Molecular Med TRI-CON 2016

23rd Annual Conference and Exhibition
Moscone North Convention Center, San Francisco · March 6-11, 2016

Visit the preeminent event on molecular medicine

BY LLOYD DUNLAP

SAN FRANCISCO—It's possible that channel-surfing may be a thing of the past now with so many people watching their shows on services like Netflix, Hulu and Amazon—does anyone really pick up the remote control much anymore to flip through TV channels?

Perhaps not, but the Molecular Medicine Tri-Conference has four channels for your needs—Diagnostics, Genomics, Cancer and Informatics—and while you may not flip through them on a screen, you might very well be flipping through them in person in the presentation rooms according to your professional and personal needs in the realm of molecular medicine.

Let's take a quick look, shall we, with the Molecular Med Tri-Con's organizers to describe them for us:

CREDIT: MOSCONE CENTER

A view of the Moscone Center North and South exteriors at night; the Moscone Center North will host the 2016 Molecular Medicine Tri-Conference.

CREDIT: MOSCONE CENTER

Pictured here is an example of an exhibit hall at a Moscone Center-hosted conference. For the Molecular Medicine Tri-Conference, more than 200 companies will exhibit.

Diagnostics Channel—Molecular technologies are essential to accurately understand and effectively diagnose disease and guide therapy. The Diagnostics Channel will bring together industry leaders to discuss best practices in the creation and implementation of tools to enable precision medicine.

Genomics Channel—As researchers continue to unveil the importance and role of the human genome in diagnosis and treatment of disease, it will be critical to maintain a multifaceted approach. Covering everything from sample preparation to data interpretation and integration, the Genomics Channel will showcase the techniques, technologies and emerging trends in precision medicine and beyond.

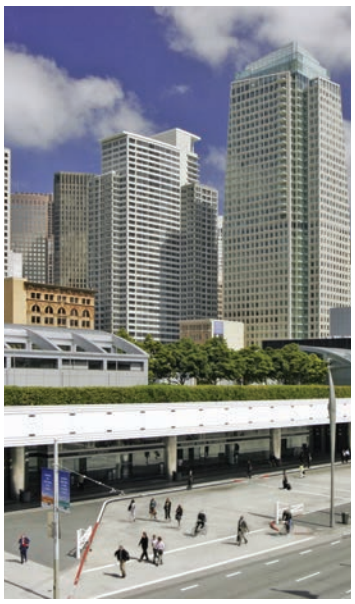
Cancer Channel—The heterogeneity and complexity of malignant tumors has changed the way we think about the initiation, progression, diagnosis and management of cancer. The Cancer Channel will explore the emerging molecular markers, improved preclinical models, genomic-based and immune-modulated therapies that are enabling precision oncology.

Informatics Channel—The Informatics Channel gathers leading experts in big data science, drug discovery informatics, bioinformatics and IT to explore cutting-edge ways to manage, analyze and integrate data that will transform our understanding of translational research and precision medicine.

TRI-CON CONTINUED ON PAGE 21

As far as specific areas covered by each, the Diagnostics Channel features two new themes this year: Precision medicine and molecular diagnostics for infectious disease. Along with those are the numerous returning topic areas of molecular diagnostics, personalized diagnostics, cancer molecular markers, circulating tumor cells, digital pathology, PCR for molecular medicine, clinical next-generation sequencing (NGS) diagnostics and, finally, genomic sample prep and biomarker assay development.

Some of the same themes are visited on the Genomics Channel: precision medicine, PCR for molecular medicine, clinical NGS diagnostics and genomic sample prep and biomarker assay development.



CREDIT: MOSCONE CENTER

The Moscone Center North, where well over 3,000 people are expected to attend the Molecular Medicine Tri-Conference this year.

The Cancer Channel is covered by a new area in cancer immunotherapy, plus the returning areas of cancer molecular markers, circulating tumor cells and predictive preclinical models in oncology.

The Informatics Channel is a bit more concise with two theme areas: bioinformatics for Big Data and integrated informatics driving translational research and precision medicine.

As stated by the organizers, "The Tri-Conference has been and will continue to be a platform in recognizing the potential for new technologies and research in molecular medicine, diagnostics, drug discovery and drug development that have a pivotal role in mitigating disease, improving access to healthcare and identifying transformative treatments."

Why attend? Here are a few of the highlights noted by the Tri-Conference organizers:

- Hear over 500 speakers from across all industries, all research fields and from all over the world
- Choose from over 400 presentations and panel discussions
- Leading molecular medicine and diagnostics program consisting of 14 conference programs, seven symposia and over 20 short courses
- Network with several thousand drug discovery and development professionals from a few dozen countries or more
- Create your conference with two options—choose from All Access or build your own program with their a la carte option
- Participate in one of 30 roundtable discussions
- Book meetings with fellow attendees using Intro-Net
- View over 150 scientific posters
- Schedule your days' events using the Tri-Conference App
- Visit with over 200 companies in the exhibit hall
- Learn about new products in the New Product Showcase

The event attracted more than 3,300 drug discovery and development professionals from over 40 countries in 2015 and as the Tri-Conference organizers put it, "If you are working in diagnostics and drug discovery, this is the must-attend event of the year." ■

EDITCONNECT: E021631

CREDIT: MOSCONE CENTER

An example of a general session setup at the Moscone Center Hall D. Attendees of the Molecular Med Tri-Con will enjoy 14 conference programs, seven symposia and over 20 short courses in this and other venues there.

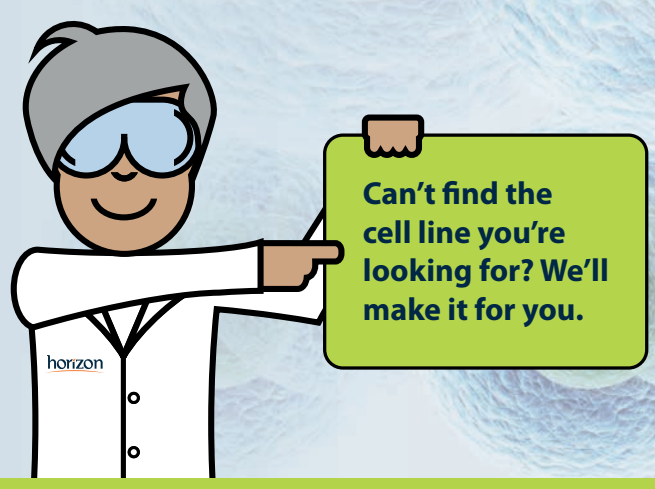
30% Discount on X-MAN® Cell Lines

for Pharmaceutical & Biotechnology customers

Innovate. Impact. Learn.

As a special offer, for a limited time we are making our unique isogenic cell line catalog and HAP1 on-demand cell line engineering service available to our commercial customers at a 30% discount

- Over **2,500** cell line pairs available **off the shelf**
- **On-demand** knockout and knockin cell line generation in **8-14 weeks** in HAP1 cells
- This is a **limited time offer**, so please **get in touch** if you would like to learn more
- And of course, our cell lines are still available to Academic researchers at **very** reasonable prices



Learn more about how X-MAN® Cell Lines at:
www.horizondiscovery.com

horizon

Symposia focus on gene editing

New Frontiers in Gene Editing

Striving for Better Design, Precision and Efficiency

March 10-11, 2016
Hilton San Francisco Union Square
Part of the 23rd International Molecular Medicine Tri-Conference

Gene editing is rapidly progressing from being a research/screening tool to one that promises important applications downstream in drug development, cell therapy and bioprocessing. Cambridge Healthtech Institute's second annual symposium on New Frontiers in Gene Editing will bring together experts from all aspects of basic science and clinical research to talk about the progress being made in gene editing and how it's being applied. Knowing the strengths and limitations of the different tools, how does one decide when to use the CRISPR (clustered regularly interspaced short palindromic repeats)/Cas system, as opposed to transcription activator-like effector nucleases (TALENs), zinc finger nucleases (ZFNs) and other systems? What is being done to overcome some of the inherent challenges with design, delivery and off-target effects associated with each of these techniques? Experts from pharma/biotech, academic and government labs will share their experiences leveraging the utility of gene editing for diverse applications.

CREDIT: SAN FRANCISCO TRAVEL ASSOCIATION

The Transamerica Pyramid is the tallest skyscraper in the San Francisco skyline. The building no longer houses the headquarters of the Transamerica Corporation, which moved their U.S. headquarters to Baltimore, Md., but it is still associated with the company and is depicted in the company's logo.

Unraveling CRISPR/Cas9-mediated gene editing

Activities and Applications of *Neisseria meningitidis* Cas9

Dr. Erik Sontheimer, professor, RNA Therapeutics Institute and the Program in Molecular Medicine, University of Massachusetts Medical School

Diverse Cas9 orthologs have the potential to provide novel activities and targeting specificities to the genome engineering toolbox. The Sontheimer lab has established *Neisseria meningitidis* Cas9 (NmeCas9) as a compact genome-editing enzyme. This presentation will describe the NmeCas9 system's features during native bacterial interference, as well as human gene targeting. These features include novel activities that are independent of the tracrRNA, which was previously considered an essential Cas9 co-factor.

Engineered Nucleases for Targeted Genome Integration

Dr. Pablo Perez-Pinera, assistant professor, Department of Bioengineering, University of Illinois at Urbana-Champaign

The CRISPR-Cas9 system can be used to inactivate genes by introducing double-strand breaks in genomic DNA that are preferentially repaired by non-homologous end joining, an error-prone DNA repair pathway that often causes mutations. However, tools for targeted gene insertion in genomes remain elusive. This talk will summarize recent advances in methods for targeted integration of heterologous DNA within complex genomes.

In-vivo Genome Engineering Using *S. aureus* Cas9: Development and Applications

Winston Yan, graduate student, M.D.-Ph.D. Program, Laboratory of Dr. Feng Zhang, Broad Institute

The small Cas9 ortholog from *Staphylococcus aureus* (SaCas9) has proven to be a versatile and efficient RNA-guided endonuclease ideally suited for *in-vivo* applications due to its ability to be packaged into the highly versatile adeno-associated virus (AAV) delivery vehicle. Here, we describe the characterization and structure of SaCas9 and its application in knocking down the cholesterol regulatory gene Pcsk9 in the adult liver as a prototype for efficient *in-vivo* genome editing using CRISPR-Cas9.

Building the CRISPR/Cas9 toolbox

Engineering CRISPR for Visualizing Genome Organization

Dr. Wulan Deng, Helen Hay Whitney Fellow, research specialist, Transcription Imaging Consortium, Janelia Research Campus, Howard Hughes Medical Institute

We have engineered the nuclease-deficient CRISPR/Cas9 for labeling genomic DNA *in-situ* in fixed cells and tissues. Using fluorescently labeled nuclease-deficient Cas9 (dCas9) protein assembled with various single-guide RNA (sgRNA), we demonstrated rapid and multi-color labeling of DNA elements and coding gene loci in mammalian cells. This rapid, less disruptive, and cost-effective technology adds a valuable tool for basic research and genetic diagnosis.

Engineered Orthogonal Drug Switchable Precise Control for CRISPR Transcription Regulation

Dr. Xin (Cindy) Xiong, research scientist, Agenovir Corporation

We have engineered the CRISPRi/a system to precisely control transcription activity and dosage by drug. We identified several drug switchable protein dimerization modules that are highly efficient and specific

EDITING CONTINUED ON PAGE 23

Plenary keynotes

Three plenary keynote presentations provide the chance to join more than 750 of your colleagues—these are the only times each day that bring all attendees from the 14 conference tracks together in one room.

MONDAY, MARCH 7

5 P.M. TO 6 P.M.

Translating Rapid Whole Genome Sequences into Precision Medicine for Babies in Intensive Care Nurseries

Stephen F. Kingsmore, president and CEO of Rady Pediatric Genomics & Systems Medicine Institute at Rady Children's Hospital, San Diego

Genetic diseases are the No. 1 cause of death in newborns in intensive care units. Rapid genome sequencing (STATseq) can diagnose genetic diseases in newborns in 26 hours. However, scaling STATseq to thousands of acutely ill newborns and implementation of precision care plans that improve outcomes are uncharted territory. Problems, potential solutions and progress to date will be discussed.

Kingsmore came to Rady Children's from Children's Mercy Kansas City, where he most recently served as executive director of medical panomics, and from the University of Missouri, Kansas, City School of Medicine where he was Dee Lyons/Missouri Endowed Chair in Genomic Medicine. He was a MedScape Physician of the year in 2012 and received the 2013 Scripps Genomic Medicine award and 2013 ILCHUN prize of the Korean Society for Biochemistry and Molecular Biology. *TIME* magazine ranked his rapid genome diagnosis method one of the top 10 medical breakthroughs of 2012.

TUESDAY, MARCH 8

8 A.M. TO 9 A.M.

Unlocking the Potential of Next-Generation Biomarkers

Jorge Soto, co-founder and chief technical officer of Miroculus

This presentation will discuss a simple, noninvasive, affordable point-of-care test that looks for early signs of multiple forms of cancer and infectious diseases based on circulating microRNAs.

Soto, a graduate of both Tec de Monterrey and Singularity University, is co-founder and CTO of Miroculus, a life-science company that aims to push forward a new test for different diseases based on circulating microRNA. Prior to founding Miroculus, he was the deputy general director of civic innovation at the coordination of national digital strategy of Mexico where he designed and launched several projects that use technology to encourage transparency and improve the communication between citizens and their institutions.

WEDNESDAY, MARCH 9

8 A.M. TO 10 A.M.

Plenary Session Panel: Emerging Technologies and Industry Perspectives

Moderator: Kristin Ciriello Pothier, head of life sciences/managing director of Parthenon-EY (Ernst & Young)

Panelists include:

Brian Feth, CEO, Xcell Biosciences
Kevin Coker, CEO, Molecular Match
Paul Diehl, director of business development, Cellecta, Inc.
Dr. Russell Garlick, chief scientific officer, SeraCare Life Sciences
Dr. Scott Marshall, managing director, analytics, Precision for Medicine
Dr. Bernard Andruss, vice president, diagnostic development, Asuragen

This panel session will feature a series of presentations on emerging and hot technologies in molecular medicine. Each speaker will have seven minutes at the podium. After all speakers have presented, there will be a moderated Q&A with attendees. The presentations are not meant to be a corporate or specific product pitch. Each speaker will focus on a technology and solution framed around a motivational clinical problem and how their particular company/organization is solving it. ■

EDITING

CONTINUED FROM PAGE 22

when combined with CRISPR. By pairing these modules with orthogonal Cas9s, we developed orthogonal drug switches that enable independent transcriptional regulation (activation/repression) of distinct target genes according to the drug inputs.

Genomic Editing, Nucleofection and the Generation of Cell Lines for Cell-Based Assays

Dr. Gregory Alberts, global subject matter expert, Lonza Pharma Bioscience Solutions

Using primary cells in cell-based assays can improve the assays, which should translate more effectively into *in-vivo* models. Lonza's Nucleofector technology easily transfects primary cells, and with CRISPR, primary cells can be specifically modified at the genomic level, creating isogenic strains of specific cells that differ in only one specific aspect.

Luncheon Presentation: CRISPR and RNAi: Gene Editing and Functional Genomic Screening Approaches

Dr. Paul Diehl, director of business development, Cellecta Inc.

While RNAi screens have proven effective genome-wide loss-of-function pooled screens, CRISPR/Cas9 provides a newer attractive alternative. We have developed pooled sgRNA libraries that complement our established shRNA ones, and then compared how each type performs in genetic screens on PDX-derived cell lines.

Identifying and modifying novel drug targets

Genome-Edited Reporter Systems to Enable Cell-Based HTS Assays for Chemical Biology and Drug Discovery

Dr. James Inglese, head of assay development and screening technologies, National Center for Advancing Translational Sciences, NIH

The targeting precision of genome editing was used in combination with advances in reporter gene design to modify the genetic loci of neurologic target genes to create HTS assays for compound library interrogation. Our goal was to identify transcriptionally active pharmacological agents acting by a variety of mechanisms, including through chromatin co-regulators accessible by our assay design. Specific case studies will serve to illustrate progress and findings to date.

Optimizing CRISPR-Cas9 System to Improve Genome-Wide Knockout Screening Performance

Dr. Haoquan Wu, associate professor, Department of Biomedical Sciences, Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center

CRISPR-Cas9 system enables genome-wide knockout screening in human cells. One of the limitations is that the knockout efficiency of sgRNAs targeting the same gene can vary significantly, or even dramatically. Here we present data to improve knockout efficiency generally to improve the screening performance of CRISPR-Cas9-mediated knockout screening.

Parallel shRNA and CRISPR/Cas9 Screens Reveal Biology of Stress Pathways and Identify Novel Drug Targets

Dr. Michael Bassik, assistant professor, Department of Genetics, Stanford University

We have developed high-complexity shRNA libraries (25 shRNAs/gene) that greatly reduce false negatives/false positives, and have adapted these libraries to knock down gene pairs to perform systematic genetic interaction maps in mammalian cells. Using this strategy in parallel with the CRISPR/Cas9 system, we have uncovered new insights into the biology of stress signaling and identified novel drug targets.

Strategies and Applications Using shRNA and CRISPR Technology for Identification of New Druggable Targets

Dr. Donald Apanovitch, director of functional genomics (oncology), Pfizer Research

The application of RNAi loss-of-function negative selection screens is a well-documented platform for the identification of essential gene function regulating oncogenic pathways and tumorigenesis. In collaboration with the Cold Spring Harbor and the IBB group of Pfizer Oncology, we have designed and validated druggable and target-specific lentiviral shRNA libraries. Provided will be an overview of our mir-based libraries and screening strategy will be presented along with CRISPR applications as an orthogonal tool to characterize differences in shRNA rescue experiments.

CREDIT: MOSCONE CENTER

The Medicine Tri-Conference invites you to network with several thousand drug discovery and development professionals from a few dozen countries or more. Pictured here is Hall D at the Moscone Center.

Recent Progress Towards Efficient Targeted Gene Modification in Primary Human Hematopoietic Cells

Dr. David Rawlings, director, Center for Immunity and Immunotherapies, Seattle Children's Research Institute; professor of pediatrics and immunology, University of Washington School of Medicine

We have utilized RNA-based nuclease and AAV-mediated donor co-delivery to drive targeted gene modification in primary hematopoietic cells. Using this approach, we achieve ~60% gene targeting in T cells and we have generated "targeted CAR" T cells with potent functional activity. We have also applied this method to edit CD34+ stem cells. Overall, primary cells with myriad novel properties can be generated with high-efficiency using this clinically feasible gene-editing approach.

Developing precise gene editing

Precise Genome Engineering in Human iPS Cells to Model and Treat Disease

Dr. Bruce R. Conklin, investigator, Roddenberry Center for Stem Cell Biology and Medicine, Gladstone Institutes; professor, Division of Genomic Medicine University of California, San Francisco

We have combined droplet digital PCR (ddPCR) technology, TaqMan PCR system, and optimized iPSC culture system to develop rare allele induction and detection (RAID). This method allows for precise base-by-base genome editing in human iPSCs followed by efficient detection, sub-selection, and isolation of mutant clones. We have made a series of >20 isogenic iPSC-derived cardiomyocytes and observed cardiomyopathy phenotypes with several heterozygous and homozygous single-base mutations.

Engineering Human Stem Cells by CRISPR

Dr. Su-Chun Zhang, Steenbock Professor in Behavioral and Neural Sciences and professor of neuroscience and neurology, Waisman Center, University of Wisconsin

We have adapted the current genome-editing technology for human cells. Using the optimized technology, we have engineered human stem cell lines with reporters, inducible gene expression and knockout, as well as functional switches. These genetically modified human cells substantially enable fundamental research, drug discovery and potentially clinical applications.

Therapeutic Genome Editing for Blood Diseases

Dr. Matthew Porteus, associate professor of pediatrics, Stanford University School of Medicine

The genome-editing toolbox now offers powerful options in designing engineered nucleases, and there are multiple different ways to utilize the engineered nucleases to create precise genomic modifications using both non-homologous end-joining and homologous recombination. Harnessing this toolbox so that it can be applied beyond just manipulating cancer cell lines and instead utilized to engineer therapeutically relevant cell types is now proceeding. Progress on modifying T cells and hematopoietic stem and progenitor cells will be presented.

Practical Considerations for Genome Engineering of Model Cell Lines

Dr. Daniel C. Teasley, genome engineering specialist, Cell Design Studio, MilliporeSigma

The widespread adoption of CRISPR-based genome editing technology has made cell line engineering more accessible than ever before. Despite these recent advances, engineering the genome of a model cell line remains a challenging task. Common decision points, such as choosing a parental cell line and nuclease, and potential stumbling blocks in the workflow, will be discussed. Several case study engineering projects will be reviewed to demonstrate best practices to manage risk and maximize success.

Designing Functional and Specific Guide RNAs for Gene Knockout or Homology-Directed Repair

Dr. John A. Schiel, research scientist, R&D, Dharmacon

We describe a CRISPR-Cas9 algorithm incorporating parameters to predict functional gene knockout of gRNAs and ability to detect potential off-target sites typically missed using existing tools. We also provide guidelines for design of donor templates for optimal HDR and knockins.

Improving efficiency and specificity of CRISPR

CRISPR Libraries for Functional Genomics: Optimizing On-Target Activity, Avoiding Off-Target Effects

Dr. John Doench, associate director, Genetic Perturbation Platform, Broad Institute

Pooled screens with CRISPR technology have proven to be a powerful means of understanding gene function. Here will be discussed experiments and computational modeling approaches to optimize sgRNA sequence to both increase on-target activity and decrease off-target effects.

CRISPR-EATING: A Method for Inexpensively Generating Large sgRNA Libraries

Dr. Andrew Lane, postdoctoral fellow, laboratory of Dr. Rebecca Heald, Department of Molecular and Cell Biology, University of California, Berkeley

CRISPR-based technologies have emerged as powerful tools to alter genomes and mark chromosomal loci, but an inexpensive method for generating large numbers of RNA guides for genome screening and labeling is lacking. Using a new method, CRISPR-EATING, to construct libraries from any source of DNA, we have labeled a single chromosomal locus in Xenopus egg extracts and show that a complex library can target the *E. coli* genome at high frequency.

Application of Genome Editing Tools to Model Human Genetics Findings in Preclinical Animals

Dr. Myung Shin, senior principal scientist, biology-discovery, genetics and pharmacogenomics, Merck Research Laboratories

Genome-editing tools have allowed for rapid generation of genetically engineered models in various preclinical species. We will present how ZFN and CRISPR have been applied to efficiently generate various animal models to recapitulate findings based on human genetics and pathobiology to aid drug discovery process. ■