In trio of papers, researcher elucidates key biochemical pathways

Andrew McMahon, director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, has recently published three papers that underscore the importance of basic science in developing 21st century medical breakthroughs.

"An important strategy in regenerative medicine is to understand normal mechanisms that generate cell types and harness those mechanisms to regenerate parts of the body,'”

—Andrew McMahon,
director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC

Massry Foundation’s $100,000 grant supports four Keck School research scholars

By Amy E. Hamaker

The Meira and Shaul G. Massry Foundation is best known for the prize in medicine that it offers to noted scientists—10 of the 33 Massry Prize winners have gone on to win Nobel Prizes.

Now, fourth-year students at the Keck School of Medicine of USC can further their scientific careers thanks to a recent $100,000 grant from the Massry Foundation to the Dean’s Fifth-Year Research Scholars program.

Fifth-year scholars receive a stipend of $25,000 each to continue their research. The new grant will support four Massry Research Scholars over the coming year.

“I believe that a student who has finished four years of medical school and is ready to postpone his or her career is motivated to be a scientist, and that’s critical,” said Shaul Massry, professor emeritus of medicine, physiology and biophysics at the Keck School and president of the Massry Foundation.

Massry served as chief of the division of nephrology at the Keck School from 1974 to 2000, and has received honorary doctorates from 14 universities.

He has published more than 600 scientific papers and 111 book chapters and has edited 52 books. He created the Massry Foundation in 1995.

According to Massry, encouraging new scientists is vital to the future of medicine. "Clinical medicine is critical," he said. "It’s very important to take care of patients. But to treat disease and to find the right avenues for medications and therapy, we need to understand the disease and what causes it. You need investigators to search for the cause of disease."

Keck School Dean Carmen A. Puliafito agrees. "I created the Dean’s Fifth-Year Scholar program to give students the opportunity to spend a full year working on focused research projects to prepare them for further research after graduation and encourage them in the development of their academic medical careers," he said. "We thank Dr. Massry for his foundation’s generous contribution to help our students meet those goals."

Massry believes that giving back to others is an integral part of life. "In America, this is often called ‘charity,’” he explained. "But in the Jewish tradition, there is no word for charity—the word in Hebrew is ‘tsedakah,’ which means ‘justice.’ I believe that to share with others and to give for good causes is a justice in this world that we are a part of. To invest as a physician in medical education and the encouragement and support of young people in their research careers is something that I believe is essential. If I can do more, I will not hesitate to do so."

By Hope Hamashige

In his brief tenure as director of the Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC, Andrew McMahon has published three articles, in two key areas of his research, that give insight to both the research that is being carried out at the center and the critical role basic science plays in developing 21st century medical breakthroughs.

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By Ina Fried

Holding a spoon, a cell phone or a baby all require bending and straightening the hand and arm. Most of the time, people take the ability for granted. But when that functionality is damaged or missing, combining microsurgery with orthopaedic surgery may help.

Using microsurgery to transplant a bundle of nerves, muscles and blood vessels restores not only motion, but also the sense of touch, said Milorad Stevanovic, professor in the Department of Orthopaedic Surgery at the Keck School of Medicine of USC. “We’re able to perform cutting-edge microsurgery and achieve a great functional outcome.”

At Keck Hospital of USC, Children’s Hospital Los Angeles, and Angeles County+USC Medical Center, Stevanovic treats a wide variety of hand and upper extremity problems in patients ranging in age from a couple of days to over 90 years old.

For example, Stevanovic and his colleagues repaired and restored function in the forearm of a 7-year-old child who had been unable to flex and extend his fingers since he was 3 years old due to an injury. They were able to do this by transplanting muscles with nerves and blood vessels from the child’s leg to his injured arm. Thanks to surgery like this, a college student with a severe spina bifida (a network of nerves that originate near the neck and shoulder) injury that kept him from bending his elbow is now planning a medical career.

“It’s really amazing that we’re able to take children without fingers and transplant their toes to their hands, significantly improving their motor function. These procedures change children’s lives,” he said.

Recognized internationally for his expertise in treating injuries of the hand, wrist, elbow and shoulder, Stevanovic has extensive experience with patients who have nerve injuries, trauma, burns, tumors and rheumatoid arthritis. A leading authority on reconstructive microsurgery and limb and digit replantation, he recently returned from Fukuoka, Japan, where he was invited to speak at a meeting of the Japanese Society of Reconstructive Microsurgery, attended by almost 1,000 participants.

The first successful replantation of a completely amputated finger occurred in Japan in 1965, and Japan is considered to be “the cradle of microsurgery,” Stevanovic said. “They absolutely dominated the field for a long time, so I was truly honored that they invited me to be a guest speaker at the annual meeting.”

At the conference, Stevanovic spoke about upper extremity reconstruction with free functional muscle transfer. He also discussed the application of microsurgery in elderly patients (those over the age of 70).

Both physicians spoke to attendees about their success rate for reconstruction of the lower and upper extremities in 70- and 80-year-olds is almost the same as in 25-year-olds as long as the older patients do not have comorbidity, such as arteriosclerosis, heart disease or diabetes.

Stevanovic has conducted research on free functional muscle transplantation for extremity reconstruction since 1983, when he began his training in microsurgery at Duke University. He came to the United States from the University of Belgrade in Serbia, where he completed his medical degree. He completed a fellowship in hand surgery at USC before going to Duke and then returned to Belgrade to serve as chief of the hand, upper extremity and replantation team.

On the USC faculty since 1994, Stevanovic is currently the director of the Joseph H. Boyes Hand Surgery Fellowship Program, the oldest such program in the country. The program usually has 60-80 applicants each year for two fellowship positions. Former fellows include five past presidents of the American Society for Surgery of the Hand.

“Fellows are able to gain a wide range of experiences in a good academic setting with outstanding clinical exposure,” Stevanovic explained. “The future of microsurgery lies in advances in supermicrosurgery, as well as in the creation of more powerful microscopes and thinner needle and suture materials,” Stevanovic said. “Even more promising,” he added, “is the combination of these developments with immunology, stem cell research and gene therapy.”

Despite the fact that the field of microsurgery will inevitably expand in the future, “the USC orthopaedic department is currently doing a remarkable job with microvascular reconstruction,” Stevanovic said. For a 10-year-old with a large tumor on her leg, surgeons used vasularized bone from the opposite leg to fill the gap. Twenty years ago, first physicians would have most likely amputated her leg, but thanks to developments in microsurgery, today her limb can be saved.

Undergrad awarded Congressional Hispanic Leadership fellowship

By Sara Reeve

USC senior Pamela Ascon has been awarded the highly coveted Congressional Hispanic Leadership Institute (CHLI) Global Leaders Internship & Fellowship for the spring 2013 Semester.

As one of only four fellowship recipients from across the country, Ascon, who is majoring in health promotion and disease prevention studies at the Keck School of Medicine of USC, will work on project-based programs that provide hands-on experience and also strengthen her understanding of public policy.

“Being selected to be part of the Congressional Hispanic Leadership Institute program has provided me with a once-in-a lifetime opportunity,” Ascon said. “I look forward to expanding my knowledge through the real life experiences this program affords—not only living in the nation’s capital, but working in corporate and nonprofit offices. I look forward to gaining more leadership skills in order to be an asset to society. I am interested in acquiring first-hand understanding of the business, health care and nonprofit worlds.

“I am excited about the doors this program will open and for the experiences I will gain that at this time I can only imagine!” she said.

Through the 12- to 15-week program, Ascon will work closely with congressional offices and private corporations in Washington, D.C., and will earn academic credit hours. The CHLI scholarship includes round trip airfare to and from Los Angeles, a monthly transportation stipend, a $2,000 living stipend, and enrollment and housing at George Washington University for the semester.

Ascon, who serves as co-chair of the USC Institute for Genetic Medicine Art Gallery Internship Program, was brought to the United States by her parents at age 10 and is the first member of her family to go to college. The spring program runs from Jan. 10 to May 5.
Saban Research Institute symposium focuses on origins of health, disease

By Elin Karnaghan
Pediatric research is at a historic moment, and clinicians have the responsibility to take this opportunity to improve the health of children and, ultimately, adults, according to Alan E. Guttmacher, keynote speaker at the third annual Saban Symposium.

Children's Hospital Los Angeles hosted the Dec. 14 symposium, which focused on the developmental origins of health and disease and, in particular, on the developmental mind.

A panel of speakers included a diverse group of nationally recognized experts in addition to keynote speaker Guttmacher, who is director of the Excellence in Shriver National Institute of Child Health and Human Development. He oversees National Institutes of Health research in pediatric health and development, intellectual and developmental disabilities, and other areas.

Drawing on his training as a pediatrician and medical geneticist, Guttmacher offered insight into how the practice of pediatrics has changed, bringing new opportunities and new challenges. He predicted a future in which new partners will be offered a genome screening that will identify all the genetic health risks for their infant. This technology will allow Children's Hospital Los Angeles to provide that family with anticipatory guidance permitting not just the treatment of disease, but also the prevention of disease from its very origin.

Brooke T. McMahon, chair of the Department of Pediatrics at the Keck School of Medicine of USC, discussed the collaborative work that is being done at the CHLA Institute for the Developing Mind, as well as his vision for the future that will include a full range of research and clinical care for children with neurodevelopmental disorders.

The discussions preceded the announcement of the Floyd H. Giles Annual Lecture in Neuroscience Research. For decades, Giles, who was head of the Children's Research Institute and a professor of pathology, has recognized and advocated for the importance of this integrated vision of research and clinical care.

The daylong program included lectures on basic and translational research into neurobehavioral diseases. Although the range of topics was broad, there was one unifying observation—all of these conditions had developmental origins, underscoring the tremendous need for investment into pediatrics research and high-quality clinical care.

MCAHON: Study results show promise

Continued from Page 1

the body to start building a kidney. That information, said McMahon, brings science much closer to the ability to develop treatments for diseased or damaged kidneys.

The other two publications both pertain to pathway signaling—called the Hedgehog pathway—that harks back to research McMahon began two decades ago on Hedgehog cells.

His initial research on the relationship between nerve cells and certain brain diseases led to research on a Hedgehog pathway, which instructs which type of nerve cells form, and where. It also appears to play a role in the development of certain types of cancers including the most common brain cancer in children, medulloblastoma, and basal cell carcinoma—a highly prevalent though usually non-lethal skin cancer.

Both of the recent publications came out of ongoing research to determine the conditions that exist when the Hedgehog pathway begins developing tumor cells and to find ways to modify them in an effort to halt the development of tumors.

The first of the articles, published in ACS Chemical Biology, examines the role of a protein, dubbed Smoothened (Smo), which acts as an on-off switch in the pathway. The research team identified a range of drugs that work in a way that would interfere with the role of Smo in the pathway. The paper tracking work identified a range of new compounds that control the pathway and potential leads for anti-tumor agents.

The second of the publications, called “A novel pathway: Synapsin I regulates Hedgehog signaling,” was published in Oncogene.

The unexpected interplay between these pathways suggests, said McMahon, that the presence of high concentration of glucocorticoids may modify the effects of the newly emerging drugs that are treating Hedgehog pathway-related cancers.

Boyer’s focus is on the Hedgehog pathway and potential leads for drugs that are treating Hedgehog effects of the newly emerging conditions. His lab was awarded a grant from the National Institute of Health to create a new drug that would inhibit the role of the protein called Smoothened (Smo), which is key to the development of cancerous tumors.

Aside from his primary research, Boyer also develops screening drugs, the findings in the other paper in Oncogene.

By Robert Perkins

Fifteen USC scientists—including two with appointments on the Health Sciences campus—have been elected fellows of the American Association for the Advancement of Science (AAAS), chosen by their peers in recognition of their efforts to advance science or its applications.

The AAAS is the world's largest general scientific society and the publisher of the journal Science, which has a readership of 1 million. The nonprofit organization was founded in 1848.

“I am delighted that so many of our faculty have been recognized by their peers with election as AAAS fellows,” said Elizabeth Garrett, USC provost and senior vice president for academic affairs. “This honor affirms the rich diversity and strengths of the scientific research that our faculty engage in on a daily basis and their commitment to create scholarship of consequence.”

This year, 702 AAAS members will be made fellows. The 15 honorees from USC come from the USC Dornsife College of Letters, Arts and Sciences, the USC Viterbi School of Engineering, the Keck School of Medicine of USC and the USC Davis School of Gerontology.

The Health Sciences campus fellows are:

• Norman Anheim, distinguished professor of Biological Sciences, Molecular Biology and Biochemistry, and holder of the Ester Dornsife Chair in Biological Sciences, who has joint appointments at USC Dornsife and the Keck School. He was selected for contributions to molecular evolution and genome structure and to polymerase chain reaction development, including single cell/molecule methods and their application to studying recombination and mutagenesis.

• Margaret Gatz, professor and chair of psychology, professor of gerontology and preventive medicine, and director of the Education Core at the USC Alzheimer Disease Research Center. Gatz has joint appointments at USC Dornsife and USC Davis. She was selected for contributions to the study of mental health of older adults, particularly the analysis of Swedish twins to resolve gene-environment interactions in Alzheimer's disease.

• Fellows are selected from among the society's membership through nomination by a steering group within the association, by three fellows who are currently AAAS members or by the association's CEO. The new fellows will be presented with a certificate and a gold and blue rosette pin symbolizing science and engineering on Feb. 16 at the annual AAAS meeting in Boston.

A Jan. 15 article in the Los Angeles Times opined that Sharon Orrange, assistant professor of clinical medicine at the Keck School of Medicine, about ways to prevent the spread of the virus.

A Jan. 14 broadcast of an America Now story interviewed Alan Nager, associate professor of clinical pediatrics of the Keck School of Medicine and division head of emergency medicine at Children's Hospital Los Angeles, about pediatric injuries related to treadmill equipment.

A Jan. 14 broadcast by NBC News San Luis Obispo affiliate KSBY-TV interviewed David Tishler, assistant professor of clinical pediatrics at the Keck School of Medicine, about a Children's Hospital Los Angeles patient battling Ewing's sarcoma.

A Jan. 14, Men's Journal featured research led by Mariana Stern, associate professor of preventive medicine at the Keck School of Medicine, finding that cooking meat at lower temperatures may lower one's prostate cancer risk.

A Jan. 14 article in U.S. News & World Report featured a HealthDay News story, featured a study led by Anirban Mitra, senior research associate in the Department of Pathology at the Keck School of Medicine, and a colleague, finding that heavy smokers are more likely to develop aggressive, deadly bladder cancers than are nonsmokers.

By Anirban Mitra, assistant professor of neurology at the Keck School of Medicine, finding that depressed stroke survivors may face a higher risk of early death.

A Jan. 11 story by CBS News Los Angeles affiliate KCBSS-TV noted that Debasish “Debu” Tripathy, professor of clinical medicine at the Keck School of Medicine, plans to travel to his native Haiti to oversee a Children’s Hospital Los Angeles donation worth more than $326,000.

A Jan. 11 post on OneLive featured an interview with Deborah “Deb” Ford, vice dean for medical education at the Keck School of Medicine, plans to travel to his native Haiti to oversee a Children’s Hospital Los Angeles donation worth more than $326,000.

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Calendar of Events

Tuesday, Jan. 22

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Noon. Broad CIMR Center Seminar. "Accelerating Human Pluripotent Stem Cell Directed Differentiation of Neural Cell Fates," Stuart Chambers, Memorial Sloan-Kettering Cancer Center. BOC Conference Room. Info: (323) 442-7874

Tuesday, Jan. 22

Thursday, Jan. 24

Friday, Jan. 25
8:30 a.m. Research Seminar. "The Lysophosphatidyls Ipa and Sip: Regulating Fisures in the Lung and Other Organs," Andrew Tager, Harvard. JBD 732-734. Info: (323) 442-7874

11 a.m. "How Pathogens Change Immune Responses – What Does Antigen Presentation Really Mean?" Jeffrey Frailing, University of Arizona College of Medicine. NRT LG505/504. Info: (323) 442-7874

Friday, Jan. 25

Saturday, Jan. 26
11 a.m. – 4:15 p.m. KSIOM 2nd Annual Women’s Health Symposium. Various speakers. KAM Mayer Auditorium. The free symposium is open to health and medical students from across Southern California. Info: (323) 442-2163

Tuesday, Jan. 29
6:30 p.m. – 8:30 p.m. Health Matters: USC physicians discuss health topics you care about. "Geriatric Management," John Lapham, Joesph Zechetter and Nikolai Bildmukzewski. University Club of Pasadena, 175 North Oakland Ave., Pasadena, CA 91101. For more info and to RSVP, log on to usc.edu/esvp (code: HEALTHMATTERS1) or call (323) 442-2805

Wednesday, Jan. 30
8 a.m. Department of Pathology and Laboratory Medicine Grand Rounds. "Cold Case Investigations – the LA County Coroner Experience," Lakshmanan Sathyavagiswaran, USC & UCLA. NOR Topping Tower 7409. Info: (323) 442-1180

Tuesday, Feb. 18

Notice: Deadline for calendar submission is 4 p.m. Monday to be considered for that week's issue—although three weeks' advance notice of events is recommended. Please note that timely submission does not guarantee an item will be printed. Send calendar items to The Weekly, KAM 400 or fax to (323) 442-2813, or email to ebialue@usc.edu. Entries must include day, time, title of talk, first and last name of speaker, affiliation of speaker, location and a phone number for information.

Gift to help create cystic fibrosis exercise room at Keck Hospital

By Amy E. Hamaker

Certified fitness instructor and cystic fibrosis (CF) patient Nikki Adams wasn’t always in the best of shape. A little over a year ago, the 28-year-old Adams was an inpatient at Keck Hospital of USC to treat her condition when a friend suggested she become certified for group fitness instruction. "I used to work in escrow and didn’t do much movement or exercise," said Adams. "I also didn’t do my treatments often enough, so my lung condition wasn’t the best. My friend suggested exercising more to keep my lungs in shape, and she helped me get my certification. My first spin bike class was really hard, but I could tell it was good for me."

The exercise helped. After a month and a half of cycling, her endurance, stamina and lung condition had all improved. This gave Adams an idea of how she could help other CF patients. Adams persuaded her grandparents Lew and Dorothy Webb, founders of the Webb Foundation, a Palm Desert, Calif.-based nonprofit organization, of the importance of exercise to CF patients. She outlined how the foundation could help by creating a special exercise room for Keck Hospital CF inpatients so that they could still exercise while confined to the hospital. Thanks to that conversation, the Webb Foundation’s recent gift of $10,000 will make the room a reality.

Cystic fibrosis is a life-threatening genetic disease that causes thick mucus to build up in the lungs and digestive tract. It is one of the most common chronic lung diseases in children and young adults. According to the National Center for Biotechnology Information, approximately 1 in 29 Caucasian Americans have the gene that causes CF, with a median life expectancy in the 30s depending on diagnosis and treatment. However, regular exercise can help patients reduce the rate of lung function loss, strengthen the heart and help increase healing from lung infections. Aerobic exercise provides the most benefits for those patients who can tolerate it.

"The biggest thing that has helped me with my CF is to stay active—whatever you can do, keep moving," said Adams. "I want to encourage other people with CF to get out there and do everything they can to stay active and keep their lungs fully functioning."

Dorothy Webb, program director for the Webb Foundation and Adams’ grandmother, believes that helping CF patients to extend their lives through exercise is a wonderful goal. "After talking to Nikki and the doctors and nurses at Keck Hospital of USC, we could see there really was a need," she said. "Nikki has gotten such marvelous care there, and we wanted to continue supporting her. "Exercise does so much good for CF patients, and we’re so pleased that we can offer them this help as adults," she continued. "It’s important to support causes you believe in, and I believe that anyone can give at least a little back.”

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