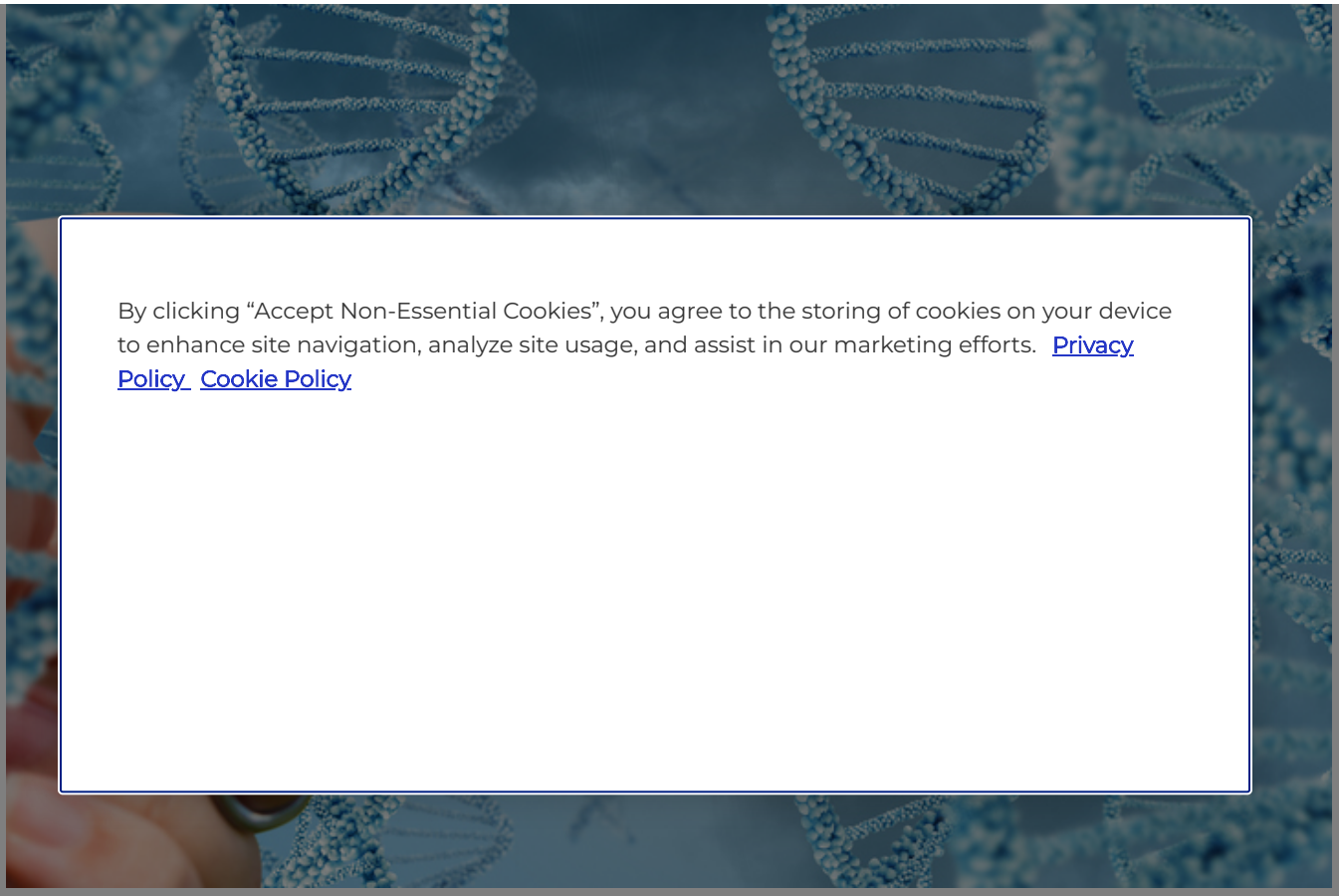
Scientists Develop Chip-Based Platform to Scan DNA for Off-Target CRISPR Effects

July 3, 2017



Despite the signficant promise of CRISPR to correct the genetic underpinnings of disease, the technology still has signficant risk off-target effects—instances when non-targeted genes are altered. Scientists from The University of Texas at Austin took an important step toward safer gene-editing cures for life-threatening disorders, from cancer to HIV to Huntington's disease, by developing CHAMP, which stands for chip-hybridized association-mapping platform. It repurposes next-generation sequencing chips to enable the massively parallel profiling of protein–nucleic acid interactions.

The scientists used CHAMP to provide the first comprehensive survey of DNA recognition by a type I-E CRISPR-Cas (Cascade) complex and Cas3 nuclease. CHAMP, the scientists showed, was able to simultaneously measure the interactions between proteins and ~10^7 unique DNA sequences.

Additional details appeared June 29 in the journal *Cell*, in an article entitled, "Massively Parallel Biophysical Analysis of CRISPR-Cas Complexes on Next Generation Sequencing Chips." These details suggest that CHAMP provides a fra
int

"Ar hat
Cas
art
[nu
nu

Ess
governing off-target DNA binding. This model, for example, suggests that Cascade pays less attention to every third letter in a DNA sequence than to the others.

"So, if it were looking for the word 'shirt' and instead found the word 'short,' it might be fine with that," explained Stephen Jones, Ph.D., a postdoctoral researcher at UT Austin and one of three co-lead authors of the Cell paper.

Knowing such rules could lead to better computer models for predicting which DNA segments a specific CRISPR molecule is likely to interact with. And that can save time and money in developing personalized gene therapies.

"You and I differ in about 1 million spots in our genetic code," said Ilya Finkelstein, Ph.D., an assistant professor in the department of molecular biosciences at UT Austin and the project's principal investigator. "Because of

this genetic diversity, human gene editing will always be a custom-tailored therapy."

The researchers took a DIY approach to developing the equipment and sof eart of t wic for a 3 the tea her res CR

"Ne t here we've turned the technology on its head to allow us to characterize how CRISPR interacts with genomes," noted Andy Ellington, Ph.D., a professor in the department of molecular biosciences, vp for research of the Applied Research Laboratories at UT Austin, and a co-author of the paper.

"If we're going to use CRISPR to improve peoples' health, we need to make sure we minimize collateral damage," commented Dr. Jones. "And this work shows a way to do that."

News & Features | Biological therapy | Clinical medicine | Computational biology | Computational molecular biology | CRISPR | Gene editing | Genetic engineering | Genetic Engineering and Biotechnology | Medicine | Medicine, Diagnosis, and Therapeutics | Molecular medicine | Research and development | Technology and Computational Biology

Therapeutics | Translational research

Al

Leu

Chi

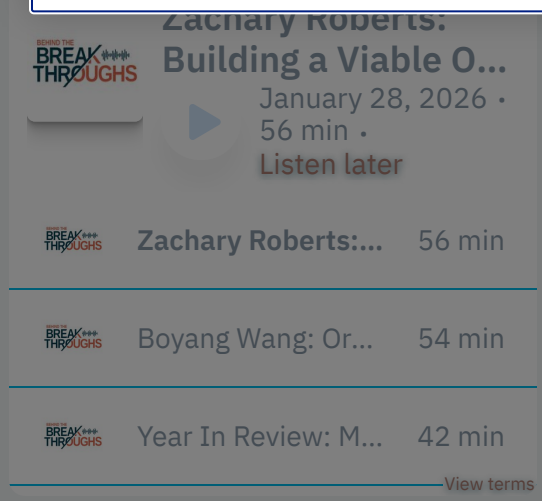
Pill Communicates from Stomach Using Biodegradable Antenna

Cancer’s Immune “Safety Switch” Identified: A Path to Stronger Immunotherapy

Asked and Answered: Prime Medicine CEO on First Prime Editing Patient Data

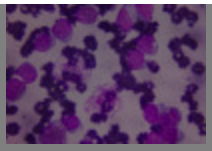
Year in Review: My Personal Genomics Journey Redux

PODCAST SERIES



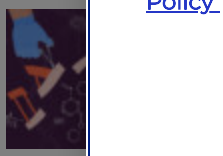
Stay up to date with the latest episodes of *Behind the Breakthroughs* by subscribing to the *IPM* eNewsletter.

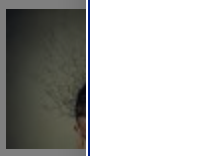
RELATED CONTENT



Leukemia Co-opts Transcriptional Memory, Revealing 'Off-Switch' Protein Targets

Precision Delivery: The Final Mile





Your email address

Sign Up

EXPLORE

About Us