Betting Against the Spread
Leading the development of flu vaccines
BCM BITES
While the driving force behind all we do at Baylor College of Medicine lies within our mission, realizing our vision requires a strong financial foundation to support work across all areas of the College.

Over the last few years considerable effort has been focused on creating this foundation. Between fiscal year 2009 and fiscal year 2013, which ended on June 30, 2013, revenue grew by 17.5% while expense growth was limited to 11.9%, demonstrating that we have successfully leveraged opportunities for revenue generation while minimizing expense growth.

In the past year revenue from medical services provided directly by the College grew 7% while our revenue from contracts with our affiliated hospitals grew 15%.
Welcome to BCM Quarterly.

Capturing the essence of an organization as large and complex as Baylor College of Medicine is no easy task. Our new branding (see story page 8) achieves this with just four words, “Giving Life to Possible.”

What does it mean to give life to possible? Creating a future in which devastating flu pandemics are not inevitable, is one example (page 5). Changing the future for one child with epilepsy (page 2) is another.

Our faculty, trainees and staff give life to possible everyday with the many discoveries they make (pages 10-12) and the work that earns them accolades from their peers nationally and internationally (page 3). While we have shared their stories with you through this publication and others, we have never pushed our message to a broader audience with a consistent brand. That’s changing now.

“Giving Life to Possible” focuses on their hands-on work to push boundaries in unraveling the mysteries of the human body. Broadcast, print and web advertising all are part of the campaign.

To see more about the campaign, visit www.bcm.edu/possible.

Best regards.
Paul Klotman, MD
President and CEO, Baylor College of Medicine
John E. and Clara B. Whitmore Chair for the President

TABLE OF CONTENTS
BCM Update ...................................................... 1
Accolades ............................................................3
Betting Against the Spread .............................4
Baylor College of Medicine
Launches First Brand Campaign ...............8
Research Briefs .........................................................10

With a strong focus on data, Katta and Desai address a variety of questions including:
What does it take to impress a medical school interviewer?
What do these interviewers care about?
What qualities would make applicants less likely to be admitted?
What personal qualities are most valued by admissions faculty?

Previous, widely acclaimed books by Katta and Desai include Success on the Wards: 250 Rules for Clerkship Success, The Successful Match: 200 Rules to Succeed in the Residency Match, and Success in Medical School: Insiders Advice for the Preclinical Years.
Baylor College of Medicine is the academic center around which the Texas Medical Center, the world’s largest health science complex, evolved.

Within the four schools of BCM our faculty creates, implements and shares new knowledge, new systems and new technologies that improve the lives of our patients, our community, our nation and our world.

**Baylor College of Medicine** – Consistently ranked as one of the leading research-intensive medical schools in *U.S. News & World Report* and ranked fourth in the nation by StudentDoc.com, BCM is the least expensive private medical school in the U.S.

**BCM Graduate School of Biomedical Sciences** – BCM’s extensive research portfolio combined with faculty who are world leaders in their fields have helped earn our graduate programs ranking among the top 10 percent of graduate programs in biological sciences.

**BCM School of Allied Health Sciences** – Drawing highly regarded applicants from throughout the region and the nation, the programs of BCM School of Allied Health Sciences consistently rank among the best in the country.

**BCM National School of Tropical Medicine** – This is the only school in the nation dedicated exclusively to patient care, research and education related to neglected tropical diseases, the most common infections of the world’s poorest people.

At BCM, leading research and technology translate to exceptional patient care. Our doctors and staff provide a patient-centered, multidisciplinary team approach to healthcare with a focus on quality and safety. More than 2,000 BCM doctors care for patients in over 40 locations across the Houston area, including:

**Baylor St. Luke’s Medical Center**
**Baylor Clinic**
**Lee and Joe Jamail Specialty Care Center**

**Affiliated Hospitals**
- Children’s Hospital of San Antonio
- Harris Health System Ben Taub Hospital and health centers
- Michael E. DeBakey Veterans Affairs Medical Center
- Texas Children’s Hospital
- TIRR Memorial Hermann
- The Menninger Clinic
- The University of Texas MD Anderson Cancer Center
Medical Students Dedicate Day to Make a Difference

First-year medical students at Baylor College of Medicine fanned out to 10 community organizations before the first day of classes, enjoying the opportunity to serve their community and work side-by-side with new classmates.

The organizations benefiting from the annual Orientation Service Project included:

- Bo's Place, a bereavement center offering support to children and their families.
- Harris Health System.
- The Center for Serving Persons, a program serving those with developmental disabilities.
- The Center for Hearing and Speech, a program that teaches deaf children to listen and speak without the use of sign language.
- Covenant House, a shelter for homeless, abused and abandoned youth up to the age of 21.
- Neighborhood Centers, a program that provides resources to the community through community centers and other outreach.
- Magnificat House, a shelter for the homeless.
- Sunnyside Multipurpose Center, a multi-service community center.
- PEBBLES (Parental Enrichment to Bring Up Babies and Learn Essential Skills) - an organization started by two second-year BCM students that engages with local homeless youth through the New Haven Center to hold workshops on sexual health and parenting for new/expecting mothers and fathers.

Activities included gardening, putting together patient waiting room care packages, playing bingo with clients, collecting donations, and taking glucose and cholesterol levels at a health fair.

Students Succeed by the Book

A survey published by the Association of American Medical Colleges in 2011 found that it is the interview, not GPA and MCAT scores, that has the greatest effect on whether a student is admitted to medical school.

Unlike the straightforward parameters of grades, tests or extracurricular activities, the components of a successful interview are less clear. Baylor College of Medicine’s Dr. Rajani Katta, professor of dermatology, and Dr. Samir Desai, assistant professor of medicine, have written a new book, “The Medical School Interview: Winning Strategies from Admissions” to help aspiring doctors master this crucial step on their journey to medical school.

With a strong focus on data, Katta and Desai address a variety of questions including:

- What does it take to impress a medical school interviewer?
- What do these interviewers care about?
- What qualities would make applicants less likely to be admitted?
- What personal qualities are most valued by admissions faculty?

Previous, widely acclaimed books by Katta and Desai include Success on the Wards: 250 Rules for Clerkship Success, The Successful Match: 200 Rules to Succeed in the Residency Match, and Success in Medical School: Insiders Advice for the Preclinical Years.
Residents participate in Intern Bootcamp.

**INTERN BOOT CAMP PROVIDES PRACTICAL FOCUS**

Each July, newly minted physicians from around the country arrive at Baylor College of Medicine ready to begin the intern year of their residency training. “Interns come from a variety of backgrounds,” said Dr. Chirayu Shah, associate program director of the Internal Medicine Residency Program at Baylor. “They are anxious to start their residencies but also very receptive to instruction.”

Pre-residency surveys completed by interns over the years showed that some of them never had formal medical school instruction in the handling of cross covers—when a resident takes over the care of another physician’s patient. Others expressed feeling uncomfortable performing certain procedures.

In 2012 Drs. Prathit Kulkarni, Kaushal Patel, Nainesh Shah and Luke Cunningham, all residents in the BCM Internal Medicine Residency Program developed the Intern Boot Camp. In 2013 the program was expanded to include residents in other specialties, opening this program up to about 125 incoming residents who participated in this full-day training before the official start of residency.

The training sessions use simulation to demonstrate common procedures, such as inserting a central line and performing a lumbar puncture. In addition, the boot camp focuses on developing communication skills through a series of presentations on topics such as presenting a patient, cross overs, consults and efficient note writing.

**PATIENT-DOCTOR RELATIONSHIP BOOSTS EPILEPSY RESEARCH**

Within days of birth, Jack Pribaz began having epileptic seizures. In 2012, at age 2, he was found to have a mutation in KCNQ2, a gene encoding a type of electrical signaling molecule, or ion channel, expressed in the developing brain.

Dr. Edward C. Cooper, an expert from Baylor College of Medicine on the KCNQ2 channel, was called in to meet with the family and the child’s medical team in Chicago. Since those first consultations, the Jack Pribaz Foundation and Cooper have collaborated in efforts to address the needs of children with KCNQ2 deficiency, a newly-discovered and severe form of infantile onset epilepsy, which resists treatment with all approved anti-seizure drugs. Patients also have impaired cognitive, language and motor development. Almost always, there is no warning and the mutations are “de novo,” meaning it was not transmitted from either parent.

Cooper, an associate professor of neurology and neuroscience and an investigator with the Baylor College of Medicine Intellectual and Developmental Disabilities Research Center, has been awarded grants from the Jack Pribaz Foundation of Winfield, Ill., the American Epilepsy Society, the Epilepsy Foundation of America, the Pediatric Epilepsy Research Foundation and the National Institute of Neurological Disorders and Stroke, all in support of finding treatments for this rare disease.

Cooper led the establishment of a national network of physicians providing care to patients with this disorder, and the Foundation has served as a resource for parents seeking support and information about the new disease.

“We’re all looking forward to making a difference through research,” said Michael Pribaz, President of the Jack Pribaz Foundation.
“At this year’s Annual Meeting of the American Association of Medical Colleges I had the privilege of accepting a plaque honoring Baylor College of Medicine as a finalist for the Spencer Foreman Award for Outstanding Community Service. I encourage you to visit www.bcm.edu/community to be inspired by the myriad of ways Baylor faculty, staff and trainees are reaching out to help those in need in Houston and around the world.”

Dr. Paul Klotman, president and CEO

Dr. Huda Zoghbi, professor of molecular and human genetics, neuroscience, pediatrics and neurology at BCM, Howard Hughes Medical Institute investigator and director of the Jan and Dan Duncan Neurological Research Institute at Texas Children’s Hospital, received the Dickson Prize in Medicine from the University of Pittsburgh.

Dr. Hardeep Singh, associate professor of medicine at BCM and chief of the Health Policy, Quality and Informatics Program at the Houston VA Health Services Research and Development Center of Excellence, was appointed by the U.S. Secretary of Health and Human Services to serve on the Clinical Laboratory Improvement Advisory Committee for a four-year term.

Dr. Jason Yustein, assistant professor of pediatrics, and Dr. Wendy Allen-Rhoades, instructor of pediatrics, at BCM were spotlighted for their research in pediatric oncology by the Conquer Cancer Foundation.

Nancy Wilson, assistant professor of medicine—geriatrics at BCM, was selected as the recipient of the 2013 Maxwell A. Pollack Award funded by New York Community Trust on behalf of the Gerontological Society of America.

Dr. Jonathan Clark, associate professor in the Center for Space Medicine at BCM, won the 2013 American Institute of Aeronautics and Astronautics’ Jeffries Aerospace Medicine and Life Sciences Research Award.

The Vallbona Health Center, formerly Harris Health System’s People’s Community Health Center, was dedicated in honor of Dr. Carlos Vallbona, professor of family and community medicine at BCM, for his legacy of care to the residents of Harris County.

Drs. Neil Hanchard and Sandesh Nagamani, both assistant professors of molecular and human genetics at BCM, have received career developmental awards from The Doris Duke Charitable Foundation to support their transition to becoming independent clinical researchers.

Dr. Laura Medford-Davis, emergency medicine chief resident at BCM, has been selected as a 2014 Robert Wood Johnson Foundation Clinical Scholar.

Drs. Neil Hanchard and Sandesh Nagamani, both assistant professors of molecular and human genetics at BCM, have received career developmental awards from The Doris Duke Charitable Foundation to support their transition to becoming independent clinical researchers.

Dr. Meenakshi Hegde, instructor of pediatrics—hematology/oncology at BCM, was awarded the 28th Schweisguth Prize from the International Society of Pediatric Oncology for the best scientific paper by a trainee.

Dr. David Berger, professor of surgery and vice president and chief medical officer of the Baylor College of Medicine Medical Center, has been appointed to the editorial board of the American Journal of Surgery.

Dr. David Burgan, a postdoctoral fellow in the laboratory of Dr. Robert Bryan, professor of anesthesiology at BCM, received both the Young Investigator Award and Best Poster Award at the 13th International Conference on Endothelin.

Drs. Ming-Jer Tsai and Sophia Tsai, professors of molecular and cellular biology at BCM, have been awarded the Lifetime Achievement Award from the Society of Chinese Bioscientists in America.
High resolution 3D image depicting anatomy of an influenza virus.
The Baylor College of Medicine Vaccine and Treatment Evaluation Unit (BCM VTEU), part of the BCM Vaccine Research Center, has been funded by the National Institutes of Health (NIH) for over 40 years. In November 2013, it was one of nine academic institutions in the country to receive a new VTEU contract from the National Institute of Allergy and Infectious Diseases of the NIH. The BCM VTEU has the potential to receive up to $135 million per year for seven years.

Over the four decades of its operations, the BCM Vaccine Research Center has led and been involved in numerous vaccine development initiatives and clinical trials, including ones for prevention of influenza, bacterial pneumonia, pertussis (or whooping cough), respiratory syncytial virus, cytomegalovirus, smallpox, tularemia, anthrax, HIV and parasitic microbes. Their work has led to the licensure of several vaccines, including those against shingles, acellular pertussis, live attenuated influenza (LAIV) and high dose and other flu vaccines. BCM Vaccine Research Center investigators also conducted community trials that documented the safety and value of LAIV, or FluMist®, a nasally administered vaccine.

Influenza, while far from the single focus of the BCM Vaccine Research Center, is a central target of the researchers there, making the College one of the first places to which public officials turn in preparing for seasonal flu and the threat of potential pandemics.

**PREDICTING UNPREDICTABILITY**

The genetic material in the flu virus consists of discrete segments of ribonucleic acid or RNA. “A person or animal may be infected with more than one strain of virus,” said Dr. Wendy Keitel, the Kyle and Josephine Morrow Chair in Molecular Virology and Microbiology at BCM and principal investigator of the BCM VTEU. “When that happens, the pieces of RNA can get rearranged (a process called reassortment), leading to new traits. Mutations also contribute to the appearance of new strains.”

These genetic changes may produce a virus that is more virulent, change an animal virus into one that can be transmitted from person to person, create resistance to drugs, or have other effects. Each year, new strains of flu emerge and vaccines must be prepared to target those strains.

Since birds and other animals can also contract flu, investigators watch these animal populations closely for any signs of new strain that can be transmitted to humans.

Anticipating unpredictability is what flu experts do each year as they try to figure out how to craft a vaccine that will protect against a form of the virus that has not yet emerged. Everyone prepares for the dramatic change that could set off a pandemic, but no one knows what it will be.
In the spring of 2013, a new and deadly strain of bird flu, H7N9, emerged in China. During the initial outbreak, 135 cases were reported in people, 44 of whom died. To date, the virus does not appear to be transmitted easily from person to person, but researchers worry that this could happen any day.

“It is difficult to predict whether H7N9 virus will cause a pandemic, but there is great concern that this virus may gain the ability to transmit easily from person to person,” said Keitel. “If that happens, then rapid worldwide spread could occur.”

Funded by the NIH, Keitel and her colleagues at the BCM VTEU are participating in a study involving nearly 1,000 adults nationwide who will receive different dosages of an investigational vaccine against this new form of the virus. The vaccine is being given with or without one of two adjuvants, substances added to vaccines to increase the body’s immune response.

Generally flu vaccines are given without an adjuvant in the U.S. However, avian flu vaccines prepared without adjuvants fail to stimulate strong immune responses. “One of our primary interests across all diseases has been to enhance understanding of the immunology of vaccine development,” said Keitel. Among other things, this work led to the discovery that adjuvants improve the immune response to avian viruses.

“This is particularly important in a pandemic as the adjuvant may allow lower doses of vaccine to be used,” said Keitel. In the midst of a pandemic, it is not always possible for manufacturers to produce enough vaccine to meet demand. By reducing the amount of virus needed to elicit an effective immune response, adjuvants may help increase vaccine supply.

Rushing against the clock to try to avert a pandemic is familiar ground for Baylor College of Medicine researchers.

In the spring of 2009, a different influenza virus suddenly appeared. The novel virus, commonly called swine flu, is named 2009 influenza A (H1N1). Unlike the H7N9 bird flu, H1N1 swine flu can spread easily from person to person. As a result of the rapid, global spread of H1N1, the first pandemic of the 21st century was declared in June 2009.

After the virus emerged, Dr. Gail Demmler-Harrison, professor of pediatrics at BCM, began the ticklish process of growing the virus in culture. Success in that endeavor enabled her to help public health experts across the world put together a genomic picture of the virus itself.

By May of 2009, Keitel and her team were collecting samples from local swine flu patients to facilitate the immunological groundwork needed to develop a vaccine against the disease. The BCM VTEU also conducted trials of vaccines for H1N1, providing critical support to bring the vaccine to the general population rapidly and curtail the impact of this pandemic.

For more than a decade, experts have anticipated the “coming out” of the avian influenza virus—known as H5N1.

“The 2009 pandemic of H1N1 influenza virus that circled the globe in short order demonstrated how quickly a new influenza virus to which we do not have previous exposure can spread,” said Dr. Andrew P.
Rice, professor of molecular virology and microbiology who holds the Nancy Chang, Ph.D. Professorship in the department. “While that virus turned out to be mildly pathogenic, the avian virus called H5N1 is highly pathogenic. Of the known human H5N1 infections, about 60 percent have died.”

The virus has yet to be transmitted efficiently from person to person. Most people acquire the infection through contact with infected birds.

In 2010, Rice and colleagues from Baylor and The University of Texas at Austin identified a special subversive weapon this organism brings to the fray – four tiny amino acids that hang off the end of a viral protein called NS1. A report of their work appeared in the *Journal of Virology.*

They demonstrated how this grouping of amino acids targets a specific protein that usually protects people by killing cells infected with a virus. This study is one example of many BCM researchers are conducting to understand the functioning of the influenza virus at the molecular level with an eye toward developing new approaches to vaccines and treatments.

Preparing for a potential pandemic of H5N1 also requires new approaches to large-scale, rapid production of vaccine. Both the antigens and the adjuvants needed for vaccine production are finite resources. In a 2009 report published in *Vaccine,* Keitel and colleagues tested the effectiveness of various doses of both antigen and adjuvant in a vaccine for H5N1.

They successfully demonstrated that dose-sparing strategies – approaches that reduce the amount of antigen and adjuvant in the vaccine – could be used without compromising the strength of the immune response. Furthermore, they used antigens grown in cell culture, thus greatly increasing the pace at which antigens can be produced as compared to traditional approaches that utilize eggs.

In addition to working to avert the next influenza pandemic, BCM Vaccine Research Center researchers are engaged in studies to reduce the toll of seasonal flu on vulnerable populations.

“If you look at people who are dying and going to the hospital during an outbreak of season influenza,” says Keitel, “the majority of those people are older individuals.”

Keitel and her team led a study funded by the NIH to compare the effect of different doses of vaccine in elderly patients. They reported in the *Archives of Internal Medicine* that elderly subjects given a higher dose of the seasonal flu vaccine produced higher levels of antibody. Increased antibody production better prepares the elderly to fight off influenza infections. The high dose vaccine is now licensed and recommended by the Center for Disease Control for elderly populations.

BCM researchers have also conducted studies targeting pregnant women and HIV-infected individuals. Some of these populations may not respond to vaccines in the same way as the general population. Since most vaccine trials do not include these populations, BCM researchers conduct separate studies to evaluate antibody responses after vaccination in these populations. These studies have helped to develop specific recommendations for treating vulnerable populations.

For information on ongoing studies related to influenza and other diseases, please contact the BCM Vaccine Research Center at 713.798.4912.
When marketing experts began work on Baylor College of Medicine’s first ever brand campaign, they got some clear direction from the top.

“Make it different from everything out there,” said Baylor President and CEO Dr. Paul E. Klotman.

And after months of research and dozens of conversations with key members of the Baylor community, the national agency Olson delivered “Giving Life to Possible.” The brand campaign debuted in July.

The campaign focuses on the people of Baylor College of Medicine, centering on their hands. “These hands give life to possible.”

Photographer Nadav Kander captured in photos the hands of several Baylor faculty members as well as those of a student for the launch campaign. “Hands can tell so much about a person. They are what we read when we are watching someone. When we talk to someone, we notice what they are doing with their hands. They are very telling,” said Kander.

The print ads feature hands in striking poses, with inspiring copy in a stylized block format.
Some center on a specific person, such as Dr. Brendan Lee, Robert and Janice McNair Chair in Molecular and Human Genetics at BCM and Howard Hughes Medical Institute Investigator. The ad touts his work in human genetics.

“The Hands of an Explorer Aren’t Always Rough.” These hands belong to Dr. Brendan Lee. Relentless in their search for knowledge, they continue to unravel the vast mysteries of the human genome, mapping the very origins of humankind. Dr. Lee’s hands, like all at Baylor College of Medicine, are giving life to possible.

Others describe work throughout the health sciences university.

“The Toughest Fighters Wear the Thinnest Gloves.” These are the hands of Baylor College of Medicine. Every day, in every surgery, lab, classroom and clinic, they push boundaries. Reach beyond expectations and shape truths. Never complacent, always eager to fight, solve and cure, these hands are giving life to possible.

The doctors featured in the first series, along with Lee, are Drs. Emily Sedgwick, assistant professor of radiology, Peggy Smith, professor obstetrics and gynecology, and Julia Nangia, assistant professor in the Lester and Sue Smith Breast Center.

Sedgwick (“Turning Cancer Diagnosis Around”) is a breast cancer imaging specialist who introduced same-day testing services in the Lester and Sue Smith Breast Clinic. Smith (“An Open Hand Can Shelter Our Most Vulnerable Souls”) oversees Baylor’s nine Teen Health Clinics that provide medical and other support services to young adults throughout the Houston area. And Nangia (“Delicate and Caring Yet Determined to Vanquish a Cancerous Foe”) is an oncologist in the Smith Breast Clinic.

“It’s the perfect description of what we do at Baylor College of Medicine every day, across all areas. We are giving life to possible,” he said.

The campaign will continue in 2014 with more stories about Baylor’s advancements and discoveries in science, medicine and education. ■
TOLL-LIKE RECEPTOR 4 A WAYSTATION ON THE ROAD TO ASTHMA

The path to asthma requires a toll – toll-like receptor 4 to be precise, said Dr. David Corry, chief of the section of immunology, allergy and rheumatology in Baylor College of Medicine’s department of medicine and colleagues in a report that appeared in the journal Science. This receptor prompts the innate or immediate immune response that drives allergic disease and asthma, as the immune system marshals its forces to fight off an invading organism or what mimics such invaders. Corry, who holds the Cullen Trust for Health Care Endowed Chair in Immunology, and his colleagues found that enzymes called proteinases carve up the protein fibrinogen, leaving fragments that signal through toll-like receptor 4 to activate the cells of the innate immune system, starting the pathway to allergic disease and asthma.

Funding for this work came from the U.S. National Institutes of Health (Grants HL75243, AI057696 and AI070973 and CA125123) and the C.N. and Mary V. Papadopoulos Charitable Fund.

ABERRANT SPlicing SAPS THE STRENGTH OF “SLOW” MUSCLE FIBERS

“Fast” muscle fibers give you the winning kick in a sprint, but the “slow” or type 1 factors keep you moving in a marathon. It’s the slow muscle fibers that waste away in people with myotonic dystrophy, a form of the disease most likely to occur in adults. In a report in the Proceedings of the National Academy of Sciences, Dr. Thomas A. Cooper, S. Donald Greenberg Chair in Pathology at BCM, and Dr. Zhihua Gao, a post-doctoral associate, describe how an aberrant alternative splicing program changes the form of an enzyme (pyruvate kinase of PKM) involved in the fundamental metabolism of these muscle cells, leaving them unable to sustain exercise as they are converted into the enzyme’s embryonic form (PKM2). (Alternative splicing is the process by which different proteins can arise from the same gene.)

Funding for this work came from the Muscular Dystrophy Association and the National Institutes of Health (Grants R01AR45653, R01HL045565, R01AR060739).

A SPECIAL TRiC PREVENTS PROTEIN AGGREGATION IN HUNTINGTON’S DISEASE

The neurological disorder Huntington’s disease occurs when a defective huntingtin protein forms aggregates, affecting brain function and dooming those who have it to slow degeneration. Inside cells, a protein called TRiC, which assists in the protein folding process, in the presence of mutant huntingtin protein sequesters the soluble huntingtin molecules to prevent them from joining together, while a separate TRiC population caps the tips of the fibrils to prevent them from elongating into larger aggregates, said Dr. Wah Chiu, professor of biochemistry and molecular biology at Baylor College of Medicine who holds the Alvin Romansky Chair in Biochemistry and led a group of researchers from Baylor College of Medicine and Stanford University in the open access journal eLife. To achieve their result they used cryo-electron tomography combined with three-dimensional mapping and computer-aided reconstruction.

Funding for this work came from the National Institutes of Health (Grants PN2EY016525, P41GM103832 and R01GM080139), the Nanobiology Interdisciplinary Graduate Training Program of the W.M. Keck Center for Interdisciplinary Bioscience Training of the Gulf Coast Consortia (NIH Grant T32EB009379).
Researchers at Baylor College of Medicine and the Michael E. DeBakey Veterans Affairs Medical Center answered a qualified yes in a report that appeared in the Journal of the American Medical Association. In a multi-year study that recruited 83 physicians and 42 other health care personnel at 12 different Veterans Affairs hospital-based outpatient clinics, Dr. Laura Petersen, professor of medicine—health services research at BCM and director of the Center for Innovations in Quality, Effectiveness and Safety (IQuEST) at Michael E. DeBakey Veterans Affairs Medical Center and her colleagues found that individual physicians who received modest monetary incentives increased by 8.36 percent the patients whose blood pressure was reduced to desirable levels or whose treatment was an appropriate response according to guidelines—a statistically significant finding. However, incentives to the whole health care team or to the physician plus health care team did not result in a statistically significant reduction.

JAMA. 2013 Sep 11;310(10):1042-50. doi: 10.1001/jama.2013.276303. Funding for this work came from the Veterans Affairs Health Services Research & Development the National Institutes of Health, the National Heart, Lung and Blood Institute, the American Heart Association, the Robert Wood Johnson Foundation, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

MICE WITH RETT SYNDROME BENEFIT FROM STATIN

Treatment with a cholesterol-lowering statin drug lengthened the lifespan and improved some symptoms of Rett syndrome in a mouse model of the disorder, said a group of researchers led by those at Baylor College of Medicine in a report in the journal Nature Genetics. Dr. Monica Justice, professor of molecular and human genetics at Baylor College of Medicine, and corresponding author of the report, did not anticipate this finding when she and her colleagues did a gene screen in mice with a mutation in MECP2, the gene associated with Rett. They found a stop codon mutation in the gene squalene epoxidase that downregulates the cholesterol pathway. When the brain has too much cholesterol, it shuts down production within the brain, stopping the normal process by which cholesterol helps the brain achieve its goals and is then scavenged by glial cells and turned over normally.


SEQUENCING PINPOINTS GENE IN PRADER-WILLI SYNDROME

As so many genetic/genome studies do, this one, published in the journal Nature Genetics, began with a single patient and his parents on a diagnostic odyssey.

The parents of this first patient sought genetic testing for Prader-Willi syndrome when he was only a year old, but the test, still in its infancy, came back negative. For the next 12 years, his parents were left in limbo. He had many features of the disease—including lack of muscle tone, feeding difficulties and failure to thrive early on. Autism spectrum disorder and mild intellectual disability became evident as he grew older.

Dr. C. Thomas Caskey, now a professor of molecular and human genetics at Baylor College of Medicine, referred the patient to Dr. Christian Schaaf, an assistant professor of molecular and human genetics at Baylor College of Medicine and a faculty member at the Jan and Dan Duncan Neurological Research Institute at Texas Children’s Hospital. Schaaf agreed that the boy had many of the outward signs consistent with Prader-Willi, but others were lacking, such as the morbid obesity, which is typically caused by a very aggressive appetite. He suggested whole genome sequencing. Dr. Manuel L. Gonzalez-Garay, another author and an assistant professor and a bioinformatics expert at the University of Texas Health Science Center’s Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases, identified a single change (called a point mutation) in the gene MAGEL2.

Prader-Willi syndrome, an imprinted disease, stems from a mutation in only one of the pair of genes inherited from the parents. (In imprinting, one copy of the gene is silenced and the other is active. If the active copy has a mutation, a disease can result.) In this case, the team from UTHealth and the California life sciences company Complete Genomics then performed an involved analysis that determined that the mutated gene was on the paternal chromosome 15.

“Because the mom’s copy of the gene is silenced and the dad’s copy is deficient, there is no functional copy of the gene in his body,” said Schaaf. Proving the gene was the cause of the disorder meant finding more patients.

A search through the Baylor Whole Genome Sequencing Laboratory found three more patients with mutations in the same gene and some symptoms of Prader-Willi.

“This is the first report of a point mutation causing Prader-Willi syndrome,” said Schaaf. Perhaps someday, he said, it might be possible to “unsilence” the silenced copy of the gene. “It’s been done in mice with other diseases involving imprinted genes, and there’s some evidence it might work in humans as well.”

A technique that pools drug-resistant bacteria with similar kinds of antibiotic resistance and then sequences the DNA of the pools can quickly identify the drugs to which the bacteria are resistant, said Baylor College of Medicine researchers led by Dr. E. Lynn Zechiedrich, professor of molecular virology and biochemistry, in a report that appeared in the open access journal PLoS ONE. “We wanted to understand what genes are changing to make these bacteria resistant to drugs and to give clinicians a way to determine quickly, by measuring just these changes—a process that should take hours as opposed to days, whether the bacterial infection is resistant to drugs—before they give them,” said Zechiedrich, who holds the Kyle and Josephine Morrow Chair in Molecular Virology and Microbiology.

PLoS One. 2013 Jun 18;8(6):e65961. Print 2013. Funding for this work came from the NIH (RO1AI054830) and from a sequencing award from the Applied Biosystems SOLiDTM System $10K Genome Grant Program.

An enzyme called Pif1 promotes the extensive DNA synthesis that occurs through a specific mechanism called D-loop migration—a mechanism very different from that used in regular chromosome replication, said a consortium of researchers led by those at Baylor College of Medicine in a report in the journal Nature. “Instead of the helicase used for replication of chromosomes called Mcm2-7, we found that the Pif1 helicase is very important for the extensive repair-specific DNA synthesis,” said Dr. Gregory Ira, associate professor of molecular and human genetics at Baylor and senior author of the report. (A DNA helicase acts like the pull on a zipper, separating the two strands of DNA during replication. The separation allows each DNA strand to be copied.)

Nature. 2013 Oct 17;502(7471):393-6. doi: 10.1038/nature12585. Epub 2013 Sep 11. Funding for this work came from the US National Institutes of Health (GM080600, ES007061, GM057814, ES015632, GM084242, T32 GM07526-34), National Research Foundation of Korea, Academia Sinica National Taiwan University, and the National Science Council of Taiwan.

Funds for this publication were provided by the BCM President’s Circle.