

TRANSLATION **BUILDER**

This newsletter is designed to provide a place for members of the APTC to share news, collaborate and network, and discover each other and the services we offer.

Investigator's Corner



Rahila Ansari, M.D., M.S.

Staff Neurologist - Louis Stokes Cleveland VA Medical Center
Assistant Professor, School of Medicine – Case Western Reserve University
APTC Research Area: Enabling Technologies

[Dr. Rahila Ansari](#) is a Neurologist at LSCVAMC and an Assistant Professor in the Department of Neurology at CWRU. Dr. Ansari is dedicated to translating engineering solutions into the clinical setting to help restore function to patients with neurological deficits. After graduate school in biomedical and polymer engineering, she obtained her medical degree from CWRU School of Medicine. Dr. Ansari completed her residency at John Hopkins Hospital, where she was a Neurology Chief Resident. Following fellowship training in Neuromuscular Diseases at University Hospitals Case Medical Center, she became faculty at the school of medicine. Her research on orthotics for patients with inclusion body myositis has been highlighted by the American Orthotic and Prosthetic Association as a keynote lecture at the annual meeting, and as a spotlight article in their journal, the O&P Almanac.

COLLABORATIONS

Due to the interdisciplinary nature of Dr. Ansari's work, she has formed multiple interdepartmental and cross-institutional collaborations with basic scientists and engineers, including other APTC Investigators, with a common goal of more rapidly translating technology into clinical applications. Some of her projects include using orthotics for individuals with myopathy that work as a dampening system to help stabilize the quadriceps and prevent knee buckling during walking (PI: Dr. Ansari; *see image on right*), and developing a portable, wearable, and wireless gait lab to quantify body kinetics (Co-PIs: Dr. Ansari, Dr. Huang, and Dr. Yu).

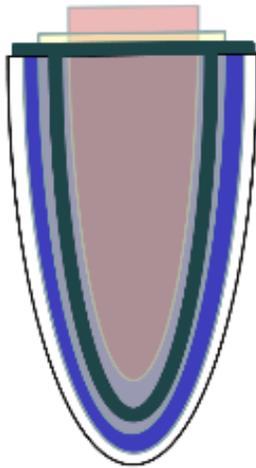
She is also involved in multiple projects with Drs. Ronald Triolo and Dustin Tyler that focus on short and long-term nerve health, evaluating for nerve cuff stability, and performing electrodiagnostic studies, including:

- ◆ Automatic Control of Standing Balance with Functional Neuromuscular Stimulation
- ◆ A Neuroprosthesis for Seated Posture and Balance
- ◆ Long Term Performance of Implanted Neuroprosthesis after Paralysis from SCI



- ✦ Verifying Operations of New Peripheral Nerve Interfaces
- ✦ A Neuroprosthesis for Prolonged Standing after SCI using Multi-Contact Peripheral Nerve Electrodes
- ✦ Restoring Natural Sensation to Lower Limb Amputees

CURRENT RESEARCH



LINER DESIGN

Residual Limb
Wicking Liner
Hydrophilic Transporting
Core
Shape Changing
Polymer
Socket

In the latter half of 2017, Dr. Ansari, along with APTC Investigator Dr. Gary Wnek (CWRU) and Dr. LaShanda Korley (University of Delaware), was awarded the Steven Garverick Innovation Incentive Program grant from the APTC. The project is titled “Smart’ Prosthetic Liners” and will focus on 1) identifying polymers with shape changing properties, 2) quantifying their mechanical, electrical, and viscoelastic properties, and 3) designing and constructing an architecture to maximize and control these properties.

Dr. Ansari has noted that, while engineering advancements have been made in artificial limb biomechanics, joint control systems, and light-weight materials, the liners that are commercially available are limited in their ability to adapt to each user. Veteran amputees report that the primary problem they face with their artificial limbs is a poor fitting socket due to changes in body weight, swelling of residual limb, development of pressure ulcers, and accumulation of sweat. In the future, Dr. Ansari hopes to provide her patients with socket liners that not only wick moisture and shape-adjust, but involve a real-time sensor system (developed by Dr. Ming-Chun Huang) in the polymer composite to allow for “smart” and auto-adjusting conformational changes to accommodate for areas of high shear stress and pressure forces.

FDA & Quality Fast Facts

THE FDA APPLICATION TRAIL

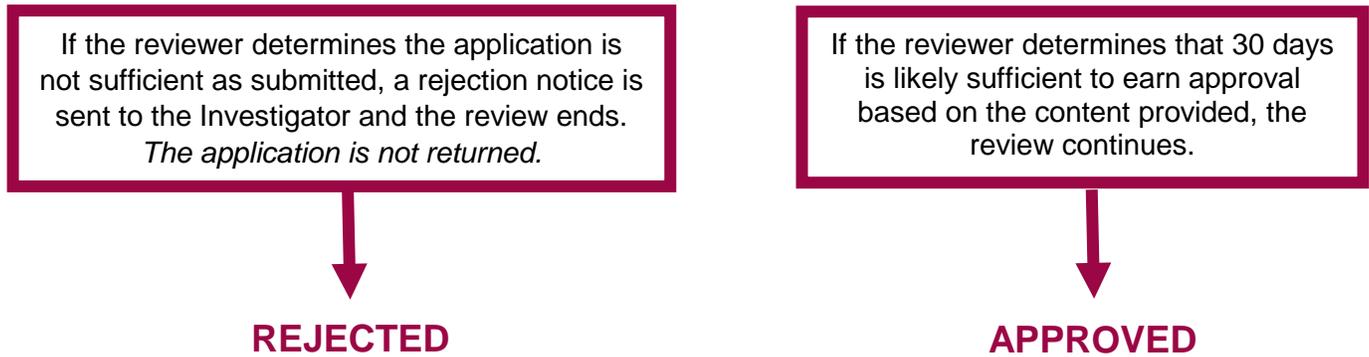
How is your application submitted to the FDA? The US Food and Drug Administration (FDA) document acceptance and review process is regimented, yet more predictable than you might imagine. All APT Center applications are sent via UPS to the FDA Document Room in Silver Spring, MD. UPS delivery allows close tracking and documentation of the delivery of applications which creates an audit trail. The recipient address is specific to the medical device, drug, or biologic an Investigator requests to investigate.

After receiving an application, a Document Room member will:

- ✦ Conduct a cursory review of the material submitted
- ✦ Ensure the requisite electronic copies load properly into the database and are labeled per FDA rules
- ✦ Confirm the packet is complete and ready for review
- ✦ Assign a numeric identifier based on its classification (e.g., supplement, annual report, notice)
- ✦ Send the Investigator a confirmation email that the application was accepted and its review process has begun

APPLICATION ACCEPTANCE AND TIMELINE

The Document Room's formal acceptance date becomes the date on which FDA's 30-day review clock begins. Within that 30-day window, FDA assigns review oversight to an individual to work with the Investigator.



INTERACTIVE REVIEW

Earning approval often includes a period of Interactive Review that occurs about three weeks into the 30-day review cycle, in which questions are forwarded to the Investigator with an expectation of rapid response. **It is not unusual for an Investigator to receive a series of questions with a notice that all must be satisfied within a period of hours for the review to continue.**

Requests can be as simple as “Can you confirm [x] to be true?” or burdensome, including requests to have additional diagrams prepared, charts or defenses drafted, or tests run -- any of which could take considerable time to complete. For very complex questions or issues, it is not unusual for FDA to request a last-minute telephone conference with the primary reviewer, any secondary reviewers, the Investigator, and perhaps study staff so that discussions can take place in real time.

The Investigator usually communicates directly with the primary reviewer, but questions could come on behalf of any of the reviewing subject matter experts.

- ◆ Sterilization and pyrogenicity questions typically originate from the Microbiology or Sterilization team
- ◆ Subject safety typically originates from a clinical team review

FORMAL APPROVAL

FDA typically sends its formal approval by email or hardcopy letter on or just prior to Day 30. If no notice of approval or rejection is received by midnight on Day 30, the Investigator may presume the application was approved and begin the investigation (always best to check to confirm).

It is important to note that all parties have the same goal – approval of every application on first ‘pass.’ Investigators are eager to begin their investigations and FDA hopes to prevent an application rejection, likely resulting in a resubmitted application circling back to their desks under another 30-day review window.

WHERE DO I TURN FOR HELP?

Please contact Jen Wall, PAHM, CCRP, at (216) 791-3800 ext. 3578 or Jennifer.wall@va.gov with questions or for assistance regarding your application.

The APTC offers regulatory and quality support, including consulting services, to investigators at any point along their research and development continuums, from earliest concept to human trials. Developing a medical device with the ultimate goal of investigation via human studies? We provide a variety of resources to assist you.

NEWS

VA Deputy Secretary Tours LSCVAMC Research Programs

On March 23, 2018, the Deputy Secretary of the VA, Mr. Thomas Bowman, toured the Louis Stokes Cleveland Veterans Affairs Medical Center and learned more about the innovative research advancements happening in Cleveland. Presentations and demonstrations, including an overview of the sensory restoration prosthetics projects, biking program (*below, left*), and self-leveling walker (*below, right*), were led by Dr. Paul Marasco (*shaking Mr. Bowman's hand, below*) and APTC staff Stephanie Bailey, Kevin Foglyano, Lisa Lombardo, and Courtney Shell.



Congratulations to [Dr. Frank Jacono](#) who received a 2018 Wings of Excellence Cleveland VA Award! This Federal Executive Board award honors those outstanding federal employees who exemplify the best in government service, recognizing employees whose outstanding performance, either on or off the job, have served as an inspiration to others and/or brought prestige to the federal service. This year marks the 32nd anniversary of this event.



Dr. Jacono is an outstanding clinician and distinguished researcher. He initiated two major clinical programs that have distinguished the medical center and resulted in far reaching impact: The Facility Medical Emergency Response System and Delirium Prevention. In the former program, his leadership established a rapid response team leading to early recognition of impending medical emergencies, enhanced stabilization of care, and significantly reduced activations of the full cardiopulmonary arrest team. In the Delirium Prevention initiative, he initiated and led a multidisciplinary delirium resource team that addressed the assessment and prevention of pain, agitation, and delirium in the critically ill. This initiative serves as a model program throughout the medical center. Lastly, he is a recognized academic scholar whose nationally funded research projects benefit the health and well-being of our Veterans. Dr. Jacono's efforts demonstrate excellence and commitment to the VA mission.

DARPA Director and HAPTIX Program Manager Visit

On January 25, 2018, the APTC was visited by the Director of Defense Advanced Research Projects Agency (DARPA), Dr. Steven Walker, and the Program Manager for the Hand Proprioception and Touch Interfaces (HAPTIX) program, Dr. Al Emondi, to see the progression of the sensory restoration projects being conducted at the VA and CWRU. The HAPTIX program aims to help restore full and natural functionality to wounded service members and Veterans. Three APTC research projects are receiving major contracts from DARPA.

Dr. Paul Marasco discusses his DARPA projects related to 1) outcome metrics for advanced bi-directionally integrated prosthetic limbs and 2) kinesthetic feedback to improve the control and agency over prosthetic devices.

A research participant in Dr. Ron Triolo's study with below-knee amputation describes how he perceives natural sensation in his missing limb. This achievement was made possible by electrically stimulating his peripheral nerves using cuff electrode technology.



In Dr. Dustin Tyler's lab, a research participant who has regained the sense of touch in his prosthetic hand using an implanted neuro-electrical stimulation system emotionally described what participation in this project has meant to him. He also demonstrated how he could control a robot hand in a different room with the Microsoft Hololens virtual reality system.



Using a Hololens headset to see the robotic hand, he controlled its movements using muscle implants in his residual arm and felt the touch on the robotic hand through the neuro-electrical stimulation. Dr. Walker was able to watch using another Hololens headset.



[Dr. Kath Bogie](#) was an **invited speaker for the first annual Association for the Advancement of Wound Care Pressure Ulcer Summit** in Atlanta, GA in February. The conference brought together leaders on an international scale in wound care and pressure ulcer prevention and management to present the latest research in the field. The purpose of this interactive program was to:

- ◆ Examine the pathophysiology of pressure induced tissue damage / ulcer development
- ◆ Explore innovations in clinical care and challenges in pressure ulcer documentation
- ◆ Identify research to advance the science of pressure ulcer prevention and management

Be sure to look for the next summit in 2019!



Nature Outlook: The future of Medicine released a collection of articles featuring research that is taking health improvement to the next level. In the article titled *The mind-reading devices that can free paralyzed muscles*, [Dr. Jeffrey Capadona](#) describes the challenges researchers are facing from the body's inflammatory response on devices implanted in the brain. He is currently developing a coating that can act as an antioxidant and prevent consequences such as scarring, device corrosion, and even neuron death.



<https://www.nature.com/articles/d41586-018-02478-0>

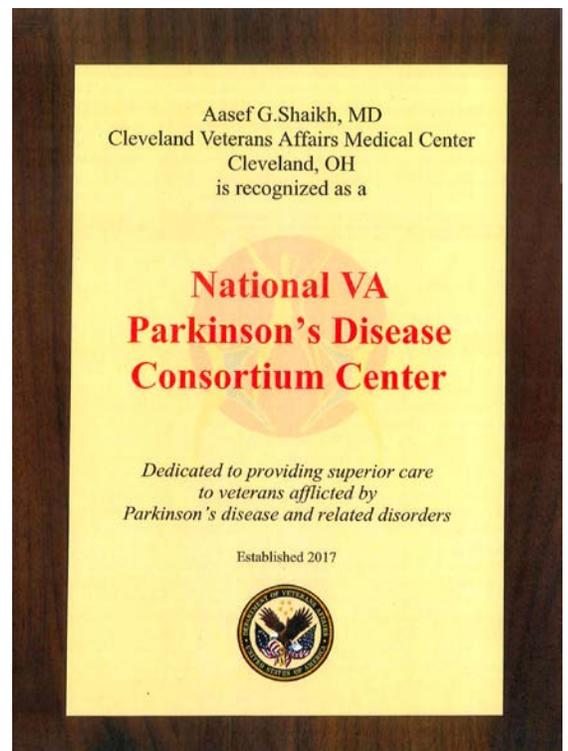
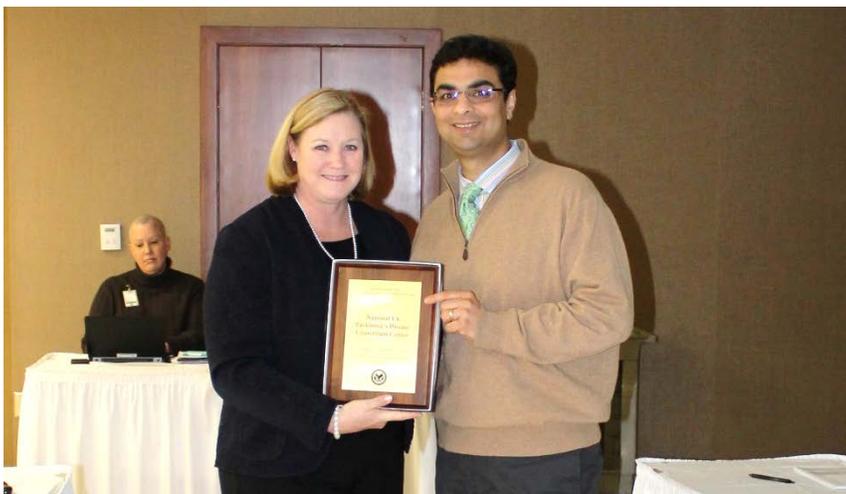
nature

The APT Center is privileged to be a part of the NorthCoast 99 winning organization Louis Stokes Cleveland Veterans Affairs Medical Center, one of the 99 great workplaces for top talent in Northeast Ohio. We are proud to be a member of this team!



<https://www.northcoast99.org/>

On April 5th, [Dr. Aasef Shaikh](#) was presented with a plaque by LSCVAMC Director Susan Fuehrer which designates our medical center as a Parkinson's Disease Consortium Center. The 51 established Consortium Centers ensure accessibility and continuity of specialized care for veterans afflicted by parkinsonism, regardless of locality. Dr. Shaikh serves as the Center's Director.



RECENT PUBLICATIONS

Neuromodulation: Comprehensive Textbook of Principles, Technologies, and Therapies

Second edition

Edited by: ES Krames, PH Peckham, AR Rezaei

Ch 20: Electrodes for the Neural Interface

Author: **Tyler DT**

Ch 28: Prospects for a Robust Cortical Recording Interface

Authors: **Shoffstall A, Capadona JR**

Ch 97: Lower-Extremity Motor System Neuroprostheses

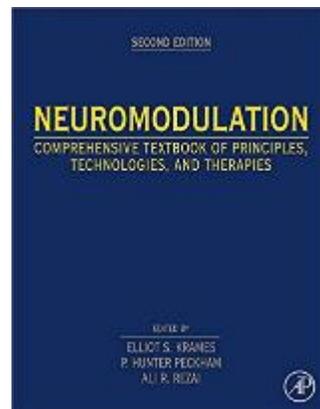
Authors: **Audu M, Kobetic R, Selkirk S, Triolo RJ**

Ch 103: Neuroprostheses for Restoring Sensation

Author: **Tyler DT**

Cha 108: Upper-Airway Neurostimulation to Treat Obstructive Sleep Apnea

Authors: Damato EG, Decker MJ, **Schiefer MA**, Baskin JZ, Benderro GF, Strohl KP



Excerpt from the Introduction: “The field of neuromodulation has become one of the premier and most innovative specialties of implanted technology in the body to improve neurological deficits and overall function of patients. New chapters and additions in this edition cover a variety of important topics that reflect the evolution and growth of neuromodulation.”

Audu ML, Odle BM, Triolo RJ

Control of standing balance at leaning postures with functional neuromuscular stimulation following spinal cord injury

Medical & Biological Engineering & Computing, 56:2, 2018.

[Link to article](#)

Benderro GF, Gamble J, **Schiefer MA**, Baskin JZ, Hernandez Y, Strohl KP

Hypoglossal Nerve Stimulation in a Pre-Clinical Anesthetized Rabbit Model Relevant to OSA

Respiratory Physiology & Neurobiology, Vol 250, 2018.

[Link to article](#)

Ereifej ES, Rial GM, Hermann JK, Smith CS, Meade SM, Rayyan JM, Chen K, Feng H, Capadona JR

Implantation of Neural Probes in the Brain Elicits Oxidative Stress

Frontiers in Bioengineering and Biotechnology, 6:9, 2018.

[Link to article](#)

Hermann JK, Ravikumar M, Shoffstall AJ, Ereifej ES, Kovach KM, Chang J, Soffer A, Wong C, Srivastava V, Smith P, Protasiewicz G, Jiang J, Selkirk SM, Miller RH, Sidik S, Ziats NP, Taylor DM, Capadona JR

Inhibition of the Cluster of Differentiation 14 Innate Immunity Pathway with IAXO-101 Improves Chronic Microelectrode Performance

Journal of Neural Engineering, 15:2, 2018.

[Link to article](#)

Marasco PD, Hebert JS, Sensinger JW, **Shell CE**, **Schofield JS**, **Thumser ZC**, Nataraj R, Beckler DT, Dawson MR, Blustein DH, Gill S

Illusory movement perception improves motor control for prosthetic hands
Science Translational Medicine, 14:10, 2018.

[Link to article](#)

Plegue TJ, **Kovach KM**, Thompson AJ, **Potkay JA**

Stability of Polyethylene Glycol and Zwitterionic Surface Modifications in PDMS Microfluidic Flow Chambers
Langmuir, 34:1, 2018.

[Link to article](#)

Shahdoost S, Frost SB, Guggenmos DJ, Borrell, JA, Dunham C, Barbay S, Nudo RJ, **Mohseni P**

A brain-spinal interface (BSI) system-on-chip (SoC) for closed-loop cortically-controlled intraspinal microstimulation

Analog Integrated Circuits and Signal Processing, 95:1, 2018.

[Link to article](#)

Shoffstall AJ, **Srinivasan S**, **Willis M**, Stiller AM, Ecker M, Voit WE, Pancrazio JJ, **Capadona JR**

A Mosquito Inspired Strategy to Implant Microprobes into the Brain
Scientific Reports, 8:122, 2018.

[Link to article](#)

(JCI Cover) Stavrou EX, Fang C, Bane KL, Long AT, Naudin C, Kucukal E, Gandhi A, et al.

Factor XII and uPAR upregulate neutrophil functions to influence wound healing
Journal of Clinical Investigation, 128:3, 2018. ----->

[Link to article](#)

Zamani H, Bahrami HR, Chalwadi P, Garris PA, **Mohseni P**

C-FSCV: Compressive Fast-Scan Cyclic Voltammetry for Brain Dopamine Recording

IEEE Transactions on Neural Systems and Rehabilitation Engineering, 26:1, 2018.

[Link to article](#)



TRAINING AND EVENTS

VENDOR AUDITS

Our Quality Systems Specialist, Ed Panek, will be conducting an audit of Ardiem Medical on May 9th.

Please contact Ed at Edward.panek@va.gov if you are having any issues or concerns with this vendor.

APT Center Distinguished Lecture Series

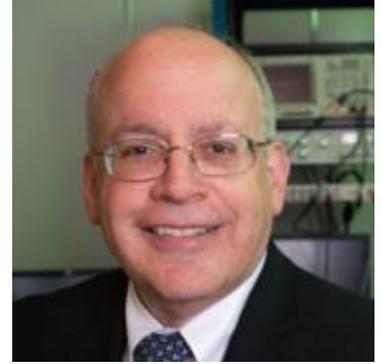
Restoring function with neural prostheses: work towards the development of more effective stimulation strategies

Presented by Shelley Fried, Ph.D.

April 13, 2018

11:00a – 12:00p

<https://friedlab.mgh.harvard.edu/>



Abstract: The Fried Lab focuses on the design, development and optimization of neural prostheses that target the CNS. Most of their work to date has focused on visual prostheses and has included devices that target the retina or the visual cortex. Retinal devices consist of electrode arrays that are implanted in subjects with outer retinal degenerative diseases, such as macular degeneration or retinitis pigmentosa. Using a combination of computational modeling, electrophysiology and immunochemistry, the team studies the responses of single neurons to artificial stimulation and uses this knowledge to develop new and more powerful stimulation strategies including approaches that better replicate certain aspects of natural signaling. *Key findings will be discussed.*

More recently, this lab has begun to develop a prosthesis designed for implantation into the visual cortex, a device that could be used by returning battlefield soldiers that have suffered traumatic injury of the eye. Their approach uses an array of implantable micro-coils that magnetically stimulate nearby neurons; such an approach is a potentially attractive alternative to conventional micro-electrodes because the asymmetric fields from micro-coils can be harnessed to selectively target or avoid specific types of cortical neurons. *Ongoing efforts to confirm the selectivity and stability of micro-coils and move this technology into clinical testing will be discussed.*

Be sure to stop by the APTC booth at **Research ShowCASE** on Friday, April 20!
9:00am – 3:00pm at the Veale Convocation Center



UPCOMING GRANT DEADLINES

- ✦ April 15 – VA HSRD LOI for CDA
- ✦ April 26 – DARPA: [Full Biological Technologies Office \(BTO\) proposals](#)
- ✦ May 1 – VA BLRD/CSRD LOI for CDA
- ✦ May 1 – VA CSRD LOI for Clinical Trial Merit
- ✦ May 1 – VA HSRD ITS for Merit
- ✦ May 1 – VA RRD LOI for Merit, RCS, CDA
- ✦ May 7 – National MS Society: [Pilot Research grants](#) (pre-appl; appl due May 9)
- ✦ June 1 – Air Force: [FY19 Young Investigator Research Program \(YIP\)](#)
- ✦ June 5 – NIH R01, U01 New Applications
- ✦ June 12 – NIH K New Applications
- ✦ June 12 – VA HSRD Merit, CDA Applications
- ✦ June 12 – VA RRD Merit, RCS, CDA Applications
- ✦ June 16 – NIH R21 New Applications
- ✦ June 27 – Howard Hughes Medical Institute (HHMI): [2018 HHMI Investigator Competition](#)

LINKS TO STANDARD ANNOUNCEMENTS

NIH - https://grants.nih.gov/grants/guide/parent_announcements.htm

VA (intranet) - <http://vawww.research.va.gov/funding/rfa.cfm>

VA (external) - <https://www.research.va.gov/services/default.cfm>

ADDITIONAL FUNDING OPPORTUNITIES

Bridge Funding: A clinician with a BLR&D Merit Award that expired on or after October 1, 2016 and has not secured another VA award can apply for up to \$30K for 6 months.

https://www.research.va.gov/services/blrd/clinician_bridge.cfm

Funding opportunities aggregated by CWRU: <https://case.edu/research/faculty-staff/funding-ops/>

APTC now offers Business Plan templates to help with Transition Plans required in grant applications, such as the NIH. Contact Ed Panek at Edward.panek@va.gov for more details.

Have something to share? Send YOUR good news and professional accomplishments to Rebecca Polito at rpolito@aptcenter.org to include in a future Translation Builder.