A multi-institutional team spanning Baylor College of Medicine, Rice University, Stanford University, and the Broad Institute of MIT and Harvard has reported the first successful genome surgery, changing how the genome is folded inside the nucleus.

The advance may lead to new methods of understanding and overcoming genetic diseases.

Last year, researchers at Baylor College of Medicine's Center for Genome Architecture demonstrated that when the 2-meter long human genome folds up inside the nucleus of a cell, it forms roughly 10,000 loops. These loops turn genes on and off, and control how long stretches of the genome are packed. Anomalies in this folding process can lead to disease. The team also discovered a DNA codeword, or “motif,” that lies at both ends of nearly all loops: a string of fewer than 20 genetic letters that causes the DNA to bind a protein called CTCF. More often than not, these motifs lie in what had previously been thought of as “junk” DNA.

Now, in a result with profound consequences for genetic research, a team at the Center, which is directed by Dr. Erez Lieberman Aiden, has demonstrated that by manipulating these motifs, it is possible to destroy, move, and create new loops in the genome. The work, led by co-first authors Adrian Sanborn and Suhas Rao, both graduate students in the Aiden lab and at Stanford University, appears this week in the journal Proceedings of the National Academy of Sciences.

Click here for downloadable video and images (and descriptions) associated with the work.

“We were able to use our insights into how loops form in nature in order to engineer genome loops artificially. This means that it is possible, at least in principle, to fix errors in genome folding by modifying a handful of genetic letters, without disturbing the surrounding DNA,” said Aiden, senior author on the new study, as well as a McNair Scholar at Baylor and a Senior Investigator at Rice University’s Center for Theoretical Biological Physics.

Like the strings on a marionette, loops often connect genes with the DNA elements that control them – even though, when the genome is viewed as a one-dimensional string of letters, those elements lie far away. To modify the code words that create loops without disrupting the surrounding sequence, the team used CRISPR/Cas9-based genome editing, which makes it possible to modify a genome sequence in an extremely targeted fashion. If the team was right about the role of the code words...
STUDENT CORNER: SCHWEITZER FELLOWS

Medical students Jennifer Lee, Diana Whitney, Peter Yeh and Christine Ogugbuaja have been selected as members of the 2015-2016 class of Albert Schweitzer Fellows from the Houston-Galveston area. They will work on yearlong projects that address community health needs.

The Albert Schweitzer Fellowship - Houston Galveston ASFHG is a non-profit organization housed at Baylor that offers students the opportunity to design and implement a health-related community project that provides direct service to an underserved population. Students are paired with mentors, field experts and community sites to meet vital local health needs, with an immediate and lasting impact in the Houston-Galveston area.

Since 2008 nearly 100 Albert Schweitzer Fellows in Houston-Galveston have completed projects in areas such as HIV/AIDS care, homeless support, oral health, nutrition, refugee health, mental health awareness, mobile health clinics, smartphone health apps, family and teen support groups, healthcare education and more.
Four BCM students have been selected to join this prestigious group.

- **Fellow Jennifer Lee** is working in partnership with the Teen Health Clinic to raise awareness of HPV associated cervical cancer among young women through education and increased access to preventative care.

READ LEE’S BLOG ON THE ASFHG WEBSITE

- **Fellows Peter Yeh and Christine Ogugbuaja** are working together to improve the quality of life of adolescent sickle cell disease patients as they transition to adulthood. They are implementing a network of support groups, mentorship programs and workshops in conjunction with Texas Children’s Hospital and community organizations throughout Houston.

READ YEH’S BLOG ON THE ASFHG WEBSITE

READ OGUGBUAJA’S BLOG

- **Fellow Diana Whitney** (in partnership with Fellow Elizabeth Mercer of UT Health Medical School) is working at The Beacon, a Houston-area day center affiliated with the HOMES Clinic, a student-run clinic for the homeless, in order to identify and address health and hygiene needs specific to homeless women.

READ WHITNEY’S BLOG ON THE ASFHG WEBSITE

ASFHG is under the new leadership of Executive Director Dr. Gabrielle Hansen of the Department of Family and Community Medicine.

“I am thrilled to be part of such a wonderful mission and delighted to facilitate links between local community agencies and these enthusiastic fellows. You only have to meet one of our fellows to truly understand that one person can really make a difference. These young people are incredibly inspiring!”

The Albert Schweitzer Fellowship program is recruiting Houston-Galveston based graduate students in all fields for the 2016-2017 fellowship. For more information, contact Hansen at Gabrielle.Hansen@bcm.edu or 713-798-1045, or visit ASFHG on the web at http://www.asfhg.org.

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**BAYLOR GLOBAL INITIATIVES INTRODUCES SMART POD, RECEIVES $1.5 MILLION GRANT FROM THE PAUL G. ALLEN EBOLA PROGRAM**

Emergency managers, first responders and healthcare professionals from around the world took the opportunity to tour the Baylor College of Medicine Emergency Smart Pod during the 2015 Regional Healthcare Preparedness Coalition Symposium in Galveston earlier this month.

The portable four-bed treatment unit that can be rapidly deployed in emergency response situations also has caught the interest of a philanthropist with a history of investing in innovation. The Paul G. Allen Ebola Program recently granted $1.5 million to the College for an enhanced, zero-impact Emergency Smart Pod.

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With lifetime giving totaling more than $2 billion, Microsoft co-founder and investor Paul G. Allen has spent his career tackling some of the world’s biggest challenges and pushing the boundaries of what’s possible. His philanthropy has sparked important developments and innovations in the areas of science, education, conservation, the arts and community improvement.

“The West Africa Ebola outbreak exposed significant gaps in the world’s ability to effectively contain emerging infectious diseases. A rapidly deployable health facility was a clear gap in the early days of the Ebola response. While the world cannot stop every outbreak, we can apply innovative solutions to more effectively fill the gaps to ensure that the next outbreak doesn’t become the next epidemic,” said Barbara Bennett, president and COO of Vulcan Inc., which manages The Paul G. Allen Ebola Program.

“The challenges we face in global health require a radical change in our approaches and models – technologically, financially and culturally,” said Dr. Sharmila Anandasabapathy, Director of Baylor Global Initiatives and the Baylor Global Innovation Center. “The Pod is designed to overcome these challenges by providing a lower-cost, ‘off-grid’ solution to areas that lack medical capacity or need augmentation of existing capacity,”

Baylor Global Initiatives’ concept of an emergency smart pod was selected by the United States Agency for International Development (USAID) earlier this year for President Barack Obama’s challenge to find innovative tools to help fight the Ebola crisis.

This new funding allows expansion of this concept and use of smart technology to build on the initial Ebola treatment unit for confirmed Ebola patients and will help build out the ancillary services of an entire Ebola Treatment Facility. Pharmacies and labs were of great need during the Ebola outbreak, and Baylor Global Initiatives’ efforts to prototype and standardize these facilities should help to improve immediate and effective care of patients with Ebola. This effort can be easily translated to any emergency response situation.

The team also will work on research and development of technologies for the pods, which include a water sanitization system, a drug and supply tracking system, a lab and innovative pharmaceutical technologies. The pharmacy’s layout will be reorganized so that the flow and functionality is appropriate for the specific emergency situation. The standardized triage process for each pod will allow an organized process for patient check-in and tracking through a wristband system where each patient is identified with a QR code.

“We realized in the process of designing and building our USAID Ebola Treatment Unit that there were other capabilities and components that were essential to clinical care in remote regions, particularly during a crisis,” said Anandasabapathy. “The Allen funds will be highly complementary to the USAID unit and, in fact, the two agencies are working together with us closely to advance this effort. You couldn’t really ask for a better team.”

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in creating loops, the results would do more than affect the sequence of the genome: they would change the fold.

“Using CRISPR allowed us to go in with a ‘molecular scalpel’ to add or remove a small number of genetic letters. By knowing exactly which letters we needed to target, we found that it was possible to change how the genome folded in a highly predictable fashion,” said Rao. The new study also demonstrates how loops form inside the genome – and the results were a huge surprise. For decades, scientists thought that loops form when bits of the genome, wiggling around in the nucleus, bump into one another. But the authors found that the cell forms loops by a different process, called extrusion. Sanborn uses the analogy of a backpack to explain how extrusion works.

“Extrusion is the process you use when you’re manipulating the plastic adjustors on your backpack: you feed the strap through on each side, and the slack forms a loop. But the genome is much longer than the strap on a backpack, so the process keeps going and going: more and more slack, a bigger and bigger loop! The key is that the extrusion process stops when it hits a CTCF site. That’s why modifying the motifs is the key to controlling the whole process,” he said.

In each experiment, the researchers modified certain CTCF sites, changing the pattern of CTCF binding. Once they knew that extrusion drives the genome folding process, the team found that knowing where CTCF bound DNA was enough to predict how whole regions of the genome would fold. Modifying the CTCF sites made it possible to destroy loops, to move loops, and to create new loops. It was also possible to predictably modify other folding features, called domains, which are stretches of the genome that all segregate into a single spatial position. In each of over a dozen cases, the team combined mathematics and high-performance computation to predict how the genome would fold in advance. In each case, the genome’s fold closely matched the team’s predictions. In one case, adding a single base pair was enough to change the folding of millions of letters of the genome.

These results are an important step in the process of understanding how the genome folds – and they come just as the National Institutes of Health is launching a 10-year initiative, called the 4D Nucleome project, to explore exactly these questions.

“CTCF sites function like a code for genome folding. Now that we’ve begun to crack the code, we can understand and control the folding process,” said Dr. Eric Lander, co-corresponding author on the paper and director of the Broad Institute.

Others who took part in this work include Su-Chen Huang, Neva C. Durand, Miriam H. Huntley, Andrew Jewett, Ivan D. Bochkov, Dhararaj Chinnapappan, Ashok Cutkosky, Jian Li, Kristopher P. Geeting, Doug McKenna and Elena K. Stamenova all with the Center for Genome Architecture at Baylor; Andreas Gнirke and Alexandre Melnikov with the Broad Institute at MIT and Harvard. Aiden, Sanborn, and Li are also with the Center for Theoretical Biological Physics at Rice University. McKenna is also with Mathemaesthetics, Inc., in Boulder, Colorado.

Funding for this work came from the Welch Foundation, IBM, Nvidia, the National Science Foundation, including a National Science Foundation Center for Theoretical Biological Physics (Grants NSF PHY-1308264 and PHY-1427654), a National Institute of Health New Innovator Award (Grant 1DP2OD008540-01), the Cancer Prevention Research Institute of Texas Scholar Award (Grant R1304), a McNair Medical Institute Scholar Award, and the President’s Early Career Award in Science and Engineering.

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– DR. EREZ LIEBERMAN AIDEN
BAYLOR’S GOLD HUMANISM HONOR SOCIETY NAMED OUTSTANDING COMMUNITY SERVICE ORGANIZATION

Baylor College of Medicine’s chapter of the Gold Humanism Honor Society received the Outstanding Community Service Organization Award from the Association of Fundraising Professionals Greater Houston Chapter on National Philanthropy Day, Nov. 19.

Dr. Vandana Shah, Assistant Professor of Medicine and the Baylor GHHS sponsor, accepted the award, made in recognition of the group’s advocacy for compassionate care through service projects focused on underserved patients, veterans and families of critically ill children.

Founded in 2007, the Baylor GHHS quickly has become one of the society’s most active chapters. Since its inception, the group has inducted more than 250 medical students and, in 2012, in recognition of the chapter’s remarkable commitment, was selected as one of only 10 chapters nationwide to pilot a new program for residents and fellows.

This year, 25 medical students and 25 residents joined the Baylor GHHS. They are leading a variety of projects, including the Gold Closet of clothes for indigent patients at Ben Taub Hospital, a Veteran Appreciation Day at the DeBakey VA Medical Center, and book collecting for the pediatrician-led Reach Out and Read program, and sharing their experiences with others. Through these efforts, the chapter is making an immediate difference in the community while fostering a culture change to relationship-centered, humanistic patient care across the continuum of medical students, residents, fellows and faculty.

ALUMNI DIRECTORY

The Alumni Association has retained the services of PCI to compile the 2016 Baylor College of Medicine Alumni Directory. The firm is reaching out to more than 18,000 Baylor alumni worldwide to confirm their contact and occupational information and accept orders for the directory, which will print this fall. The directory is a great way for alumni to reconnect with classmates for social and business networking and for the College to ensure it has up-to-date information on all alumni. Thank you for participating in this project.