

PALMETTO HEALTH • Vol. 3 Issue 3 Summer 2017

Neuroscience Journal

Stem cell therapy –
a promising new
stroke treatment?

pg. 5

Neurology residency program
congratulates inaugural graduating
class of resident physicians

pg. 9

As physician co-leaders of Palmetto Health's neuroscience service,

we share a vision to provide the most advanced neurology and neurological surgery treatments available to the residents of South Carolina. We are excited to share this latest edition of our neuroscience journal featuring articles about stem cell therapy and our inaugural graduating class of neurology resident physicians.



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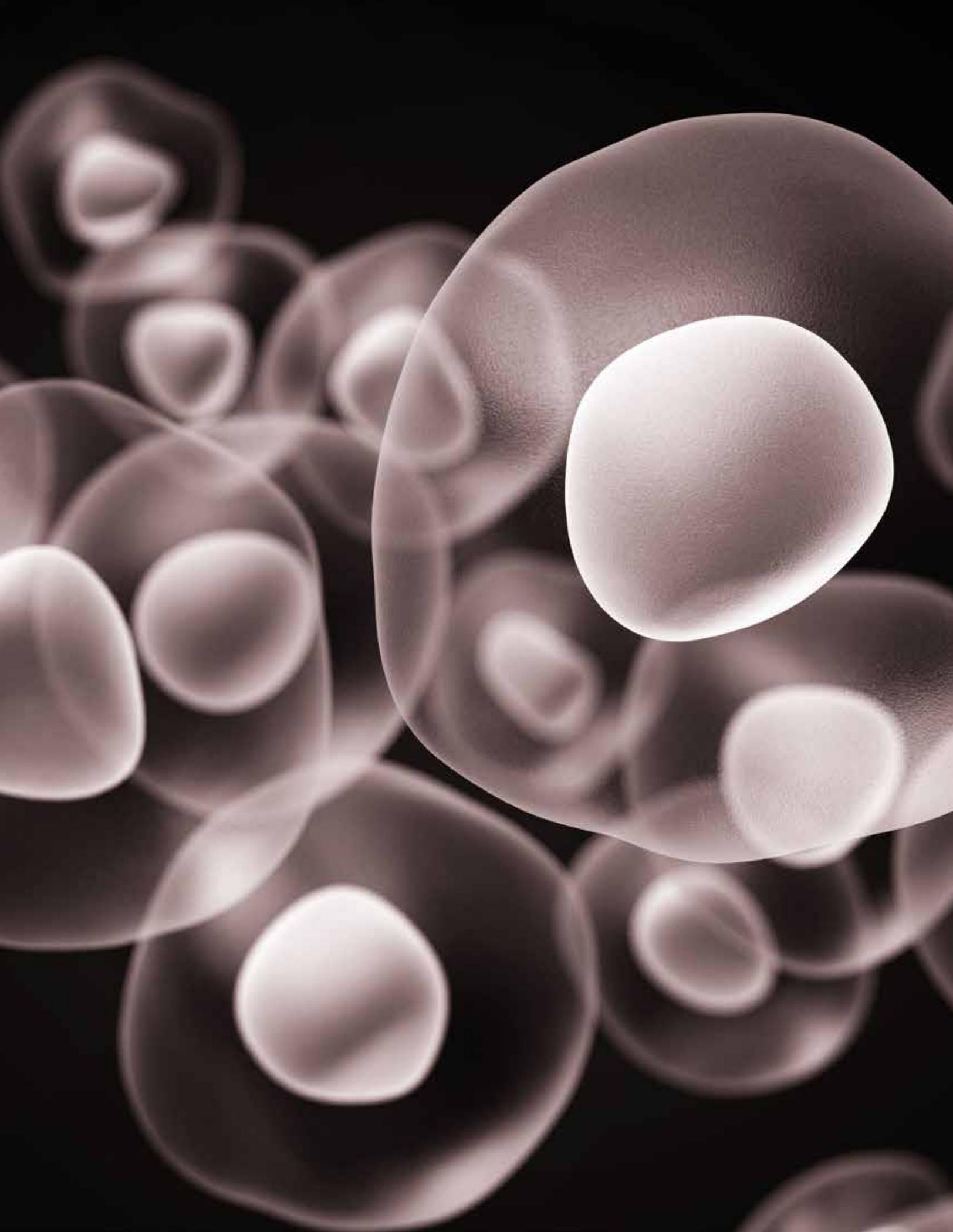
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Call 844-64-BRAIN (27246) for emergent neurosurgical transfers.





Stem cell therapy shows promise for stroke treatment

by Souvik Sen, MD, Neurologist, and Nimit Patel, MD, Senior Neurology Resident

Stroke often is caused by a clot that obstructs blood flow to a region of the brain, resulting in nerve cell death.

Treatments for stroke have largely focused on two methods: dissolving the clot by way of an intravenously administered “clot buster,” known as tissue plasminogen activator; or through catheter-based clot removal, known as endovascular thrombectomy. However, in addition, it is thought that stem cells can potentiate repair of the nerve cells. Acting as a neurorepair agent, stem cell therapy shows promise to be a new stroke treatment avenue.

Although both intravenous tissue plasminogen activator and endovascular thrombectomy continue to be effective treatments for acute stroke, the time window for these treatments from symptom onset limits the majority of patients from benefiting from these therapies.¹ Furthermore, thrombectomy can only be performed at well-equipped stroke centers. Given this, there remains a large and unmet need for safe and widely available treatment for acute stroke.

Basis for stem cell therapy

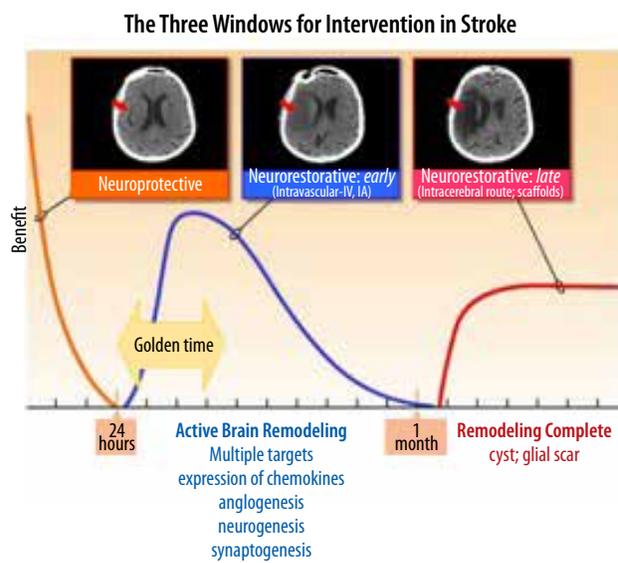
In the first week after a stroke, the activation of the immune system with immune cells, including splenocytes, targets the brain and likely aggravates the ischemic area and prevents remodelling and recovery.^{3,6} This is assumed to be an optimum time window for the administration of bone marrow derived cell therapies for therapeutic benefit. The mechanism of this is not fully understood, but instead of a neuro-restorative mechanism, there is growing evidence suggesting that the benefits may be due to an indirect mechanism such as trophic support of the nervous system and immunomodulation of the immune system and peripheral immune organs, such as the spleen. Regarding the latter, activation and inflammation of the spleen have been shown to occur in rodent models with more recent studies suggesting splenic contraction occurring in humans with acute stroke.^{2,8,9} In addition, T lymphocytes seem to be the leukocyte population that is key in the mediation of the neuroinflammatory response.¹⁰

Stem cell therapy has been promising in animal studies to limit ischemic injury and promote recovery after ischemic stroke in extended time windows.^{2,3} In two Phase 1 clinical trials in patients with stroke, delivery of either neural stem cell line or a mesenchymal stem cell line were shown to be safe.^{4,5} More recently, Palmetto Health played a significant role in a Phase 2, multicenter, double-blind, randomized, placebo-controlled trial of multipotent progenitor cells for treatment in patients with acute ischemic stroke. This study, called MultiStem in Acute Stroke Treatment to Enhance Recovery Study (MASTERS), aimed to establish the highest, well-tolerated, and safest dose of multipotent adult progenitor cells and if there was efficacy for treatment for stroke recovery.¹

Results of MASTERS successfully established that multipotent adult progenitor cell therapy was well tolerated and safe up to a dose of 1,200 million cells. According to the study, this is the largest single dose of intravenous cell therapy given in patients with any disease. The basis of studying this dose was because animal stroke models showed a dose equivalent to this when adjusted for body mass had maximal efficacy.¹

This study also presented some of the first data to show that multipotent adult progenitor cells reduced secondary peripheral immune response after acute stroke by measuring a reduction in serum cytokines, regulatory T cells, and CD3 positive T cells.¹

Regarding the primary efficacy outcome for stroke recovery, there was no difference between multipotent adult progenitor cells and placebo in global stroke recovery at 90 days. However, post-hoc analysis of one-year results for some secondary stroke outcomes such as mRS ≤ 1 , NIHSS ≤ 1 , and Barthel index ≥ 95 , did have statistical significance.¹ These trends of stroke recovery lead us to a larger trial to test the effectiveness of this promising stroke treatment in a Phase 3 trial. Palmetto Health Richland is proud to be a participant in the experimental trial of this innovative treatment for stroke patients in South Carolina. ◀

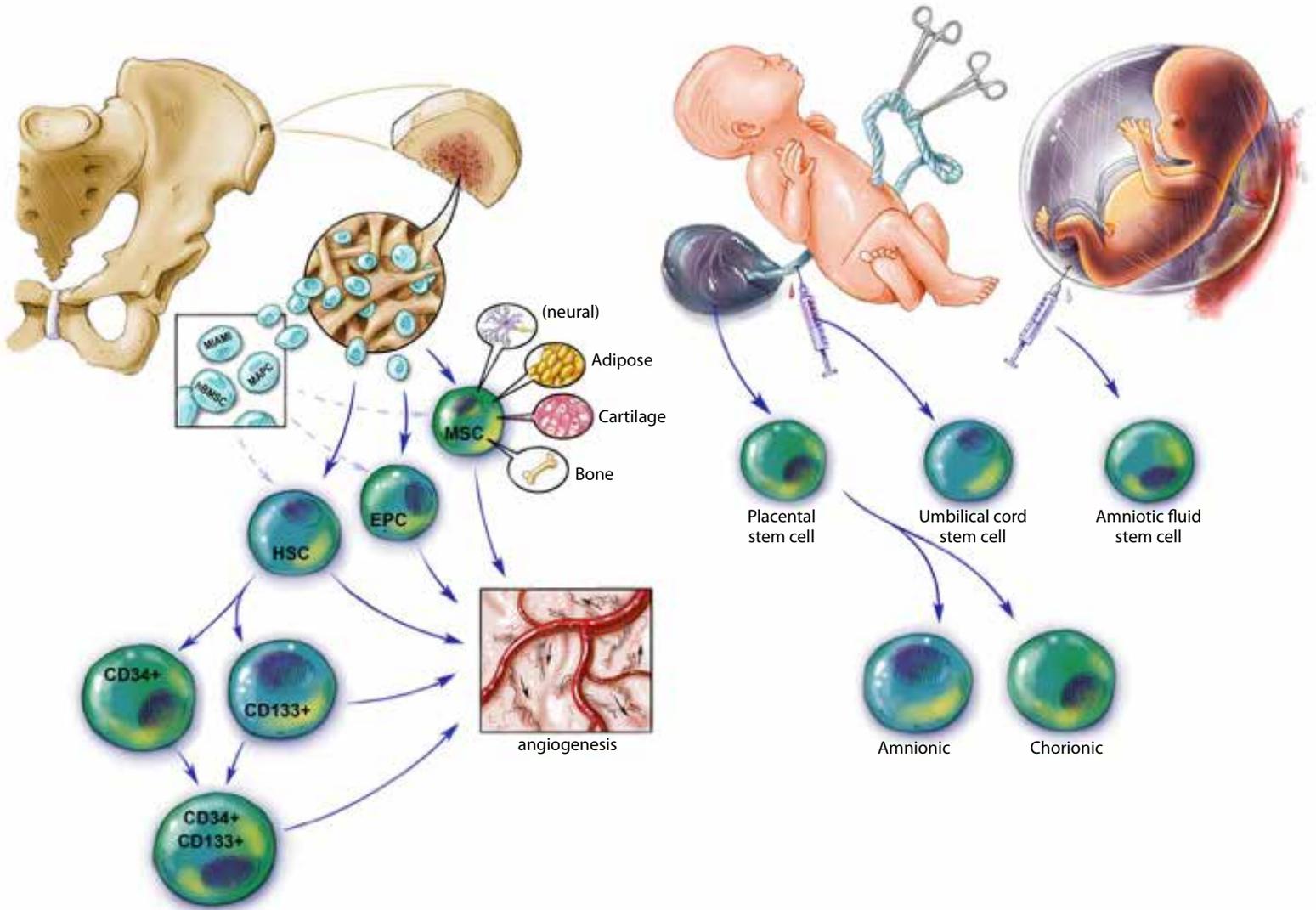


Progression of ischemic changes and the potential "golden time" for stem cell therapy

References

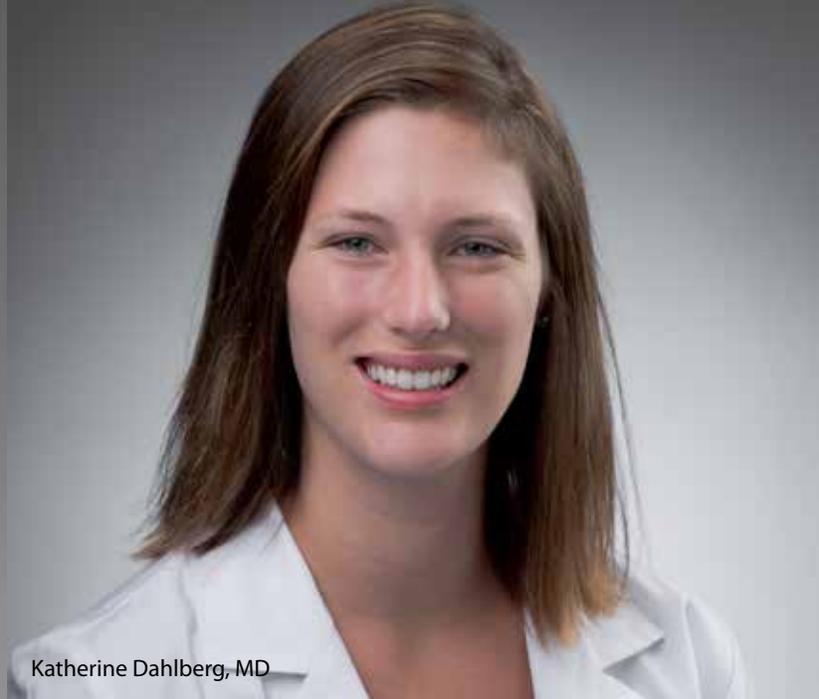
1. David C Hess, Lawrence Wechsler, Wayne Clark, Souvik Sen, et al. Safety and efficacy of multipotent adult progenitor cells in acute ischaemic stroke (MASTERS): a randomized, double-blind, placebo-controlled, Phase 2 trial. *Lancet*, 16 (2017), pp 360-368
2. M Janowski, DC Wagner, J Boltze. Stem cell-based tissue replacement after stroke: factual necessity or notorious fiction? *Stroke*, 46 (2015), pp. 2354–2363
3. SI Savitz, SC Cramer, L Wechsler, S Consortium. Stem cells as an emerging paradigm in stroke 3: enhancing the development of clinical trials. *Stroke*, 45 (2014), pp. 634–639
4. D Kalladka, J Sinden, K Pollock, et al. Human neural stem cells in patients with chronic ischaemic stroke (PISCES): a Phase 1, first-in-man study. *Lancet*, 388 (2016), pp. 787-796
5. GK Steinberg, D Kondziolka, LR Wechsler, et al. Clinical outcomes of transplanted modified bone marrow-derived mesenchymal stem cells in stroke: a Phase 1/2a study. *Stroke*, 47 (2016), pp. 1817–1824
6. H Offner, AA Vandenbark, PD Hurn. Effect of experimental stroke on peripheral immunity: CNS ischemia induces profound immunosuppression. *Neuroscience*, 158 (2009), pp. 1098–1111
7. DC Hess, CA Sila, AJ Furlan, LR Wechsler, JA Switzer, RW Mays. A double-blind placebo-controlled clinical evaluation of MultiStem for the treatment of ischemic stroke. *Int J Stroke*, 9 (2014), pp. 381–386
8. FS Vahidy, KN Parsha, MH Rahbar, et al. Acute splenic responses in patients with ischemic stroke and intracerebral hemorrhage. *J Cerebral Blood Flow Metabolism*, 36 (2016), pp. 1012–1021
9. P Sahota, F Vahidy, C Nguyen, et al. Changes in spleen size in patients with acute ischemic stroke: a pilot observational study. *Int J Stroke*, 8 (2013), pp. 60–67
10. A Liesz, X Hu, C Kleinschnitz, H Offner. Functional role of regulatory lymphocytes in stroke: facts and controversies. *Stroke*, 46 (2015), pp. 1422–1430

Multipotent cells can be derived from bone marrow





Amar Anand, MD



Katherine Dahlberg, MD



Ravish Kothari, MD



Neil Patel, MD

“I feel confident that this program has trained me well to be able to diagnose and treat my future patients.”

Neil Patel, MD



Nikil Swamy, MD

Palmetto Health-USC School of Medicine Neurology Residency Program congratulates inaugural graduating class of resident physicians

by Y. Swamy Venkatesh, MD, Program Director, Palmetto Health-USC School of Medicine Neurology Residency Program, and Rhonda S. Harden, C-TAGME, Palmetto Health-USC School of Medicine GME Program Coordinator II

Neurology is one of the fastest growing specialties in medicine. We are training the next generation of physicians to provide the full spectrum of neurological services and to be at the forefront of patient care, teaching, technology and research. The Palmetto Health-University of South Carolina School of Medicine Neurology Residency Program was established in 2012 to serve the needs of residents of South Carolina who face a severe shortage of neurologists. In June 2017, our first group of recruits celebrated the completion of their residency training.

“We are proud of our first class of graduates,” Dr. Y. Swamy Venkatesh, program director, said at the recent graduation. “It took a lot of courage for these residents to come to a new program,” he said. “Every resident has been instrumental in developing the program curriculum and paved the way for every year of training. Their participation has been key in recruiting more excellent residents to the program. This class will be remembered for their hard work and dedication for many years to come as our program continues to grow stronger.”

Four of the graduating residents will continue their advanced training in the following fellowships: Amar Anand, MD, Neuro Imaging Fellowship at DENT in Buffalo, New York; Ravish

Kothari, MD, Vascular Neurology Fellowship at Palmetto Health-USC School of Medicine, Columbia, South Carolina; Neil Patel, MD, Epilepsy Fellowship at the Medical University of South Carolina, Charleston; and Nikil Swamy, MD, Neuro Critical Care Fellowship at California Pacific Medical Center, San Francisco, California. Katherine Dahlberg, MD, joined a private practice, South Carolina Neurological Clinic in Columbia.

The program is fully accredited by the Accreditation Council for Graduate Medical Education (ACGME), and emphasizes a multidisciplinary approach to the core competencies of patient care, medical knowledge, practice-based learning and improvement, interpersonal skills and communication, professionalism and systems-based practice. It is a four-year training program, with the first year in medicine internship, and then three years specifically dedicated to neurology training.

The first year’s training is a comprehensive clinical experience in the areas of internal medicine and its specialties, including emergency medicine. First-year residents provide medical care for patients within the confines of the team, and gain skills and develop confidence in independent medical decision-making.

Message from Neil Patel, MD, Class of 2017, Chief Resident

“Having been a part of a blossoming program and watching it develop into a neurological powerhouse for the Midlands and surrounding areas of South Carolina over the past four years has been an amazing experience. Residents play an integral role in our program’s development, thus allowing residents to obtain significant exposure to clinical neurophysiology, vascular neurology, headache medicine, neuromuscular disease, neuro-immunology, movement disorders and neuro-ophthalmology. I feel confident that this program has trained me well to be able to diagnose and treat my future patients. The faculty are second to none, and looking back years from now on my experience here, I will certainly value the knowledge I obtained, and more so the friendships formed with faculty and co-residents.”

In their second year, residents are provided comprehensive clinical experience in adult neurology and psychiatry for both outpatient and inpatient diagnosis and management. Thirteen blocks of clinical rotations include adult neurology at Palmetto Health Richland and William Jennings Bryan Dorn VA Medical Center (VAMC).

Third-year residents have an exceptional opportunity to increase their depth of understanding of the field of neurology and to lay the foundation for their future development. The clinical experience during this year is spent at Palmetto Health Richland, Palmetto Health Children’s Hospital, the Neurology Outpatient Clinic and the Dorn VA Medical Center. All the while, residents experience increasing levels of responsibility for patient care and teaching as they attain supervisory roles for residents at earlier levels of training.

In the fourth year, residents develop an extensive knowledge base in neurology and the neurosciences that are both broad and deep. They gain competence at using the medical literature to guide patient care decisions (evidence-based medicine). Residents demonstrate competence in all facets of care provided to neurology patients. The fourth year allows extensive elective options for mentoring, protected time for formulating a career path, intensive literature study, and a clinical or basic neuroscience research QI project. Chief Residents Neil Patel, MD, and Doug Davis, MD, traveled to Washington, D.C., to lobby at the American Academy of Neurology’s “Neurology On the Hill” annual event.

Our program is very collegial and the teaching faculty have an open-door policy which provides an excellent environment of inquiry. Residents support one another and have a great time learning and playing together, as well. Renu Pokharna, MD, served as Game Day host for our first “Neuro Bowl” which pitted fourth-year residents against faculty. The friendly competition proved very valuable in preparing the residents for boards and made learning fun.

In addition, we have a newly accredited Vascular Neurology Fellowship program starting July 2017. The fellowship will provide further training in the subspecialty of Vascular Neurology (Stroke). Ravish Kothari, MD, recent graduate of the residency program, will begin his Vascular Stroke Fellowship this summer as our first fellow in the new program. ◀



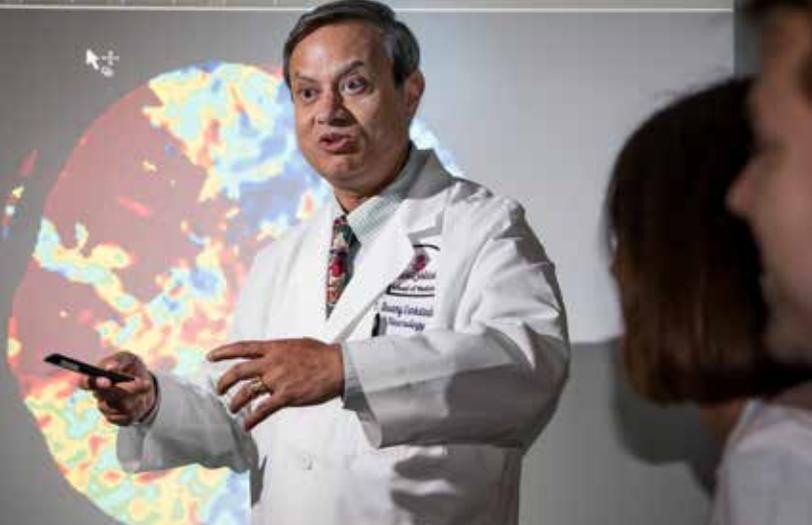
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