Programme

14:00 **Opening remarks** - **Michel Deneken**
President, University of Strasbourg

14:05 **Presentation USIAS Fellows 2017**
Thomas Ebbesen, Director of USIAS

14:15 **Introduction** - **Jules Hoffmann**
Professor of Integrative Biology, USIAS, IBMC, university of Strasbourg

14:20 **Anti-cancer immune reactions in the tumour microenvironment, a guide for efficient immunotherapies**
Wolf-Hervé Fridman
Professor emeritus in Immunology, Cordeliers Research Centre and University of Paris Descartes

15:10 **Innate immunity, inflammation and cancer: from bench to bedside**
Alberto Mantovani
Professor in Experimental Medicine and Physiopathology, Humanitas University, Milan

16:00 **Discussion** moderated by **Jules Hoffmann**

16:30 **Reception**

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USIAS
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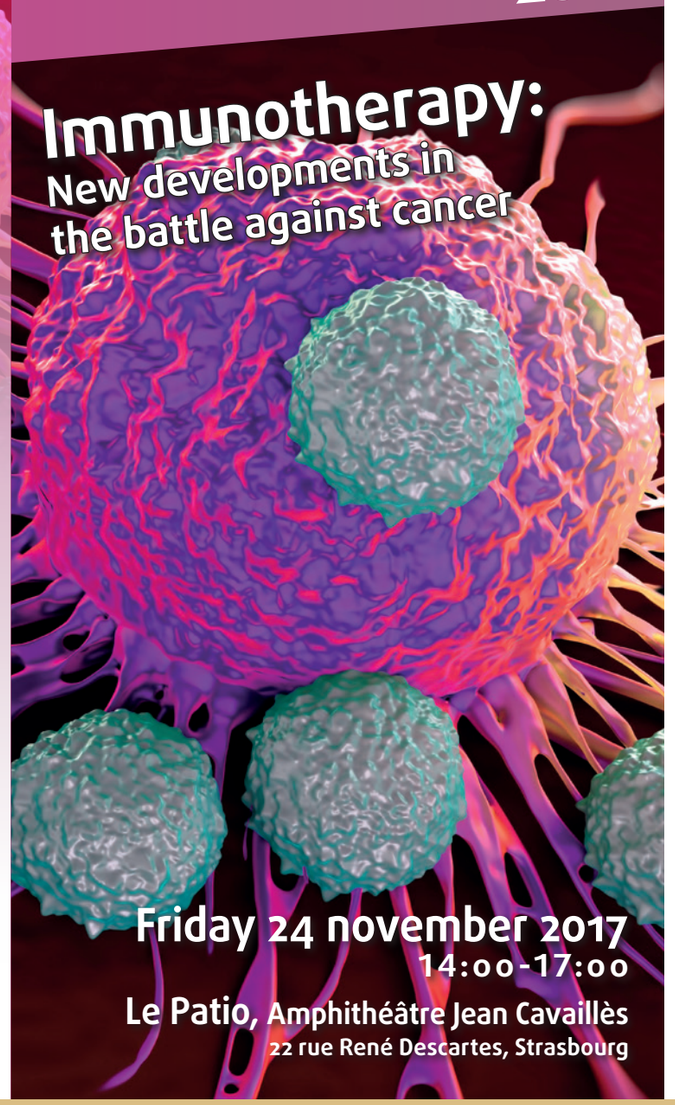
Annual Symposium 2017

Immunotherapy: New developments in the battle against cancer



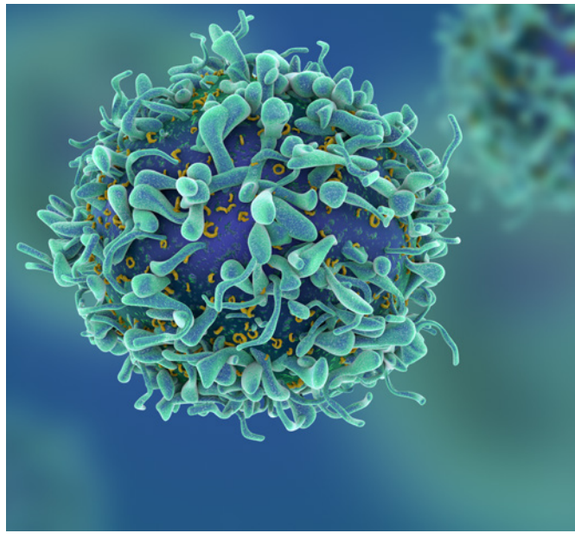
Friday 24 november 2017
14:00-17:00

Le Patio, Amphithéâtre Jean Cavaillès
22 rue René Descartes, Strasbourg

Introduction

Tumour immunology has become, in recent years, the most promising approach in the fight against cancer: cancer cells can be targeted and destroyed by the immune system of the patient. But how can the immune system be stimulated so that it only destroys cancer cells? The direct solicitation of certain proteins belonging to the immune system is a key factor in the implementation of effective therapeutic strategies.

Two of the leading pioneers in the field of cancer immunotherapy, who have fundamentally changed the way cancer and its treatment are perceived, will be present at the symposium. The theme and the two keynote speakers will be introduced by Jules Hoffman, who holds the Chair of Integrative Biology at USIAS, and who was awarded the 2011 Nobel Prize for Medicine for his work on innate immunology. The discussion will focus on the next steps in cancer immunotherapy.



Jules Hoffmann is Professor at the University of Strasbourg Institute for Advanced Study (USIAS) and the University of Strasbourg as well as senior researcher at the CNRS. He has dedicated his work to the study of the genetic and molecular mechanisms responsible for innate immunity in insects, thus providing new insights into the defence mechanisms that organisms, from the most primitive level up to humans, employ against infectious agents. By demonstrating the marked conservation of innate defence mechanisms between insects and humans, the work initiated by Hoffmann and his collaborators has led to a re-evaluation of the role of innate immunity in mammals.

More generally, the Drosophila model has enabled biologists throughout the world to make considerable progress, not only in development genetics and innate immunity but also in the study of certain human pathologies and in the understanding of memory, behaviour, sleep and nutrition phenomena.

In 2011, Jules Hoffmann was awarded the Nobel Prize for Medicine, with Bruce A. Beutler and Ralph M. Steinman.

Wolf-Hervé Fridman is Professor emeritus in Immunology at the University of Paris Descartes. His research is focused on the role of the immune system in controlling human tumours and the biological functions of receptors for IgG antibodies, both through basic and translational approaches.

In 1969 he published, with François Kourilsky, the first demonstration of a patient's immune response to his own cancer, in acute leukaemia. He then focused on the analysis of the tumour microenvironment. The studies of Wolf-Hervé Fridman and his collaborators Jérôme Galon and Franck Pagès have changed the paradigm of host/cancer interactions by demonstrating that the "immune contexture" is the major prognostic factor for human cancers. These findings open the way for immune-based tools for efficient prognosis and therapy of cancers.

In 2007 Professor Fridman founded and became the first director of the Cordeliers Research Centre, a joint research structure between INSERM, the University of Paris -Descartes, and Pierre and Marie Curie University with over 400 research staff.

Professor Fridman is co-author of over 470 original peer-reviewed publications in high-impact journals. He has received numerous prizes and honours, among which - with Jérôme Galon and Ohtani Haruo - the 2010 William B. Coley Award from the Cancer Research Institute, for their work on the key role of immune response, in particular of T lymphocytes, in the defence against cancer.

Anti-cancer immune reactions in the tumour microenvironment, a guide for efficient immunotherapies

Tumours grow within a complex microenvironment composed of immune cells, fibroblasts, endothelial cells and other non-malignant cells. The study of the composition of tumour microenvironments has led to classifications with prognostic and theranostic values, as well as to treatments modulating its composition and its functional orientation. Concurrently, molecular classifications of tumours have proposed taxonomies that define groups of patients with different prognosis and which predict responses to treatments.

The density, location and functional orientation of tumour-infiltrating lymphocytes form the immune contexture which composition is positively correlated in most cases with patient's survival. Colorectal cancer represents a paradigm for tumour immunology, as it is the human cancer in which it was exemplified that an adaptive immune response can control tumour growth and metastasis. A high infiltration of Th1/cytotoxic T cells is associated with longer disease or progression free and/or overall survival both in primary and metastatic sites. High infiltration by myeloid cells and fibroblasts is generally associated with poor prognosis in cancer.

Immunotherapy is aimed to substitute or activate the patient's immune reactions to its tumour in order to control the disease in the long run. It has already revolutionized the management of several deadly and major cancers such as lung cancer, melanoma and hematopoietic malignancies. It shows efficacy in many other cancers including, bladder cancer, renal cell cancer, etc. The arsenal of immunotherapies is diverse with the use of anti-tumour monoclonal antibodies, T cell therapies and antibodies that revigorate the natural anti-tumour immune responses. The use of a given immunotherapy, and of therapeutic combinations, depends on the type of interactions of malignant cells with their microenvironment. Evaluating the tumour microenvironments allows the most appropriate selection of patients for an immunotherapeutic approach, to unveil mechanisms of resistance and provides novel therapeutic targets.

In colorectal cancer, the molecular and immune classifications confirmed that Microsattelite instable (MSI) tumours, which have defects in DNA repair enzymes and therefore are highly mutated, are characterized by a favorable immune contexture with high Th1/cytotoxic infiltration. It is responsive to anti-checkpoint therapy as well as other MSI cancers. These findings led to the first approval of an immuno-oncology therapy based on a molecular diagnosis. Other subtypes exhibited poor immune infiltration or, in the worst prognostic case, high T cell infiltration in the context of a major inflammatory, angiogenic and desmoplastic reaction which should be addressed differently in terms of immunotherapy.

Such analyses form the basis of a unification of molecular and immune classifications of human cancers, challenge our current views of the relationship between the composition of the tumour microenvironment and patient's prognosis, and I will discuss how they support targeted immunotherapeutic approaches that could benefit subgroups of patients in different cancers.

Alberto Mantovani is Professor in Experimental Medicine and Physiopatho-logy, Humanitas University, Milan. He was born October 29, 1948 in Milan, where he graduated in Medicine in 1973. After specializing in oncology, he worked at the Chester Beatty Research Institute in London (1975-1976), in the United States at the National Institutes of Health (1978, 1979 and 1985-1986) and as Head of the Department of Immunology and Cell Biology of the Mario Negri Institute for Pharmacological Research in Milan (1996-2005). From 1994 to 2001 he was Professor of General Pathology, University of Brescia and from 2001-2014 Full Professor of General Pathology, Faculty of Medicine, University of Milan.

Since October 2005 he is Scientific Director of the Istituto Clinico Humanitas and President of the Humanitas Foundation for Research. Since October 2014 he is Full Professor of General Pathology at Humanitas University in Rozzano, Milan, Italy. As of August 2017 he holds the Chair of Inflammation and Therapeutic Innovation at the William Harvey Research Institute, Queen Mary University of London.

His interests have always been focused on the mechanisms of immunological defense, innate immunity in particular, and cancer. He has contributed to the advancement of knowledge in this area both formulating new paradigms and by identifying new molecules and functions.

For his research activity he has received several national and international awards, including in 2016 the Triennial OECI Award from the Organisation of the European Cancer Institutes and the Robert Koch Award. He is President of the International Union of Immunological Societies. He served in the Board of the Global Alliance for Vaccines and Immunization (GAVI) (2007-2010). He has served in the Board of national and international scientific societies, including the International Cytokine Society (President, 2009-2010). He is EMBO Member and Member of Accademia dei Lincei. He is the most quoted Italian scientist and one of the most quoted immunologists worldwide The broad impact of the contribution of Alberto Mantovani is testified by citations. As of July 2017 he has over 95,380 (Scopus), 68,900 (Web of Science) or 132,751 (Google Scholar) citations and an H-index of 148 (Scopus), 123 (Web of Science) and 174 (Google Scholar).

Innate immunity, inflammation and cancer: from bench to bedside

The tumour microenvironment (TME) is a complex network, which includes soluble factors and components of the extracellular matrix as well as stromal, endothelial and immune cells. Immune cells and, among them, myeloid cells, play important roles in cancer development and can promote or inhibit cancer initiation and progression.

Among tumour-infiltrating immune cells, macrophages are well-known determinants of cancer-related inflammation and are typically characterized by their remarkable plasticity. This consists in the ability to acquire a wide spectrum of activation states in response to various signals derived from the microenvironment. Classical M1 and alternative M2 macrophages represent the paradigm of this property. Tumour-associated macrophages (TAMs) usually display a so-called "M2-like" phenotype that can foster tumour progression in different ways, namely by promoting genetic instability, angiogenesis and metastasis and by restraining anti-tumour adaptive immunity. Notably, TAMs can also play a dual role in the response to conventional anti-tumour therapies: they can enhance the anti-neoplastic effect or, in contrast, they can sustain a tumour-promoting response and so foil the anti-cancer power of these drugs.

Given their roles in tumour development, a number of macrophage-targeted anticancer approaches are currently being evaluated. They include inhibition of macrophage recruitment and/or survival at tumour sites, functional re-programming of TAMs to the antitumour M1-like phenotype and enhancement of killing and/or phagocytosis of cancer cells. Moreover, TAMs express checkpoint proteins that modulate T-cell activation in such a way that they can be targeted by checkpoint-blockade immunotherapies. Therefore, macrophages are involved in the regulation of the innate and adaptive immune responses in various inflammatory situations, including cancer.