The Immunosuppression Summit 2016 will bring together scientists from all over the world in order to discuss the many aspects of immunosuppression, immunotherapy and vaccination. With topics ranging from tumour immunosuppression and HIV, to antibodies and biomarkers, this event promises to appeal to all scientists working within this ever-growing field. The problems of immunosuppression will be discussed, and research into overcoming them will be debated in an informal, academic setting.

This event has CPD accreditation

This abstract book will be finalised two weeks before the event
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Invited Speakers Abstracts

Immunological heterogeneity in type 1 diabetes
Dr. Sefina Arif, King's College London, London, United Kingdom
The concept that Type 1 diabetes (T1D) is a heterogeneous disease in terms of its pathological presentation and rate of progression is currently gaining some traction, but data are scant. Theoretically the identification of heterogeneity would be of considerable importance; it could significantly impact upon prediction algorithms and on stratification for immune-based therapies. We have obtained preliminary evidence for heterogeneity in the adaptive autoimmune response that is associated with T1D development. Using a novel combinatorial approach to examining autoreactive T by T cell ELISpot and autoantibody responses coupled with a bioinformatics approach to data analysis, we have uncovered significant immunological heterogeneity in subjects at T1D diagnosis. We find that responses cluster into “pro-inflammatory” and “partially regulated” autoimmune inflammatory phenotypes (AIPs). Pilot data now shows that the same two clusters also divide at-risk subjects.

Induction of Immunosuppression with polyclonal ATGs: New perspectives
Professor Andres Beiras-Fernandez, Department of Thoracic and Cardiovascular Surgery, Johann Wolfgang Goethe University, Frankfurt, Germany
Polyclonal anti-thymocyte globulins (ATGs) are immunosuppressive drugs widely used in induction of immunosuppression and treatment of acute rejection after solid organ transplantation. The main mechanism of action has been widely reported, and is based on the depletion of activated T-cells through complement activation and induction of apoptosis through CD95. However, these drugs present other mechanisms of action not related to T-cell depletion, allowing different immunosuppressive strategies. Among them, modulation of endothelial cells and regulation of dendritic cells and B-cells, are some interesting features of these drugs.

Immunosuppression strategies in liver transplantation in patients with HCC or renal impairment
Dr Dimitrios Giakoustidis, Aristotle University of Thessaloniki, Thessaloniki, Greece
Recurrent HCC tumors after liver transplantation have significantly faster growth rate than the non-transplanted patients with HCC subjected to surgical resection due to immunosuppression and reduced host immunity. CNI-based immunosuppression is associated with TGFβ expression and HCC development. Moreover, CNI-induced nephrotoxicity is the leading cause of renal dysfunction after liver transplantation and has been associated with significant morbidity and mortality. Diverging and minimizing the intensity of immunosuppression to the minimum level without compromising effectiveness should be the target of future immunosuppression maintenance.

Mesenchymal Stromal Cells with Enhanced Immunosuppressive Activity
Dr John Girdlestone, Stem Cells and Immunotherapies, NHSBT Oxford, John Radcliffe Hospital, Headington, Oxford, UK
MSC have generated a great deal of interest in the field of regenerative medicine. Beyond their potential to differentiate into bone and cartilage, they possess immunosuppressive activities that are being exploited in the clinic to treat undesired immune reactions in autoimmunity and transplantation. We have developed a simple method to substantially increase the suppressive potency of MSC, and demonstrated their superior efficacy in a pre-clinical model of GvHD.
Stabilizing regulatory T cells for tolerance inducing immunotherapy
Dr. Irma Joosten, DVM, PhD, Director Laboratory of Medical Immunology, Department of Laboratory Medicine, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands
Regulatory T cells (Treg) are important for immune homeostasis and of great interest for clinical immunosuppressive therapy in transplantation and autoimmunity. The paucity of Treg numbers obviates the need for ex vivo expansion. Due to Treg plasticity, it is not only crucial to develop expansion protocols that maximize ex vivo Treg proliferative rates, but also maintain Treg stability and preserve their suppressive function. This talk will focus on the recent discovery of selected immunomodulatory agents (drugs and biologicals) that successfully improve Treg function upon expansion and will thus be of potential use in clinical protocols.

The infection status and its influences to methadone maintenance treatment
Dr Yu-Li Liu, National Health Research Institutes, Zhunan, Miaoli County, Taiwan
Methadone maintenance treatment (MMT) program was a policy used to reduce the heroin use, to prevent infectious disease, and to control the crime rate. As the patients had high individual dosage variability, pharmacogenomics study was applied in a population recruitment to study the dosage regulatory mechanism. In 328 of MMT patients, we found that 95% patients infected with hepatitis C virus (HCV) and 24% patients infected with human immunodeficiency virus (HIV). In order to understand the impact of these infections to methadone treatment responses, we have analyzed the immunological chemokines and cytokines for their influences.

Intrinsic inhibitors of T cell signals in the control of tumor-induced immunosuppression
Dr Isabel Mérida, Dept of Immunology and Oncology, National Center for Biotechnology, Darwin 3. Campus UAM/CSIC, Madrid, Spain
The immune system constitutes the internal defense to infection but also to cancer. In recent years T lymphocytes are becoming central players in anticancer therapies. In particular, blocking antibodies against proteins that constitute T-cell activation brakes, such as CTLA-4 and PD-1, are yielding very promising results in trials with patients in advanced stages of cancer. However, the striking variability in the outcomes of these treatments illustrates the need to gain more detailed knowledge of these promising strategies. Understanding the mechanisms by which tumors hijack intrinsic mechanisms of T cell tolerance will allow to fully exploit the potential of immunotherapy for cancer.

Autoimmunity diseases and cutaneous melanoma
Dr Guglielmo Pranteda, NESMOS Departement, Università "Sapienza", Roma, Italy
Association between autoimmune disease and malignant melanoma (MM) was reported as a positive prognostic factor. Revising our data from 1992 to 2014, we found 49 MM patients with autoimmune disease and matched them with control group. Statistical analysis of disease-free survival (DFS) and overall survival (OS) showed a range of results, from a worsening of DFS and OS to a lack of any difference. In conclusion autoimmune disease was not associated with better prognosis in MM patients. Therefore the relationship between autoimmunity and MM may be a result of individual variation influenced by autoimmune disease, tumour and/or treatments.

Malignancies in HIV-infected patients
Dr Bernardino Roca, Hospital General, Jaume University, Castellon, Spain
Most malignancies affecting HIV-infected patients are those recognized as acquired immunodeficiency syndrome (AIDS)-defining cancers, i.e., Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL), and invasive cervical cancer (ICC). However, other
cancers, such as Hodgkin's lymphoma (HL), and lung cancer are more common among the HIV-infected people than in the general population. While not classified as AIDS-defining conditions, these last malignancies have been referred to as HIV-associated malignancies. Treating cancer in HIV-infected patients remains a challenge in most cases, because of drug interactions, compounded side effects of the medications needed, and the potential effect of chemotherapy on CD4 count and HIV viral burden.

**Use of biologic agents in inflammatory eye conditions: benefits and potential risks**

Dr. Bernardino Roca and M. Roca, Hospital General, Jaume University, Castellon, Spain

Biologic agents have supposed a major advance in control of inflammatory and autoimmune diseases. Noninfectious uveitis is a potentially sight threatening inflammatory condition that was traditionally treated with local or systemic steroids and other immunosuppressant drugs. The availability of biologic agents has markedly improved the clinical control of the disease and considerably increased the possibility of long-term remissions. Several studies have demonstrated the usefulness of tumor necrosis factor inhibitors, anti-interleukins, interferon alpha and other related agents for the treatment of uveitis, including refractory cases. However, there are still few studies available to validate most of the practical applications of the drugs. The medications show in general a favorable safety and efficacy profile, but knowledge on when to commence treatment, which agent to choose, or how long to continue therapy is still limited. Moreover, high cost and potential for serious and unpredictable complications are limiting factors to their broad scale use.

**Immunosuppression in Chronic Lymphocytic Leukemia: the key role of c-MET/HGF interaction.**

Dr. Daniela DeTotero, IRCCS AOU San Martino-IST, Molecular Pathology Lab, Genoa, Italy

Chronic lymphocytic leukemia (CLL), the most common leukemia in the Western World is characterized by accumulation of monoclonal CD5+ B cells in blood, lymph-nodes and bone marrow (BM). Leukemic infiltration of lymph-nodes and BM correlates with clinical stages: these districts may represent sanctuary sites where leukemic cells are protected from apoptosis. We demonstrated that in CLL, Hepatocyte Growth Factor (HGF), produced by stromal cells, has a dual role: enhances CLL cells survival and drives mono/macrophages towards the M2 phenotype. Collectively our data support a model for ongoing immunosuppression through autocrine/paracrine secretion of HGF, subsequent M2 polarization and Treg expansion.

**Soluble CTLA-4 and its role in immune regulation**

Dr. Frank Ward, Institute of Medical Sciences, Aberdeen, United Kingdom

Dr Frank Ward completed his PhD at King's College London, studying mechanisms of tolerance induction in systemic lupus erythematosus. Currently at the University of Aberdeen, his interest centres on a secretable molecule called soluble CTLA-4, a crucial modulator of immunity, which has been less well-studied than its celebrity counterpart, full length CTLA-4 receptor. Recently, he has generated reagents including antibodies and recombinant proteins to allow study of sCTLA-4 mechanisms in isolation from other isotypes. He welcomes productive collaborations with those seeking to understand how sCTLA-4 contributes to immune regulation in different disease settings.

**Targeting donor rather than recipient cells to prevent rejection of transplanted organs**

Dr. Wilson Wong, MRC Centre for Transplantation, King's College London, Guys' Hospital, London, United Kingdom
Rejection of transplanted organs is a main cause of graft loss. This depends on the trafficking of donor passenger leukocytes to the secondary lymphoid organs of the recipient to elicit an immune response. Therefore, the depletion of passenger leukocytes may be clinically applicable as a strategy to improve graft survival. As MHC class II+ cells are most efficient at inducing immune responses, selective depletion of this population from donor grafts may dampen the alloimmune response and prolong graft survival. We have constructed an immunotoxin against donor MHC class II+ cells. It depletes donor MHC class II+ cells specifically in vitro and in vivo. When given to recipients of kidney allografts, it resulted in indefinite graft survival with normal graft function, presence of Foxp3+ cells within donor grafts, diminished donor-specific antibody formation and delayed rejection of subsequent donor type skin grafts. Strategies aimed at the donor arm of the immune system using agents such as immunotoxins may be a useful adjuvant to existing recipient orientated immunosuppression.