Gene Editing Workshop

MAY 11, 2020

ASGCT
23rd ANNUAL MEETING

BOSTON
MAY 12-15 • 2020
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WORKSHOP SPONSORS

Gene Editing Workshop: Value, Evidence, and Reimbursement Sponsors

The American Society of Gene & Cell Therapy is honored to acknowledge the following organizations for their support of the Gene Editing Workshop:

- Homology Medicines, Inc.
- Beam Therapeutics
- Bluebird Bio
Homology is a clinical-stage genetic medicines company harnessing its broad and proprietary dual gene therapy and gene editing platform into potential one-time treatments for the rare disease community.

Dual Technology
We have a family of 15 adeno-associated virus vectors derived from human hematopoietic stem cells (AAVHSCs) that are capable of in vivo gene therapy and nuclease-free, homologous recombination-based gene editing. Our AAVHSCs have shown broad tissue tropism (ability to enter disease-relevant cells), enabling the selection of the best vector and approach based on disease biology, target tissue and patient population.

Clinical Program
Our investigational gene therapy for adults with the rare disease phenylketonuria (PKU) is being studied in the Phase 1/2 pheNIX trial. To learn more, please visit phenixpku.com.

Homology’s ASGCT 2020 Presentations:

Molecular Characterization of Precise In Vivo Targeted Gene Editing in Human Cells using AAVHSC15, a New AAV Derived from Hematopoietic Stem Cells (AAVHSC)
Abstract #: 227
Date/Time: Tuesday, May 12; 5:30–6:30 p.m.

Molecular Design and Characterization of Packaging Plasmid Sequences for Improved Production of Novel Clade F AAVHSCs
Abstract #: 445
Date/Time: Tuesday, May 12; 5:30–6:30 p.m.

Role of Terminal Galactose in Cellular Uptake, Intracellular Trafficking, and Tissue Tropism Using Adeno-Associated Viruses Isolated from Human Stem Cells (AAVHSCs)
Abstract #: 570
Date/Time: Wednesday, May 13; 5:30–6:30 p.m.

Gene Therapy for Metachromatic Leukodystrophy (MLD) That Crosses the Blood-Nerve and Blood-Brain Barriers in Mice and Non-Human Primates
Abstract #: 590
Date/Time: Wednesday, May 13; 5:30–6:30 p.m.

In Vivo Transduction of Murine Hematopoietic Stem Cells after Intravenous Injection of AAVHSC15 and AAVHSC17
Abstract #: 600
Date/Time: Wednesday, May 13; 5:30–6:30 p.m.

AAVHSCs Transduction Does Not Significantly Elicit p53-Mediated Apoptosis or Alter Cell Cycle in Human iPSCs and Primary Cells When Compared to Non-Clade F AAV Vectors
Abstract #: 1011
Date/Time: Thursday, May 14; 5:30–6:30 p.m.

Development and Scalability of Transfection-Based Production and Purification of Novel Clade F Adeno-Associated Viruses Isolated from Human Hematopoietic Stem Cells (AAVHSCs)
Abstract #: 1248
Date/Time: Thursday, May 14; 5:30–6:30 p.m.

HOMOLOGY MEDICINES’ mission is focused on curing disease and transforming patients’ lives.

www.homologymedicines.com
Gene Editing Workshop

PROGRAM SCHEDULE

All times are listed in Eastern Daylight Time (EDT UTC -4).

1:00 PM - 5:00 PM
ROOM: Ballroom B
CO-CHAIRS: Nicole Gaudelli, PhD and Kris Saha, PhD

1:10 PM - 1:30 PM
Prime Editing: Precise and Versatile Genome Editing without Double-Strand Breaks or Donor DNA
Andrew Anzalone, PhD

1:30 PM - 1:50 PM
Analyzing CRISPR Experiments - From Amplicons to Whole Genome Sequencing
Kendell Clement, PhD

1:50 PM - 2:10 PM
Harnessing Novel CRISPR Systems for Genome Engineering and Human Health
Omar Abudayyeh, PhD and Jonathan Gootenberg, PhD

2:10 PM - 2:30 PM
Assessing Unintended Off-target Mutations Caused by Cas9 and Other Gene Editing Enzymes
Vikram Pattanayak, MD, PhD

2:30 PM – 2:50 PM
Unbiased Detection of CRISPR Off-targets Using DISCOVER-Seq
Beeke Wienert, PhD

2:50 PM – 3:10 PM
Break

3:10 PM - 3:30 PM
AAV Design Strategies for Different Genome Edits
Nicole K. Paulk, PhD

3:30 PM – 3:50 PM
Delivering Cas9 outside the liver by testing thousands of DNA barcoded nanoparticles in vivo
James Dahlman, PhD

3:50 PM - 4:10 PM
Translating Base Editing Technology into a Potential Treatment for Alpha-1 Antitrypsin Deficiency
Michael Packer, PhD

4:10 PM - 4:30 PM
Building a Modular CRISPR/Cas9 Platform for Human Therapeutic Applications
Jessica Seitzer

4:30 PM - 4:50 PM
Best Practices for Achieving Optimal Ex Vivo Genome Editing in Your Research
John A. Zuris, PhD

Eastern Time Zone (EDT UTC -4)
Gene Editing Workshop

CO-CHAIRS

Nicole Gaudelli, PhD
Beam Therapeutics
Cambridge, MA

Kris Saha, PhD
University of Wisconsin-Madison
Madison, WI

Andrew Anzalone, PhD
Broad Institute
Cambridge, MA

Kendell Clement, PhD
Massachusetts General Hospital
Boston, MA

James Dahlman, PhD
Georgia Tech
Atlanta, GA

Jonathan Gootenberg, PhD
Massachusetts Institute of Technology
Cambridge, MA

Michael Packer, PhD
Beam Therapeutics
Cambridge, MA

Vikram Pattanayak, MD, PhD
Massachusetts General Hospital
Boston, MA

Nicole K Paulk, PhD
University of California San Francisco
San Francisco, CA

Kris Saha, PhD
University of Wisconsin
Madison, WI

Jessica Seitzer
Intellia Therapeutics Inc.
Cambridge, MA

Beeke Wienert, PhD
University of California, San Francisco
San Francisco, CA

John A Zuris, PhD
Editas Medicine
Cambridge, MA

Join the Beam Team!

Beam Therapeutics is developing precision genetic medicines through the use of base editing. Proprietary base editors create precise, predictable and efficient single base changes, at targeted genomic sequences, without making double-stranded breaks in the DNA. Breakthroughs in genetic medicines require a unique combination of cutting-edge exploratory science to enable new possibilities.

Our values define how we work together:

- A community of fearless innovators
- Rigorous and honest in our research
- Listening with open minds
- Committed to each other

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The Boston Globe
TOP PLACES TO WORK 2019

May 11, 2020
Omar Abudayyeh is a McGovern Institute Fellow at MIT where he directs a lab exploring microbial diversity for developing next-generation cell profiling, gene editing and gene delivery technologies. These tools, including the popular genome editing system CRISPR, allow for unprecedented manipulation and profiling of cellular states with multiple applications in basic science and for programmable therapeutics and diagnostics. Dr. Abudayyeh also applies many of these tools towards answering fundamental questions about the effect of aging on the brain and other organs with the goal of developing regenerative therapeutics for degenerative disease.

He previously was at Harvard Medical School and MIT as a graduate student in Feng Zhang’s lab at the Broad Institute, where his research centered on novel CRISPR enzymes for genome editing, therapeutics, and diagnostics. He is also co-founder of Sherlock Biosciences, which is commercializing CRISPR-based diagnostics for healthcare. Dr. Abudayyeh was recognized as 2018 Forbes 30 under 30, Business Insider 30 under 30, and a 2013 Paul and Daisy Soros Fellowship. Dr. Abudayyeh graduated from MIT in 2012 with a B.S. in mechanical engineering and biological engineering, where he was a Henry Ford II Scholar and a Barry M. Goldwater Scholar.

Andrew Anzalone, PhD
Andrew is currently a Jane Coffin Childs postdoctoral fellow at the Broad Institute of Harvard and MIT, working in the laboratory of David R. Liu. There, he aims to develop next-generation genome editing technologies for therapeutic applications and basic biological research.

Andrew received his MD and PhD in chemical biology from Columbia University. He carried out his thesis research in the laboratory of Virginia Cornish, where he developed chemical probes for biological imaging and RNA tools for reprogramming the protein translation machinery of the cell. Andrew earned his bachelor’s degree in chemistry from Brown University.

Kendell Clement, PhD
Kendell Clement is currently a postdoctoral research fellow at the Massachusetts General Hospital under the mentorship of Drs. Luca Pinello and Keith Joung. As a computational scientist, he is interested in developing and building analytical methods to understand complex biological processes, particularly using novel assays or approaches. During his PhD in the Harvard-MIT Division of Health Sciences and Technology, he studied epigenetic signatures that are dynamic in development and disease progression, and defined a measure of DNA methylation disorder that utilizes information on individual next-generation sequencing reads. His postdoctoral research has resulted in several software tools to aid in genome editing design and analysis, including the widely used tool CRISPResso2 which is used to quantify genome editing using amplicon sequencing data. In addition to developing fundamental computational strategies for CRISPR applications, he is also part of the NIST Genome Editing Consortium working group charged with defining data and metadata standards.

Jonathan Gootenberg, PhD
Jonathan Gootenberg draws from fundamental microbiology to engineer new molecular tools, which he applies to the study of aging. These tools, including the popular genome editing system CRISPR, allow for unprecedented manipulation and profiling of cellular states in the body, and have multiple applications in basic science, diagnostics, and therapeutics. Along with McGovern Fellow Omar Abudayyeh, Gootenberg uses gene editing, gene delivery, and cellular profiling methods to understand the changes that occur in the brain and other organs during aging, with the goal of generating new therapies for degenerative disease.
group at Harvard University and the Broad Institute. During this time, I
became fascinated by the mechanisms underlying Alpha-1 Antitrypsin Deficiency and I remain motivated to find solutions to serve the unmet needs in this patient population. Before Beam, I was a PhD candidate in Prof. David Liu’s group at Harvard University and the Broad Institute. During this time, I performed research on the directed evolution of proteases. Although it was not the focus of my work, I was exposed to genome editing and the nascent field of base editing.

Vikram Pattanayak, MD, PhD
Vikram Pattanayak, MD, PhD is an Assistant in Pathology at Massachusetts General Hospital and an Instructor in Pathology at Harvard Medical School. He has developed methods to study and/or improve the specificities of homing endonucleases, zinc finger nucleases, TALENs, Cas9, Cas12a, and base editors. In addition to his research activities, Dr. Pattanayak is also a practicing board-certified clinical pathologist and is the medical director of the clinical histocompatibility (HLA) lab at Massachusetts General Hospital.

Nicole Paulk, PhD
Dr. Nicole Paulk is an Assistant Adjunct Professor in the Department of Biochemistry and Biophysics at the University of California San Francisco, as well as an Advisor in Genome Engineering for the Chan Zuckerberg Biohub. Dr. Paulk’s translational gene therapy lab is species/organ/disease agnostic and instead focuses on forging new paths for the entire field by engineering new ways to make AAV cheaper, easier and faster. Her lab combines bioengineering, viral gene therapy and ‘omics profiling to transform therapeutic AAV delivery. Dr. Paulk is well known for her prior work in AAV gene repair for rare diseases, humanized animal model development for preclinical gene therapy validation, directed evolution of novel AAV capsid serotypes (most notably NP59 for human liver and NP66 for human skeletal muscle), and deep proteomic profiling of AAV to uncover novel AAV biology. As part of the Somatic Cell Genome Engineering Consortium, the Paulk lab is developing new AAV tools for performing genome edits in humans. Dr. Paulk sits on the Scientific Editorial Boards of the journals Human Gene Therapy and Gene Therapy. She is currently a member of the ASGCT Viral Gene Transfer Vectors Committee and Translational Science & Product Development Committee. Dr. Paulk holds a BS in Medical Microbiology, a PhD from OHSU with Dr. Markus Grompe where she worked on AAV gene targeting and therapeutic liver repopulation, she did her Postdoctoral Fellowship with Dr. Mark Kay at Stanford University in the Human Gene Therapy Program, and has a K01 mentored by Dr. Joseph DeRisi at UCSF on various aspects of AAV gene therapy.

Jessica Seitzer
Jessica Seitzer is the Director of Genomics at Intellia Therapeutics. Jessica is a researcher with over 15 years of industry experience in the development of oligonucleotide therapies. Prior to joining Intellia, Jessica was at Merck working on RNAi Therapeutics with a focus on lipid nanoparticle and GalNac delivery of siRNAs. She joined Intellia in 2015 during the beginning of company’s inception. She has since built out their genomics and high throughput screening core with a focus on next generation sequencing. More recently, Jessica has been co-leading Intellia’s in vivo emerging pipeline leveraging their lipid nanoparticle platform to develop CRISPR/Cas9 therapies for genetic diseases.

Beeke Wienert, PhD
Beeke earned her PhD in Molecular Genetics in 2016 from the University of New South Wales in Sydney, Australia, studying hemoglobinopathies and therapeutic upregulation of fetal hemoglobin using CRISPR. In 2017, she became a postdoctoral researcher at the Innovative Genomics Institute in the Bay Area and specialized in CRISPR-Cas9 off-target discovery and DNA repair as part of Jacob Corn’s team. In 2018, she joined Bruce Conklin’s team at the Gladstone Institutes in San Francisco to study rare genetic diseases using patient-derived stem cells as disease models. Her work focuses on the development of safe CRISPR reagents for therapeutic genome editing and the development of novel gene editing strategies for alpha-thalassemia major.

John Zuris, PhD
John Zuris has long been drawn towards developing protein-based medicines and found a perfect home in the emerging CRISPR field. As a Scientist at Editas Medicine, he heads the CRISPR Engineering group, which focuses on using both the CRISPR-Cas12a and the CRISPR-Cas9 modalities for achieving the best editing outcome for a chosen disease cell type. Prior to joining Editas Medicine, John completed his postdoctoral training in the laboratory of Dr. David Liu (Harvard University-Broad Institute) where he developed a lipid nanoparticle delivery system for CRISPR-Cas9 RNPs which allows for highly efficient genome editing both ex vivo as well as in vivo, as demonstrated in the mammalian inner ear. This delivery technology was later utilized to successfully treat a rare form of deafness in an animal model using genome editing. Before entering the CRISPR-space,
he spent his graduate career elucidating the redox and iron-sulfur cluster transfer mechanisms for a novel metalloprotein involved in Type II diabetes. His first opportunity for protein engineering came during those studies when he discovered that he could alter the redox potential of this metalloprotein over a broad range through mutagenesis, showing that this protein could serve as a tool for measuring cellular redox potentials across many organelles, cell types, and tissues. This work lead to the successful completion of his doctoral thesis in the laboratory of Dr. Patricia Jennings at University of California, San Diego.
## DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIPS

<table>
<thead>
<tr>
<th>Name</th>
<th>Disclosure</th>
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<tbody>
<tr>
<td>Omar Abudayeh, PhD</td>
<td>Sherlock Biosciences, Equity/Cash, Co-Founder/Advisor; Beam Therapeutics, Equity/Cash, Advisor</td>
</tr>
<tr>
<td>Andrew Anzalone, PhD</td>
<td>Prime Medicine, Ownership interest, Future employee</td>
</tr>
<tr>
<td>Kendell Clement, PhD</td>
<td>Edilytics, Inc., Shares, employee, shareholder, and officer</td>
</tr>
<tr>
<td>James Dahlman, PhD</td>
<td>Guide Therapeutics, Stock and consulting fees, Co-Founder, Board Member</td>
</tr>
<tr>
<td>Michael Packer, PhD</td>
<td>Beam Therapeutics, Salary, stock options, employment</td>
</tr>
<tr>
<td>Vikram Pattanayak, MD, PhD</td>
<td>Harvard University, payments related to licensing, intellectual property; Massachusetts General Hospital, payments related to licensing, intellectual property; Excelsior Genomics, equity, co-founder of company</td>
</tr>
<tr>
<td>John A Zuris, PhD</td>
<td>Editas Medicine, Salary, Stock options, Employment</td>
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