

Massry Prize winners discuss mechanics of protein movement in cells

By Ryan Ball

Next time you're sitting in freeway gridlock, consider the complex system of traffic moving through each and every one of your cells — proteins and other molecules all trying get to the right place at the right time to perform a specific function, such as contacting muscles so you can lay on the horn when the distracted driver in front of you doesn't move.

Uncovering the mechanisms through which that intracellular traffic works earned researchers Michael P. Sheetz, PhD, of Columbia University, James A. Spudich, PhD, of Stanford University and Ronald D. Vale, PhD, of the University of California, San Francisco, the 2013 Massry Prize.

The multidisciplinary trio, who began working together in the 1980s, visited the Health Sciences Campus on Oct. 10 to discuss their work in defining the protein motors that move molecules inside the cell. They also identified the fuels for those motors, a multifunctional nucleotide known as ATP that transports chemical energy within cells.

According to Shaul G. Massry, MD, professor emeritus of medicine and physiology & biophysics at the Keck School of Medicine of USC, the discovery is significant because many diseases develop because of abnormal transport of proteins.



James A. Spudich, PhD, of Stanford University (center) answers a question while Michael P. Sheetz, PhD, of Columbia University (left) and James A. Spudich, PhD, of Stanford University (right) look on during their USC Massry Prize lecture on Oct. 10.

"Imagine a post office," Massry said. "You put your mail in, and they need to take it to a certain address. If they take it to another address, there is chaos. If we don't understand how cells function, we'll never be able to treat derangements."

One abnormality Spudich has been studying is hypertrophic cardiomyopathy, a hereditary condition that affects one in 500 people and is often to blame when seemingly healthy athletes suddenly die during strenuous exercise. A

mutation in the cardiac myosin protein causes cardiac muscle to grow so thick that the heart stops pumping blood efficiently.

While Spudich admits it will be some time before science finds an answer to why the mutations cause the disease, he said that with new understanding of protein motility they can already begin thinking about small molecule therapies that will lower the muscle power output back to normal.

Vale's work over the past decade has been focused on dynein, a motor

protein that is one of the largest protein complexes found in cells. He said dynein has the massive challenge of communicating small chemistry over a relatively long distance from its fuel-bonding site to its "feet" so that it can walk along its microtubule track within the cell.

Vale and his team are detectives investigating how this protein moves, they have uncovered a lot of clues, but have not yet solved the mystery. Still, each clue brings science closer to understanding how to study the many proteins that remain to be studied in biological systems.

"I think we're really going to need to understand the details of how these protein machines work if we're going to think of new strategies of treating disease," said Vale.

Sheetz focused his lecture on how cells use their protein motors and other motility mechanisms to sense their neighbors and their environment to interact dynamically and create the shape of the organism. He's interested in the feedback mechanisms through which cells sense surface rigidity, an issue at the heart of cancer and many other diseases when rigidity-dependent growth becomes abnormal.

"How the cell reacts to that environment and tests that environment decides whether that

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Humayun named inaugural USC Eye Institute director

By Leslie Ridgeway

Mark Humayun, MD, PhD, internationally known for his work on the Argus II artificial retina implant intended to restore sight to the blind, has been named the inaugural director of the USC Eye Institute and interim chair of the USC Department of Ophthalmology.

In his new role, Humayun will take the reins in overseeing advanced surgical techniques and comprehensive care for patients. He will also continue to lead and guide cutting edge transformative research.

"The USC Eye Institute and the USC Department of Ophthalmology together offer a top-ranked clinical practice and world-class research with the potential to cure prevalent and challenging diseases of the eye," said Humayun. "The groundbreaking work at the USC Eye Institute will lead to transformative new solutions for preserving and restoring sight and the USC

Department of Ophthalmology will be the conduit that provides these treatments safely and effectively to patients with vision problems."

Humayun is professor of ophthalmology, biomedical engineering and cell and neurobiology at the Keck School of Medicine of USC and the USC Viterbi School of Engineering. He is a University Professor (the highest recognition for a professor at USC) and also is the inaugural Cornelius J. Pings Chair in Biomedical Sciences. He is a member of both the USA National Academies Institute of Medicine and the National



Mark Humayun, MD, PhD, with the Argus II artificial retina implant.

Academy of Engineering.

In a joint statement, Elizabeth Garrett, JD, USC provost and senior vice president for academic affairs, Carmen Puliafito, MD, MBA, dean of the Keck School of Medicine of USC, and Tom Jackiewicz, MPH,

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USC study: Alzheimer's-linked genetic mutation doubles brain tissue loss rate

By Alison Trinidad

People who carry a genetic mutation associated with Alzheimer's disease may develop the disease three years earlier than expected, according to a new study from Keck Medicine of USC.

Scientists at the Keck School of Medicine of USC have mapped the effects of that genetic mutation, showing for the first time how the Alzheimer's risk factor affects the living human brain. The discovery is detailed in the Oct. 17 edition of *The New England Journal of Medicine* alongside five other studies focused on the TREM2 gene variant, whose link to Alzheimer's was first reported in January.

"Our lab studies the rate of brain tissue loss in elderly people, trying to discover factors that protect you as you age," said Paul M. Thompson, PhD, professor of neurology, psychiatry,

engineering, radiology and ophthalmology and the study's principal investigator. "We have never seen such a dramatic effect as with this genetic variant. If you carry this genetic mutation, we've found that there is this wildfire of tissue loss in the brain."

Healthy people typically lose less than 1 percent of their brain tissue a year, offset by normal tissue generation from mental stimulation, Thompson said. Symptoms of Alzheimer's begin to manifest when approximately 10 percent of the brain's tissue has eroded away.

"This is the first study to use brain scans to show what this gene variant does, and it's very surprising," Thompson said. "This gene speeds up brain loss at a terrific pace. Carriers of this genetic mutation, who comprise about 1 percent of the population, lose about 3

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Keck School researchers awarded grant to study Kaposi's sarcoma-associated herpesvirus

By Jon Nalick

The National Institutes of Health (NIH) have awarded Keck School of Medicine of USC researchers a five-year, \$7.5 million grant to investigate how Kaposi's sarcoma-associated herpesvirus (KSHV) evades the immune system and triggers certain cancers.

Principal investigator Jae Jung, PhD, the Fletcher Jones Foundation Chair and Hastings Foundation Professor of Molecular Microbiology and Immunology at the Keck School, said the research aims to find ways to short circuit the development of Kaposi's sarcoma. This malignant tumor, often caused by KSHV, is more prevalent among people with compromised immune systems, such as patients with AIDS.

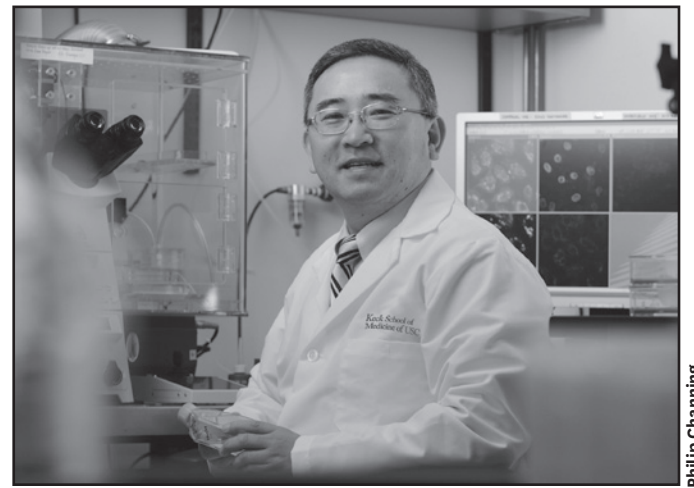
In Africa, he said, where AIDS is endemic and advanced medical treatment is spotty, Kaposi's sarcoma causes as many as half of all cancer deaths.

The NIH grant, awarded through the National Institute of Cancer, will fund three related projects, led by Jung, Pinghui Feng, PhD, associate profes-

sor of molecular microbiology and immunology, and Shou-Jiang Gao, PhD, professor of molecular microbiology and immunology. Each project will be assisted by a genetic core, led by Paula Cannon, PhD, associate professor of molecular microbiology and immunology, and a virology core, led by Hyera Lee, PhD, research assistant professor of molecular microbiology and immunology.

The projects as a whole will examine various biochemical and immunological aspects of how KSHV eludes and manipulates the human immune system to persist indefinitely within the body — and how it initiates the growth of Kaposi's sarcoma.

At present, Jung said, KSHV and other herpesviruses are especially difficult to attack medically: "Herpes is forever. We cannot get rid of it, and it stays with us until we die because the virus has a number of ways to establish a persistent infection. We



Philip Channing

hope our research will become the cornerstone of vaccine development and anti-viral therapy."

Principal investigator Jae Jung received a \$7.5 million grant to help discover how to short circuit development of Kaposi's sarcoma.

HUMAYUN: Best work in clinical practice/translational, basic vision research a priority

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senior vice president and CEO for USC Health, expressed their support for Humayun.

"We look forward to his continued commitment to the highest levels of basic and translational research through his leadership of the USC Eye Institute," the statement said, adding that they "are confident that USC's tradition of strong leadership will be maintained."

Working closely with physicians and researchers to enable them to do their best in clinical practice as well as translational and basic vision research is a priority for Humayun. "We plan to achieve our new goals through continued emphasis on clinical, research and educational missions," he said.

Humayun is internationally recognized for his work on the

treatment of the most debilitating and challenging eye diseases through advanced engineering. This includes the development of therapies for retinal degenerations such as retinitis pigmentosa; macular degenerations such as age-related macular degeneration; retinovascular diseases such as vein occlusions; diabetic retinopathy and retinal detachments.

Humayun was the principal member of a team that developed the Argus II implant, which has been shown to restore sight to some people blinded by retinitis pigmentosa (RP). The Argus II (manufactured and sold by Second Sight Medical Products) was approved for use in the United States by the U.S. Food and Drug Administration in February 2013.

New USC Verdugo Hills Hospital chief operating officer comes home to USC

Paul Czajka, past associate administrator of support services of the former USC University Hospital (now Keck Hospital of USC), has been named chief operating officer (COO) of USC Verdugo Hills Hospital, effective Nov. 4.

Czajka brings more than 20 years of health-care leadership experience, including responsibilities in the areas of nonclinical and clinical operations, construction management, patient electronic health record and Computerized Physician Order Entry (CPOE) implementation, strategic planning and business development.

"This is a new position at USC Verdugo Hills Hospital — one that is crucial as we move forward with our construction and expansion plans and implementation of the electronic health record," said Debbie Walsh, RN, MSN, CEO of USC Verdugo Hills Hospital. "Paul's knowledge and experience make him a perfect fit for the COO position."

Czajka's most recent position was COO at Fountain Valley Regional Hospital and Medical Center. There, his work helped earn the hospital quality awards and accreditations, including



Jason Wallis Photography

Paul Czajka, the new chief operating officer of USC Verdugo Hills Hospital

Joint Commission (JC) Primary Stroke Center, JC Advanced Inpatient Diabetes Care, Society of Cardiovascular Patient Care for Chest Pain Center,

Tenet Innovation Award for Inpatient Diabetes Program and Bariatric Center of Excellence. In addition, he was responsible for all construction projects as well as the successful implementation of its Cerner patient electronic health record and CPOE.

"I am thrilled to be a part of USC-VHH, which offers high-quality and compassionate patient care to the surrounding Foothills community," said Czajka. "This hospital has provided four decades of clinical excellence. I know that there has been a long history for the community to support the

mission and vision of the hospital during these 40 years, which enabled the physicians and staff to provide the highest level of care to its patients.

"It's also exciting for VHH to be a part of the USC family, which will open the door for our patients and community to gain access to specialty services offered by a world-class academic medical center," he added. "This is a very exciting time for Verdugo and USC. I look forward to contributing to the growth and development of health-care services at USC-VHH, and I'm delighted to be appointed COO of USC-VHH."

The Weekly

Next Issue: Dec. 13

The Weekly is published for the faculty, staff, students, volunteers and visitors in the University of Southern California's Health Sciences campus community. It is written and produced by the Health Sciences Public Relations and Marketing staff. Comments, suggestions and story ideas are welcome. Permission to reprint articles with attribution is freely given.

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Courtesy Dawn Fishback

PHYSICIAN ASSISTANTS CELEBRATE Keck Hospital of USC celebrated Physician Assistant (PA) Week for the first time on Oct. 6 - 12. Held every year during those dates, PA Week is a celebration of the PA profession. Pictured here (left to right), Chris Justino, PA-C, Bob Sachs, PA-C, Leah Lovely, PA-C, Dawn Fishback, PA-C, and Lindsay Lapierre, PA-C, helped assemble a table at the Keck Hospital cafeteria to increase awareness of PAs and the importance of a healthy lifestyle; USC PA student Lisa Beedle (not pictured) also helped man the table.

\$4 million grant received to study maternal stress/childhood obesity links

By Sara Reeve

The National Heart, Lung and Blood Institute has awarded a five-year, \$4 million grant to a USC research team to discover whether stress in the lives of working mothers influences risk of childhood obesity in their children.

The project, "Maternal Stress and Children's Obesity Risk," led by Genevieve Dunton, PhD, MPH, will monitor stress levels in mothers through the use of a smartphone app, as well as through salivary cortisol.

"We will examine how parenting practices related to children's eating and physical activity such as modeling, restriction, and encouragement may be compromised on days when mothers experience higher levels of stress," said Dunton, assistant professor in the Departments of Preven-

tive Medicine and Psychology at the Keck School of Medicine of USC.

Approximately 200 ethnically and economically diverse working mothers and their 9- to 11-year-old children will participate in the study over a three-year period, allowing the research team to track obesity risk trajectories during the pre-teen and early teen years.

"Parental stress is an understudied factor that may undermine parenting practices related to children's dietary intake and physical activity," said Dunton. "This study will help to identify families whose children are at greater risk of obesity progression into adolescence based on working mothers' levels of stress."

In addition to recognizing at-risk children, researchers will working on the project will develop

tools to help mothers reduce the impact of stress on their children's eating habits and physical activity.

"The results will inform the development of novel interventions that help working mothers to reduce the negative effects of stress on weight-related parenting practices, and foster family environments that can buffer the effects of maternal stress on children's obesity risk," Dunton said. "Given the detrimental health effects and enormous costs of childhood obesity, such information could be of significant value to efforts to improve public health."

This study brings together an interdisciplinary team of researchers from the Keck School; the USC Dornsife College of Letters, Arts, and Sciences; the USC Davis School of Gerontology; and the USC Spatial Sciences Institute.



Did you know?

In 2012, USC announced an expansion of cancer care facilities made possible by a \$15 million donation from the Kenneth T. and Eileen L. Norris Foundation. The gift supports the construction of the Norris Healthcare Consultation Center, a new outpatient clinic building currently under construction on the USC Health Sciences Campus.

Established in 1963, the Norris Foundation has a long and extensive history of giving to USC, beginning with the philanthropic work of Eileen and Kenneth T. Norris, who funded the Norris Medical Library, the Eileen L. Norris Cinema Theatre and the Norris Dental Center at USC.

That tradition of giving was continued under the guidance of Kenneth T. Norris, Jr., whose lead donations helped establish the USC Norris Comprehensive Cancer Center.

New Keck Medicine PR exec to lead Creative Services

USC Health Sciences Public Relations and Marketing has appointed Tom DeSanto as executive director to lead its newly minted creative services division, bringing with him nearly 20 years' experience working with more than 50 hospitals and health systems as a health-care communications leader.

As executive director, DeSanto will be responsible for further developing the department's creative services team, as well as the materials it produces. He will oversee *Keck Medicine*, *USC Norris Cancer Report*, *The Weekly* and other Keck Medicine of USC publications, as well as new publications being developed for consumers and referring physicians.

DeSanto will guide strategic communications initiatives and lead creative and design services in support of the hospitals and health system, Keck School and health-sciences development. He also will be instrumental in the further

development and implementation of Keck Medicine brand identity guidelines.

"Tom comes to us with a substantial background in



Tom DeSanto

advertising and an extensive work history with health-care organizations across the nation," said Deborah S. Fullerton, MBA, associate vice president of USC Health Sciences Public Relations and Marketing. "His experience, knowledge, leadership and overall work ethic will serve us well as we build a new infrastructure to best support Keck Medicine as it grows."

Prior to joining USC,

DeSanto was president and lead consultant for San Diego-based Tom DeSanto Strategy & Communications. He also served for 15 years as executive vice president of strategic and creative services for an East Coast agency that specialized in health-care marketing.

DeSanto has provided strategic planning, creative direction and brand positioning support to organizations such as Loyola University Health System, NYU Langone Medical Center, Geisinger Health System, Thomas Jefferson University Hospital, Blue Cross Blue Shield of Delaware and University of the Sciences in Philadelphia.

"I'm excited about this opportunity to join such a flourishing organization at such a transformational time," said DeSanto. "I look forward to supporting the important creative and communications needs — both internally and externally — necessary to help advance Keck Medicine as the emerging health-care leader in Los Angeles and beyond."

Amy E. Hamaker

The Weekly ETCETERA

The V Foundation for Cancer Research has awarded **Ite A. Laird-Offringa**, PhD, associate professor of surgery and of biochemistry and molecular biology, a three-year, \$600,000 translational grant to fund her research on the development of immunotherapy for small-cell lung cancer using novel modified antigens. The V Foundation, one of the nation's leading cancer research funding organizations, focuses on aiding cancer researchers transforming lab discoveries into clinical applications and "rising star" scientists.

Keck Hospital of USC was recently awarded the Blue Distinction Centers for Cardiac Care program designation by insurers Blue Shield and Blue Cross for the quality of its cardiac care program. Selection criteria are based on the medical team's expertise, the number of times the hospital has performed various procedures and its track record for results. Blue Distinction

Centers for Cardiac Care must provide a full range of services, including inpatient cardiac care, cardiac rehabilitation, cardiac catheterization and cardiac surgery (including coronary artery bypass graft surgery), and demonstrate better quality and improved outcomes for patients.

The Pediatric Cardiothoracic Intensive Care Unit (CTICU) at **Children's Hospital Los Angeles** has been awarded the national gold-level Beacon Award for Excellence from the American Association of Critical-Care Nurses (AACN). The Beacon Award for Excellence is a three-year designation that merits individual units and its caregivers who distinguish themselves by successfully improving patient care and achieving healthy work environments. Units also meet national criteria consistent with Magnet Recognition, the Malcolm Baldrige National Quality Award, and the National Quality Healthcare Award.

ALZHEIMER'S: Mutation multiplies risk

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percent of their brain tissue per year. This is a silent time bomb in one percent of the world."

Thompson and colleagues compared brain magnetic resonance imaging (MRI) scans of 478 adults (average age 76 years old) participating in the Alzheimer's Disease Neuroimaging Initiative over two years. The group included 283 men and 195 women from across North America; 100 participants had Alzheimer's disease, 221 had mild cognitive impairment and 157 were healthy elderly adults.

Keck researchers found that mutation carriers lost 1.4 percent to 3.3 percent more of their brain tissue than noncarriers, and twice as fast. The loss appears to be concentrated in the brain's temporal lobe and hippocampus, areas that play important roles in memory.

"This TREM2 mutation appears to multiply the risk of Alzheimer's by three or four times, which is very useful information. Enrolling those people who carry the mutation in clinical trials for Alzheimer's treatments could help us reach quicker and more meaningful results," Thompson said.

Co-authors include Priya Rajagopalan, MB, MPH, post-doctoral researcher; and Derrek P. Hibar, PhD, assistant professor, at the USC Imaging Genetics Center, which is directed by Thompson. The study was supported by numerous agencies, including the National Institutes of Health (grants U01 AG024904, P30 AG010129, K01 AG030514, EB008281, EB015922, MH097268, NS080655, AG40060, AG016570).

USC Coulter Translational Program accepting funding applications

The USC Coulter Translational Research Partnership Program is seeking USC faculty applicants for its Pilot and Seed Programs. The submission deadline for pre-proposals is Jan. 15, 2014. The program is open to all faculty members, and the multistep review includes development of a full proposal and an investor pitch.

The one-year awards are for up to \$100,000. Project proposals are evaluated on their clinical merit, potential health-care impact and significance, time line and pathway to commercialization and potential for obtaining further financial investment to translate the particular solution to health care.

The program seeks to fund groundbreaking projects that solve an unmet or underserved clinical need through the use of engineering solutions. The goal of the USC Coulter Program is to support the development of novel health-care

solutions for partnership with a commercial entity and investors to bring concepts to market. Project proposals at all stages of development from concept to implementation are invited for assessment, although the program does not fund discovery research.

The USC Coulter Program is a collaboration between the Wallace H. Coulter Foundation and the Biomedical Engineering Department at the Viterbi School of Engineering. USC partners in the program include the USC Viterbi School of Engineering, the Southern California Clinical and Translational Science Institute within the Keck School of Medicine of USC, and the USC Stevens Center for Innovation.

Applications are available online at <http://coulter.usc.edu/programs-services/>. Inquiries can be directed to coulterusc@gmail.com.

Calendar of Events

Friday, Nov. 22

Noon – 1 p.m. Department of Medicine Grand Rounds. “Glucocorticoid Induced Osteoporosis,” Jennifer Johnson, USC. New Facility, Inpatient Tower, Room C2J104-B. Info: (323) 226-7556

Tuesday, Nov. 26

Noon. Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research at USC. “Directed Differentiation of Human Pluripotent Stem Cells,” Gordon Keller, University Health Network, Toronto. Broad CIRM Center Seminar Room. Info: (323) 442-8084

Noon – 1 p.m. Research Ethics Forum. “Ethical Dilemmas in the New World of Electronic and Mobile Health Technologies,” Alexander Captron, Donna Spruijt-Metz, USC. Aresty Conference Room, LG 503/4. Info: www.uscethics.net

Wednesday, Dec. 4

11:30 a.m. – 2 p.m. USC Health Systems Improvement Collaborative. “Can We Master Patient Safety? Tools, Trends, and Technologies” panel discussion, various speakers. Broad CIRM Center Seminar Room. Info: <http://hsic.usc.edu/>

Friday, Dec. 6

Noon – 1 p.m. Department of Medicine Grand Rounds. “History and Future of the Treatment of Myocardial Infection,” David Shavelle, USC. Inpatient Tower Conference Room B. Info: (323) 226-7556

Noon – 1 p.m. Department of Cardiovascular Medicine Grand Rounds. “Biomarkers in Heart Failure,” Alan Maisel, UCSD. Herklotz Seminar Room, ZNI 112. Info: (323) 442-6130

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) 442-2832, or email to hscwkly@usc.edu. Entries must include day, date, time, title of talk, first and last name of speaker, affiliation of speaker, location and a phone number for information.

The busy lives of KSOM students

Keck School of Medicine of USC students lead busy lives in their clinical and academic studies.

A SAFE HARBOR FOR PATIENTS

Third-year Keck School of Medicine of USC medical student Martin Tolosa examines a patient at the Care Harbor clinic held Oct. 31 to Nov. 3 at the Los Angeles Memorial Sports Arena. The annual event provides free medical and dental care to hundreds of people with limited or no access to health care.

A DAY IN THE LIFE

Keck School of Medicine of USC Dean Carmen A. Puliafito, MD, MBA, speaks at the Parents Association Mini-Medical School on Oct. 25. The annual event offers medical school students’ parents tours of the campus as well as brief seminars about the lives of doctors-in-training.



Photos/Jon Nalick



MASSRY: Discovering how to study proteins

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cell lives or dies,” Sheets said.

The Meira and Shaul G. Massry Foundation established the Massry Prize in 1996 to recognize outstanding contributions to the biomedical sciences and the advancement of health. Each year, a scientific theme is chosen by the Foundation, and a committee of distinguished professors representing both USC and UCLA selects the laureates. The Massry Prize activities at USC are hosted by the USC Institute for Genetic Medicine.

Sheetz, Spudich and Vale find themselves in good company, considering 12 of the 31 Massry recipients have gone on to receive the Nobel Prize. Most recently, 2010 Massry laureates James E. Rothman and Randy Schekman were awarded the 2013 Nobel Prize in

Physiology or Medicine. The full 2013 Massry

Prize lectures can be viewed at <http://tinyurl.com/l1nalme>.

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