# TECHNOLOGIES, TOOLS AND APPLICATIONS

within **Genome Editing**, **Transgenics** and **Synthetic Biology**

**USA** Pre-Event Newsletter

### NEPA21 from Bulldog Bio

Product details and recent publications highlighting the advances the NEPA21 has allowed in transgenic EP

### Genome Editing in Regenerative Medicine

RegMedNet looks at the obstacles, considerations, forecast, and more

### Expert Q&A Sessions

Industry insights from 6 individual field experts from Novartis, Pfizer, and several leading USA Universities

HYATT REGENCY BOSTON

*10-11 MAY 2018 | BOSTON, USA*

OXFORD GLOBAL CONFERENCES

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## Meet the Team

**Peter Franko**
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Conference Producer

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**Jamie Morris**
Delegate Sales Executive

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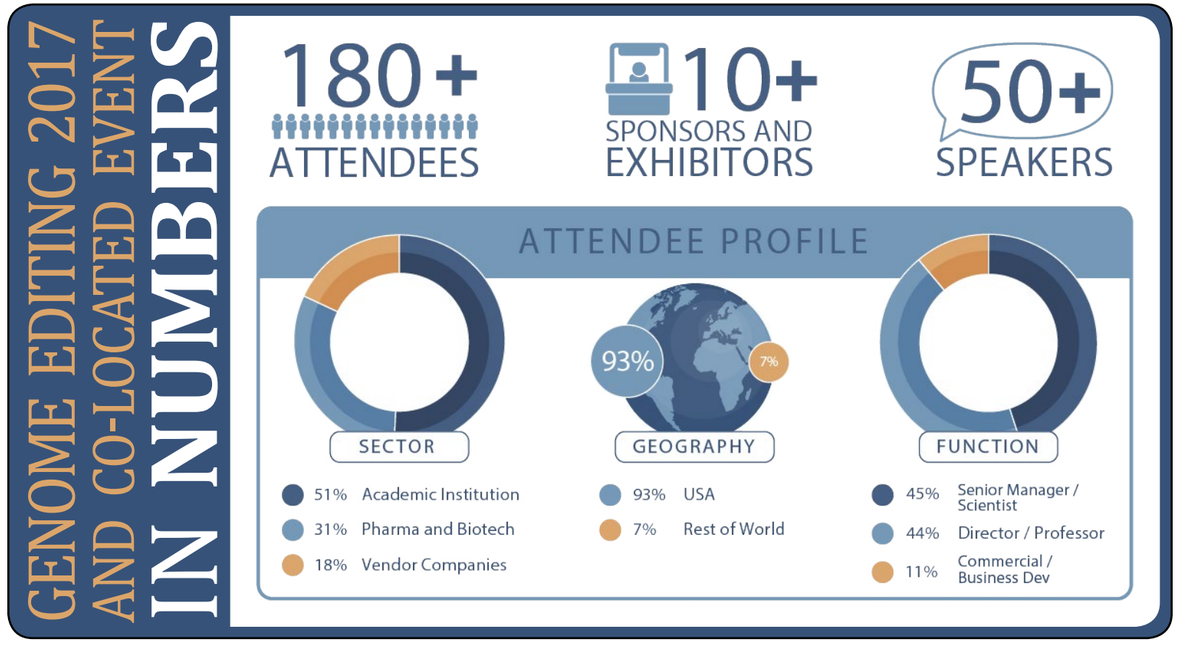


# WELCOME TO THE INAUGURAL EDITION OF OXFORD GLOBAL'S TECHNOLOGIES, TOOLS AND APPLICATIONS NEWSLETTER!

With the 2nd Genome Editing, Transgenic Technologies and co-located Synthetic Biology USA Congresses taking place in Boston on 10-11 May 2018, I am delighted to invite you to join us at our forum but before that we would like to give you a quick recap on the 2017 event and a tour of what you can expect to learn and who you can expect to meet this year.

Our inaugural event last year brought together over 180 attendees to hear 50 + presentations covering aspects of Genomic and Transgenic Genome Editing alongside technology workshops from experts who discussed the systematic state of the art high throughput screening, novel CRISPR-Cas systems and 3D mouse imaging systems. Attendees were able to discover new solutions from key technology providers of the industry across the two days and of course have the chance to network at our popular drinks reception.

Whilst the commitment and excitement to gene editing as a ground-breaking technology continues to rise, there is a compelling need to improve the collective understanding around the functional biology and the mechanism of action of the CRISPR/Cas9 system itself. As such, our congress will showcase only the most reliable, reputable and cutting-edge data to help you optimize your CRISPR workflows. Our event will host 4 distinct tracks on each day that will enable you to delve deeper into the basic research, synthetic biology and therapeutic applications of CRISPR.

We will feature over 70+ presentations on key topics within Gene Editing Technologies, Drug Discovery & Development Applications of Gene Editing, Therapeutic Applications of Gene Editing, Technical Advances In Transgenic Genome Editing, Transgenic Models Of Disease, CRISPR And Synthetic Biology Tools & Biomedical Applications of Synthetic Biology.

After a full day of learning, knowledge sharing and meeting new people, what better way to unwind after the first day of the congress than with a networking drinks reception at the venue.

Read on for a range of interesting interviews and insights with some of 2018's industry-leading speakers and participating sponsors, and I look forward to welcoming you to the 2018 Congress in May. **- Peter Franko, Commercial Director**


## WHO IS ATTENDING?

For the full attendee list please contact
marketing@oxfordglobal.co.uk

- **300+ senior level attendees** from leading pharmaceutical, biotechnology, CRO and solution provider companies
- **Highly esteemed members** of internationally renowned research & academic institutions
- **Professors, Directors and Heads** of gene editing, synthetic biology, biomedical engineering, transgenic technologies and translational genomics

**These companies and many more:**

Genentech – A Member of the Roche Group · Pfizer · NOVARTIS · janssen · Bristol-Myers Squibb · NERx BioSciences · Intellia THERAPEUTICS · addgene – The nonprofit plasmid repository · ETAGEN pharma · Massachusetts Institute of Technology · abbvie · CRISPR THERAPEUTICS · HARVARD UNIVERSITY · Berkeley UNIVERSITY OF CALIFORNIA · Yale University





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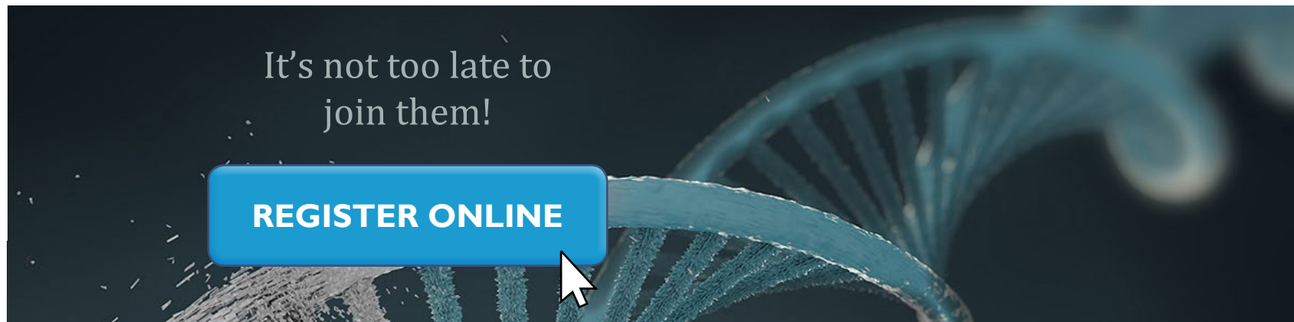


# Q&A SESSION WITH **DR. LEV FEDOROV**

**We spoke to Dr. Lev Fedorov about the future of the transgenic technology industry and the ongoing interest in mouse genome editing with CRISPR *in vivo*.**

Lev Fedorov Ph.D., Research Assistant Professor and Director of OHSU Transgenic Mouse models Shared Resource, Knight Cancer Institute at Oregon Health & Science University

Lev Fedorov gained the PhD degree in genetics in 1987 in N.I. Vavilov Institute of General Genetics of Russian Academy of Sciences, in Moscow. After that he worked as Junior Scientist (1986-1990) and Group Leader of Mouse Developmental Genetics Group (1990-1993) in Medical Genetics Research Center, Moscow, Russia. Later he continued his scientific career in Germany as guest scientist at the Max-Planck-Institute in Freiburg (1993-1995), as staff scientist and Group Leader of Mouse Genetics at the University in Wurzburg (1995-2004) and as Head of Transgenic Animal Core, University of Jena (2004-2008). After 15 years' work in Germany, Dr Fedorov moved to Portland, Oregon, USA. Since 2008, he is Research Assistant Professor and Director of the Transgenic Mouse Models Core Laboratory at Oregon Health & Science University (OHSU). Additionally, he is a Faculty Member of the Program in Cancer Biology of OHSU Knight Cancer Institute. His scientific interests cover several topics: a) Transgenic Technology and modeling of human diseases; b) Spindle Assembly Checkpoint (SAC) and its potential role in recurrent pregnancy loss in the human; and c) Oncogenes and cellular molecular mechanisms underlying embryonic development and cancer progression.

**The transgenic technology industry is experiencing steady growth. What do you think are likely to be the most exciting developments for the industry over the next couple of years?**

**LF:** I think the industry will expand its use and development of the CRISPR genome editing technology; its applications, which have stirred excitement in several areas, were published recently:

**CRISPR/cas9 application for prokaryotes:** For example, in the area of antibiotic resistance, CRISPR/ca9 has been used to eliminate pathogenic bacteria (Beisel et al., 2014). Another example is the modification of Lactococcus lactis, an important fermentation strain, with an insertion of spacer sequences from lactococcal phage that enhances resistance against phage and therefore highlights the utility of this tool for the dairy industry (Millen et al., 2012). Another use of CRISPR-Cas9 is within the industrially-important Actinomycetales, a bacterial order that is a well-established source for the production of secondary metabolites and pharmaceutically active components. (Tong et al.2015).

**CRISPR/cas9 for one cell's eukaryotes:** The editing of the yeast, *Saccharomyces cerevisiae*, genome by CRISPR-Cas9 system was published recently (DiCarlo et al. 2013). This will be useful for the food and wine industry.

**CRISPR/cas9 for mammalian cells - Medicine:** Genome editing with CRISPR/cas9 on a number of organisms including mouse, monkey etc. *in vitro* and *in vivo* indicated the possibility of using CRISPR-Cas9 to manipulate the human genome. It also suggested that the efficiency and specificity of CRISPR-Cas9 could have clinical applications. It seems a gene/tissue therapy will soon be used for the autologic correction of a mutant gene in somatic tissues of a patient. It will be possible to repair genes in hematopoietic stem cells *in vitro* and return the corrected cells back to patient. Similar manipulations with other somatic tissues are possible but need more time for development. Another application of CRISPR/cas9 is in cancer therapy where it may be used to prevent the development of resistance in tumor cells to anticancer drugs. It is very promising, but will take more time.

**CRISPR/cas9 for mammalian cells - Farm animals:** CRISPR/cas9 will be used to develop useful properties of farm animals and for veterinary purposes, but it will take more time.

**What do you feel are the biggest challenges the industry is currently facing, as well as the challenges you are facing in your own research and how do you overcome this?**

**LF:** Every area of CRISPR/cas9 applications has own challenges. A general challenge is the prejudice that transgenic experiments and genetically modified organisms are harmful. Our own challenge is the low efficiency of repair in mouse genome manipulations (knock-in) *in vivo*. We are testing and optimizing different conditions.

**Mouse genome editing with CRISPR *in vivo* including the efficiency of Cas9 protein versus Cas9 mRNA is a particularly hot topic at present. Why is this?**

**LF:** Many papers were published recently about successful gene editing in the mouse and other animals via CRISPR *in vivo*. Various laboratories are using different approaches and having different success. Some researchers use Cas9 mRNA or Cas9 protein in combination with gRNA or PX330 plasmid that contain Cas9 and gRNA to cut DNA. Other researchers have injected a CRISPR cocktail into the cytoplasm or pronuclei of zygotes. Gene targeting by CRISPR is working (with different efficiency) in general. Of course, it is interesting to compare and discuss these approaches and optimize different conditions. Moreover, according to our results, a Knock-in by CRISPR is more difficult because it has a low efficiency compared with CRISPR KO and integration of the repair template via homologous recombination after cutting DNA by Cas9 occurs in only a few percent of newborns. This may be dependent on several factors including the design and length of repair template (ssDNA oligo or length dsDNA), number of available PAMs, concentration of CRISPR components etc. Testing of CRISPR in cell culture is useful but does not reflect exactly what will happened *in vivo*. Therefore, analysis and discussion of different approaches will help to save time and money. I think it can be particularly useful for the farm animal industry, because their process is more expensive and the animals have a much longer time of pregnancy ■



# WEBINAR EXCERPT: Q&A SESSION WITH **SHANRONG ZHAO**

Shanrong Zhao, Director of Computational Biology and Bioinformatics, Pfizer

Shanrong Zhao is Director, Computational Biology and Bioinformatics at Pfizer Inc. More than 20 years of experience in computer science and computational biology. A recognized pioneer in the field of RNA-seq, big data analysis and cloud computing. Deep scientific knowledge in immunology, antibody design and biomarker discovery. He published more than 30 peer-reviewed publications, and has been invited to speak at more than 20 international meetings. Enthusiastic about applying next generation sequencing, system biology and machine learning to drive drug discovery and biological research.

**What are the main hurdles for RNA-seq data analysis at the isoform and exon levels?**

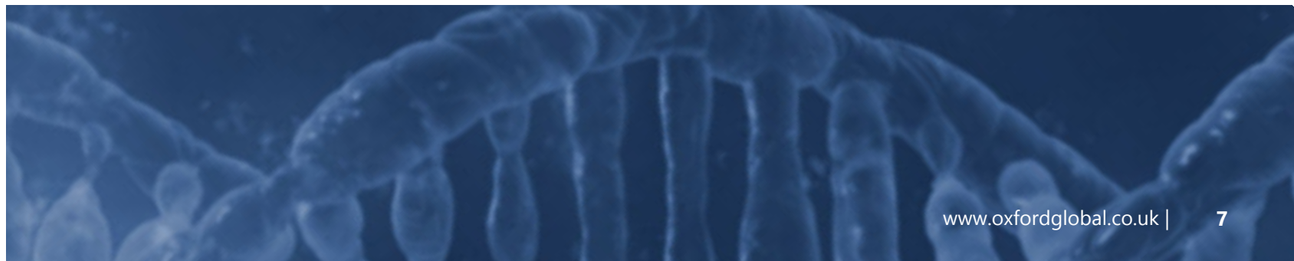
**SZ:** Of course, the computational analysis itself is challenging, but it's more challenging in terms of biological functions. The functions of most genes are annotated at the gene level, not at the isoform level. Let's say we see isoform switch between two conditions, what's the biological significance? Without understanding the functionalities of individual isoforms, it's difficult to interpret the difference at the isoform and exon levels.

**Any comments on different algorithms for computational alternative splicing?**

**SZ:** There are quite a few algorithms available for alternative splicing, including MAJIQ, rMATs, leafcutter and SUPPA. One problem is: different algorithm define its own splicing pattern, and the outputs from different algorithms can be compared directly, quite often. We need consensus on alternative splicing and a standard on how to represent alternative splicing ■

This is an excerpt from the free webinar, 'Latest CRISPR Genome Editing and Therapeutic Applications of Mouse and Rat Models'.

**The full webinar recording is available on our website at:**
www.genomeeditingusa-congress.com/2018-free-webinar-recordings



# WEBINAR EXCERPT: Q&A SESSION WITH **HIUMIN ZHAO** AND **ADAM ARKIN**

**There are so many reported DNA assembly methods, what should I use for my experiments?**

**HZ:** This is a good question and I think it will depend on the specific application. If your goal is to build a small DNA molecule, i.e. less than 20 kb, then either the Golden Gate method or the Gibson assembly method can work pretty well. If you want to build a large DNA molecule such as a 30 kb natural product biosynthetic pathway, then I think that you must rely on the DNA assembler method or other *in vivo* assembly methods.

**There are so many existing DNA assembly methods, but why is there still a need to develop a new DNA assembly method?**

**HZ:** That is because no existing method works perfectly. Every method has its advantages and disadvantages. Since there is an increasing need to work with very long or more complex DNA molecules that have repetitive sequences or high GC content, it is highly desirable to develop a method that is more versatile or more generally applicable. Furthermore, it is desirable to automate the entire DNA assembly process.

**Is there a machine that can perform automated DNA assembly?**

**HZ:** This is a goal that many academic and industrial labs are working towards. Synthetic Genomics has developed a machine that automates the Gibson DNA assembly method, but its capability is still rather limited. I believe that in 5-10 years there will be a more powerful and versatile machine that many labs will use to build custom-designed large DNA molecules, similar to what we do with DNA sequencing these days.

**What are the challenges for using HT genetics for optimising microbial function in complex environments?**

**AA:** There are few problems here, the first being that it is often very difficult to transform the most important microbes. Of the 60 or so human microbial members that we've tries, there are only a few of them that are very efficient in their transformation capabilities. By using things like CRISPRi or CRISPR itself with bacteria, it can be very difficult to transfer that particular technology from bacteria to bacteria. There are maybe 10 or so where it works very effectively in not so well in others in general. This means that transforming them and doing the manipulation remains difficult.

The second thing is that there is a problem with simulation the environments that where we want to understand the gene function. It would be ideal if we could get very specific biochemical adaptations but in general there are conditions which are specific to certain mutations and we still don't know how to simulate realistic environments very well. If we could figure out a way to make CRISPRi very transportable that would be great.

Adam Arkin, Professor of Bioengineering, University of California, Berkeley

Adam Arkin is the Dean A. Richard Newton Memorial Professor in the Department of Bioengineering, University of California, Berkeley and Senior Faculty Scientist in the Environmental Genomics and Systems Biology Division at the Lawrence Berkeley National Laboratory.

Huimin Zhao, Professor of Chemical and Biomolecular Engineering, University of Illinois

Dr. Huimin Zhao is the Steven L. Miller Chair of chemical and biomolecular engineering, and professor of chemistry, biochemistry, biophysics, and bioengineering at the University of Illinois at Urbana-Champaign (UIUC). He received his B.S. degree in Biology from the University of Science and Technology of China in 1992 and his Ph.D. degree in Chemistry from the California Institute of Technology in 1998.

**What are the next generation technologies that will help solve these problems?**

**AA:** I think that there are three of them. I think that clearly recombineering and CRISPR are the future in bacteria just like it is elsewhere. There are, however, barriers to using these which are not well understood and so that need to be explored much better. In bacteria it is still very difficult though, and if we can break that barrier it would help us in using them for biomanufacturing and for manipulating even microbial and plant microbial material which is really important technology. It turns out that its much easier in eukaryotes as there are no barriers to using CRISPR in eukaryotes so far.

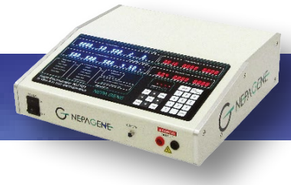
The second big innovation has to be the ability to simulate targeted environments in the laboratory. People are now building these things called eco-trons that are simulations of plant and agricultural environments that are meant to math what goes on tin the field so they can do things in that lab which will translate to the field in agriculture. People are also trying to do that for humans as well, trying to build artificial guts and the like, but those are very primitive right now, so it would be fantastic if we could get that to work.

The third and final one is being able to query multiplex manipulations with CRISPRi. For example, it is relatively trivial to knock down or knock up one gene at a time and that allows us to map epistasis and if we could get these epistatic maps and understand them better that would allow us to better understand what traits could be stacked together and thereby save us time on the engineering side of things ■

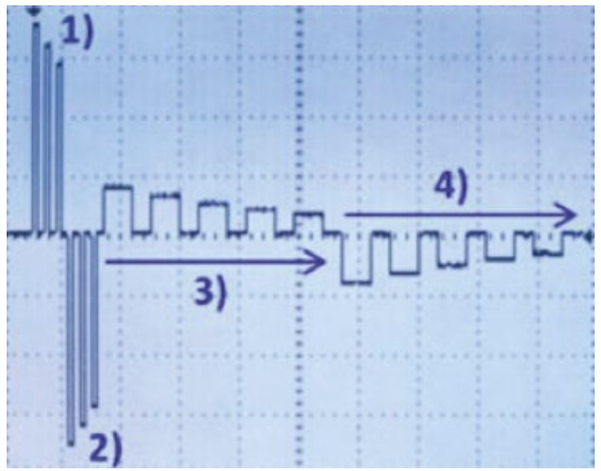
This is an excerpt from our Synthetic Biology webinars, **available on our website at:** www.genomeeditingusa-congress.com/2018-free-webinar-recordings

# NEPA21

## Electro-Kinetic Transfection System



The most popular transfection procedures all require costly specialized chemicals — running as much as $8 or more per sample. These additives can have unwanted effects on the cell and create another parameter which must be considered. Though electroporation has been around for many years, no protocols exist for high efficiency transfections without the use of such reagents. That is, not until the NEPA21. Nepa Gene has created THE most sophisticated apparatus for delivering DNA, RNA, and proteins into cells. Your cells stay in standard media, so all that's required are the reusable electrodes. With a combination of low voltage short-and-long pulses and unique polarity reversal, the NEPA21 can transfect a huge variety of cells, tissues, and even organisms with amazing efficiencies. This patented pulsing technology has been shown to be both superior to and far more flexible than other techniques. And because most living cells are not bothered by low voltages, and transfections can be done in standard growth media, cytotoxic effects are nearly eliminated.




**Typical 4-Step Electro-kinetic Protocol**

**Novel 1-, 2-, 3- or 4-step Pulsing Technology**

By creating complex patterns of square wave pulses, the NEPA21 can open pores in cellular tissues and then carry charged particles into these cells. The high amplitude, short duration Poring Pulse uses voltage decay to minimize damage to nuclear and cellular membranes (1). By reversing polarity of the Poring Pulse, the channels in the plasma membrane can be further stabilized (2). The lower-voltage longer-duration Transfer Pulses deliver DNA and RNA into the cells while continuing to ameliorate the cytotoxic effects (3). Significant improvements in transfer efficiency can also be generated by cleverly reversing polarity of the pulses (4).

### *In vitro* transfection of suspension, adherent and primary cells

The NEPA21 utilizes one of two electrode types to deliver nucleic acids to live cells in culture. The first type, for standard electroporation cuvettes, is used for suspension cells without the need for expensive buffering conditions with unknown additives. Simply add cells and pulse — then save money and time. For adherent cells, we offer a unique cell-culture plate electrode for 2-dimensional electro-kinetic transfer of RNA and DNA. The NEPA21 is the best option for efficacious transfection of primary cells. Stem cells, primary neurons, and immune cells all exhibit high cell viability and high transfection efficiency when pulsed by the NEPA21.

### Gene Editing for Transgenic Zygotes

Microinjection has been the traditional way to get nucleic acid machinery into zygotes. Electroporation has now proven easier, faster and more effective. The TAKE method was developed with the NEPA21 and is a direct replacement of the microinjection technique. The GONAD method obviates the need to harvest oocytes, but rather directly electroporates eggs while they still reside in a female mouse's oviduct. These mice can be mated naturally at greatly reduced cost by eliminating the need to individually handle hundreds of zygotes.

### *In vivo* transfection in mice and rats

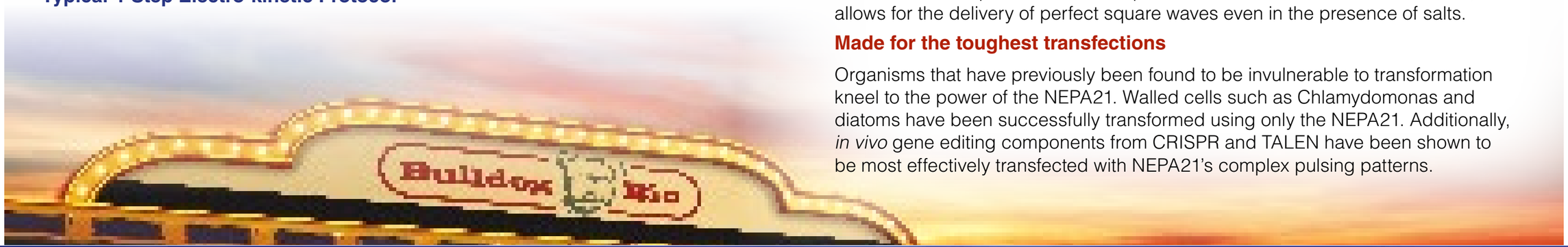
The NEPA21 is offered with more than 100 electrodes. These specialized tools can be used to gently pulse organs and tissues in live animals. This system allows previously difficult – or impossible – transfection experiments to be executed, opening new avenues of scientific inquiry. Transfections have been successfully performed on muscle, skin, liver, kidney, testis, ovary, brain, retina, cornea, and other organs. And if you need to study tissue outside of the organism, the NEPA21 offers specialized electrodes for the *ex vivo* transfer of nucleic acids to a variety of tissue explants including brain.

### *In utero, ex utero* and *in ovo* transfections for developmental studies

Nepa Gene has developed tools and techniques for transfecting embryonic tissues – or even whole embryos – in mice, rats, and chickens. Whether it's specific regions in a mouse embryonic brain, a chicken cortex, or a rat leg muscle, we can provide a protocol and an electrode set. Flexibility is almost limitless, as these electrodes have been adopted for use with a variety of other animals and plants including honey bee, Xenopus, and even plant seeds. The unique "non-capacitor" design of the NEPA21 is perfect for tissues perfused in PBS or other saline solutions, as it allows for the delivery of perfect square waves even in the presence of salts.

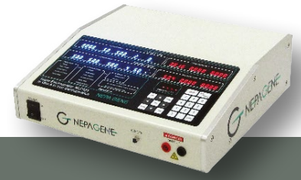
### Made for the toughest transfections

Organisms that have previously been found to be invulnerable to transformation kneel to the power of the NEPA21. Walled cells such as Chlamydomonas and diatoms have been successfully transformed using only the NEPA21. Additionally, *in vivo* gene editing components from CRISPR and TALEN have been shown to be most effectively transfected with NEPA21's complex pulsing patterns.



# NEPA21

## Electro-Kinetic Transfection System



| SPECIFICATIONS | | | |
|---|---|---|---|
| Size | 346(W) x 330(D) x113(H) mm | # transfer pulses | 0-99 |
| Weight | 7.5 kg | Decaying pulses | Yes |
| Warranty | 2 Year | Reverse polarity | Yes |
| Types of pulses | Poring & Transfer | Impedance readout | Yes |
| # pulsing steps | Up to 4 | Total energy readout | Yes, in Joules |
| # poring pulses | 0-9 | | |

| ITEM # | SIZE | DESCRIPTION | APPLICATION |
|---|---|---|---|
| NEPA21 | 1 | NEPA 21 Electro-Kinetic Transfection System | Per electrode type. See below |
| CU500 | 1 | Electrode chamber for electroporation cuvettes | Cells and cell clusters in suspension such as stem cells, immune cells, organoids and all cell lines |
| CUY900-13-3-5 | 1 | Electrode for 24-well culture plate | Adherent cells such as neurons |
| CUY505P5 | 1 | Electrode on slide with parallel platinum plate electrode 8mm x 3mm, 5mm gap | Transgenic animal zygotes and tissue explants |
| CUY650P5 | 1 | Tweezer-style electrode w/5mmϕ platinum disk electrodes | In vivo EP of organs, muscle, skin and mouse embryos |
| CUY652P2.5X4 | 1 | Tweezer-style electrode w/ cupped platinum disk electrodes | Mouse oviduct for transgenic iGONAD |
| CUY611P7-2 | 1 | Platinum chopstick-style elec¬trodes, 7mm bend, 2mm tip length, 2/pkg | For targeted tissue *in vivo* such |
| CUY701P7E/7L | 1 | 7mm x 7mm platinum square electrodes; one on stick and one on petridish w/1mm frame for tissue explants | For *ex vivo* EP using tissue explants |

More than100 other *in vivo*, *in utero*, *in ovo* and *ex vivo* electrodes available at www.bulldog.com

Bulldog Bio, Inc.
One New Hampshire Ave
Suite 125
Portsmouth, NH 03801

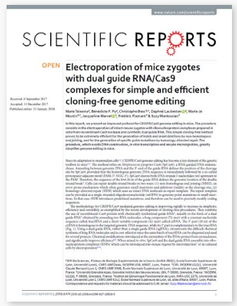




# Advances in Transgenic EP using the NEPA21

The NEPA21 system can be used for a very wide variety of applications and has been cited in over 170 publications since 2017. The system is now installed in nearly 100 transgenic labs worldwide.

**Here are some key recent publications highlighting advances in transgenic EP using the NEPA21:**


SCIENTIFIC REPORTS

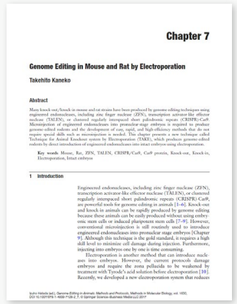
OPEN

Electroporation of mice zygotes with dual guide RNA/Cas9 complexes for simple and efficient cloning-free genome editing

### Electroporation of mice zygotes with dual guide RNA/Cas9 complexes for simple and efficient cloning-free genome editing

"In this report, we present an improved protocol for CRISPR/Cas9 genome editing in mice. The procedure consists in the electroporation of intact mouse zygotes with ribonucleoprotein complexes prepared *in vitro* from recombinant Cas9 nuclease and synthetic dual guide RNA."

> Read More


Chapter 7

Genome Editing in Mouse and Rat by Electroporation

Takehito Kaneko

### Genome Editing in Mouse and Rat by Electroporation

Dr. Takehito Kaneko

Dr. Kaneko is one of the founders of this technique and this chapter highlights the basics of his procedure using the nEPA21 system.

> Read More


nature biotechnology

BRIEF COMMUNICATIONS

Highly efficient RNA-guided base editing in mouse embryos

### Highly efficient RNA-guided base editing in mouse embryos

Base editors composed of a cytidine deaminase fused to CRISPR–Cas9 convert cytidine to uridine, leading to single-base-pair substitutions in eukaryotic cells. We delivered BE mRNA or ribonucleoproteins targeting the Dmd or Tyr gene via electroporation or microinjection into mouse zygotes. F0 mice showed nonsense mutations with an efficiency of 44–57% and allelic frequencies of up to 100%, demonstrating an efficient method to generate mice with targeted point mutations.

> Read More

# FROM TRANSGENIC CORE TO GENOME EDITING CORE FACILITY

## GHASSAN YEHIA, PH.D.

**Scientific Director, Genome Editing Core Facility, Office of Research Advancement, Rutgers New Brunswick**

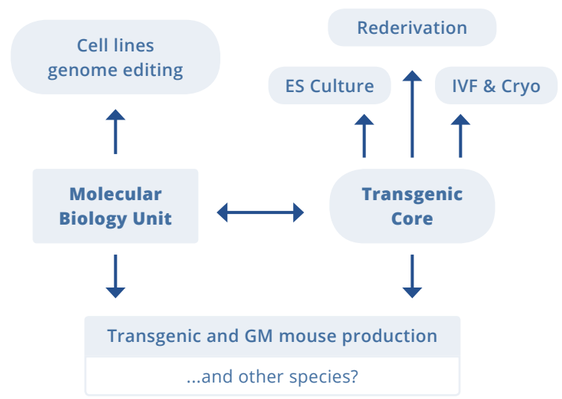
Dr. Ghassan Yehia, Scientific Director, Genome Editing Core Facility, Office of Research Advancement, Rutgers

Dr. Ghassan Yehia has over 20 years of experience in all aspects of mouse transgenesis. He received his doctorate from Strasbourg, France in the Institute of Genetic, Molecular and Cell Biology, where he first started generating knock-out and transgenic mice. He then joined the University of Medicine and Dentistry of New Jersey to work on cancer research and cell signaling. While there, he helped establish and then manage the mouse transgenic facility. In 2016, he joined the Genome Editing Core facility at Rutgers, where he helped implement CRISPR/Cas9 platform for genome editing in mouse.

### A paradigm shift in the services provided and the role of transgenic cores in the future

Institutional transgenic core facilities play a central role in advancing biological and biomedical research by providing research communities with services to generate and preserve transgenic and genetically modified (GM) mice. Traditional mouse transgenesis methods for the last 30 years allowed great advances in science, generating thousands of GM mice to model human diseases and to study gene functions *in vivo*. Transgenic facilities applying these methods require a dedicated and highly skilled staff in ES cell culture and early stage embryo microinjection. The design and the materials used to generate GM mice were often not part of a transgenic core but, to certain extent, incumbent on the research laboratory. Recently, the advent of CRISPR/Cas9 technology for genome editing directly in the zygote, completely revolutionized transgenesis technologies with its simplicity and efficiency. This exciting new technology was of great appeal to many facilities and most moved quickly to adopt it for their services. Nevertheless, in the last 3 years, at a remarkable rapid pace, several CRISPR/Cas9 technologies were published; this dynamic pace poses a challenge to any facility on deciding which methods to deploy for their services. In addition, transgenic facilities found themselves with no control over the quality production of CRISPR components, like the gRNAs and donor templates.

At Rutgers University, the role of the Genome Editing Core Facility (GECF) was redefined to include a molecular biology unit, as an integral part of the core, in order to take control of the design, production and testing of all CRISPR components, including genotyping of CRISPR-generated mouse founders. This unit was essential for the successful implementation of CRISPR/Cas9 technologies and for the efficiency in generating GM mice. As such, the GECF will soon bypass conventional steps to generate GM mice, using instead CRISPR/Cas9 components to electroporate zygotes either *in vitro* or in situ, directly in the oviduct. For sure, core facilities are outgrowing their original role as producers of transgenic mice to expand the range of their services, including genome editing in species where gene targeting was not available. The GECF organization could be used as a blueprint for other institutions seeking to fully integrate CRIPSR technologies into their own transgenic cores for the research of the future ■




RUTGERS THE STATE UNIVERSITY OF NEW JERSEY

**Organization of the Genome Editing Core Facility at Rutgers University:**

In addition to its transgenic core, including Embryonic Stem cell culture, mouse rederivation, IVF and cryopreservation, a fully equipped molecular biology unit is added to give a quality control over the production of all CRISPR components. This unit is also used for genotyping and sequencing mouse founders. Services provided by GECF could be extended to cell lines genome editing and to possibly other species.

# WEBINAR EXCERPT: Q&A SESSION WITH **DANILO MADDALO** AND **NIREN MURTHY**

**How is pharma integrating CRISPR based animal models into the drug discovery pipeline?**

**DM:** This is great question but the answer is not actually that straight forward. It is a case by case approach and it depends a lot on the target and translatability of the target. What I can say is that it is definitely a type of model that is not pre-placing the previous system models but rather an additional way of investigating oncogenes or drugs or doing drug discovery.

**How do you envision the implementation of such technology in other aspects of the pharma workflow?**

**DM:** The implementation of such technology is something that will require time. It will probably be something that will be along the lines of working *in vivo* screening and generating animals that can then be used to screen for multiple compounds and for examples *in vivo* at the same time and to also check for the interaction between the same tumour and so on. This is probably what is going to happen.

**In your mouse experiments you stopped at 6mg/ kg, assuming that there was dose limiting toxicity what effect was observed?**

**NM:** So, the reason that we stopped at 6mg/ kg wasn't really because of toxicity, we measured for a lot of it but didn't observe a lot of toxicity. We measured for cytokines and we measured for formation but didn't see a lot of toxicity. It turns out that this was the maximum concentration that we could make a formulation for CRISPR Gold while keeping to the proper size. To inject more than 6mg/ kg would we would have to make too concentrated a solution of CRISPR Gold and at that concentration it starts to aggregate

**Can you do intravenous systemic injections of CRISPR Gold?**

**NM:** We have tried to do this but we see that this is certainly much less efficient after an intravenous injection and we think that it's just too big to go through the vasculature system. We believe that if you do an IV injection that you may be able to get some macro factions and things like that but the size is really too big to get to the cells outside of phagocytic cells ■

Danilo Maddalo,
Novartis Institutes for Biomedical Research

Danilo Maddalo graduated in Pharmaceutical Chemistry and Pharmacy with honors from Naples University (Italy) and gained his PhD in molecular biology with honors from Karlsruhe University (Germany) investigating stress response in cancer development and chemoresistance in murine models of prostate cancer. He joined Memorial Sloan Kettering Cancer Center in New York City as Research Fellow where he generated the first mouse model of chromosomal rearrangements by viral delivery of the CRISPR/Cas9 to the mouse lung. Dr. Maddalo is currently leading a laboratory in the Novartis Institute for Biomedical Research (NIBR) in Basel (Switzerland) to continue his work in translational medicine making use of mouse models.

Niren Murthy,
University of California, Berkeley

Dr. Niren Murthy is a professor in the Department of Bioengineering at the University of California at Berkeley. Dr. Murthy's laboratory is an interdisciplinary laboratory that focuses on the development of new materials for drug delivery and molecular imaging. Dr. Murthy received the NSF CAREER award in 2006, and the 2009 Society for Biomaterials Young Investigator Award. The Murthy laboratory has developed several new biomaterials for drug delivery and molecular imaging, such as the hydrocyanines.

(Opinions expressed by individual speakers are personal opinion and are not related to their company's product and/or commercial activity)

This is an excerpt from the free webinar, 'Genome Editing – Tools and Technologies for Drug Discovery and Bioinformatics'.

**The full webinar recording is available on our website at:**
www.genomeeditingusa-congress.com/2018-free-webinar-recordings

# FORTHCOMING EVENTS

OXFORD GLOBAL

## Biologics Series

| | | |
|---|---|---|
| APR | 11th Annual Proteins & Antibodies Congress | London, UK |
| | 5th Annual Peptides Congress | London, UK |
| | 5th Biennial Biosimilars & Biobetters Congress | London, UK |

Co-located Events

## Genomics Series

| | | |
|---|---|---|
| MAY | 2nd Annual Genome Editing USA Congress | Boston, USA |
| | 2nd Annual Advances in Transgenic Technology USA Congress | Boston, USA |
| | Synthetic Biology USA Congress | Boston, USA |
| OCT | 4th Annual Next Generation Sequencing & Clinical Diagnostics USA Congress | Boston, USA |
| | 4th Annual Single Cell Analysis USA Congress | Boston, USA |
| | Industrial Synthetic Biology Congress | Munich, Germany |
| NOV | 10th Annual Next Generation Sequencing & Clinical Diagnostics Congress | London, UK |
| | 6th Annual Single Cell Analysis Congress | London, UK |
| | 4th Annual Genome Editing Congress | London, UK |
| | Synthetic Biology Congress | London, UK |

Co-located Events

## Cell Series

| | | |
|---|---|---|
| NOV | 4th Annual Cell & Gene Therapy Congress | London, UK |
| | 7th Annual Cell Culture & Bioprocessing Congress | London, UK |
| | 5th Annual Stem Cell & Regenerative Medicine Congress | London, UK |
| | Biobanking Congress | London, UK |

Co-located Events

## R & D Series

| | | |
|---|---|---|
| FEB | 14th Annual Biomarkers Congress | Manchester, UK |
| MAR | 2nd Annual Formulation & Drug Delivery USA Congress | San Diego, USA |
| | 2nd Annual Inhalation & Respiratory Drug Delivery USA Congress | San Diego, USA |
| MAY | 4th Annual Formulation & Drug Delivery Congress | London, UK |
| | 3rd Annual Inhalation & Respiratory Drug Delivery Congress | London, UK |
| | 3rd Annual Advances in Immuno-Oncology Congress | London, UK |
| JUN | 19th Annual Drug Discovery Summit | Berlin, Germany |
| | 6th Annual Discovery Chemistry & Drug Design Congress | Berlin, Germany |
| | 2nd Annual Microbiome Discovery & Development Congress | Berlin, Germany |
| | 2nd Annual Precision Medicine Congress | Munich, Germany |
| OCT | 5th Annual Drug Discovery USA Congress | San Diego, USA |
| | 3rd Annual Biomarkers & Precision Medicine USA Congress | San Diego, USA |
| | Advances in Immuno-Oncology USA Congress | San Diego, USA |

Co-located Events

## PharmaTec Series

| | | |
|---|---|---|
| SEP | 16th Annual Pharmaceutical IT Congress | London, UK |
| | 2nd Annual Artificial Intelligence in Drug Development Congress | London, UK |
| | Digital Health and Digital Technologies Congress | London, UK |

Co-located Events

## Biotech Investment Series

| | | |
|---|---|---|
| MAY | Biotech Investment Showcase & Start Up Slam | London, UK |

Register your interest, e-mail us:

info@oxfordglobal.co.uk