Kisaco Research Presents...

Reduced Rates for Academia Available.

Adoptive T-Cell Therapy Congress

CAR T, TCR's and Beyond

15-16 March 2016
Millennium Knightsbridge Hotel
London, UK
www.tcellcongress.com

Join thought leaders to discuss new adoptive cell therapies for cancer looking at ways forward in improving efficiency and efficacy, case studies on liquid and solid tumours and investigations into human and clinical trials.

Gain insight from speakers including:

Renier Brentjens
Memorial Sloan Kettering Cancer Centre

David Gilham
University of Manchester

Inge Marie Svane
University of Copenhagen

Martin Pule
CSO, Autolus

Andrew Sewell
Cardiff University

Emma Morris
University College London

Michal Besser
Tel-Aviv University

Hans Stauss
Royal Free Hospital, UK

We aim to foster further consensus with a focus on academic collaboration, networking and business partnering within the fields of CAR-T, TCR's and TIL's.

Key topics we'll address include:

- T-Cell Engineering: Processes for scalability and manufacturing
- Cancer Models: Efficiency and efficacy on liquid and solid tumours
- Investigations in Human and Clinical Studies: Effect on human patients

5 Key Reasons You Need to Attend this Event:

- This is the only European congress dedicated specifically to the 3 core Adoptive T-Cell Therapies.
- There is a focus on real case studies with real tumours, and quality presentations uncovering new data from human clinical trials.
- Network with Professors, Directors and Heads of Lab from premier institutions globally.
- Hear from Adaptimmune, one of the leading commercial players in transforming T-cell therapy.
- There are over 6 hours of networking across the 2 day congress, allowing participants to build collaborative relationships.

Meet and Network with Representatives from:

Adaptimmune · Leucid Bio · cellulartherapeutics · alacrita · CAGT · Cardiff University · Dartmouth · Netherlands Cancer Institute · Memorial Sloan Kettering Cancer Center · University of Birmingham · UCL · Sheba Medical Center · Uniklinik Köln · University of Copenhagen · Penn · UCSF

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Register online at www.tcellcongress.com. Call us at +44 (0)20 3696 2920 or email events@kisacoresearch.com

Over the past 3 years, the industry has been a hive of activity, with 6 companies forging deals valued at over half a billion dollars in total.

Welcome to the Adoptive T-Cell Therapy Congress

There have been huge leaps forward in recent years with the further development of new adoptive T-cell therapies for cancer. CD19 CAR T therapy has shown the world how effective it can be, but many significant challenges remain.

- Safety is of primary concern with toxicity being a key topic of discussion
- Dealing with escape and relapse from treatment
- Managing effective translation in the clinic
- Targets - Finding out what makes an antigen a good antigen? And for what tumour?
- When a patient comes in with a list of mutations what do you practically do next? How do you resolve it?

The **Adoptive T-Cell Therapy Congress** is a platform committed to furthering consensus on developing state of the art T-cell therapies focusing on safety, efficacy and commercialisation.

Join the industry's scientific and business leaders as we discuss adoptive T-cell therapies for cancer by looking at ways forward in improving efficiency and efficacy, case studies on liquid and solid tumors, scalability, manufacture and progress within industry regulation. The congress will focus on academic collaboration, networking and business partnering within the fields of CAR-T, TCR's and TIL's with sessions including: advancements in T-cell engineering; efficacy in different cancer models and results from human and clinical studies.

Attending the congress brings you together with thought leaders from biotech, big pharma, academia and the wider service community and gives you access to strategies that are critical to furthering the development of viable T-cell therapies.

Joining us are thought leaders such as:

- **Renier Brentjens,** Memorial Sloan Kettering Cancer Centre, USA
- **David Gilham,** University of Manchester, UK
- **Inge Marie Svane,** University of Copenhagen, Denmark
- **Andrew Sewell,** Cardiff University, UK
- **Emma Morris,** University College London, UK
- **Michal Besser,** Sheba Medical Centre, Israel
- **Hans Stauss,** Royal Free Hospital, UK

Now is the time to discover more about the exciting new developments within adoptive T-cell therapies. Join us in London this coming March 15-16, 2016 for an exciting networking, learning and benchmarking forum. We offer special early bird prices off industry rates as well as reduced academic rates, so book now online at www.tcellcongress.com.

I look forward to meeting you in London.

Best Regards
Calan Smith
Event Director, **Kisaco Research**

Who Should Participate in this Congress?

- Pre-clinical and clinical scientists
- Clinical investigators
- Postdoctoral fellows involved in cancer research
- Regulatory scientists
- Healthcare professionals
- Pharmaceutical industry

Industry:

- Reagents and equipment suppliers
- Distributors
- Cold Chain logistics
- Biopharma
- Research Institutes
- Associations

Kisaco Research's Global 'Next in Pharma' Conference Portfolio

- Conferences in the Human Microbiome, Adoptive T-Cell Therapy, Plant Improvement Technologies and more
- Over 100+ academia, scientists and industry executives onsite
- Global industry partners including BaseClear, Libragen, List Laboratories, Synthetic Biologics, BioMed Central, Gen Eng News, All Seq and more
- CPD Accreditation-Approved by the Royal College of Physicians

About Kisaco Research

Kisaco Research works with the early adopters and leaders of growth markets in driving their respective industries forward and in providing the right knowledge, learning and social opportunities to stimulate business growth quickly and effectively.

Kisaco Research produces, designs and hosts B2B industry conferences and exhibitions. Our platforms are neutral, so that our attendees get the right information from the most relevant people. Our level of research ensures the topics and products we offer are of utmost relevance and timeliness; our 30+ years of combined experience in the event industry means we have an unmatched level of strategic social engineering onsite.

Join our conferences to ensure you benefit from the high-quality knowledge, learning and networking opportunities. Find out more about our upcoming events by emailing events@kisacoresearch.com.

Speakers

Renier Brentjens
Memorial Sloan Kettering Cancer Centre
USA

David Gilham
University of Manchester
UK

Emma Morris
University College London
UK

Hinrich Abken
University of Cologne
Germany

Inge Marie Svane
University of Copenhagen
Denmark

Alexander Marson
University of California, San Francisco
USA

Michal Besser
Tel-Aviv University
Israel

Hans Stauss
Royal Free Hospital
UK

Anthony Walker
Partner, **Alacrita LLC,** CEO, **Leucid Bio**

Weidong Ha
PLA General Hospital
China

Nabil Ahmed
Baylor College of Medicine
USA

Joost van der Berg
Netherlands Cancer Institute
Netherlands

Andrew 'Jez' Gerry
Director of Preclinical Research
Adaptimmune

John S. Bridgeman, Ph.D.
Director, Cell Therapy Research
Cellular Therapeutics Ltd.

Andrew Sewell
Cardiff University
UK

Daniel Trey Lee
NIH, NCI
USA

Martin Pule
CSO
Autolus

Aaron Foster
Senior Director of Product Discovery
Bellicum Pharmaceuticals

Conference Day One

TUESDAY,
15 March 2016

09:30 **Registration for Conference Opens for All Attendees**

10:00 **Chairperson's Opening of Conference**

10:10 **Pre-clinical models of CAR T cell toxicity**

CD19 targeted CAR T cell therapy is delivering impressive clinical responses in patients with advanced B-cell leukaemia. This therapy is associated with acute toxicity associated with high levels of several cytokines including IL-6. In syngeneic mouse models, we have observed a similar cytokine driven acute toxicity in Balb/c mice receiving mouse CD19-specific CD28-based second generation CAR T cells; however, there was little evidence of raised levels of IL-6. Additionally, we have observed a chronic toxicity associated with the long term production of cytokines form CD4+ CAR T cells and a concomitant expansion of the myeloid cell compartment resulting in granuloma formation.

These observations suggest that prolonged cytokine production as a result of the continuous activation of second generation CAR T cells may have long term adverse effects. Importantly, both acute and chronic toxicities appear to be strain related with much reduced effects observed in C57 bl/6 mice. Taken together, this observed toxicity appears to be related to Th2 based cytokine production while there is little evidence of an involvement of IL-6 which raises questions relating to the relevance of toxicity seen in the mouse model for extrapolation to the human situation.

David Gilham, **UNIVERSITY OF MANCHESTER, MANCHESTER, UK**

10:40 **Improving anti-tumour potential of CD19 CAR T cells**

Dr. Lee was among the first to develop chimeric antigen receptor (CAR) modified T cell therapy for children and young adults with pre-B cell acute lymphoblastic leukaemia and B-cell lymphomas. The clinical trial he leads genetically engineers patient's own T cells with a CAR targeting the antigen CD19 resulting in remissions in the vast majority of patients with refractory or relapsed disease. Capitalizing on the success of the CD19-CAR T cell therapy, Dr. Lee's laboratory now aims to develop other CAR-based therapies for the treatment of medulloblastoma, ependymoma, and other paediatric brain tumours.

Daniel Trey Lee, Assistant Clinical Investigator, NIH, **NCI**

11:10 **Potential and Tentative Strategy and Protocol of CART-based treatment in Solid Tumours**

Brief introduction of CART design and clinical breakthrough in hematopoietic liquid tumours. Crucial barriers and current dissolving protocols of CART treatment in solid tumours. Summarization of clinical trials of CART therapy in Chinese PLA General Hospital from Feb. 2013 to Mar. 2016. Except in hematopoietic malignancies (CART-19, CART-33, CART-20, CART-30 for B-ALL, AML, NHL, and HL, respectively), safety and clinical efficacies for EGFR-, HER2-, and CD133-trageted solid tumours will be highlighted, the underlying mechanism by which differential toxicity between target antigen-expressing normal and tumour cells will be addressed as well).

Proposal for more rational clinical strategy and protocol for CART-based therapy in solid tumors (including stroma-targeting and lymph depleting agents, then repeated and/or alternative antigen-targeted CART cells infusions given the heterogeneous nature of tumor cells, and sequential administration of CD133-directed CART cell therapy targeting both tumor stem cells and myeloid-derived suppressive cells in tumor microenvironment.

Wei Dong Han, Director of Department of Molecular and Cellular Biology, **THE GENERAL HOSPITAL OF PLA, CHINA**

11:40 **Morning Networking Break: Coffee, Tea & Refreshments**

12:10 **Tumor Infiltrating Lymphocytes for Metastatic Cutaneous and Non-Cutaneous Melanoma:**

We have established the UK's only GMP-compliant and MHRA (Medicines and Healthcare Products Regulatory Agency) licensed unit capable of producing multiple T cell product types (CAR or TCR-modified and natural T cells (TIL)) using 'clean room free technology'. This unit has produced melanoma-derived TIL products which have been successfully returned to patients. This study supports the success of melanoma TIL therapy seen in other centers worldwide and suggests that this is a viable means of treating a disease which has few effective options.

John S. Bridgeman, Ph.D., Director, Cell Therapy Research, **CELLULAR THERAPEUTICS LTD.**

12:40 **Commercialization of Adoptive T-Cells: Prospects and Hurdles**

Successful commercialisation of a cell therapy requires more than proving safety and efficacy to the regulators. The inherent complexity of cellular products poses particular manufacturing, logistical and reimbursement hurdles that threaten commercial viability for any therapy with a less than spectacular clinical profile that truly changes the standard of care. This is particularly acute for autologous cell therapies where patients receive bespoke treatments manufactured from a sample of their own cells and where economies of scale, which play an important role in containing the production costs for small molecule and antibody therapeutics, are highly limited. Nevertheless, the promise of game-changing efficacy, as exemplified by very high levels of complete responses in refractory haematological malignancies, has attracted capital investments on a vast scale, and the attendant pace of technology development provides promising indicators for future clinical and commercial success.

Anthony Walker, PhD, Managing Partner **ALACRITA CONSULTING**, CEO **LEUCID BIO**

13:10 **Networking Lunch**

14:30 **Adaptimmune – Transforming T Cell Therapy**

Adaptimmune are a clinical-stage biopharmaceutical company focused on novel cancer immunotherapy products. They utilize the body's own machinery – the T cell – to target and destroy cancer cells by increasing the affinity of naturally occurring T cell receptors (TCRs). Their lead program, utilizing their NY-ESO TCR therapeutic, has generally been well tolerated in Phase 1/2 trials in solid tumors and in hematologic cancer types and they have seen responses and preliminary evidence of tumor reduction in patients with highly refractory cancers. An IND is now open for their MAGE-A10 TCR therapy. The initial clinical program will be in patients with advanced stage NSCLC. They continue to build a pipeline of TCR therapeutic candidates targeting a number of additional cancer targets. They have a research base in Oxford, UK and a clinical base in Philadelphia, US.

Andrew Gerry, Director of Preclinical Research, **ADAPTIMMUNE**

15:00 **Rounded Panel Discussion: Pre-Clinical Trial Decision Making.**

What do we need in the pre-clinical setting? What background data is needed to appropriately move forward to a clinical trial? What are the triggers involved?

We explore the level of information and confidence required when going into clinical trials and what those implications are for business development.

Moderator: **David Gilham, UNIVERSITY OF MANCHESTER**

Panellists:

Nabil Ahmed, BAYLOR COLLEGE OF MEDICINE

Andrew Gerry, Director of Preclinical Research, **ADAPTIMMUNE**

Joost Van Der Berg, Netherlands Cancer Institute, **NETHERLANDS**

16:00 **Afternoon Networking Break: Coffee, Tea & Refreshments**

16:30 **Adoptive Transfer of Autologous T Cells in Advanced Stage Melanoma Patients**

The aim of our research is straightforward 1). To design novel technologies that can be used to examine and modify antigen-specific T cell immunity 2). To use these tools to unravel and manipulate the molecular processes underlying immune recognition by T lymphocytes. Within these projects, a main focus is on the design and testing of novel concepts for adoptive immunotherapy of cancer.

Joost van der Berg, NETHERLANDS CANCER INSTITUTE, NETHERLAND

17:00 **Development of CAR T Cells for Solid Tumors: Adopting Realistic Pragmatism!**

Dr. Ahmed is a physician scientist engaged in translational research focusing on adoptive immunotherapy with genemodified effector cells, to improve therapy for brain tumors. Dr Ahmed's initial studies demonstrated that antigen-specific cytotoxic T cells could eradicate established brain tumors in medulloblastoma and Glioblastoma models. Subsequent studieshave demonstrated that the tumor-specific T cells, unlike conventional therapies, can effectively target the stem cell compartment in the tumor eradicating experimental tumors in animal models. Aligning with his primary interest is studying the role of T cells in creating a tumor niche and studying T cell migration to distant tumor sites in the brain. Dr. Ahmed therefore has experience in developing and translating cell and gene therapy studies to the clinic. Currently, Dr. Ahmed is the principal investigator on 3 clinical trials targeting Glioblastoma and Osteosarcoma by administering tumor-specific T cells to. All studies are FDA, IRB, RAC and IBC approved.

Nabil Ahmed, Baylor College of Medicine, **TEXAS, USA**

17:00 **Close of Conference Day One and Networking & Welcome Drink Reception**

About Our Sponsor:

Miltenyi Biotec

Miltenyi Biotec provides cutting-edge products and services that advance biomedical research and cellular therapy. Our innovative tools support research at every level, from basic research to translational research to clinical application. Used by scientists and clinicians around the world, our integrated technologies cover techniques of sample preparation, cell isolation, cell sorting, flow cytometry, cell culture, molecular analysis, and preclinical imaging. Our more than 25 years of expertise spans research areas including immunology, stem cell biology, neuroscience, and cancer. Today, Miltenyi Biotec has more than 1,400 employees in 25 countries – all dedicated to empowering discovery and impacting lives.

Thank You To Our Media Partners:

Conference Day Two

WEDNESDAY
16 March 2016

08:30 **Registration for Conference Opens for All Attendees**

09:00 **Chairperson's Opening of Conference**

09:10 **Moving Car T Cell Therapy Forward: Cars and Armored Cars**

T cells may be genetically modified to express chimeric antigen receptors (CAR) targeted to antigens expressed by tumor cells. Treatment of patients with CD19 targeted CAR T cells has resulted remarkable remission rates in relapsed B cell acute lymphoblastic leukemia (B-ALL). Specifically, based on currently updated clinical outcomes, we have achieved CR rates in adult patients with relapsed B-ALL treated with CD19 targeted CAR T cells which far exceed historical expectations. Further, by deep sequencing analysis, most treated patients were MRD- after CAR T cell therapy. Significantly, remissions were observed in both patients with overt morphological residual disease at the time of therapy as well as in patients with only residual MRD+ disease. Clinical trials from other centers which confirm the presented clinical trial outcomes from our center and toxicities associated with CAR T cells therapy will be reviewed. In contrast, far more modest responses were seen in patients with relapsed chronic lymphocytic leukemia (CLL). The discordant clinical outcomes between B-ALL and CLL patients treated with CD19 targeted CAR T cells remains a subject of conjecture although the tumor microenvironment is a strong focus of further investigation. To this end, we will present novel data on a next generation of CAR T cells, termed "armored CARs" further genetically designed to overcome an immune suppressive tumor microenvironment through further genetic modification of CAR T cells. Promising preclinical studies utilizing these "armored CAR" T cell approaches and their role in future clinical trials will be discussed.

Renier Brentjens, Director, Cellular Therapeutics Centre, **MSKCC**

9:40 **T-Cell Receptors**

The research of our group is focussed on T cell immunology, with a particular focus the role of the T cell receptor (TCR) in the recognition of cancer antigens. We were amongst the first to show that cytotoxic T cells can selectively attack cancer cells by recognising point mutations in transforming proteins expressed in tumours (J Exp Med. 1993; 177:1493). We have since developed strategies to isolate monoclonal TCR that are specific for tumour antigens, and we use these TCR for gene therapy to redirected the specificity of patient T cells and equip them with the ability to selectively recognize and attack cancer cells. The use of TCR gene therapy to produce antigen-specific cytotoxic and helper T cells is one area of active research in our group. We also use TCR and chimeric antigen receptor (CAR) gene transfer to produce antigen-specific regulatory T cells. This provides the opportunity to achieve highly selective immune suppression and treat autoimmune conditions without the need for systemic immune suppression

Prof Hans Stauss, ROYAL FREE HOSPITAL, UNITED KINGDOM

10:10 **TCRs in Immunotherapy**

The Cardiff T-cell modulation group consists of a number of world-class researchers with a diverse skill and knowledge base that covers all areas of T-cell biology including T-cell genetics, molecular biology, protein chemistry, crystallography, cell biology and clinical investigations. The overall goal of the Cardiff T-cell modulation group is to understand the genetic, biochemical and cellular mechanisms that govern T-cell responses to human disease. Our research outputs are extremely wide ranging and include basic studies which are aimed at understanding how the T-cell immune response is regulated, through to translational studies which are aimed at developing tools, diagnostics and treatments for human diseases such as cancer, HIV, EBV, tuberculosis and many more.

Andrew Sewell, CARDIFF INSTITUTE OF INFECTION & IMMUNITY, UK

10:40 **Morning Networking Break: Coffee, Tea & Refreshments**

11:10 **The fourth generation of CAR T cells: TRUCKs**

Adoptive therapy with engineered T cells with an antigenspecific chimeric antigen receptor (CAR) is achieving impressive efficacy in early phase trials, in particular in hematologic malignancies, strongly supporting the notion that the immune system can control cancer. Such CAR T cells can substantially reduce the tumor burden as long as the targeted antigen is present on the cancer cells, however, loss of target antigen make them invisible to CAR T cells and may contribute to deadly tumor relapses. We discuss the fourth generation of CAR T cells, so called TRUCKs, which release inducible IL-12 or any other cytokine upon CAR engagement in the targeted tumor lesion. Locally accumulating IL-12 in turn attracts an innate immune cell response towards those cancer cells that are invisible to CAR T cells. Elimination of antigen-loss tumor cells was accompanied by the accumulation of activated macrophages through a TNF-alpha mediated process. The IL-12 supplement by CAR T cells has the advantage to target otherwise not accessible tumor lesions, to achieve therapeutic levels in a localized fashion, to reduce systemic toxicity and to recruit and activate innate immune cells. The strategy combines antigen-redirected immunotherapy with an antigen-independent anti-tumor response. We discuss major consequences for future strategies the immune therapy of malignant diseases and other applications of TRUCKs as targeted living factories.

Hinrich Abken, Professor, Genetics & Immunology, **UNIVERSITY OF COLOGNE**

11:40 **Controlling CAR-T cell safety and efficacy using molecular switches**

Regulating CAR-T survival, persistence and expansion in vivo following adoptive transfer is critical for maximizing therapeutic efficacy while also managing CAR-T-related toxicity. We present two molecular switches, inducible Caspase-9 (iCasp9) and inducible MyD88/CD40 (iMC) that can be used to control T cell levels and function in vivo by systemic administration of the small molecule dimerizing ligand, rimiducid. Here, we first demonstrate that CAR-T cells containing iCasp9 can be partially or completely eliminated in a rimiducid dose-dependent manner, which corresponds to a rapid reduction of cytokine levels and toxicity. Conversely, activation of iMC in CAR-T cells by rimiducid provides a potent costimulatory signal which, together with CAR activation, drives T cell proliferation, survival and anti-tumor efficacy in multiple tumor models. Thus, iCasp9 and iMC can be used as "off" and "on" molecular switches, respectively, to control T cell behavior in vivo to maximize therapeutic efficacy and mitigate potential toxicities.

Aaron Foster - Senior Director of Product Discovery at **BELLICUM PHARMACEUTICALS**

12:10 **Adoptive Transfer of Tumor Infiltrating Lymphocytes (TIL): Current Status and Future Directions**

Clinical cell production. Dr. Besser manages the clean room facility of the Ella Institute and is responsible for the production of cellular products for our patients. Basic and translational research. Tumor immunology serves as a platform for a wide range of research projects. Main research focus is to identify predictive markers for clinical success with the aims (1) to improve the response rate of T cell immunotherapy and (2) to select cancer patients upfront, who are most likely to benefit from the treatment. In addition, the laboratory validates the combinational effects of cellular therapy with immune check point inhibitors and tests the effectiveness of T cell immunotherapy in cancers, other than melanoma.

Michal Besser, SHEBA MEDICAL CENTER, ISRAEL

12:40 **Networking Lunch**

14:00 **TCR gene modified T cells: From bench to bedside**

Novel approaches for generation of antigen-specific T cells for leukaemia and cancer immunotherapy.

- Retroviral gene transfer of T cell receptor (TCR) genes into T cells and haematopoietic stem cells to re-direct antigen-specificity.
- The generation of MHC class I-restricted tumour antigen-specific CD4+ helper T cells to augment CD8+ T cell mediated tumour immunotherapy.
- Analysis of functional avidity and signalling pathways of tumour antigen-specific TCRs.
- Investigation of the role of the CD8 co-receptor in TCR transduced CD4+ helper T cells and conventional CD8+ T cells.
- The generation of pre-clinical models for the evaluation of WT1-specific immunotherapy (WT1 is a tumour associated antigen over-expressed in myelodysplasia (MDS), leukaemias (AML, CML), breast, ovarian, prostate and colon cancers.
- Isolation of TCRs from T cell clones specific for tumour antigens.
- Generation of antigen-specific regulatory T cells using TCR gene transfer.

Emma Morris, Professor, **UCL INSTITUTE OF IMMUNITY AND TRANSPLANTATION**

14:30 **TIL based adoptive cell therapy - exploring indications and combinations**

Professor in clinical cancer immune therapy and director of the translational research centre, Center for Cancer Immune Therapy (CCIT). CCIT is working translational and has a broad experience in preclinical as well as clinical research within cancer immunology and immunotherapy. Since 2005 CCIT has conducted numerous clinical trials including more than 200 cancer patients. It is an aim for CCIT to develop immunotherapeutic strategies for a broad spectrum of cancer diseases. Therefore, clinical trials have been carried out in diseases such as myeloma, melanoma, lung, -kidney, breast- and prostate cancer.

Inge Marie Svane, UNIVERSITY OF COPENHAGEN, DENMARK

15:00 **Rounded Panel Discussion: Safety Concerns in T-cell Therapy**

Despite the growing number and length of remissions using T-cell therapy to treat leukaemias and lymphomas, key challenges remain with the first and foremost being, safety.

What new methods are being considered to overcome high levels of toxicity and other adverse effects? - Immunoescape.

Moderator:

Andrew Sewell, CARDIFF UNIVERSITY, UK

Panellists:

Inge Marie Svane, UNIVERSITY OF COPENHAGEN, DENMARK

Renier Brentjens, MEMORIAL SLOAN KETTERING CANCER CENTRE, USA

Emma Morris, UNIVERSITY COLLEGE LONDON, UK

16:00 **Afternoon Networking Break: Coffee, Tea & Refreshments**

16:30 **Chimeric Antigen Receptors (CAR)**

Current approaches in Chimeric Antigen Receptor (CAR) adoptive T-cell therapy have focused on single targets limiting its utility to cancers with a well characterised antigen that is exclusively expressed on the tissue. Given the autonomous nature of CAR T-cell activity on-target off-tumour activity can result in fulminant toxicity. Recognition of patterns of antigens on a cancer cell surface should greatly broaden the scope and safety of CAR T-cell therapy. The kinetic-segregation model of T-cell activation explains how antigen recognition and immunological synapse formation leads to T-cell activation. This model also provides a means of cleanly modulating the activity of phosphatases on the T-cell surface. We have developed a strategy to engineer T-cells to recognise a pattern of two antigens through integration of signals from two CARs based on kinetic-segregation. The mechanistic deconstruction of these boolean logic gates demonstrate that CAR triggering responses are governed by a local balance in kinase/phosphatase activity. These gates advance the safety and broadens the applicability of CAR based therapies.

Martin Pule, CSO, **AUTOLUS**

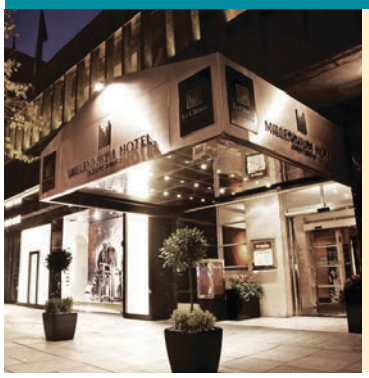
17:00 **Engineering Human T Cell Circuitry**

T cell genome engineering holds great promise for immunotherapies for cancer, HIV, autoimmune diseases, immune deficiencies and organ transplantation. We have overcome the poor efficiency of CRISPR/Cas9 genome engineering in primary human T cells using Cas9:single-guide RNA ribonucleoproteins (Cas9 RNPs). Cas9 RNPs can promote targeted genome sequence replacement in primary T cells by homology-directed repair (HDR), which was previously unattainable. This Cas9 RNP technology enables unprecedented explorations of genetic mechanisms that regulate T cell differentiation and function. We aim to understand how sequence variation throughout the human genome affects T cell circuits in health and disease. T cell engineering should accelerate development of novel drug-based and cell-based therapeutics for human diseases.

Alexander Marson, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, USA

17:00 **Close of Conference**

Venue & Accommodation



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Kisaco Research is pleased to announce that all attendees of the Adoptive T-Cell Therapy Congress will be able to access an exclusive group rate at the Millennium Hotel Knightsbridge.
Rates start from **£150 + VAT per night,** including English breakfast, single occupancy. This special rate will be valid until 13 February 2016. Book your room now: http://www.4cityhotels.com/adoptivetcelltherapy2016.html

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