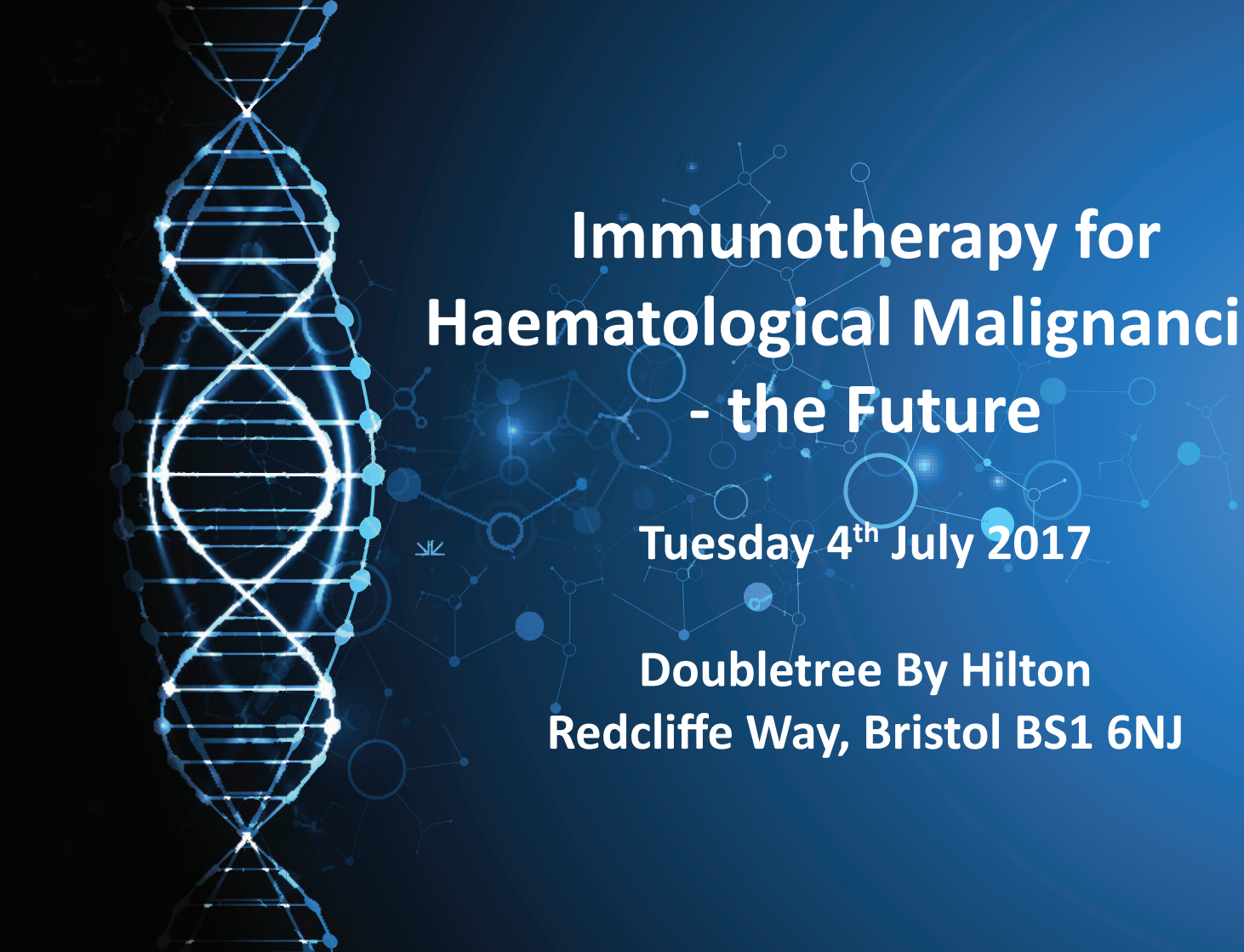


# Immunotherapy for Haematological Malignancies - the Future

**Tuesday 4th July 2017**

**Doubletree By Hilton**
**Redcliffe Way, Bristol BS1 6NJ**

# Welcome

In 1891 the American surgeon William Coley, demonstrated that the immune system could be harnessed to attack human malignancies by injecting Coley's toxin. Ever since these seminal observations, clinicians and scientists have endeavoured to elaborate the nature of the immune response to malignant cells and how this could be employed for therapeutic benefit. Although progress has been slow, we now have a much clearer understanding of how both the innate and acquired immune systems work at a molecular, cellular and systemic level and this has facilitated the development of a variety of immune therapies. We now have available a growing array of monoclonal antibodies, bi-specific antibodies, gene modified T lymphocytes, allogeneic donor lymphocytes and immune checkpoint inhibitors that have all been shown to induce effective anti-tumour immune responses. The challenge we now face is how to optimize these potent immune-therapies and incorporate them alongside conventional treatment strategies for patient benefit.

Todays meeting brings together an eminent panel of speakers who have been involved in the development of immune based therapies. Sessions on checkpoint inhibitors, novel monoclonal antibody based therapy, CAR T cell therapy, ECP and mesenchymal stem cells will initiate a discussion of how these potential new initiatives may be employed throughout the Southwest.

I wish you a warm welcome to Bristol and an enjoyable day.

Dr Stephen Robinson
Organiser & Chairman

# Organiser & Chairman

Dr Robinson trained in medicine at the Royal Free Hospital, London graduating in 1992. He trained in Haematology between 1995 and 2002 at University College London. He was awarded a PhD for research into developmental aspects of human dendritic cells in 1998. Since 2002 he has worked as a Consultant Haematologist in the Bone Marrow transplant Unit at University Hospital Bristol with a specialist interest in malignant lymphoma and stem cell transplantation. Since 2014 he has been the Clinical Director of the Bristol Cancer Institute. Dr Robinson is currently conducting research into reduced intensity allogeneic stem cell transplantation in lymphoma and is the Scientific Secretary of the EBMT Lymphoma Working Party.

# Programme

## Chair: Dr Stephen Robinson *(Bristol)*

| | | |
|---|---|---|
| 09.00 | *Registration, tea, coffee and pastries* | |
| | **IMPACT Transplant Group** | |
| 09.30 | Immunotherapy in the transplant setting | **Professor David Marks** *(Bristol)* |
| | **Immune Checkpoint Inhibitors** | |
| 09.45 | Immune checkpoint inhibitors in solid tumours - experience, opportunities and challenges | **Professor Jeff Evans** *(Glasgow)* *Director of Translational Cancer Research* |
| 10.10 | Experience in haematological malignancies | **Dr Graham Collins** *(Oxford)* |
| 10.35 | Discussion: Incorporating CIs into the treatment algorithm of lymphoma and leukaemia - guidance | **Panel:** Stephen Robinson, Jeff Evans, Graham Collins, Gordon Cook |
| 10.50 | *Coffee* | |
| | **Novel Antibodies** | |
| 11.15 | New anti-B cell antibodies | **Dr Graham Collins** *(Oxford)* |
| 11.40 | BITE technology science and clinical results | **Professor Oliver Ottmann** *(Cardiff)* |
| 12.05 | The antibody era dawns in multiple myeloma | **Professor Gordon Cook** *(Leeds)* |
| 12.30 | Discussion | **Panel:** Stephen Robinson, Hannah Hunter, Oliver Ottmann, Gordon Cook, James Griffin |
| 12.45 | *Lunch* | |

**Plenary Session:**

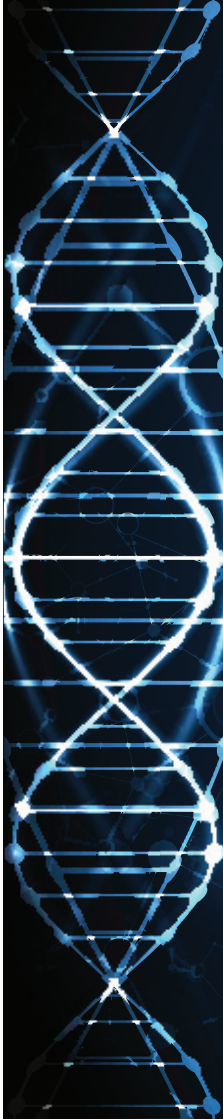
| | | |
|---|---|---|
| 13.30 | Cellular immunotherapies ... old dogs and new tricks | **Professor Mark Vickers** *(Aberdeen)* |

**CAR T Cells**

| | | |
|---|---|---|
| 14.00 | How to build a CAR T - what are they and how are they made | **Dr James Griffin** *(Bristol)* |
| 14.25 | Experience of CAR T cells in leukaemia and lymphoma | **Dr Reuben Benjamin** *(London)* |
| 14.50 | Challenges in delivering CAR T cell therapy regionally | **Professor David Marks** *(Bristol)* |
| 15.05 | *Coffee* | |

**Immunotherapy in GVHD**

| | | |
|---|---|---|
| 15.25 | ECP in acute and chronic GVHD | **Dr James Griffin** *(Bristol)* |
| 15.50 | ECP in combination therapy | **Dr Fiona Dignan** *(Manchester)* |
| 16.15 | Potential mesenchymal stem cells | **Professor Francesco Dazzi** *(London)* |
| 16.40 | Discussion | **Panel:** James Griffin, Fiona Dignan, Francesco Dazzi, David Marks |
| 16.55 | Chair's summary | |
| 17.00 | *Close* | |



# Professor David Marks

## Professor David Marks
### Professor of Haematology and Stem Cell Transplantation
### Bristol BMT Unit

Professor David Marks received his medical education at the University of Melbourne and his clinical training largely at the Royal Melbourne Hospital. He was awarded his FRACP in 1988 and his PhD in 'Mechanisms of cytotoxic drug action' in 1990. He then moved to London to receive further training in stem cell transplantation with Professor Goldman at the Hammersmith Hospital as MRC/LRF fellow and senior registrar. A 3 year stint in Philadelphia as Assistant Professor in Haematology/Oncology enabled him to set up a new unrelated donor transplant programme and work in p53 research in acute lymphoblastic leukaemia (ALL). He returned to the UK in 1996 and was appointed to a consultant position in the Bristol BMT Unit (which he directs) and Honorary Senior Lectureship at the University of Bristol. Professor Marks' research and scientific papers focus on clinical aspects of stem cell transplantation (particularly the use of alternative donors), ALL and infection. In 1999 he worked to initiate the Clinical trials committee of the British Society of BMT, the first national transplant trial group and chaired that group for 5 years. In 2004 he was promoted to Reader and in 2007 to Professor at the University and was Lead Clinician of the Bristol BMT Unit from 2003-9 and 2014 till now. He received FRCPath in 2006. He is Transplant Coordinator and Deputy Chair of the NCRI ALL working group and from 2007-2009 was President of the BSBMT. He currently chairs the Adjudication committee of BSBMT and is a current Member of the ASBMT Practice Guidelines Committee. He is currently Vice Chair (Europe) of the Advisory Committee of the CIBMTR and recently was Scientific Secretary for EBMT London 2013. He was the CI of the Improvit study, a large multinational study of fungal prophylaxis. He is married to Dr Jenny Bird (also a haematologist) and has two teenage children. He is interested in surfing, Australian Rules football, travel and cinema.

# Impact Transplant Group

## Immunotherapy in the Transplant Setting

David Marks, the Medical Director of the newly formed Impact Clinical Trials Platform, will discuss the goals of Impact and briefly introduce the new transplant trials network and then discuss past and upcoming immunotherapy studies that may receive Impact. He will briefly describe some transplant immunotherapy trials Impact is currently considering.

IMPACT
THE UK'S STEM CELL TRANSPLANT CLINICAL TRIALS PLATFORM

mail@bsbmt.org

**IMPACT Aims**

The overarching aim of IMPACT is to accelerate and facilitate the delivery of a portfolio of randomised phase 2 and 3 trials by UK transplant centres. It is anticipated that 9-12 trials will be delivered over the four-year pilot, with approximately 400-500 patients participating.

By reducing set-up and creating new capacity, the IMPACT trials network represents a potentially transformative development within the UK transplant community with the potential to accelerate trial delivery and improve patient outcomes.

In addition, the platform offers the opportunity, through the provision of high-quality biological samples with matching clinical data, to drive basic scientific research in areas such as predictive biomarkers, genomic mechanisms of resistance to therapy and drug discovery. Discussions with the MRC have confirmed the substantial contribution that the initiative can make to the UK's scientific infrastructure in areas such as stem cell biology and regenerative medicine.

Grantholder: Professor Charles Craddock

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ANTHONY NOLAN saving the lives of people with blood cancer
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PARTNERSHIP FOR ACCELERATED CLINICAL TRIALS
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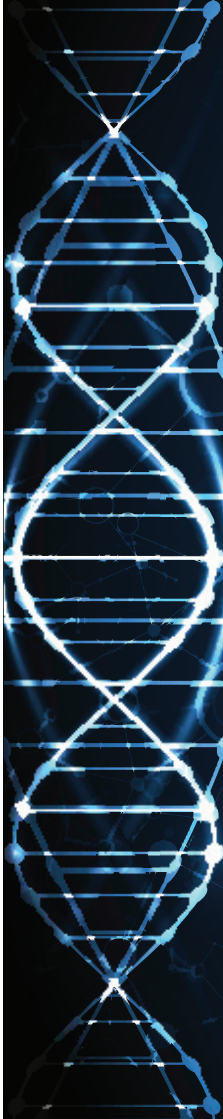

# Professor Jeff Evans

## Professor Jeff Evans
### Director of Translational Cancer Research
### University of Glasgow

Professor Jeff Evans is a Group Leader (Translational Cancer Therapeutics Laboratory) at the CR-UK Beatson Institute, Glasgow, Professor of Translational Cancer Research and Director of the Institute of Cancer Sciences, University of Glasgow, and Honorary Consultant in Medical Oncology at the Beatson West of Scotland Cancer Centre, Glasgow, and Lead of the Glasgow Experimental Cancer Medicine Centre (ECMC).

His research interests are in the pre-clinical and clinical development of novel anti-cancer agents, and his clinical interests are in Upper GI Cancers and Melanoma, and he leads the Phase I clinical trials and drug development team in Glasgow.

He is a member of the NCRN Upper GI Cancer Pancreatic Cancer and Gastro-Oesophageal Cancer sub-groups, member of the ECMC – Industry Combinations Alliance Joint Steering Committee, member of CR-UK's Clinical Experts Review Panel, and former member of Cancer Research UK's New Agents Committee. He is co-editor of the clinical research section of the British Journal of Cancer.

# Immune Checkpoint Inhibitors

## Immune checkpoint inhibitors in solid tumours - experience, opportunities and challenges

Human cancers contain numerous genetic and epigenetic alterations, generating neo-antigens that are potentially recognisable by the immune system. However, tumours evolve diverse mechanisms of immune evasion and immunosuppression to prevent or restrain anti-tumour T-cell responses (1, 2). In addition, cancer and/or the tumour microenvironment can produce molecules that actively inhibit any tumour-specific T-cells that do manage to enter the tumour (3-5). These processes are potential targets for therapeutic interventions that aim to induce, enhance or de-repress anti-tumour T cell responses, including immune checkpoint inhibitors that target Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) or programmed cell death protein 1 (PD-1) pathways.

A number of agents that target CTLA-4, PD-1, or PDL-1 pathways have been approved for the treatment of several solid tumours including metastatic melanoma, non – small cell lung cancer, renal cell carcinoma, Merkel cell carcinoma, bladder cancer, recurrent / metastatic squamous cell carcinoma of the head and neck, and colorectal cancer (MSI – H subgroup) (6-18). Promising signals of activity have been observed in a number of other tumour types including small-cell lung cancer, gastro-oesophageal adenocarcinoma and hepatocellular carcinoma, and the results of phase III trials are eagerly awaited. However, these agents have unique immune-mediated toxicities that include cutaneous, gastro-intestinal, hepatic, endocrine, and other less common inflammatory events, requiring treatment with immunosuppression following established algorithms.

Current clinical trials are exploring the efficacy of immune checkpoint inhibitors administered in combination with cytotoxic chemotherapy, radiotherapy, targeted agents, or with agents that target the tumour micro-environment. Identifying robust predictive biomarkers that can optimally select patients for treatment with immune checkpoint inhibitors remains a significant challenge.

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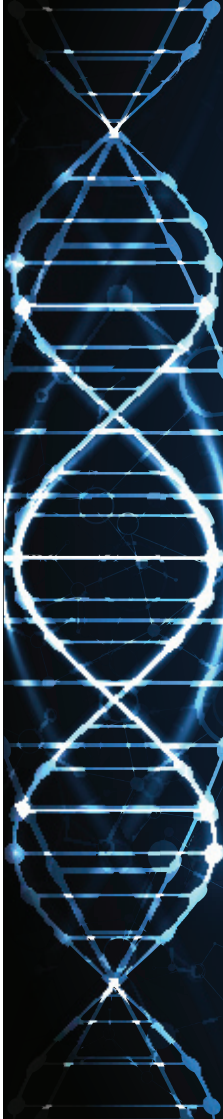




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# Dr Graham Collins

**Dr Graham Collins**
**Consultant Haematologist**
**Oxford University Hospitals**

Dr Collins trained in medicine at Cambridge and St Bartholomew's and the Royal London Hospitals. His specialist haematology training was in Oxford. Dr Collins chairs the Hodgkin lymphoma national study group and T cell lymphoma working group. He was also a member of the lymphoma guidelines development group of NICE and co-authored the national guidelines for relapsed Hodgkin Lymphoma.

# Immune Checkpoint Inhibitors

## Experience in haematological malignancies

Recently nivolumab and pembrolizumab have received their first approvals for use in a haematological malignancy: Hodgkin lymphoma. This is based on unprecedented activity in this disease which surpasses that of any other cancer investigated. The data behind the licensing will be discussed along with emerging data of their use in Hodgkin lymphoma post-allogeneic stem cell transplantation and in combination with other agents. Results in non-Hodgkin lymphoma appear more modest and a routine place in treatment is not yet established. The rationale for investigation in specific subtypes will be discussed along with early data on efficacy. Although we will focus on lymphoma a mention will also be made of other haematological malignancies.

# Novel Antibodies

**Dr Graham Collins**
**Consultant Haematologist**
**Oxford University Hospitals**

## New anti-B cell antibodies

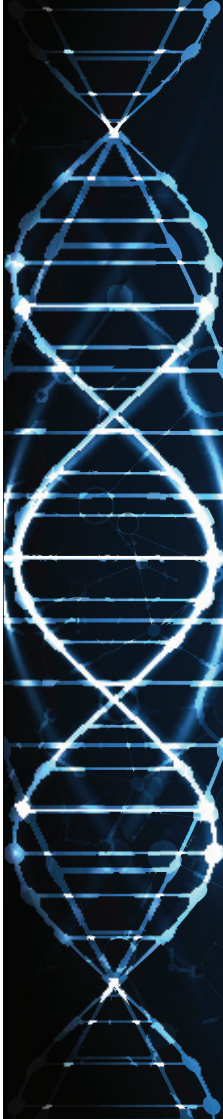
The introduction of rituximab into lymphoma practise has represented the single most important advance in lymphoma therapeutics over the last 20 years. Next generation anti-CD20 antibodies have been developed and are finding a place in CLL and lymphoma management. Other B-cell antigens are also being targeted with variable success. The introduction of linker chemistries has made it possible for the development of antibody-drug conjugates which have an established role in Hodgkin lymphoma and increasing so in acute lymphoblastic leukaemia. Ongoing investigations are assessing their use in other non-Hodgkin lymphoma subtypes.

# Professor Oliver Ottmann


## Professor Oliver Ottmann
### Professor and Head of Haematology
### Cardiff University School of Medicine


Oliver Ottmann is Professor and Head of Haematology at Cardiff University School of Medicine, UK. After obtaining his medical degree from the Heinrich-Heine University in Düsseldorf, Germany, Professor Ottmann undertook a postdoctoral research fellowship at the Memorial Sloan Kettering Cancer Center in New York, USA, before specialising in internal medicine and hematology at the Johann Wolfang Goethe University in Frankfurt, Germany. Prior to assuming his current position, he was Head of the Division of Molecular Therapeutics and Professor for Molecular Therapy Research of the Deutsche Jose Carreras Leukemia Foundation at JW Goethe University.

Professor Ottmann's scientific interests focus on malignant hematology and include the development and delivery of early phase clinical trials, translational research including bio-marker identification and validation, minimal residual disease, pre-clinical drug development as well as mechanisms of leukaemogenesis and drug resistance. Over the past decade, he has contributed particularly to the therapy for BCR-ABL positive leukemias. Prof. Ottmann is a member of many international professional societies including the European Hematology Association (EHA), the European Working Group for Adult ALL (EWALL) and the American Society for Hematology (ASH). Professor Ottmann has authored or co-authored more than 254 articles in international peer-reviewed journals.



# Professor Gordon Cook

## Professor Gordon Cook
## Professor of Haematology
## University of Leeds

Gordon Cook is a graduate of the University of Glasgow School of Medicine & received his higher professional training in haematology in the West of Scotland. After completion of his PhD, he was appointed as a Consultant Haematologist in the West of Scotland before moving to take up the post of Director of Stem Cell Transplantation at Leeds Teaching Hospitals in 2002. In 2013 he was appointed as Professor of Haematology, University of Leeds where he leads the myeloma clinical and translational research portfolio with a primary interest in tumour immunology and immunotherapy.

After 15 years executive service to the British Society of Blood & Marrow Transplantation he recently stepped down from his final position as the President of the Society representing the transplant community at the Government strategic and national commissioning level. He is the Chair of the UK Myeloma Research Alliance and NCRI Myeloma sub-group as well as a member of the NCRI Haematology-Oncology Clinical Studies Group. He holds the position of secretary and chair-elect of the UK Myeloma Forum and has represented the interests of both myeloma clinicians and patients in NICE reviews. He is Chief Investigator for NCRI Myeloma X (completed), Myeloma XII (in recruitment), MUKeight (in recruitment) and MUKeleven and MUKfifteen (in set-up) as well as Co-Chief Investigator for Myeloma XIV (in set-up phase). His collaboration with industry includes his position as the UK Chief investigator for 4 industry international phase III and IIIb studies & he is the chair of the Myeloma UK Research Advisory Group and Medical Editor of Myeloma Today. Finally, he holds the posts of Clinical Director of National Institute of Health Research Diagnostic MedTech Cooperative (Leeds) and the Scientific Secretary for the British Society of Haematology.

# Novel Antibodies

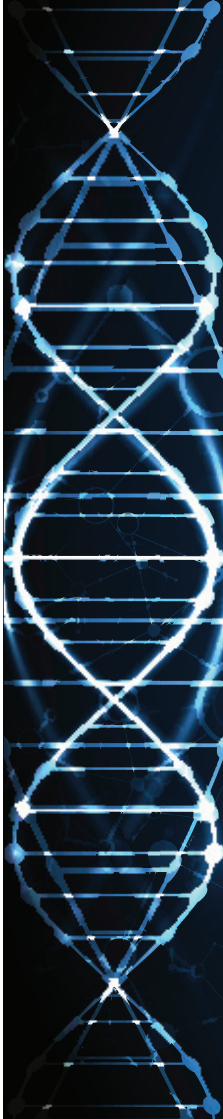
## The antibody era dawns in multiple myeloma

Multiple myeloma (MM) is a mature B-cell malignancy associated with significant cellular and humoral immune defects. As a consequence, there has been a long standing desire to re-direct the host immune response in an immunotherapeutic strategy. Immunotherapy can be considered as pharmco-immunotherapy (IMiDs), serotherapy (monoclonal antibodies; MoAb), T cell re-direction therapy (BiTE technology, CAR T cells).

Until recently, the field of MM clinical practice has been devoid of a suitable MoAb, and now there are two classes of tumour-directed and one class of immune check-point MoAb in clinical study. Tumour-directed MoAb include Elotuzumab, directed against SLAMF7 and the CD38-directed (a transmembrane glycoprotein uniformly expressed at high levels in MM plasma cells) MoAb, of which Daratumumab is the most developed, clinically. Daratumumab is a fully humanized IgG1 antibody targeting CD38, capable of direct tumour cell apoptosis as well as mediating complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC), and antibody-dependent cellular phagocytosis (ADCP). It has defined single agent and combinational anti-MM activity. Furthermore, daratumumab can also modulates the immunosuppressive bone marrow microenvironment favorably by suppressing production of of adenosine and deleting regulatory T-cells and myeloid-derived suppressor cells. Isatuxumab and MOR202 are other examples of CD38-directed MoAb in development for MM.

Immune checkpoints are an important part of the immune system's ability to differentiate self/non-self and to limit the extent of the immune response to minimize off-target damage. Cancer cells can exploit this system to crate immune dysfunction and evade eradication, thus blockade of this feedback system may evoke an anti-tumour immune response. Ipilimumab [a cytotoxic T-lymphocyte-associated protein (CTLA)-4 inhibitor] and pembrolizumab [anti- programmed cell death (PD) 1 inhibitor] are check-point inhibitors targeting the central and peripheral check-points respectively. Pembrolizumab is under clinical trial in patients with RRMM in combination with either lenalidomide/dexamethasone or pomalidomide/dexamethasone.

T-cell re-direction therapy is best characterized by the development of BiTE technology, an innovative investigational approach that is designed to help engage the body's endogenous T cells to target malignant cells. Bi-specific engager antibodies bind polyclonal cytotoxic T-cells to tumour cells. Several BiTE are under development including suing the B-cell Maturation Antigen (BCMA) are a MM-specific target. Another T-cell re-direction strategy is CAR T-cells. Chimeric antigen receptors (CARs) are engineered receptors, which graft an arbitrary specificity onto a T-cell, typically with the specificity of a MoAB. CAR T-cells are adoptively transferred and have shown promising results in ALL, when the CD19 surface marker is the target. In MM, several potential CAR targets are being developed, the most advanced being BCMA-directed CAR T-cells.



# Professor Mark Vickers

**Professor Mark Vickers**
**Senior Lecturer**
**University of Aberdeen**

Mark Vickers graduated from Oxford in 1983, having completed a Biochemistry Part II at Cambridge. After general medical jobs in London and an MRC Fellowship in Oxford, he then trained in Haematology at the Hammersmith, Reading and John Radcliffe Hospitals (1990–1996). He moved to Aberdeen in 1996.

His elective comprised an abortive attempt to clone the spectrin gene. His Fellowship was with Doug Higgs on genes surrounding the alpha-globin gene cluster. His research in Aberdeen has been eclectic, / disorganised, and includes modelling mutation accumulation in stem cells to understand the age specific incidence of leukaemias, genetic associations of thrombotic disorders, the Immunology of EBV infection, the use of cytotoxic lymphocytes directed against EBV in post-transplant lymphoproliferative disorders and how effete red cells are removed from the circulation.

# Cellular Immunotherapies

## Cellular Immunotherapies ... old dogs and new tricks

The development of cellular therapies against EBV driven disease will be reviewed, including the difficulties of moving from research projects to clinical practice. More recently, the work on how damaged red cells are removed by splenic macrophages, which involves novel classes of glycans carried on spectrin, has led to some interesting therapeutic possibilities. Most cell disposal in the body is carried out by macrophages rather than T cells and their exploitation may be a useful way forward in cellular therapies of the future.

# Dr James Griffin

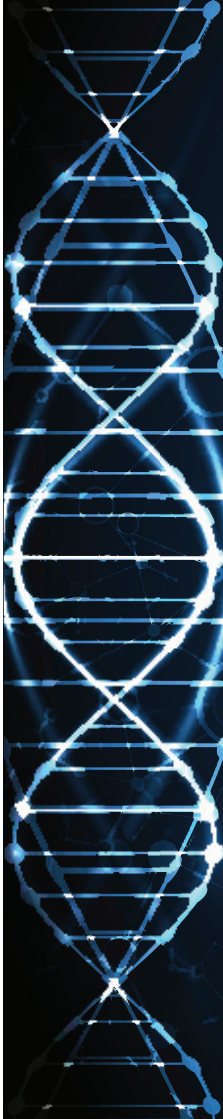
**Dr James Griffin**
**Consultant Haematologist**
**University Hospital Bristol**

Dr Griffin is Clinical Director of NHSBT Therapeutics, responsible for the 8 clinical apheresis units, 8 stem cell laboratories and the UK tissue collection and provision. He is based in Bristol where he works as a consultant in Haematology and Stem Cell Transplantation at Universities Hospital Bristol. He completed a PhD at UCL in the field of adoptive immunotherapy.

# CAR T Cells

## How to build a CAR T - what are they and how are they made

The development of cellular therapies against EBV driven disease will be reviewed, including the difficulties of moving from research projects to clinical practice. More recently, the work on how damaged red cells are removed by splenic macrophages, which involves novel classes of glycans carried on spectrin, has led to some interesting therapeutic possibilities. Most cell disposal in the body is carried out by macrophages rather than T cells and their exploitation may be a useful way forward in cellular therapies of the future.



# Dr Reuben Benjamin

**Dr Reuben Benjamin**
**Consultant Haematologist**
**King's College Hospital**

Reuben Benjamin is a haematologist with an interest in multiple myeloma, stem cell transplantation and cell therapy. He completed his haematology training at University College Hospital, London and then spent a period at Memorial Sloan Kettering Cancer Center, NY undertaking research in CAR-T cell therapy for leukaemia and myeloma. Since 2014 he has been based at King's College Hospital, London where he leads the plasma cell disorder service and CAR-T cell programme. He is currently leading the first allogeneic off-the-shelf CAR-T cell study for relapsed adult B-ALL (CALM Trial).

# CAR T Cells

## Experience of CAR T cells in leukaemia and lymphoma

Chimeric antigen receptor (CAR) T cells are an exciting new form of therapy that has shown great promise in B-acute lymphoblastic leukaemia, lymphoma and myeloma. The first reports in 2014 of >90% complete response rates in patients with relapsed B-ALL who received CD19 targeted CAR-T cells has led to an explosion of interest in this technology. Subsequent trials in lymphomas and more recently myeloma have confirmed the early promise of this novel therapy. Whilst the response rates to CAR-T cell therapy are impressively high the toxicity has also been considerable. In this talk I will summarise some of the early CAR-T cell trial results in both leukaemia and lymphoma and discuss some of the significant adverse events that are commonly seen following this therapy. I will also highlight the hospital setup required to deliver such a therapy based on our experience in conducting a phase 1 trial with the first allogeneic off-the shelf CAR-T cells (UCART19) at King's.

## CAR T Cells

**Professor David Marks**
**Professor of Haematology and Stem Cell Transplantation**
**Bristol BMT Unit**

### Challenges in delivering CAR T cell therapy regionally

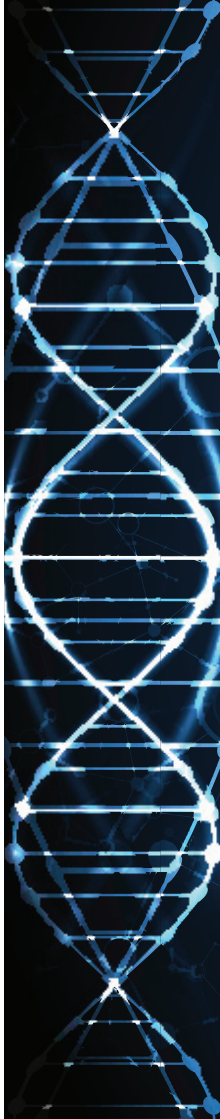
Professor Marks will briefly discuss the challenges in delivering CAR T cell therapy regionally. He will focus on the requirements to deliver this therapy, the necessary interactions and the reasons why this therapy should not be just delivered in London.

## Immunotherapy in GVHD

**Dr James Griffin**
**Consultant Haematologist**
**University Hospital Bristol**

### ECP in acute and chronic GVHD

Graft versus Host Disease (GvHD) is a potentially life-threatening complication of allogeneic stem cell transplantation. Treatment is usually immunosuppressive and for many patients, the infections acquired during treatment can cause significant morbidity and mortality. Extracorporeal phototherapy (ECP) is an immunomodulatory treatment that has potential benefit in both acute and chronic GvHD. ECP causes less immune suppression than other therapies, whilst retaining good efficacy. NHS England have recently commissioned ECP as second line therapy in acute GvHD in addition to previous funding agreement for chronic GvHD. This talk will review the mechanism of action and evidence for use in GvHD.



# Dr Fiona Dignan

## Dr Fiona Dignan
### Clinical Lead for Haematology
### Manchester Royal Infirmary

Dr Fiona Dignan is a consultant in haemato-oncology and clinical lead for haematology at Manchester Royal Infirmary. Her main clinical interests are acute leukaemia, chronic myeloid leukaemia and allogeneic transplantation. She is the lead author of national clinical practice guidelines on graft-versus-host disease and veno-occlusive disease following haematopoietic stem cell transplantation. She is also treasurer for the British Society for Blood and Marrow Transplantation and has been a member of the working party for the National Institutes of Health consensus project on chronic graft-versus-host disease.

She undertook her haematology training at The Royal Marsden in London and developed a research interest in post-transplant complications including infection and graft-versus-host disease. She undertook an MD research degree from University College London on novel strategies for managing graft-versus-host disease which has led to a number of national and international presentations and peer-reviewed journal articles.

## ECP in combination therapy

Graft versus host disease remains one of the main complications of stem cell transplantation and steroid-refractory disease remains a challenge. Extracorporeal photopheresis is used as a second line option in the treatment of both acute and chronic GVHD. ECP is often used in combination with steroids and other agents in day to day practice and appears to be safe and feasible. Novel combinations have recently been explored including ECP and etanercept in the prophylactic setting and ECP and ruxolitinib and ECP and imatinib in the treatment of chronic GVHD. In the future, ECP may be used in combination with novel agents to improve the response in patients with both acute and chronic GVHD.

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Ruxolitinib and ECP Bonmann et al, poster EBMT 2017 (N.Kroger)

Imatinib and ECP Magro et al, EBMT poster 2017

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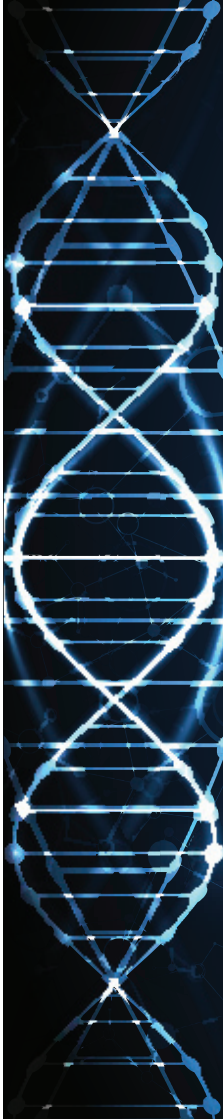


# Professor Francesco Dazzi

## Professor Francesco Dazzi
### Professor of Regenerative and Haematological Medicine
### King's College London

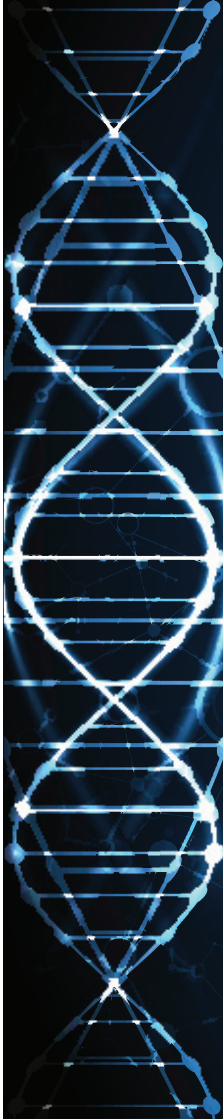
Prof Francesco Dazzi has been working on the biology and clinical applications of cellular therapies in stem cell transplantation for the last 20 years. His activity both as a scientist and a clinical Haematologist has enabled him to establish a very productive cross-talk between bench and bedside. He obtained an MD and a PhD at Padua University Medical School (Italy), and subsequently trained as a Haematologist at Verona University and at the Royal Postgraduate Medical School (now Imperial College). He was appointed Senior Lecturer and then Reader in Transplantation Biology at Imperial and in 2005 he became Professor of Stem Cell Biology. He recently moved to King's College where he is Professor of Regenerative and Haematological Medicine and leads Cellular Therapies.

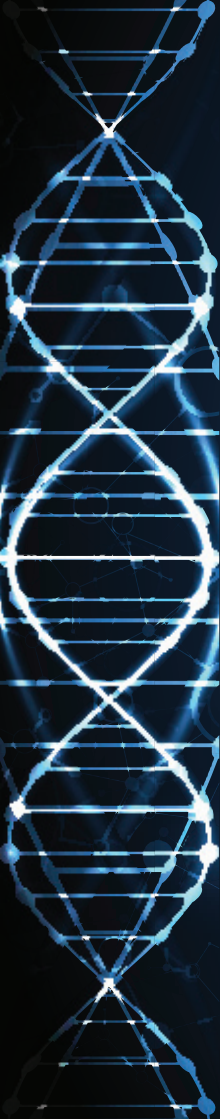
Francesco pioneered a large and highly successful cellular immunotherapy programme for leukaemia (donor lymphocyte infusions) and in parallel he developed animal models to investigate outstanding clinical problems. He described and characterised the immunosuppressive effects of mesenchymal stromal cells (MSC) thereby identifying a new mechanism of immune tolerance with distinctive tissue repair activity. His team successfully tested MSC in pre-clinical models of immune mediated diseases and the work has formed the basis of UK wide clinical studies.

# Immunotherapy in GVHD

## Potential of mesenchyman stem cells

Mesenchymal stem/stromal cells (MSC) are probably amongst the most promising cell-based reagents for immunomodulation. They are a heterogenous cell populations that can be found on virtually every tissue. They exhibit a potent immunosuppressive action which is not antigen specific and does not require MHC compatibility. Because of these properties MSC have been successfully exploited for the treatment of graft-versus-host disease whereby they can produce dramatic clinical benefits. The initial encouraging results were confirmed in subsequent studies. In the UK we have developed a clinical programme that has allowed several patients to be treated with MSC. We have recently analyzed the data collected from a cohort of patients treated with MSC that will be discussed at the meeting. Understanding the underlying mechanisms of MSC immunosuppression would be fundamental to deliver the best treatment. Currently, the most accredited modality involves the reprogramming of aminoacid metabolism. However, a fundamental concept underpinning MSC immunobiology is their plasticity. MSC are not constitutively inhibitory, but they deliver immuno-suppressive functions only after being exposed to an inflammatory environment that 'licenses' these properties. Therefore, choosing the appropriate timing for MSC infusion is fundamental for clinical efficacy and that timing is not necessarily related to disease severity but rather to the inflammatory features of the disease stage. Therefore, the pattern of molecular cues that triggers MSC therapeutic activity in disease has the potential to identify which patients are more likely to benefit from MSC therapies.





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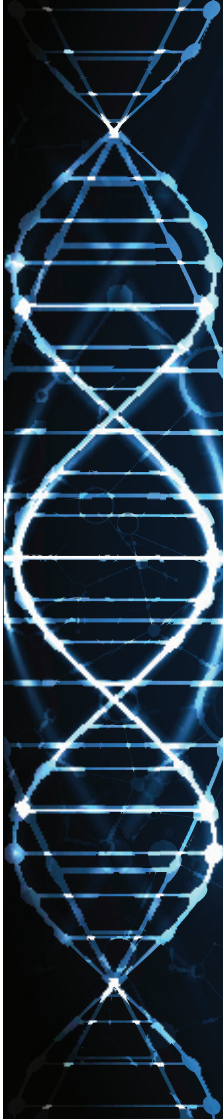

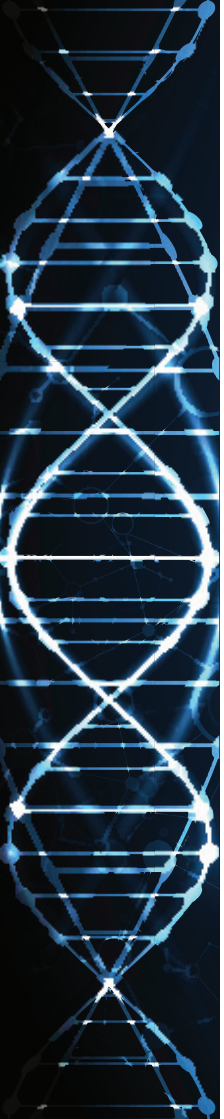

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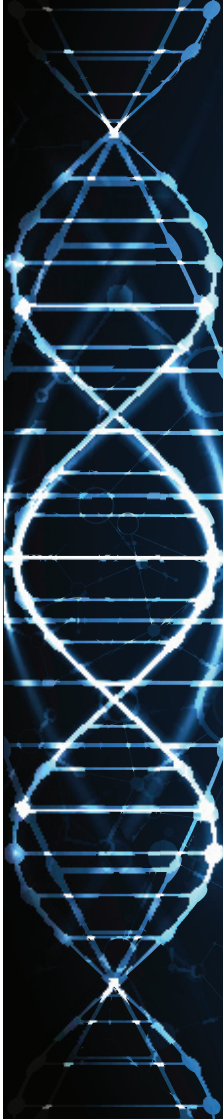
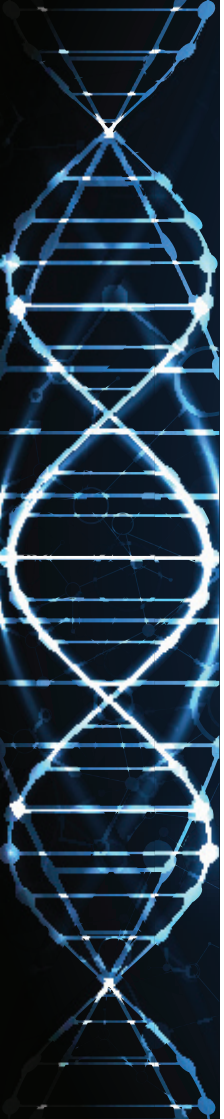




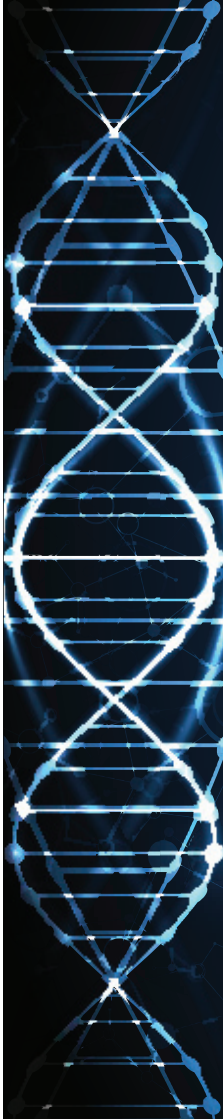
## Notes

This meeting is one in a series to be held in the UK during 2017 – 2018.

The programme was designed by the Chairs with an Expert Panel's opinion and organised by Hartley Taylor Ltd. Sponsors have had no input into the agenda or choice of speakers

Sponsorship has been provided by Mallinckrodt.

Therakos
ECP Immunomodulation



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