-2023). I laid the groundwork for the proposed research by using the comprehensive approach and reliable measures.

I have established several collaborative research teams. In recent years, we investigated Parkinson's disease-induced changes in the human pharynx involving a long-term collaboration between my laboratory and the neuropathology laboratory under the direction of Dr. Thomas Beach at Banner Sun Health Research Institute (BSHRI). Our collaborative studies on Parkinsonian pharynx with BSHRI and the Mayo Clinic Arizona (Dr. Charles H. Adler) have already produced novel discoveries described in C.2.

The current proposal builds logically on my prior work. Due to my broad knowledge and expertise in this field, I am uniquely qualified to conduct and lead this research. In addition, we have a very strong investigative team and the world-class consultants. I believe that the proposed work will be successfully completed.

Ongoing and recently completed projects that I would like to highlight include:
DoD/W81XWH2010195
Mu (PI)
04/15/2020-04/14/2023
Reinnervation of paralyzed limb muscle by nerve-muscle-endplate grafting technique

R01DC014679
Mu (PI)
04/01/2016-03/31/2021
Neuromuscular specializations of the human soft palate

DoD/W81XWH-14-1-0442
Mu (PI)
09/15/2014-09/14/2018
Reinnervation of paralyzed muscle by nerve-muscle-endplate band grafting

Michael J. Fox Foundation
Mu (PI)
09/24/2013-09/23/2014
Is dysphagia in Parkinson's disease caused by Lewy pathology in the upper aerodigestive tract?

R01DC004728
Mu (PI)
09/01/2009-08/31/2013
Anatomical specializations of the human pharynx

5R01DC008599
Mu (PI)
12/01/2007-11/30/2012
Reinnervation of Paralyzed Muscle by Nerve-Muscle-Endplate Band Grafting

5R01DC004728
Mu (PI)
02/01/2005-01/31/2009
Anatomical Specializations of the Human Pharynx

1R01DC004728
Mu (PI)
02/01/2001-01/31/2005
Anatomical Specializations of the Human Pharynx

Citations:

1. **Mu L,** Chen J, Li J, Fowkes M, Benson B, Nyirenda T, Sobotka S, Christopherson M, Sanders I. Innervation of human soft palate muscles. Anat Rec (Accepted 5 August 2020) DOI: 10.1002/ar.24531
2. **Mu L,** Sanders I. Neuromuscular compartments and fiber-type regionalization in the human inferior pharyngeal constrictor muscle. Anat Rec 264(4):367-377, 2001. PMID: 11745092.
3. **Mu L,** Sobotka S, Su H. Nerve-muscle-endplate band grafting: a new technique for muscle reinnervation. Neurosurgery 69(2 Suppl Operative):ons208-224, 2011. PMID: 21796004.
4. **Mu L,** Sobotka S, Chen J, Su H, Sanders I, Adler CH, Shill HA, Caviness JN, Beach TG. Alpha-synuclein pathology and axonal degeneration of the peripheral motor nerves innervating pharyngeal muscles in Parkinson's disease. J Neuropathol Exp Neurol 72(2):119-129, 2013. PMID: 23334595.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2021-present	Senior Scientist, Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ
2011-2020	Senior Scientist, Hackensack University Medical Center (HackensackUMC), Hackensack, NJ
2018-present	Member, Journal of Otolaryngology Ent and Head
2010-present	Member, American Society for Neuroscience
2010-present	Member, Surgical Science
2008-2011	Associate Scientist, Department of Research, HackensackUMC, Hackensack, NJ
2006-2008	Research Associate Professor, Department of Otolaryngology, Mount Sinai School of Medicine (MSSM), New York, NY
1997-2005	Research Assistant Professor, Department of Otolaryngology, MSSM, New York, NY

1991-1997 Research Associate with Associate Professor Ira Sanders, Department of Otolaryngology, MSSM, New York, NY
1996-2005 Professor, Department of Otolaryngology, China Medical University (CMU), Shenyang, China
1990-1996 Associate Professor, Department of Otolaryngology, CMU, Shenyang, China
1990-1991 WHO Scholarship - Laryngeal EMG and voice analysis, Goteborg University, Sweden
1989-1993 Ph.D., Department of Otolaryngology, CMU, Shenyang, China
1985-1990 Co-Director, Liaoning Voice Center, CMU, Shenyang, China
1981-1989 Lecturer and Attending Physician of Otolaryngology, CMU, Shenyang, China
1978-1981 M.S., Department of Otolaryngology, CMU, Shenyang, China

Honors

2017 Cover photograph, Brain & Behavior, June 2017
2015 Cover photograph, Dysphagia, August 2015
2013 "A 3-Dimensional Atlas of Human Tongue Muscles" published in the Anatomical Record (Anat Rec 296:1102-1114, 2013) has been featured in ScienceNOW entitled “Your Tongue, Inside Out” (7 May 2013; http://news.sciencemag.org/sciencenow/2013/05/scienceshot-your-tongue-inside-o.html?ref=hp).
2010 Cover photograph, Clinical Anatomy, October 2010
2010 Cover photograph, Biotechnic & Histochemistry, January 2010
2007 Cover photograph, Annals of Otology, Rhinology & Laryngology, August 2007
2003 The Broyles-Maloney Award, The American Broncho-Esophagological Association
1998 Cover photograph, The Anatomical Record, December 1998
1998 Cover photograph, The Anatomical Record, February 1998
1997 The Broyles Maloney Award, The American Broncho-Esophagological Association
1992 President’s Award for best scientific exhibit, American Academy of Otolaryngology
1990 WHO Scholarship, Department of Otolaryngology, Sahlgren’s Hospital, University of Goteborg, Goteborg, Sweden

C. Contributions to Science

1. ***The larynx:*** The human larynx is critical for voice production, respiration and upper airway protection. Laryngeal dysfunction results in serious clinical situations such as dysphonia, aspiration, and respiratory difficulty. In order to better understand laryngeal functions and related disorders, we investigated neuromuscular organization of the human larynx. My early work was to document the neuromuscular compartments in the human laryngeal muscles by determining the nerve supply patterns and muscle fiber type distribution. I served as a major co-investigator and was involved in NIH-funded 2 R01’s projects (R01DC001764; 12/01/1993-11/30/2001; PI: Ira Sanders). Our results challenged the traditional view on the laryngeal innervation. First, the external superior laryngeal nerve not only innervates the cricothyroid muscle, but also supplies thyroarytenoid muscle. Second, the internal superior laryngeal nerve (generally believed to be a sensory nerve) may contribute motor innervation to the laryngeal muscles as it also supplies the interarytenoid muscle and communicates with the recurrent laryngeal nerve. Third, we were the first to document that most of the human laryngeal muscles are composed of functional neuromuscular compartments. Finally, we found that the human laryngeal muscles contained specialized myofibers expressing unusual myosin heavy chain isoforms that are not found in the limb muscles. Our new discoveries have been published in scientific journals and modern text books.
    a. Sanders I, Wu BL, **Mu L,** Li Y, Biller HF. The innervation of the human larynx. Arch Otolaryngol Head Neck Surg 119(9):934-939, 1993. PMID: 7689327
    b. Wu BL, Sanders I, **Mu L,** Biller HF. The human communicating nerve: an extension of the external superior laryngeal nerve that innervates the vocal cord. Arch Otolaryngol Head Neck Surg 120(12):1321-1328, 1994. PMID: 7980895.
    c. **Mu L,** Sanders I, Wu BL, Biller HF. The intramuscular innervation of the human interarytenoid muscle. Laryngoscope 104(1 Pt 1):33-39, 1994. PMID: 7507545.
    d. **Mu L,** Sanders I. The human cricothyroid muscle: three muscle bellies and their innervation patterns. J Voice 23(1):21-28, 2009. PMID: 18191374.

2. ***The pharynx and Parkinson’s disease:*** The human pharynx, a tubelike structure, serves both the respiratory and digestive systems and aids in speech. Motor innervation of the pharyngeal constrictors (PCs) and upper esophageal sphincter (UES) has long been controversial. In the past 20 years, I have

served as the PI to lead one R03 (R03 DC002695; 05/01/1996-04/30/1998) and three R01 (R01 DC004728; 02/01/2001-01/31/2005; 02/01/2005-01/31/2009; 09/01/2009-08/31/2013) projects investigating the neuromuscular specializations of the human pharynx and Parkinson's disease (PD) induced neuromuscular alterations in the pharynx. These studies have yielded a number of important discoveries. First, the pharyngeal branch of the IX nerve contributes motor innervation to the PCs and UES. This novel finding challenged the current and prevailing view that the IX nerve only provides motor innervation to the stylopharyngeus muscle. Second, we were the first to document that the adult human PCs and UES are divided into two distinct and specialized neuromuscular layers: a slow inner layer (SIL) innervated by the IX nerve, and a fast outer layer (FOL) innervated by the X nerve. These novel findings lead us to tender a new theory that the human PCs and UES are controlled by two neuromuscular systems, the SIL of nerve IX (IX-SIL) and the FOL of nerve X (X-FOL). As neither fiber layer was found in human newborns, but was identified in two-year-old humans and was well defined in human adults, the appearance of the SIL appears to be related to the development of human speech. The X-FOL contains a predominance of fast type II fibers that facilitate powerful contraction and rapid movement used when swallowing. Our new discoveries and proposed theory are included in medical books for otolaryngologists/laryngologists. Finally, we also investigated the neuromuscular alterations in the pharynx in subjects with PD because motor disturbances of the upper aerodigestive tract such as oropharyngeal dysphagia and speech and voice disorders in PD are very common. Our studies funded by NIH (R01DC004728; 09/01/2009-08/31/2013) and Michael J Fox Foundation (09/24/2013-09/23/2014) documented for the first time that the pharyngeal motor and sensory nerves and muscles were affected in PD. Specifically, α-synuclein aggregates and degenerated axons in the pharyngeal nerves were identified in PD. We also found that the swallowing-related X-FOL became very slow in PD patients with dysphagia. Our data have improved our understanding of the neural control of the human pharynx and disease-induced neuromuscular alterations. These findings suggest that the neuromuscular changes in the pharynx could be a contributing factor leading to dysphagia in PD. Our discoveries would be helpful for developing novel therapies to treat dysphagia and other PD-related upper airway disorders.

a. **Mu L,** Sanders I. Neuromuscular specializations within human pharyngeal constrictor muscles. Ann Otol Rhinol Laryngol 116(8):604-617, 2007. PMID: 17847729.
b. **Mu L,** Wang J, Su H, Sanders I. Adult human upper esophageal sphincter contains specialized muscle fibers expressing unusual myosin heavy chain isoforms. J Histochem Cytochem 55(3):199-207, 2007. PMID: 17074861.
c. **Mu L,** Sobotka S, Chen J, Su H, Sanders I, Adler CH, Shill HA, Caviness JN, Samanta JE, Beach TG. Altered pharyngeal muscles in Parkinson's disease. J Neuropathol Exp Neurol 71(6):520-530, 2012. PMID: 22588389.
d. **Mu L,** Sobotka S, Chen J, Su H, Sanders I, Adler CH, Shill HA, Caviness JN, Beach TG. Alpha-synuclein pathology and axonal degeneration of the peripheral motor nerves innervating pharyngeal muscles in Parkinson's disease. J Neuropathol Exp Neurol 72(2):119-129, 2013. PMID: 23334595.

3. ***The tongue:*** The human tongue is vital for speech, swallowing, and respiration. However, little is known about how each of the tongue muscles is involved in and contributes to the complex and coordinated motor tasks. Therefore, the motor control of the tongue movements is poorly understood. I served as a major co-investigator on the tongue research project funded by NIH (R01 DC004684; 08/01/2001-07/31/2005; PI: Ira Sanders) to study the anatomy of human tongue. Findings from our work on the hypoglossal nerve and neuromuscular organization of the human tongue have been directly applicable to the development of Inspire therapy for obstructive sleep apnea (OSA), an FDA-approved electrical "pacing" device for the tongue. We have demonstrated for the first time that lingual nerve (LN) also supplies the superior longitudinal muscle, suggesting that the LN may contain motor fibers to supply the tongue. Our studies, "A three-dimensional atlas of human tongue muscles" published in the Anatomical Record 296:1102-1114, 2013 has been featured in ScienceNOW entitled "Your Tongue, Inside Out" (http://news.sciencemag.org/sciencenow/2013/05/scienceshot-your-tongue-inside-o.html?ref=hp). Our data are very useful for the development of new techniques to treat tongue-related disorders.

a. **Mu L,** Sanders I. Neuromuscular organization of the canine tongue. Anat Rec 256(4):412-424, 1999. PMID: 10589027.
b. **Mu L,** Sanders I. Human tongue neuroanatomy: Nerve supply and motor endplates. Clin Anat 23(7):777-791, 2010. PMID: 20607833.
c. Sanders I, **Mu L,** Amirali A, Su H, Sobotka S. The human tongue slows down to speak: Muscle fibers of the human tongue. Anat Rec (Hoboken) 296(10):1615-1627, 2013. PMID: 23929762.

d. Sanders I, **Mu L.** A three-dimensional atlas of human tongue muscles. Anat Rec (Hoboken) 296(7): 1102-1114, 2013. PMID: 23650264.

4. ***The soft palate:*** There are considerable controversies regarding the innervation of the soft palate and little is known about the internal properties of the palatal muscles, which play an important role in upper airway motor tasks. More recently, I have completed a NIH-funded research (R01DC014679; 04/01/2016-03/31/2021) investigating the neuromuscular specializations of the human soft palate. There were several notable findings. First, the human palatal muscles were innervated by multiple cranial nerves, including the pharyngeal branches of the IX and X, and lesser palatine nerve (LPN). The most important finding is that the LPN innervated the musculus uvulae, palatopharyngeus, and levator veli palatine muscles. These findings suggest that LPN may contribute motor innervation to the soft palate muscles. These findings challenge the current view that the LPN is a sensory nerve that innervates the palatal mucosa and palatine glandular tissue. Second, we were the first to demonstrate that some palatal muscles received dual or triple innervation from different nerves. Some soft palate muscles such as palatopharyngeus and palatoglossus were composed of neuromuscular compartments. Finally, adult human palatal muscles contained myofibers expressing unusual myosin heavy chain (MyHC) isoforms such as slow-tonic and embryonic MyHCs that are not found in the limb muscles. These specialized MyHC fibers may play an important role in muscle contractile properties needed for speech, respiration and swallowing. These findings could improve our understanding of the neural control of the soft palate and are useful for developing novel neuromodulation therapies to treat certain soft palate-related speech, breathing and swallowing disorders.
    a. **Mu L,** Chen J, Li J, Arnold M, Sobotka S, Nyirenda T, Fowkes M, Christopherson M, Sanders I. Sensory Innervation of the Human Soft Palate. Anat Rec (Hoboken) 301(11):1861-1870, 2018. PMID: 30079585
    b. **Mu L,** Chen J, Li J, Sobotka S, Fowkes M. Soft palate and its motor innervation: A brief review. Anatomy Physiol Biochem Int J 5(5):555672. 2019. DOI: 10.19080/APBIJ.2019.05.555672
    c. **Mu L,** Chen J, Li J, Fowkes M, Benson B, Nyirenda T, Sobotka S, Christopherson M, Sanders I. Innervation of human soft palate muscles. Anat Rec 304:1054-1070, 2021.
    d. **Mu L,** Chen J, Li J, Benson B, Sobotka S, Nyirenda T, Christopherson M, Sanders I. Morphometric and immunohistochemical characterization of the adult human soft palate muscles. J Histochem Cytochem (in press), 2021.

5. ***Development of a novel technique for muscle reinnervation:*** Traumatic peripheral nerve injury (PNI) to the extremities and resultant muscle paralysis represent a significant cause of morbidity and disability in both military and civilian populations. Although a number of surgical procedures have been used to restore motor function following PNIs, the currently available surgical procedures result in poor functional recovery. On the basis of our experience and knowledge of the neural organization patterns of the skeletal muscles from our previous muscle studies and others, I developed a new technique called “nerve-muscle-endplate band grafting (NMEG)” for muscle reinnervation in a rat model. The concept is that a paralyzed muscle can be reinnervated by transplanting a NMEG from a non-essential muscle to a more functionally important denervated muscle for restoring its motor function. As the PI, I led this research funded by one NIH grant (R01 DC008599; 12/01/2007-11/30/2012) and two DOD grants (W81XWH-14-1-0442; 09/15/2014-09/14/2018; W81XWH2010195; 4/15/2020-4/14/2023). Our pre-clinical studies showed that the NMEG technique resulted in improved functional recovery (82%) as compared with traditional nerve repair methods (50%). We believe that NMEG will become a clinically useful technique in the near future.
    a. **Mu L,** Sobotka S, Su H. (Nerve-muscle-endplate band grafting: A new technique for muscle reinnervation. Neurosurgery 69(2 Suppl Operative):ons 208-224, 2011. PMID: 21796004.
    b. **Mu L,** Sobotka S, Chen J, Nyirenda T. Reinnervation of denervated muscle by implantation of nerve-muscle-endplate band graft to the native motor zone of the target muscle. Brain Behav 7(6):e00668. doi:10.1002/brb3.668, 2017. PMID: 28638701.
    c. **Mu L,** Sobotka S, Chen J, Nyirenda T. Nerve growth factor and basic fibroblast growth promote reinnervation by nerve-muscle-endplate grafting. Muscle Nerve 57(3):449-459, 2018.
    d. **Mu L,** Chen J, Li J, Nyirenda T, Fowkes M, Sobotka S. Immunohistochemical detection of motor endplates in the long-term denervated Muscle. J Reconstr Microsurg 34(5):348-358, 2018.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/liancai.mu.1/bibliography/40843970/public/?sort=date&direction=ascending