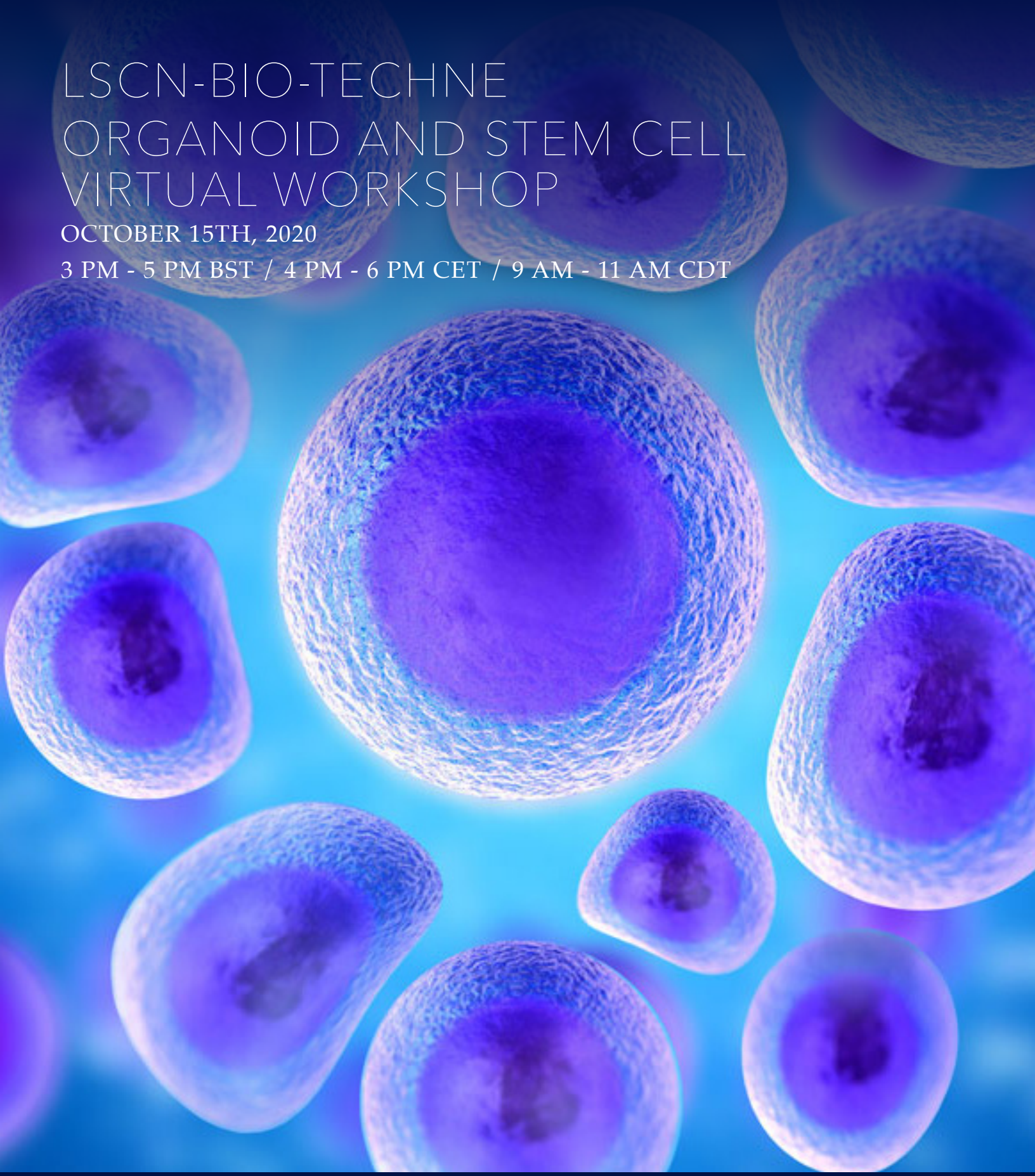


LSCN-BIO-TECHNE ORGANOID AND STEM CELL VIRTUAL WORKSHOP

OCTOBER 15TH, 2020

3 PM - 5 PM BST / 4 PM - 6 PM CET / 9 AM - 11 AM CDT

bio-techne®

WELCOME

Dear attendees,

Bio-Techne is delighted to welcome you to our first virtual workshop in partnership with the London Stem Cell Network (LSCN).

This meeting aims to bring together scientists to discuss the diverse topics being explored using stem cell cultures and organoids as model systems. Discover some of the latest, most exciting findings in the field of organoids, drug screening, and stem cell therapy from guest speakers who will be joining us from multiple locations across the globe. There will also be a live lab demonstration from our scientists in HQ.

We will be running a scientific quiz in between the sessions with the opportunity to win great prizes. The prize winners will be announced at the closing of the session.

We are extremely grateful to our speakers and all who have contributed to making this such an exciting event. We really hope that you enjoy this event, and we look forward to hearing from you at this or future events!

Sincerely,

Yas Heidari, Ph.D.

Product Manager, Protein & Cell Biology, Europe, Bio-Techne

Dr. Rob Hynds

Committee Chair, The London Stem Cell Network

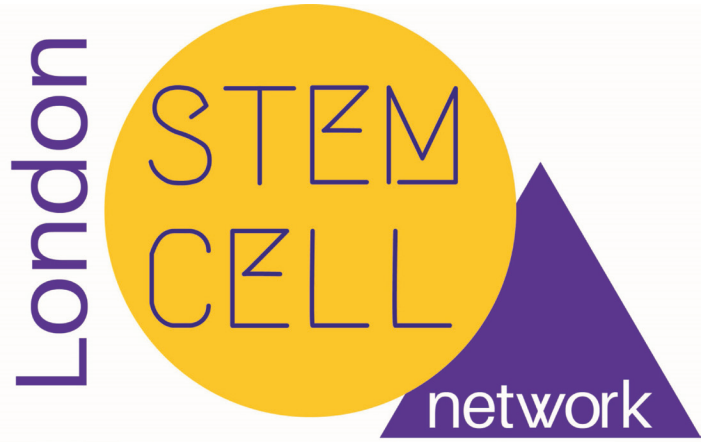
University College London and The Francis Crick Institute

BIO-TECHNE

Bio-Techne Corporation (NASDAQ: TECH) is a global biotechnology company which manufactures consumables and instrumentation for scientific and medical research. We aim to meet the expanding needs of scientific discovery by combining disciplines and expertise to offer a full portfolio of solutions.

Bio-Techne is a public company which was founded in Minneapolis, Minnesota, USA in 1981. We have 2,200 employees globally, and today our product line extends to over 500,000 products, many of which are manufactured in-house. we specialise in recombinant proteins such as cytokines, growth factors, and antibodies, biologically active small molecules, immunoassays, cell culture products and kits, laboratory equipment, and specialty diagnostics.

Bio-Techne aims to help its customers accelerate life sciences research, solve complex challenges, improve patient diagnostics, and increase laboratory productivity. Our key brands include R&D Systems, Novus Biologicals, Tocris, Protein Simple, Biospacific, Cliniqa, and ACD. Products from across our brands have been cited over 350,000 times in scientific journals. We strive to be one of the world's most trusted companies by offering our customers a combination of innovative technologies together with commitment to reliability, and ease of doing business.



The London Stem Cell Network is an international platform for research groups working across universities and institutes. The LSCN aims to provide a networking platform for the research community through events including workshops on specific stem cell-related areas and annual symposia. The ultimate goal of the LSCN is to highlight the wide breadth of stem cell research performed and facilitate interdisciplinary collaboration.

You can join LSCN as a member free-of-charge to receive regular updates on news, events and jobs in the stem cell field, as well as discounted attendance at their workshops and symposia. Further details can be found on the website (https://lscn.crick.ac.uk) and LSCN can be followed on Twitter @LSCN_UK!

PROGRAM

THURSDAY 15TH OCTOBER 2020, 3-5 PM BST

3:00-3:10 pm

INTRODUCTION BY YAS HEIDARI (BIO-TECHNE), AND ROB HYNDS (LSCN)

3:10-3:25 PM

"INTESTINAL TISSUE ENGINEERING FOR CHILDREN WITH INTESTINAL FAILURE".

Dr Vivian Li, Crick Institute, London, UK

QUIZ ROUND 1: OXFORD

3:25-3:40 PM

'INFLAMMATORY NICHES DIRECT LUNG REGENERATION"

Dr Joo-Hyeon Lee, Cambridge University, Cambridge, UK

QUIZ ROUND 2: MINNEAPOLIS

3:40-3:55 PM

"COMPARISON OF DNA DAMAGE RESPONSES BETWEEN 2D AND 3D HUMAN HEPATIC CELL MODELS USING THE COMETCHIP™ ASSAY"

Dr Xiaoqing Guo, Food And Drug Association (FDA), Jefferson, US.

3:55-4:10 PM

"THE COMETCHIP™ ASSAY AND ITS APPLICATION IN THE DETECTION OF DNA DAMAGE IN LUNG ORGANOIDS"

Dr Cyrus Munshi, Bio-Techne, MN, US joining us direct from the lab to demonstrate CometChip technology

QUIZ ROUND 3: BRISTOL

4:10-4:30 PM

STEM CELL TRANSLATIONAL STREAM, HOSTED BY DR LINDSEY CLARKE, BIO-TECHNE

A panel of industry and academic experts performing translational research discuss how stem cell therapy may help solve some of the key challenges around delivering therapies at scale such as having a universal donor, standardizing products, and one chance manufacturing of single batches.

PANELISTS

Dr Stefan Braam, CEO of Ncardia

Dr Amanda Carr, Lecturer, Pete Coffey Lab, Institute of Ophthalmology, UCL

Mr Tristan Pritchard-Moore, BDM, Necstgen

Dr Jiagang 'Jack' Zhao, CEO of Alpine BioTherapeutics

4:30-4:50 PM
GRAND Q&A PANEL

4:50-5:00 PM
QUIZ AWARDS AND CLOSING OF SESSION BY YAS HEIDARI (BIO-TECHNE), AND ROB HYNDS (LSCN)

ABSTRACTS, BIOGRAPHIES, AND REFERENCES

"INTESTINAL TISSUE ENGINEERING FOR CHILDREN WITH INTESTINAL FAILURE"

Dr Vivian Li, Crick Institute, London, UK

ABSTRACT

Intestinal failure, following extensive anatomical or functional loss of small intestine, has debilitating long-term consequences for children. The priority of patient care is to increase the length of functional intestine, particularly the jejunum, to promote nutritional independence. Here we construct autologous jejunal mucosal grafts using biomaterials from pediatric patients and show that patient-derived organoids can be expanded efficiently in vitro. In parallel, we generate decellularized human intestinal matrix with intact nanotopography, which forms biological scaffolds. Proteomic and Raman spectroscopy analyses reveal highly analogous biochemical profiles of human small intestine and colon scaffolds, indicating that they can be used interchangeably as platforms for intestinal engineering. Indeed, seeding of jejunal organoids onto either type of scaffold reliably recon- structs grafts that exhibit several aspects of physiological jejunal function and that survive to form luminal structures after transplantation into the kidney capsule or subcutaneous pockets of mice for up to 2 weeks. Our findings provide proof-of-concept data for engineering patient-specific jejunal grafts for children with intestinal failure, ultimately aiding in the restoration of nutritional autonomy.

BIOGRAPHY

Vivian Li obtained her PhD at the University of Hong Kong in 2008, studying human colonic development and tumourigenesis. She then received the Croucher Foundation Fellowship to pursue her post-doctoral training in Hans Clevers' lab at the Hubrecht Institute, the Netherlands, where she studied Wnt regulatory mechanisms in the intestine. Vivian Li is now group leader at the Francis Crick Institute. Her lab investigates signalling regulation of intestinal homeostasis and cancer, with primary focus on Wnt signalling pathways. With the use of patient-derived organoids, Vivian is also developing innovative strategies to treat patients with intestinal failure.

REFERENCE

Meran, L., Massie, I., Campinoti, S., Weston, A.E., Gaifulina, R., Tullie, L., Faull, P., Orford, M., Kucharska, A., Baulies, A., Novellasdemunt, L., Angelis, N., Hirst, E., KÖnig, J., Tedeschi, A.M., Pellegata, A.F., Eli, S., Snijders, A.P., Collinson, L., Thapar, N., Thomas, G.M.H., Eaton, S., Bonfanti, P., De Coppi, P., Li, V.S.W. (2020). Engineering transplantable jejunal mucosal grafts using patient-derived organoids from children with intestinal failure. *Nature Medicine.* Doi: 10.1038/s41591-020-1024-z. [Ahead of print]

"INFLAMMATORY NICHES DIRECT LUNG REGENERATION"

Dr Joo-Hyeon Lee, Wellcome–MRC Cambridge Stem Cell Institute,
Cambridge University, Cambridge, UK

ABSTRACT

Numerous epithelial stem and progenitor cells have been identified and shown to play a role in lung homeostasis and injury repair, yet the precise cellular events and molecular mechanisms that direct stem cell fate behaviours remain elusive. We used a combination of genetic lineage tracing, single cell RNA-seq and three-dimensional organoid co-culture approaches to identify the functional roles of critical niche cell populations that control lung stem/progenitor cell populations and the key regulatory networks at individual levels. We will discuss how inflammatory signals regulate alveolar regeneration via directing stem cell fate dynamics during regeneration process and its further implication in lung chronic diseases.

BIOGRAPHY

Dr Joo-Hyeon Lee established her research group at the Wellcome-MRC Cambridge Stem Cell Institute, University of Cambridge, in 2016. Her group focuses on understanding how stem and progenitor cells regulate their fate behaviours to specify and maintain tissues. Their goal is to define the identity and heterogeneity of stem cell populations, understand the key stem-niche interactions and the precise mechanisms that maintain tissue homeostasis and regeneration. Specifically, her team is investigating how the quiescent state is maintained and becomes activated, how cell fate or/and state is determined, and how niches develop and remodel in lung homeostasis, injury repair and disease states. Joo-Hyeon is a Wellcome Trust Sir Henry Dale Fellow and an ERC Starting Grant Awardee.

REFERENCE

Choi, J., Park, J.E., Tsagkogeorga, G., Koo, B.K., Han, N., and Lee, J.H. (2020). Inflammatory signals induce AT2 cell-derived Damage-Associated Transient Progenitors that mediate alveolar regeneration. *Cell Stem Cell.* 27, 366-382.

"COMPARISON OF DNA DAMAGE RESPONSES BETWEEN 2D AND 3D HUMAN HEPATIC CELL MODELS USING THE COMETCHIP™ ASSAY"

Dr Xiaoqing Guo, National Center for Toxicological Research, Food And Drug Association (FDA), Jefferson, US.

ABSTRACT

In vitro genotoxicity testing is an important part of the safety assessment for various xenobiotics. An important drawback of current in vitro systems is that the genotoxicity assays are usually conducted in cell models without metabolic competency. To evaluate the appropriateness of metabolically competent HepaRG cells, a human hepatoma cell line, for the genotoxicity testing, the DNA damage effect of 16 compounds known to have different genotoxic or carcinogenic mode-of-action were evaluated using the high-throughput in vitro CometChip assay; and the resulting DNA damage responses were compared with those from primary human hepatocytes (PHHs). The results showed that HepaRG cells expressed similar level of CYP450 enzyme activities to PHHs. Following a 24-h treatment, PHHs demonstrated an overall higher sensitivity (90%) for detecting DNA damage from 11 genotoxicants or carcinogens than those of HepaRG cells (70%) in 2D cultures. Both PHHs and HepaRG cells demonstrated a high sensitivity in detecting indirect-acting genotoxic carcinogens that require metabolic activation and showed a perfect specificity in detecting 5 non-carcinogens. We further used advanced 3D HepaRG spheroids to evaluate DNA damage effect of two compounds that produced weak or negative responses in 2D HepaRG cells. As a result, both compounds significantly increased the % DNA in tail in 3D HepaRG spheroids at levels comparable to those of PHHs. These results demonstrated that the high-throughput CometChip technology can be applied using 3D hepatic spheroids for genotoxicity testing; and that 3D HepaRG spheroids may have unique potential benefits for generating data better predicting human in vivo responses.

BIOGRAPHY

Dr. Xiaoqing Guo is a Research Biologist in the Division of Genetic and Molecular Toxicology (DGMT) at the National Center for Toxicological Research (NCTR)/Food and Drug Administration (FDA), USA. She has 20+ years scientific training and research experience in the field of cancer research, genetic toxicology, general toxicology, and molecular biology. Since joined the DGMT/NCTR in 2008, Dr. Guo has been working on the evaluation of the mutagenicity of chemicals of FDA regulatory interest using genotoxicity assays. Her current research interest is developing advanced in vitro cell modes using pathway-based, high-throughput, and high-content (HTHC) approaches for risk assessment. Her scientific efforts resulted in the publication of 70+ peer-reviewed manuscripts, 9 book chapters, and multiple oral or poster presentations at national and international scientific meetings.

REFERENCE

Seo, J., Tryndyak, V., Wu, Q., Dreval, K., Pogribny, I., Bryant, M., Zhou, T., Robison, T. W., Mei, N., Gou, X. (2019). Quantitative comparison of in vitro genotoxicity between metabolically competent HepaRG cells and HepG2 cells using the high-throughput high-content CometChip assay. *Archives of Toxicology*. 93, 1433–1448.

"THE COMETCHIP™ ASSAY AND ITS APPLICATION IN THE DETECTION OF DNA DAMAGE IN LUNG ORGANOIDS"

Dr Cyrus Munshi, Bio-Techne, MN, US
joining us direct from the lab to demonstrate CometChip technology

ABSTRACT

The CometChip platform is a high-throughput single-cell gel electrophoresis (SCGE) version of the comet assay, a sensitive technique to detect and measure DNA strand breaks and repair in various cell types. The comet assay is now a standard technique for assessment and quantitation of DNA damage and repair in genotoxicity studies. However, the high degree of variation associated with the traditional slide-based comet assay between studies has had an adverse impact on the reproducibility of the assay. The CometChip was developed to overcome the various complications associated with this lack of reproducibility by introducing uniformly dispersed micropores into the gel. In order to demonstrate the high-throughput and versatility of the system, we present highlights of experimental data derived using the CometChip to assess DNA damage in lung organoids.

BIOGRAPHY

Cyrus Munshi's scientific disciplines encompasses biochemistry, pharmacology, cell signalling, antibody engineering, and biologics manufacture. He currently leads efforts to produce and engineer recombinant antibodies from multiple species. In addition, he spearheads the development of products relating to DNA damage and repair, most notably the CometChip platform. At Bio-Techne, he has also guided efforts to produce difficult to express proteins in heterologous expression systems. Cyrus holds M.S. and Ph.D. degrees from Cornell University. Prior to joining Bio-Techne, Cyrus pursued postdoctoral studies at the University of Minnesota and Ohio State University. His postdoctoral experience covered Structure, function and kinetics of campthothecin compounds for anti-tumor properties, Calcium signalling through IP3-independent mechanisms mediated by cyclic ADP-ribose (cADPR) and nicotinic acid dinucleotide phosphate (NAADP), and structure and function characterization of cyclases and CD38. He is a co-author of more than 50 scientific publications, book chapters and proceedings.

STEM CELL TRANSLATIONAL STREAM, HOSTED BY DR LINDSEY CLARKE, BIO-TECHNE

A panel of industry and academic experts performing translational research discuss how stem cell therapy may help solve some of the key challenges around delivering therapies at scale such as having a universal donor, standardizing products, and one chance manufacturing of single batches.

PANELISTS

DR LINDSEY CLARKE heads up Bio-Techne's newly formed Global Cell and Gene Therapy Product Marketing team, having joined the company in late 2018 to establish their European Cell and Gene Therapy specialist team. Overseeing a portfolio of tools, technologies, and instrumentation applicable to cell and gene therapies, her role has focused on building the team to support customers applications, planning the roll out of new innovations, and developing strategic partnerships within the industry.

DR STEFAN BRAAM is the Co-Founder, CSO and CEO of Ncardia. Earlier in his career, Stefan obtained his Ph.D. in stem cell biology under the supervision of Prof. Dr. Mummery and obtained international experience in labs in the UK and Australia. Stefan won the NGI venture challenge (2009), the Niaba bio-business Masterclass (2010). Stefan has published in leading scientific journals, is actively involved in a number of commercial research collaborations, and is an inventor on multiple patent families.

DR AMANDA CARR obtained her Ph.D. from University of Manchester examining the molecular nature of seasonal and circadian clocks. In 2007, Amanda began working with Professor Pete Coffey, contributing to the development of a cellular therapy for age-realted macular degeneration using human embryonic stem cell-derived RPE which is now in clinical trials at Moorfields Eye Hospital, London. Amanda is currently a lecturer at the UCL Institute of Ophthalmology, carrying on with this vital work.

MR TRISTAN PRITCHARD-MOORE is Business Development Manager for Netherlands Center for the Clinical Advancement of Stem Cell and Gene Therapies (NECSTGEN). He is responsible for commercial strategy, business development, and collaborations at NECSTGEN. NECSTGEN is a state of the art research development and GMP production facility enabling ground breaking cell and gene therapy development in the Netherlands.

DR JIAGANG "JACK" ZHAO is the founder and CEO of Alpine BioTherapeutics. Jack received his Ph.D. from Icahn School of Medicine at Mount Sinai, and was most recently faculty investigator at the Shiley Eye Institute at the University of California, San Diego, where he focused on ocular stem cell research. Jack formed Alpine BioTherapeutics in 2017 with the mission to develop next generation stem cell-based therapies to treat progressive blindness.

BIO-TECHNE RESOURCES FOR ORGANOID RESEARCH

Organoid and 3-D cell culture are emerging as pivotal systems for understanding human organ development, modelling disease, screening for drug efficacy or toxicity, and investigating personalized medicine. The reagents and protocols needed to culture these advanced multi-cellular in vitro tissues vary by organ, species, and whether they are being generated from tissue or pluripotent stem cells.

Bio-Techne offers you a multitude of research tools and resources for organoid research covering the essential workflow below:

Culture your organoids using our highly consistent scaffolding matrix, Cultrex™ BME, and super low-endotoxin media supplements such as N-2-MAX, and N21-MAX. Ensure optimal culture and differentiation of your organoids through use of highly bioactive and stable R&D Systems cytokines and growth factors, and small molecules. Isolate your cultures using our defined organoid harvesting solution.

All-in-one cell verification and differentiation kits, a large selection of lineage specific and sensitive antibodies, RNAscope® *in situ* hybridization assays, our blockbuster Quantikine® ELISAs, and Luminex® assays ensure that the analysis and investigation part of your projects get off to a flying start!

REVIEWS OF BIO-TECHNE'S ORGANOID AND STEM CELL RESOURCES

"We utilise organoids as powerful research tools to study the underlying regulation of stem cell and cancer and to develop innovative strategies for regenerative medicine. We cultured these 3D organoids in the lab using the R&D Systems Cultrex™ reduced growth factor BME, which gave very consistent and reliable results. Other R&D Systems reagents such as growth factors and ACD's RNAScope™ technology have all contributed significantly to our findings."

Vivian Li, Ph.D., Crick Institute, London, UK

"Cultrex™ Ready BME has worked very well for our lab. H9 hESCs (WA09) were grown on Cultrex ReadyBME and was directly compared side-by-side to our normal basement membrane. So far, I've grown the cells for more the 5 passages and haven't observed any changes in proliferation rate, viability, cell morphology or the increased appearance of differentiated cells."

Amar M. Singh, Ph.D., University of Georgia

"Once I learned you were releasing an animal-free GMP N2 Media Supplement, I began converting away from my current supplier. Now I'm using the RUO version and testing the GMP grade N-2 MAX"

Jiagang "Jack" Zhao, Ph.D., Alpine Biotherapeutics

"When we switched to the Bio-Techne Pluripotent Functional Identification Kit we found it was absolutely super efficient. In a few days you can have results about the 3 germ layers, especially endoderm that we could never see before. And it was very easy to use."

Barbara Corneo, Ph.D.
Director, Columbia Stem Cell Core Facility

"The immunofluorescent staining of wholemount 3D self-organising organoids allows us to visualise molecular markers of cellular behaviours and fate choices in lung organoid models. By using lineage-specific antibodies for human lung epithelial cells from R&D Systems (anti-SCGB1A1, RAGE/AGER, E-Cadherin antibodies) we could characterise the differentiation capacity of human lung epithelial stem and progenitor cells at a clonal level in vitro."

Dr Joo-Hyeon Lee
Wellcome–MRC Cambridge Stem Cell Institute, Cambridge University

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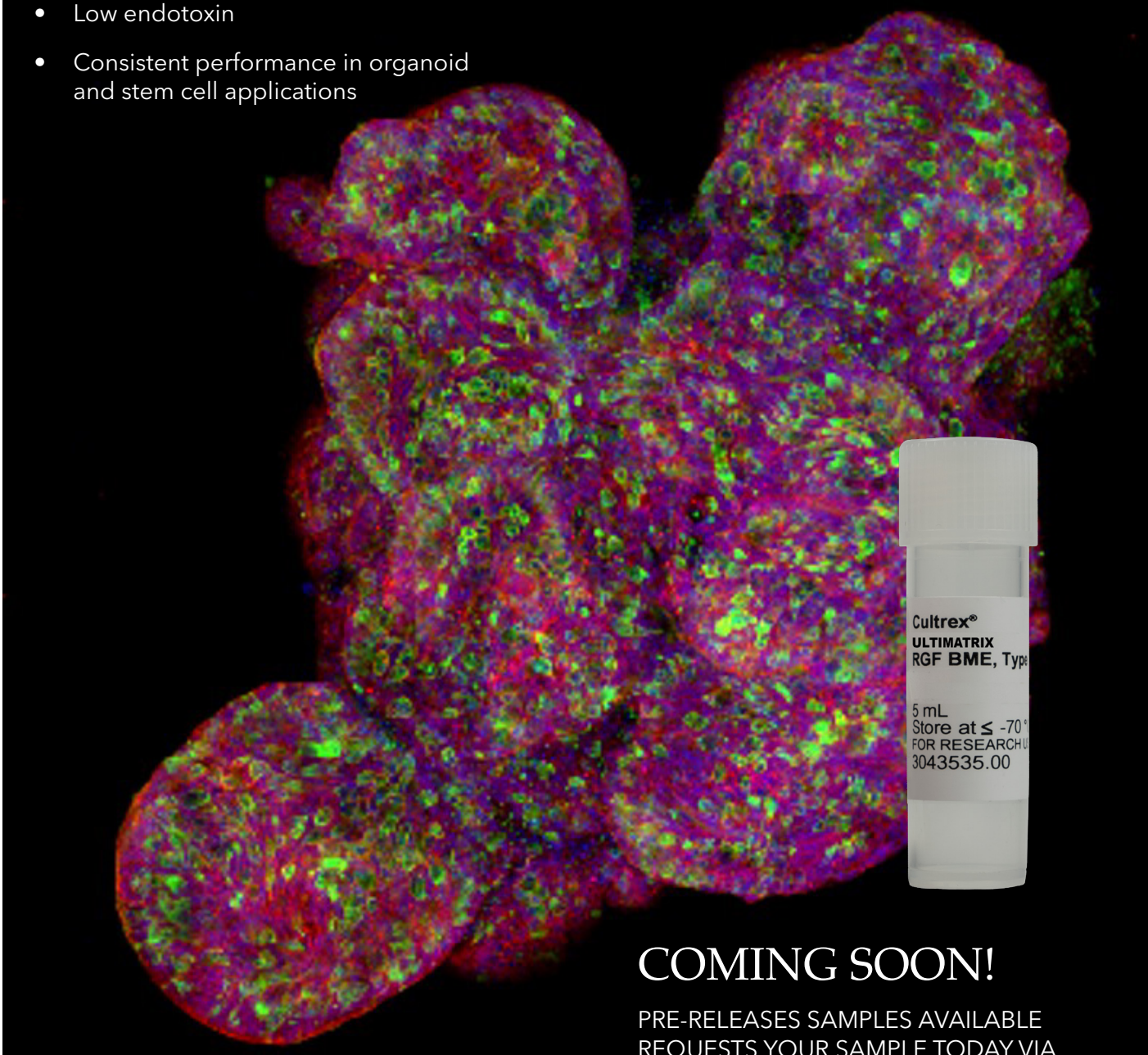

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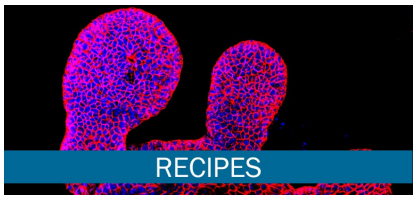
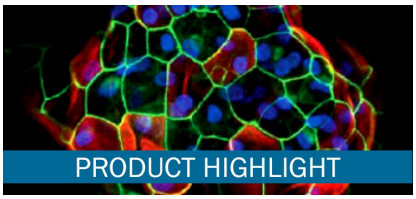
ORGANOID RESOURCES AT BIO-TECHNE

Organoid and three-dimensional (3-D) cell culture are emerging as pivotal systems for understanding human organ development, modeling disease, screening for drug efficacy or toxicity, and investigating personalized medicine. The reagents and protocols needed to culture these advanced multi-cellular *in vitro* tissues vary by organ, species, and whether they are being generated from tissue or pluripotent stem cells. This page serves as a reagent and technical resource to help researchers build robust and consistent organoid cultures designed to provide you with a central location to access protocols, view webinars, stay up to date on organoid recipes and blogs, and discover new products relevant to your work in organoid research. Navigate below to find information for culturing organoids from all tissue types.

Read more about the development and future of organoids for research.





Find out more | rndsystems.com/products/organoid-and-3d-culture-reagents