Advances in IMMUNO-ONCOLOGY

Pre-Event Newsletter Apr 2019

ILEC CONFERENCE CENTRE

20 - 21 MAY 2019 | LONDON, UK

OXFORD GLOBAL CONFERENCES

Contents

This is an Interactive Newsletter.
You can click on elements such as website links or the contents below.

Meet the Team

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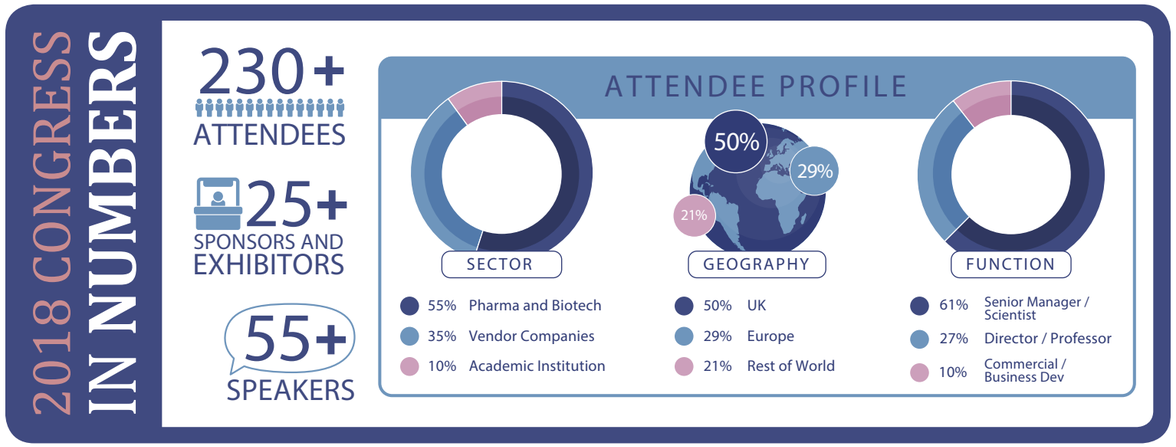

WELCOME TO THE SECOND EDITION OF OXFORD GLOBAL'S ANNUAL ADVANCES IN IMMUNO-ONCOLOGY NEWSLETTER!

With the Advances in Immuno-Oncology Congress returning to London once again in May, I am delighted to look back at some of the highlights of the 2018 congress and provide some details on a few of the key features & exciting additions for 2019.

This event has grown year on year since its launch and 2018 was no different, bringing together over 300 attendees and 24 sponsors to discover collaborative solutions to immuno-oncology discovery and development. Alongside innovative scientific case studies and extensive networking opportunities, last year's event saw the launch of our breakfast roundtables, with attendees advising they provided an invaluable opportunity to discuss key challenges and knowledge share with their peers.

In 2019, our forum will feature over 65 presentations across six conference tracks, allowing you to benefit from leading scientists sharing their knowledge and experiences across the whole spectrum of Immuno-Oncology R&D, from early discovery through to translation and clinical development. Across all tracks, the event now features case studies into bispecific antibodies, cell & gene therapies, cancer vaccines, oncolytic viruses and microbiome-derived therapies, reflecting industry's push to utilise new therapeutic strategies to complement or supersede checkpoint inhibition. In order to better evaluate the likely long-term success of these strategies, we have also incorporated a panel on Ensuring the Longevity of Immuno-Oncology Therapies into our Discovery track.

Another important focus area is the development of targeted immunotherapies. With significant subsets of patients failing to respond to immunotherapies, and others suffering adverse events, there is a significant need to identify biomarkers that can better predict patient response and guide patient and treatment selection. Through our sessions on Translational Immuno-Oncology and Precision Medicine & Personalised Therapy, you can hear case studies on how companies are tackling challenges in this space, as well as take part in our discussion on Determining the Right Approach to Understand and Model Tumour Response.

I am pleased to inform you that the 2019 event will be held in a new venue, the ILEC Conference Centre, and we will also be launching a new and improved event app!

Read on for a range of interesting interviews and insights with some of 2019's industry-leading speakers and participating sponsors, and I look forward to welcoming you to the event in May.

- Peter Franko, Commercial Director

4TH ANNUAL

ADVANCES IN IMMUNO-ONCOLOGY CONGRESS

ILEC CONFERENCE CENTRE

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WHO IS ATTENDING?

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

- **300+ senior level attendees** from leading pharmaceutical, biotechnology and solution provider companies
- **Directors, Heads and Professors** of preclinical, translational and clinical immuno-oncology, alongside cancer vaccines, bispecifics, checkpoint inhibitors and cell & gene therapies
- **Highly esteemed members** of internationally renowned academic institutions

These companies and many more:

GlaxoSmithKline · Kite · pieris PHARMACEUTICALS · AstraZeneca · OXFORD BioTherapeutics · JUNO THERAPEUTICS A Celgene COMPANY · SANOFI · Roche · Boehringer Ingelheim · MSD · AMGEN · novimmune · Adaptimmune TRANSFORMING T CELL THERAPY · MedImmune · IMMUNOCORE targeting T cell receptors

GOLD

abcam · Personalis

SILVER

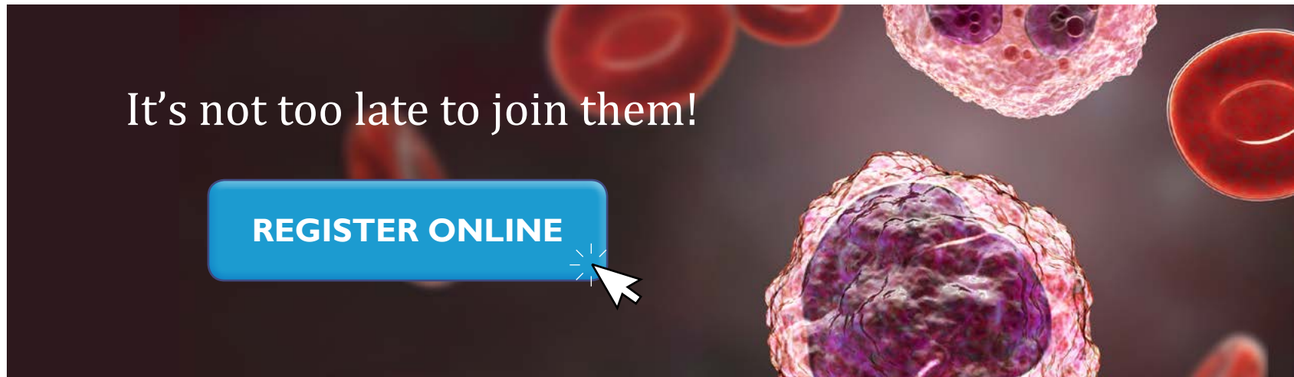
PerkinElmer For the Better · MITRA BIOTECH · pharmatest · COVANCE SOLUTIONS MADE REAL

BRONZE

FLUIDIGM · CONCEPT LIFE SCIENCES · biogazelle · charles river · ULTIVUE ILLUMINATING BIOLOGY

NETWORK AND PROGRAMME

10X GENOMICS · biotechne · BPES cytena SYNENTEC · chemometec · eurofins · flash THERAPEUTICS · HistologiX IHC and Contract Histology · HTG · ImmunXperts · myriad RBM · OracleBio Image Analysis Solutions · PEPROTECH OUR SUPPORT, YOUR DISCOVERY · Promega · proteome sciences · sartorius stedim biotech · Tissue Solutions Working with you, For you · TriStar TECHNOLOGY GROUP



HERA-LIGANDS ARE NOVEL POTENT CO-STIMULATORY TNF RECEPTOR AGONISTS FOR IMMUNO-ONCOLOGY THERAPIES

DR. KATHARINA BILLIAN-FREY

Senior Scientist Drug Discovery / Protein Engineering, Apogenix AG

Apogenix' TNFSF Receptor Agonists

The diverse functions of the immune system are orchestrated by a complex and delicately balanced interplay of stimulatory and inhibitory signals. Many key regulators of immune cell function belong to the tumour necrosis factor superfamily (TNFSF) and their cognate receptors, the TNF receptor superfamily. The TNFSF consists of 19 structurally related ligands, each binding to one or more of the 29 members of the TNF receptor superfamily. TNFSF receptors are of great importance in the anti-tumour immune process. They are expressed by a wide variety of immune cells including T cells and antigen-presenting cell populations, such as dendritic cells and macrophages, as well as by tumour cells themselves. This diverse expression pattern highlights the critical role that TNFSF receptors play in many parts of the body and in the various phases of the anti-tumour immune response.

TNFSF-mediated signaling induces a wide range of biological effects, including programmed cell death (i.e., apoptosis), proliferation, differentiation, and tumour growth. Therefore, TNFSF signaling is an attractive target for therapeutic intervention. TNFSF ligands naturally exist as homo-trimers with three receptor binding sites. The interaction of trimeric TNFSF ligands with their specific cell surface receptors leads to clustering of these receptors, followed by intracellular signal transduction. The trivalent structure of the TNFSF proteins and the resulting receptor clustering are prerequisites for the transmission of a signal delivered into the cell.

Apogenix is developing a novel class of TNFSF receptor agonists (HERA-ligands, see Figure) for the treatment of various types of cancer. Their unique hexavalent molecular structure perfectly mimics the endogenous ligands and overcomes the known limitations of antibodies and other biologics targeting TNFSF receptors. Antibodies can only bind two TNFSF receptors in a spatially undefined manner and require secondary cross-linking via Fcγ receptors. In contrast, Apogenix' HERA-ligands lead to well-defined TNFSF receptor clustering without the need for further cross-linking. This results in a sufficient level of the appropriate signal being transmitted into the target cell, whereas agonistic antibodies transmit these signals at insufficient levels. Preclinical work at Apogenix has demonstrated the producibility and biological activity of these novel TNFSF receptor agonists as well as their superiority over agonistic antibodies.

HERA-CD40L Induces T-Cell-Mediated Anti-Tumour Immune Response through Activation of Antigen-Presenting Cells

Exemplarily, efficacy data for one HERA-ligand family member are presented here. CD40 - the receptor for HERA-CD40L - is expressed on the surface of antigen presenting cells (APCs) as well as some tumour cell types. Binding of CD40 to its natural ligand leads to increased APC activation and an enhanced immune response. CD40 agonist therapy plays an important role in APC maturation and their migration from the tumour to the lymph nodes, resulting in elevated antigen presentation and T cell activation.

HERA-CD40L provides efficient receptor agonism on CD40-expressing cells and, importantly, does not require FcγR-mediated cross-linking. Strong activation of NFκB signaling was observed upon treatment of B cells with HERA-CD40L. Monocyte treatment with HERA-CD40L promoted differentiation towards the M1 spectrum and repolarization of M2 spectrum macrophages towards the M1 spectrum phenotype. Treatment of in vitro co-cultures of T and B cells with HERA-CD40L triggered robust anti-tumour activation of T cells, which depended upon direct interaction with B cells. In contrast, bivalent anti-CD40 antibodies and trivalent soluble CD40L displayed weak activity which critically depended on cross-linking.

In vivo, a murine surrogate of HERA-CD40L stimulated clonal expansion of OT-I specific murine CD8+ T cells without affecting non-specific immune cells. In the syngeneic CT26wt mouse model mHERA-CD40L treatment converts cold into hot tumours by increasing infiltration of CD8+ and CD4+ T cells. In addition, mHERA-CD40L showed single-agent anti-tumour activity in the CD40-negative syngeneic MC38-CEA mouse model, suggesting an involvement of the immune system in controlling tumour growth.

In summary, HERA-CD40L is a potent agonist that is able to establish single-agent anti-tumour immune responses. In comparison to bivalent benchmark antibodies, HERA-CD40L showed superior biological activity which qualifies this molecule as an ideal candidate for combinatorial cancer treatments.

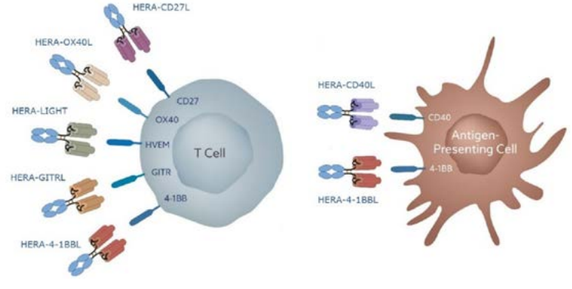


Fig: Apogenix' HERA-ligands in preclinical development

WEBINAR EXTRACT: Q&A SESSION WITH RUSSELL LAMONTAGNE

Russell LaMontagne,
President and Chief Executive Officer, Boston Immune Technologies and Therapeutics Inc

Russell LaMontagne is Co-Founder, President and CEO of Boston Immune Technologies and Therapeutics, Inc. He has been senior advisor to biotechnology and pharmaceutical companies for over 20 years. He played a predominant role in the development of several early stage companies and has advised pharmaceutical companies regarding commercialization strategies. Russell is also co-founder of Endobiome, Inc.

Why is TNFR2 a new target?

It's a new target in the sense that it is low expressional and a lot of people didn't look for it for a long time. Also, if you are looking at healthy cells it is something that isn't going to come up. There has been some work done in auto-immunity to look at it because we knew that it was potentially a way to grow and to proliferate Treg in auto-immunity. This is what you would want to do but we tend to think of it as new because it was ignored for so long and didn't seem to be particularly important.

I think that this would be true of a lot of Treg targets. If you were to look at an immunology textbook and it was 10 years old, the chapter on Tregs just wouldn't exist but there would maybe be a little section on what they then called T suppressor cells. If you looked at a text book from 5 years ago there would be a couple of paragraphs but now Tregs are the hot topic.

I think that those two factors have kept it under the radar for a long time.

How widely expressed is the TNFR2 oncogene?

It seems to be widely expressed. We know that in certain cancers it would be the degree of expression so it is heavily expressed in leukaemia. We know from the screening that we have done that it's highly expressed in ADDC lymphoma, we can also see this in some of our work in ovarian, breast, and colon cancers. It will be interesting as we move forward as the pace of the data is really increasing. More and more people are coming out to say that we see it in this particular cancer and hopefully the expression is high because it is potentially a very low toxic way to treat some of these cancers.

What cancers would you be interested in targeting first?

I don't want to tip our hand too much but I would say all the cancers that I've already mentioned that have a high expression. Certainly those which contain a T Cell lymphoma have an unmet need and those patients unfortunately don't have much that works, so I think that any cancer that expresses TNFR2 and the oncogene and has a lot of Tregs. Not all cancers induce a big Tregs response, but I think those cancers will be our first target.

Have you considered constructing bi-specific antibodies?

The way our patent portfolio would allow us to do that is to stop anyone else who would try to put TNFR2 into something else. If you look at the way our antibodies bind and the fact that we don't need cross licking and ADDC I don't think that a bi-specific is a good idea. I'm sure two immunologists in a room could have a much more heated argument about that but that's not an approach that we would take right now ■

Tumor necrosis factor receptor 2 (TNFR2), also known as tumor necrosis factor receptor superfamily member 1B (TNFRSF1B) and CD120b, is a membrane receptor that binds tumor necrosis factor-alpha (TNFα).

The protein encoded by this gene is a member of the tumor necrosis factor receptor superfamily, which also contains TNFRSF1A. This protein and TNF-receptor 1 form a heterocomplex that mediates the recruitment of two anti-apoptotic proteins, c-IAP1 and c-IAP2, which possess E3 ubiquitin ligase activity. The function of IAPs in TNF-receptor signalling is unknown, however, c-IAP1 is thought to potentiate TNF-induced apoptosis by the ubiquitination and degradation of TNF-receptor-associated factor 2 (TRAF2), which mediates anti-apoptotic signals. Knockout studies in mice also suggest a role of this protein in protecting neurons from apoptosis by stimulating antioxidative pathways.

This is an extract from our free webinar *'The Role For TNFR2 In The Tumor Microenvironment'* presented by Russell La Montagne. To listen to the full recording, please visit www.oxfordglobal.co.uk/immuno-oncology/webinar-recordings/

MASS SPECTROMETRY TOOLS FOR CHARACTERISATION OF THE IMMUNE SYSTEM

MARTINE ROUDIER

Head Pathologist, AstraZeneca

Inflammatory bowel diseases of the gastrointestinal track are not well characterized yet. However characterization of a complex immune ecosystem will facilitate understanding of their differences. For example, it has been reported that the variation of PD-L1 expression underpins the development and pathogenesis of Crohn's disease. Infectious diseases of the gut can be modulated by macromolecules. For example, using MSI (mass spectrometry imaging) palmitoyl-carnitine (PalC), a long chain fatty acid ester of carnitine, was found to play a significant role in modulating the host response to infection by Salmonella Typhimurium. Both methodologies can be associated to localize investigational drugs and their local effects on immune inflammatory ecosystems.

IMC (imaging mass spectrometry) with its spatial resolution of up to 40 antibody on the same slide and MSI (mass spectrometry imaging) with its spatial distribution of metabolites, can help understanding ICs (immune cells) distribution and macromolecule distribution in situ. However IMC and MSI need to be carefully validated prior to their use, using mouse and human specimen controls ■

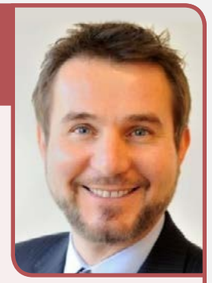
HOW CD8 IMAGING IS USEFUL TO PHARMA REGARDING DRUG RESEARCH & CLINICAL DECISION MAKING

IVAN PLAVEC

ImaginAb has developed a minibody [89Zr-Df-IAB22M2C] for non-invasive imaging of CD8 T cells in immuno-oncology patients using PET/CT. ImaginAb's completed Phase 1 study and the ongoing Phase 2 clinical study highlight the utility of CD8 imaging to provide insights in the mechanisms of immunotherapy and predict treatment responses. Pharmaceutical companies such as Merck & Co, Boehringer Ingelheim and Nektar Therapeutics have already started to incorporate CD8 imaging in clinical trials to facilitate the development of investigational immunotherapies.

Our free webinar is for clinical development experts interested in learning more about the latest Immuno-Oncology work. This is a free event open to all, so why not register and benefit from the expertise of our speakers?

Ivan Plavec,
Chief Business Officer, ImaginAb



Ivan Plavec, Ph.D. is Chief Business Officer at ImaginAb, an immuno-oncology company developing imaging agents for precision medicine. His previous roles include president and founder of Ascellna, a consulting firm supporting life science companies, executive and business development positions at BioSeek and Asterand and senior research positions at Novartis and Systemix. Dr. Plavec is an author on over thirty peer-reviewed publications, has filed numerous patents and has a track record of scientific accomplishments and broad scientific experience in drug discovery, gene therapy, immunology, and oncology. He holds a Ph.D. in Molecular Biology from the University of Zürich, Switzerland

REGISTER (FREE)

This free webinar will take place on:
Thursday 29th August 2019 at 5:00 PM - 6:00 PM BST
Can't make the date? Register to receive the recording free!

WHAT DO YOU THINK THE FUTURE OF IMMUNO-ONCOLOGY WILL BE?

TIM WYANT, DOMINIC EISINGER, TROELS JORDANSON

At last year's Advances in Immuno-Oncology Congress, we interviewed 6 key speakers for their thoughts on the future of the industry. Read their answers below:

Tim Wyant: I think combinations are going to be the future: being able to use compounds that will stimulate in one end, as well as inhibit these inhibitors in the other aspect. So those things that are suppressing the immune system you want to stop, while augmenting the stimulation aspect of it, and that could be with combinations with vaccines and agonists and things of that sort. I think one of the biggest things for those are going to be trying to understand how those combinations work best so that you again are highlighting the way the immune system should be normally working.

Dominic Eisinger: The future of immuno-oncology really will be a personalized approach. Everyone's immune system is different - it won't be able to be predicted from our genomic DNA, the immune system changes over time, and incorporating these different technologies into a cost-effective, robust way of being able to determine the status of an immune system of an individual patient. And then with all these multiple tool boxes, we'll see so many approvals of all these different current products that are in clinical trials right now. It really will be an a la carte sort of menu in choosing the right therapies based on all these different approved inhibition and immune activation, and it will be quite interesting and personalized. It will stress the health system and the current pharma development system of blockbusters, but we'll just have to sort that out as time goes on, but that is the future well.

Troels Jordanson: Off the shelf is a major opportunity. You know, many more patients can actually get treated when it's off the shelf instead of waiting for the production and delivery process. I also believe that CAR NK cells is going to be an important addition to the sector. We believe that there are safer transduction opportunities than the viral options currently available, so 2018 and 2019 are looking very promising ■

This interview is an excerpt from our Speaker Insight videos, in which experts at our events answer questions on the state of the industry, including:

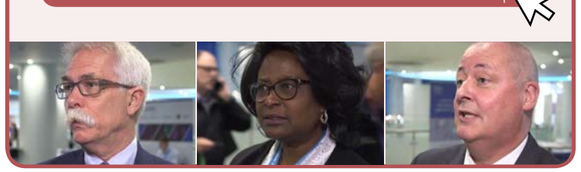
"What are the important developments in biomarker development and patient stratification for immuno-oncology?"

"How do you think genomic approaches could affect the Immuno-Oncology field"

Follow the link below to hear answers from:

- Tim Wyant, Senior Director Cancer Immunology, Curis
- Dominic Eisinger, Vice President, Sales & Marketing Operations, Myriad RBM
- Troels Jordanson, CEO, Glycostem
- Jon Waterman-Smith, Director of Business Development, Mitra Biotech
- Steven Anderson, Chief Scientific Officer, Covance
- Grace Macaulay, Safety Physician in Oncology, Medimmune

>> Watch the videos



OXFORD GLOBAL CONFERENCES

FORTHCOMING EVENTS

OXFORD GLOBAL CONFERENCES

Biologics Series

UK

12th Annual Proteins & Antibodies Congress
24 - 25 April 2019 | London, UK

6th Annual Peptides Congress
24 - 25 April 2019 | London, UK

6th Annual Biosimilars & Biobetters Congress
24 - 25 April 2019 | London, UK

Co-located Events

Biomanufacturing Congress
17 - 18 September 2019 | London, UK

US

Proteins & Antibodies USA Congress
18 - 19 November 2019 | Boston, USA

Biomarkers Series

UK

15th Annual Biomarkers Congress
February 2020 | Manchester, UK

US

4th Annual Biomarkers & Precision Medicine USA Congress
08 - 09 October 2019 | San Diego, USA

Cell Series

UK

8th Annual Cell Culture & Bioprocessing Congress
24 - 25 October 2019 | London, UK

6th Annual Stem Cell & Regenerative Medicine Congress
24 - 25 October 2019 | London, UK

5th Annual Cell & Gene Therapy Congress
24 - 25 October 2019 | London, UK

Co-located Events

US

Cell Culture & Bioprocessing USA Congress
14 - 15 May 2019 | Boston, USA

Cell & Gene Therapy USA Congress
14 - 15 May 2019 | Boston, USA

Co-located Events

Formulation & Delivery Series

UK

6th Annual Formulation & Drug Delivery Congress
April 2020 | London, UK

5th Annual Inhalation & Respiratory Drug Delivery Congress
April 2020 | London, UK

Co-located Events

US

2nd Annual Formulation & Drug Delivery USA Congress
18 - 19 March 2019 | San Diego, USA

2nd Annual Inhalation & Respiratory Drug Delivery USA Congress
18 - 19 March 2019 | San Diego, USA

Co-located Events

Immuno-Oncology Series

UK

4th Annual Advances in Immuno-Oncology Congress
20 - 21 May 2019 | London, UK

US

2nd Annual Advances in Immuno-Oncology USA Congress
08 - 09 October 2019 | San Diego, USA

PharmaTec Series

UK

17th Annual Pharmaceutical IT & Data Congress
25 - 26 September 2019 | London, UK

3rd Annual Artificial Intelligence in Drug Development Congress
25 - 26 September 2019 | London, UK

Cyber Security & Data Protection in Pharma & Healthcare Congress
25 - 26 September 2019 | London, UK

SmartLabs & Laboratory Informatics Congress
25 - 26 September 2019 | London, UK

Co-located Events

R&D Series

EU

20th Annual Drug Discovery Summit
11 - 12 June 2019 | Berlin, Germany

7th Annual Discovery Chemistry & Drug Design Congress
11 - 12 June 2019 | Berlin, Germany

Neuroscience in Discovery & Development Congress
11 - 12 June 2019 | Berlin, Germany

Bispecifics in Discovery & Development Congress
11 - 12 June 2019 | Berlin, Germany

Co-located Events

SynGen Series

UK

11th Annual Next Generation Sequencing & Clinical Diagnostics Congress
07 - 08 November 2019 | London, UK

7th Annual Single Cell Analysis Congress
07 - 08 November 2019 | London, UK

5th Annual Genome Editing Congress
07 - 08 November 2019 | London, UK

2nd Annual Synthetic Biology Congress
07 - 08 November 2019 | London, UK

Digital PCR Congress
07 - 08 November 2019 | London, UK

Co-located Events

US

5th Annual Next Generation Sequencing & Clinical Diagnostics USA Congress
14 - 15 May 2019 | Boston, USA

5th Annual Single Cell Analysis USA Congress
14 - 15 May 2019 | Boston, USA

3rd Annual Genome Editing USA Congress
14 - 15 May 2019 | Boston, USA

2nd Annual Synthetic Biology USA Congress
14 - 15 May 2019 | Boston, USA

Co-located Events

Register your interest, e-mail us:
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