
Co-organized by
Macrophage Club of Montpellier
&
Macrophage Club of Toulouse
1st Symposium of the Occitanie Network on Monocytes-Macrophages
« From ontogeny to regeneration and disease »
SoMM2017
https://somm2017.sciencesconf.org
LABEL TOULOUSE EUROPEAN CITY OF SCIENCE ESOF 2018
Monday 20 November 2017
KEYNOTES SPEAKERS
Florent GINHOUX, Singapore
Paul MARTIN, Bristol
Allan MOWAT, Glasgow
Jeffrey W. POLLARD, Edinburgh
Jessica QUINTIN, Paris
MAISON DES ÉTUDIANTS
Aimé Shoenig
Espace Richter
MONTPELLIER
REGISTRATION : FROM MAY 15TH, 2017
DEADLINE FOR A ABSTRACT SUBMISSION: OCTOBER 1ST, 2017

1st Symposium of the Occitanie Network on Monocytes-Macrophages

GENERAL MEETING INFORMATION

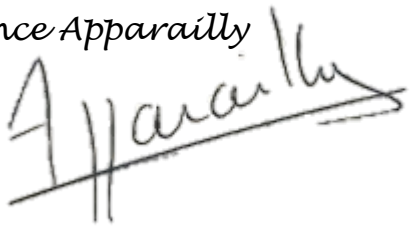
The **Montpellier Club Macrophage (MCM)** and **Macrophage Club of Toulouse (MCT)** organise the first Symposium of the Occitanie network of Monocytes-Macrophages (**SoMM2017**). This meeting is a joined initiative between the scientific communities of Montpellier and Toulouse aiming at gathering experts of the novel district named Occitanie around the biology of monocytes/macrophages.

In an intense 1 day meeting of 180 selected junior and senior researchers from the academic and private fields, cutting edge work on monocyte/macrophage biology and their involvement in inflammation and diseases will be presented, new collaborations will be established, networking is facilitated and partnership with other biomedical fields and the industry promoted. Each year will have a specific flavor and be alternatively held in Montpellier or Toulouse. For this first edition in Montpellier, we choose to address topics more specific of the local scientific community, which include ***ontogeny, regeneration and disease.***

We hope that SoMM2017 will be an interesting meeting for you and that you will enjoy your stay in Montpellier.

On behalf of the scientific Committee,

Florence Apparailly



François Canonne-Hergaux

SCIENTIFIC AND ORGANIZING COMMITEE

Florence Apparailly	***(INSERM, IRMB, Montpellier)***
Farida Djouad	***(INSERM, IRMB, Montpellier)***
Karima Kissa	***(UMR5235/CNRS, Montpellier)***
Christian Jorgensen	***(INSERM, IRMB, Montpellier)***
Béryl Laplace-Builhe	***(INSERM, IRMB, Montpellier)***
Nadège Nziza	***(INSERM, IRMB, Montpellier)***
Stéphanie Barrere	***(CNRS, IGH, Montpellier)***
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Rafael Contreras	***(INSERM, IRMB, Montpellier)***
Pascal Brugioti	***(INSERM, IRMB, Montpellier)***
Jocelyne Bihi	***(INSERM, IRMB, Montpellier)***
Florent Trecanne	***(INSERM, DR, Montpellier)***
Willam Lepetit	***(INSERM, IRMB, Montpellier)***
Michèle Moyat	***(CNRS, IGH, Montpellier)***
François Canonne-Hergaux	***(INSERM, IRSD, Toulouse)***
Céline Deraison	***(INSERM, IRSD, Toulouse)***
Céline Cougoule	***(CNRS, IPBS, Toulouse)***
Guillaume Tabouret	***(INRA, Toulouse)***
Séverine Fruchon	***(INSERM, CPTP, Toulouse)***
Christophe Carrat	***(CNRS, IPBS, Toulouse)z***
Giulia Trimaglio	***(CNRS, IPBS, Toulouse)***

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VENUE

Maison des étudiants (MDE)- Aimé Shoenig - Espace Richter

Adresse : Rue Vendémiaire, 34000 Montpellier

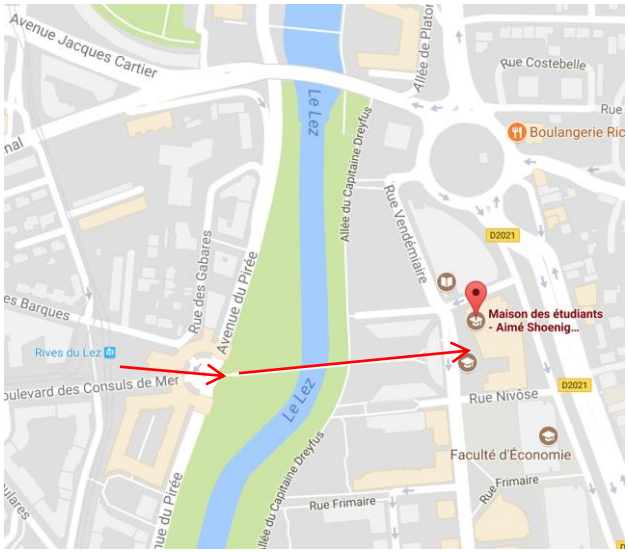
Coordonnées GPS : Latitude : 43.604524 et Longitude : 3.898905

Download Access Map (from Train station)

How to reach the meeting SoMM2017?

By Tramway

Tram 1 (blue birds) : either from the train station « Gare Saint Roch » (in front of the small garden) for people arriving by train, or from the main plazza of montpellier « Place de la Comédie » for people hosted at the « Grand hôtel du Midi ». In both cases, take direction « Odysseum » and stop at « Rives du Lez ». Once outside, walk under the building (between the purple bakery and the pharmacy) and through the footbridge for pedestrians. Cross straight the plazza, walk under the building till the « rue Vendémiaire ». MDE is straight in front.



INVITED SPEAKERS

FLORENT GINHOUX

Singapore Immunology Network (SIgN) Agency for Science, Technology and Research (A*STAR), Singapore / RESEARCH FOCUS : Dendritic Cell and Macrophage Ontogeny /

KEYNOTE LECTURE I :

Dendritic Cell and Macrophage Biology: from Development to Functions

KARIMA KISSA

Team "Emergence of haematopoietic stem cells and cancer", UMR5235/CNRS, Université Montpellier/ RESEARCH FOCUS Haematopoiesis and Cancer /

LECTURE I :

Role of macrophages in haematopoiesis

PAUL MARTIN

Professor of Cell Biology, University of Bristol, UK / RESEARCH FOCUS : Inflammation in repair and cancer /

KEYNOTE LECTURE II :

Macrophages in wound inflammatory response

CHRIS JOPLING

IGF, the Montpellier Institute of Functional Genomics, Department: Physiology - Research axis : Biology of ion channels, Montpellier / RESEARCH FOCUS : Molecular mechanisms of regeneration /

LECTURE II:

The role of macrophages during heart regeneration

JEFFREY W. POLLARD

Director of the Medical Research Council Centre for Reproductive Health and Professor of Resilience Biology at the University of Edinburgh, The Queen's Medical Research Insitiute, Edinburgh, UK / RESEARCH FOCUS: Macrophages in cancer /

KEYNOTE LECTURE III:

Macrophages: Bad Actors in Cancer.

INVITED SPEAKERS

REMY POUPOT

Professor of Paul Sabatier University - Toulouse III, Centre de Physiopathologie de Toulouse Purpan - UM1043-INSERM , Toulouse, France / RESEARCH FOCUS : A Imunomodulatory properties of dendrimer on the immune system/

LECTURE III:

Targeting monocytes-macrophages for clinical applications

JESSICA QUINTIN

Immunology of Fungal Infections, Mycology Department, Institut Pasteur, Paris, France RESEARCH FOCUS : Mechanisms of the host immune response to human fungal pathogens /

KEYNOTE LECTURE IV :

New concepts revisiting old concepts

CELINE COUGOULE

CNRS. Team: Migration and differentiation of phagocytes -IPBS-Toulouse, France / RESEARCH FOCUS: Processes of human monocyte and macrophage polarization and migration during inflammation and infectious diseases /

LECTURE IV:

Mechanisms of macrophage tissue infiltration

ALLAN MOWAT

Professor of Mucosal Immunology (Immunology), Associate - Life Sciences (School of Life Sciences), Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, UK. / RESEARCH FOCUS : Mucosal Immunology /

KEYNOTE LECTURE V :

Development and functions of intestinal macrophages

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PROGRAMM

8:00 am	**OPENING OF THE REGISTRATION DESK** – Registration for participants
	WELCOME COFFEE
8:55 am - 9:00 am	**SYMPOSIUM INTRODUCTION** Florence Apparailly (CMM, Montpellier) François Canonne-Hergaux (CMT, Toulouse)
9:00 am - 10:30 am	**SESSION I:** **MACROPHAGE ONTOGENY AND DIFFERENTIATION** Chairs : Stéphanie Barrère, (IGF, CNRS, Montpellier) Béryl Laplace-Builhe (INSERM, IRMB, Montpellier)
9:00 am - 9:45 am	***KEYNOTE LECTURE I:*** ***Dendritic Cell and Macrophage Biology: from Development to Functions*** Florent Ginhoux (Singapore Immunology Network, Singapore)
9:45 am - 10:15 am	**LECTURE I:** ***Role of macrophages in haematopoiesis*** Karima Kissa (UMR5235/CNRS, Université Montpellier)
10:15 am - 10:30 am	**SELECTED ABSTRACT 1** ***Developmental Origin and maintenance*** ***of distinct testicular macrophage populations*** Noushin Mossadegh-Keller (CIML, Marseille)
10:30 am - 10:45 am	**COFFEE BREAK (15')**
10:45 am - 12:30 pm	**SESSION II** **TISSUE REPAIR AND REGENERATION** Chairs: Farida Djouad (INSERM, IRMB, Montpellier) Mary Poupot (INSERM CRCT, Toulouse)
10:45 am - 11:30 pm	**KEYNOTE LECTURE II** ***Macrophages in wound inflammatory response*** Paul Martin (Bristol, UK)
11:30 pm - 12:00 pm	**LECTURE II** ***The role of macrophages during heart regeneration*** Chris Jopling (CNRS, IGF, Montpellier)
12:00 pm - 12:15 pm	**SELECTED ABSTRACT 2** ***AMPK activation controls LTBP4-dependent TGFβ & secretion*** ***by proinflammatory macrophages responsible of fibrosis*** ***in Duchenne muscular dystrophy*** Gaëtan JUBAN (CNRS/INSERM Institut NeuroMyoGène Lyon)
12:15 pm - 12:30 pm	**SELECTED ABSTRACT 3** ***The microglial reactome signature revealed by RNAseq from individual mice*** Hélène Hirbec,(CNRS, IGF, Montpellier)
12:30 pm - 1:30 pm	**LUNCH / NETWORKING (1H)**

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1:30 pm - 3:15 pm	**SESSION III** **FROM BASIC RESEARCH TO CLINICAL APPLICATION** Chairs: Yannick Degboé (INSERM, CPTP, Toulouse) Séverine Fruchon (INSERM, CPTP, Toulouse)
1:30 pm - 2:15 pm	**KEYNOTE LECTURE III** ***Macrophages: Bad Actors in Cancer.*** Jeffrey W. Pollard (Queen's Medical Research Institute, UK)
2:15 pm - 2:45 pm	**LECTURE III** ***Targeting monocytes-macrophages for clinical applications*** Rémy Poupot (University Paul Sabatier, CPTP, Toulouse)
2:45 pm - 3:00 pm	**SELECTED ABSTRACT 4** ***Role of the dendritic cell immunoreceptor (DCIR) in the immune regulation of colorectal cancer*** Giulia Tramaglio (CNRS IPBS, Toulouse)
3:00 pm - 3:15 pm	**SELECTED ABSTRACT 5** ***The potential impact of dual IL-17A and IL-17F neutralization: Re-evaluating the role of IL-17F in immune-mediated chronic inflammation*** Meryn Griffiths (UCB)
3:15 pm - 3:45 pm	**COFFEE BREAK (30')**
3:45 pm - 6:00 pm	**SESSION IV:** **MACROPHAGES & IMMUNITY** Chairs: Christian Jorgensen (INSERM, IRMB, Montpellier) Yoann Rombouts (CNRS IPBS, Toulouse)
3:45 pm - 4:30 pm	**KEYNOTE LECTURE IV** ***New concepts revisiting old concepts*** Jessica Quintin (Pasteur Institute, Paris)
4:30 pm - 5:00 pm	**LECTURE IV** ***Mechanisms of macrophage tissue infiltration*** Céline Cougoule (CNRS IPBS, Toulouse)
5:00 pm - 5:15 pm	**SELECTED ABSTRACT 6** ***Tuberculosis boosts HIV-1 production by macrophages through IL-10/STAT3-dependent tunneling nanotube formation*** Shanti Souriant (CNRS IPBS, Toulouse)
5:15pm - 5:30 pm	**MACROPHAGES & INTESTINE** Chairs : Céline Deraison (INSERM IRSD, Toulouse) Karima Kissa (UMR5235/CNRS, Université Montpellier)
5:15pm - 6:00 pm	**KEYNOTE LECTURE V** ***Development and functions of intestinal macrophages*** Allan Mowat (Univ Glasgow, UK)
6:00pm - 6:15 pm	**PRICES AND CONCLUSIONS**

ABSTRACTS

KEYNOTE LECTURE I

Dendritic Cell and Macrophage Biology: from Development to Functions

Florent Ginhoux

Singapore Immunology Network, Singapore

Abstract

Dendritic cells (DCs), monocytes and macrophages play crucial and distinct roles in tissue homeostasis and immunity, but also contribute to a broad spectrum of pathologies and are thus attractive therapeutic targets. Potential intervention strategies aiming at manipulation of these cells will require in-depth insights of their origins and the mechanisms that govern their homeostasis. DCs and monocytes arise from common bone marrow (BM) precursor named macrophage-dendritic cell precursors (MDP), branching into exclusively DC- or monocyte-committed progenitors named common dendritic cell progenitors (CDPs) or common monocyte progenitor (cMoPs) respectively. CDPs give rise to plasmacytoid DC and migratory DC precursors termed pre-DCs. Pre-DCs seed tissues where they differentiate into the two major functionally specialized DC lineages, CD8α+/CD103+ DC1 and CD11b+ DC2. Recent evidence from our laboratory and others has showed that monocytes do not substantially contribute to all tissue macrophage populations in steady state and inflammatory conditions. Rather certain tissue macrophages in mice are derived from embryonic precursors, are seeded before birth and maintain themselves in adults by self-renewal. In addition, we now provide evidence that commitment to DC1 and DC2 subsets is imprinted early in the BM. Combining single cell sequencing with conventional transcriptomic analysis, we identified for the first time DC subset-specific precursors in the BM as well as previously unknown molecular checkpoints for DC lineage commitment as early as the CDP stage. Using again single cell sequencing and CyTOF, we also identified homologous DC progenitors in humans and redefined the human DC lineage from the BM to the tissues. These new insights into the origins of DCs, monocytes and macrophages should aid the rational design of therapies aimed at harnessing the functions of these cells in homeostasis and inflammation and will allow efficient targeting and manipulation during health and disease.

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LECTURE I

Role of macrophages in haematopoiesis

Jana Travnickova[1,2], Vanessa Tran Chau[1,2,3], Emmanuelle Julien[4,5,6,] Julio Mateos-Langerak[7], Catherine Gonzalez[1,2], Georges Lutfalla[1,2], Manuela Tavian[4,5,6] and Karima Kissa[1,2,8,*]

1CNRS UMR 5235, F-34095 Montpellier, France
2Univ Montpellier 2, Dynamique des Interactions Membranaires Normales et Pathologiques, F-34095
3Institut Pasteur, Département de Biologie du Développement, F-75015 Paris, France
4INSERM UMR_S949, F-67000, Strasbourg, France
5Univ de Strasbourg, F-67000, Strasbourg, France
6Etablissement Français du Sang, F-67000, Strasbourg, France
7Montpellier RIO Imaging, F-34396 Montpellier, France
8INSERM, DIMNP, F-34095 Montpellier, France

Abstract

Blood cells are continuously produced from self-emerging progenitors with multi-lineage differentiation potential, called haematopoietic stem/progenitor cells (HSPC). In vertebrates, haematopoiesis occurs in two successive ways. The first wave produces only myelo-erythroid cells while the second gives rise to HSPCs. HSPCs themselves first emerge in the aorta-gonad-mesonephros (AGM) by a specific transition from aortic endothelial cells before colonising transitory and subsequently definitive haematopoietic organs.

We identified an unexpected macrophage population originating from the first wave of haematopoiesis that specifically accumulates in the dorsal mesenteric mesoderm surrounding the dorsal aorta of the human and zebrafish embryo. We therefore studied its role in haematopoiesis development in the transparent zebrafish embryo. Our study reveals dynamic interactions occurring between HSPCs and primitive macrophages in the AGM. Specific chemical and inducible genetic depletion of macrophages prevent the haematopoietic organ colonisation and lead to an accumulation of HSPCs in the place of origin (AGM). The rescue assay confirmed the specific and crucial role of macrophages in the migration of HSPCs through the stroma and the vein intravasation. Matrix metalloproteinase (Mmp) chemical inhibition together with whole mount in situ hybridisation of selected Mmps confirmed the proteolytic role of macrophages on the AGM stroma. Finally, in vivo zymography directly demonstrates the function of primitive macrophages in extracellular matrix degradation, which allows HSPCs migration through the AGM stroma, their intravasation, leading to the colonisation of haematopoietic organs, and the establishment of definitive haematopoiesis.

Keywords: Haematopoiesis, macrophage, zebrafish, live imaging

*Correspondence: karima.kissa@univ-montp2.fr

SELECTED ABSTRACT 1

Developmental origin and maintenance of distinct testicular macrophage populations

Noushine Mossadegh-Keller [1,@] , Rebecca Gentek [1] , Gregory Gimenez [1,2] , Sylvain Bigot [1] , Sebastien Mailfert [1] , Michael Sieweke [1,2*]

1 : Centre d'Immunologie de Marseille Luminy (CIML) -
Aix Marseille University, CNRS, INSERM Marseille - France
2 : Max-Delbrück-Centrum für Molekulare Medizin in der Helmholtzgemeinschaft, Berlin, Germany
* : Corresponding author

Abstract

Testicular macrophages (tMφ) are the principal immune cells of the mammalian testis. Beyond classical immune functions, they have been shown to be important for organogenesis, spermatogenesis, and male hormone production. In the adult testis, two different macrophage populations have been identified based on their distinct tissue localization and morphology, but their developmental origin and mode of homeostatic maintenance are unknown. In this study, we use genetic lineage–tracing models and adoptive transfer protocols to address this question. We show that embryonic progenitors give rise to the interstitial macrophage population, whereas peritubular macrophages are exclusively seeded postnatally in the prepuberty period from bone marrow (BM)–derived progenitors. As the proliferative capacity of interstitial macrophages declines, BM progenitors also contribute to this population. Once established, both the peritubular and interstitial macrophage populations exhibit a long life span and a low turnover in the steady state. Our observations identify distinct developmental pathways for two different tMφ populations that have important implications for the further dissection of their distinct roles in organ homeostasis and testicular function.

KEYNOTE LECTURE II

Macrophages in wound inflammatory response

Paul Martin

University of Bristol, UK

Abstract

We model various aspects of tissue repair in several genetically tractable model organisms from the fruitfly, Drosophila, through to mice. We know that inflammation is both beneficial for healing in that it fights infection and drives wound angiogeneisis, but it has negative consequences also, in that it causes scarring and is aberrant in chronic wounds. We use Drosophila and translucent zebrafish, which are both amenable to live imaging and mathematical modelling, to make movies of immune cell migration into the wound and to dissect the genetics of inflammatory cell recruitment towards tissue damage, and its consequences, and, its parallels with cancer inflammation. Most recently we have also begun to investigate how adipocytes and obesity might link into wound repair and cancer.

LECTURE II

The role of macrophages during heart regeneration

Chris Jopling

CNRS, IGF, Montpellier, France

Abstract

Zebrafish are capable of completely regenerating their heart after an extensive insult. Immediately after injury a blood clot seals the wounded area which is subseqeuntly replaced by a collagenous/fibrin scar. As regeneration proceeds the scar is progressively removed as new cardiomyocytes proliferate and eventually completely regenerate the heart. Here we show that the expression of the extracellular matrix degrading enzyme, matrix metalloproteinase 14 (MMP14), correlates with scar regression during heart regeneration. Furthermore, we demonstrate that the source of MMP14 is provided by infiltrating macrophages which remain in the scar region long after the initial injury. Consistent with a role for MMP14 producing macrophages in scar regression, we show that chemical inhibition of MMP signaling completely arrests heart regeneration and leads to extensive scar formation. Together, our data points to a model of scar removal by MMP14 positive macrophages and that this process is required for successful heart regeneration to occur.

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SELECTED ABSTRACT 2

AMPK activation controls LTBP4-dependent TGFβ1 secretion by pro-inflammatory macrophages responsible of fibrosis in Duchenne Muscular Dystrophy

Gaëtan Juban [1,*,@] , Marielle Saclier [2,@] , Rémi Mounier [1,@] , Bénédicte Chazaud [1,@]

1 : Institut NeuroMyoGène (INMG) -
CNRS : UMR5310, - INSERM : U1217, Université Claude Bernard - Lyon I (UCBL)
2 : University of Milan
* : Corresponding author

Abstract

Macrophages play a critical role in skeletal muscle regeneration. After an injury, they infiltrate the injured tissue as inflammatory macrophages, expressing the marker Ly6C, that phagocyte damaged myofibers and stimulate myogenic progenitor proliferation. Then, they switch into Ly6Cneg anti-inflammatory/restorative macrophages that favor myogenic differentiation and fiber growth. Degenerative myopathies are associated with mutations in genes coding for structural proteins causing great fragility of the myofibers. This leads to repeated, asynchroneous cycles of injury/regeneration, leading to chronic inflammation and fibrosis. Here, we characterized the phenotypes and functions of macrophage subsets associated with fibrosis in both mouse and human Duchenne muscle.

Our results showed that fibrosis is associated with macrophages expressing pro-inflammatory markers. Importantly, these macrophages actively contribute to the fibrosis as skewing their phenotype towards an anti-inflammatory phenotype using several pharmacological treatments decreases necrosis and fibrosis in dystrophic muscles.

Sorted populations from mouse skeletal muscle showed that Ly6Cpos and Ly6Cneg macrophage subsets exhibit opposite functions towards fibroblasts in regenerating *versus* dystrophic muscles. During muscle regeneration, Ly6Cneg macrophages stimulate collagen I production by fibroblasts whereas Ly6Cpos macrophages trigger their apoptosis. On the contrary, in dystrophic muscles, Ly6Cpos macrophages strongly stimulate fibroblasts to produce collagen I and protect them from apoptosis, thus participating in fibrosis.

Moreover, we could show that this effect is mediated by an AMPK-controlled increased expression of the muscular dystrophy modifier Ltbp4 gene, leading to a high production of latent TGFβ1 by Ly6Cpos macrophages only in dystrophic muscles. Concomitantly, we identified Fibro/Adipogenic Progenitors (FAPs) as the main cell population in the dystrophic muscle expressing latent TGFβ-activating enzymes, suggesting their involvment in the activation of latent TGFβ1.

These results identify a Ly6Cpos macrophage population expressing pro-inflammatory markers but with modified functions as a key player in fibrosis in degenerative myopathies. A local cross-talk between highly secreted latent TGFβ1 (via LTBP4 in Ly6Cpos macrophages) and secreted activating enzymes (by FAPs) promotes local fibrosis. In accordance, we observed in both human and mouse dystrophic muscle a privileged colocalization of collagen deposition and pro-inflammatory macrophages. Favoring the switching of the latter into Ly6Cneg macrophages could be of therapeutical interest to improve muscle function in Duchenne Muscular Dystrophy.

SELECTED ABSTRACT 3

The microglial reactome signature revealed by RNAseq from individual mice

Hélène Hirbec [1,@] , Camille Marmai [1] , Isabelle Richard-Durroux [2] , Christine Roubert [3] , Arnaud Esclangon [3] , Severine Croze [4] , Joel Lachuer [4] , Ronan Peyroutou [1] , Franois Rassendren [1]

1 : IGF, CNRS, INSERM, Montpellier, France *IGF*
2 : Institute of Regenerative Medicine and Biotherapy [CHRU Montpellier] (IRMB)
INSERM : U1203, Université de Montpellier, Montpellier - France
3 : Sanofi-Aventis R&D *SANOFI Recherche*
4 : ProfileXpert *ProfileXpert Lyon - France*

Abstract

Microglial cells have a double life as the immune cells of the brain in times of stress but have also specific physiological functions in homeostatic conditions. In pathological contexts, microglia undergo a phenotypic switch called “reaction” 'that promotes the initiation and the propagation of neuro-inflammation. Reaction is shaped by the nature and the intensity of the triggering signals and is therefore complex, molecularly heterogeneous and still poorly characterized. Recent genome-wide studies have established the specificity and the dynamism of microglial transcriptome in different pathological conditions. However, it remains unknown whether microglia in different reactive states share a common molecular signature, which could define generic molecular markers of microglial reaction with broad application from research to clinic.

Here, we improved previous experimental framework to purify microglia and used a RNAseq approach with higher statistical power to study the remodeling of the microglial transcriptome in a mouse model of sepsis evoked by intra-peritoneal lipopolysaccharide administration. Through bioinformatic comparison of our results with previously published RNAseq datasets, we identified and validated in a model of hippocampal status epilepticus, genes that are specific to microglia and define their reactive state. Further, we define the microglial reactome as a set of 341 genes that discriminates LPS-reactive from homeostatic microglia. Ultimately, we identified a subset of 86 genes of the microglial reactome that is commonly deregulated in both acute and neurodegenerative disease states. Our data provide a high-resolution transcriptomic map of microglial reaction, and a new comprehensive resource that includes both functional analysis and specific molecular makers of microglial reaction. These data represent new tools to unambiguously characterize microglia reactivity in diverse neuropathological conditions.

KEYNOTE LECTURE III

Macrophages: Bad Actors in Cancer.

Jeffrey W. Pollard

MRC Centre for Reproductive Health, The University of Edinburgh, Edinburgh EH16 4TJ, UK

Abstract

The majority of deaths caused by cancer are due to metastasis. This fact indicates that metastatic tumours are resistant to available therapies. Tumors consist not only of malignant cells but also a wide-range of non-mutated normal cells including those of the immune system. Among these immune cells, macrophages are particularly abundant in a wide range of tumors. Our studies focussing on breast cancer have indicated that macrophages promote tumor progression to malignancy in mouse models. Recently we have identified a sub-population of metastasis-associated macrophages (MAM) that help metastatic tumour cells seed at distant sites and prosper. Lineage tracking indicates that MAMs derive from the Ly6Chi population of circulating monocytes that are recruited by tumour cell produced chemokine CCL2 at the metastatic site. CCL2 signals via CCR2 in the monocytes to upregulate expression of CCL3 that in turn binds to CCR1 in an autocrine manner. This signaling pathway results in the retention of the monocytes and their differentiation into MAMs that then deliver a survival signal to the tumour cells. Differentiation of the monocytes to MAMs involves several intermediate steps whereby these cells also attain immunosuppressive phenotypes against activated T cells. Inhibition of any of these steps of MAM recruitment or differentiation using genetic or inhibitor approaches reduces metastasis in these mouse models. Such data suggest that therapeutics directed against the pro-tumoral functions of these myeloid cells might become part of a strategy that will improve survival of patients with metastatic disease.

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LECTURE III

Targeting monocytes-macrophages for clinical applications

Rémy POUPOT

University - Toulouse III, Centre de Physiopathologie de Toulouse Purpan - UM1043-INSERM , Toulouse, France

Abstract

Dendrimers are soft matter, hyper-branched, and multivalent nanoparticles whose synthesis theoretically affords monodisperse compounds. They are built from a multivalent core on which successive series of branches are grafted thanks to a repeated sequence of quantitative reactions. At the end of each branch, a point of divergence is added which enables arborescence to be implemented at the next series of branches. Generally, the number of branches of a given series is twice or three times the number of branches of the previous series. The total number of series of branches determines the generation of the dendrimer: if it has one series of branches, it is a first generation (or generation 1) dendrimer; if it has two series of branches, it is a second generation (or generation 2) dendrimer, and so on. Once the desired generation is obtained, the last step of the synthesis consists in the addition of the surface groups which will afford the outer shell of the dendrimer. The tuneable addition of surface groups gives birth to multivalent nano-objects which are generally intended for a specific use.

Previously, we showed that a phosphorus-based dendrimer capped with twelve anionic AzaBisPhosphonate groups (so-called ABP dendrimer) has immuno-modulatory and anti-inflammatory properties towards the human immune system by specifically targeting monocytes-macrophages [1-3]. The ABP dendrimer dramatically inhibits the onset and development of experimental arthritis [4] and of Experimental Auto-immune Encephalomyelitis (EAE) [5] in mouse models relevant for human Rheumatoid Arthritis and Multiple Sclerosis, respectively. Moreover, we have shown in a sub-chronic toxicity study in non-human primates that it does not induce adverse effects nor immuno-suppression [6]. These studies make the case for the ABP dendrimer as an innovative drug-candidate for the treatment of chronic inflammatory diseases by targeting monocytes-macrophages.

[1] Fruchon S, Poupot M, Martinet L, Turrin CO, Majoral JP, Fournié JJ, Caminade AM & Poupot R. Anti-inflammatory and immuno-suppressive activation of human monocytes by a bio-active dendrimer. *J. Leukoc. Biol.* 2009, *85*, 553-562.

[2] Ledall J, Fruchon S, Garzoni M, Pavan GM, Caminade AM, Turrin CO, Blanzat M & Poupot R**.** Interaction studies reveal specific recognition of an anti-inflammatory polyphosphorhydrazone dendrimer by human monocytes. *Nanoscale* **2015**, *7*, 17672-17684.

[3] Caminade AM, Fruchon S, Turrin CO, Poupot M, Ouali A, Maraval A, Garzoni M, Maly M, Furer V, Kovalenko V, Majoral JP, Pavan GM & Poupot R. The key role of the scaffold on the efficiency of dendrimer nanodrugs. *Nat. Commun.* **2015**, *6*, 7722.

[4] Hayder M, Poupot M, Baron M, Nigon D, Turrin CO, Caminade AM, Majoral JP, Eisenberg RA, Fournié JJ, Cantagrel A, Poupot R & Davignon JL. A phosphorus-based dendrimer targets inflammation and osteoclastogenesis in experimental arthritis. *Sci. Transl. Med.* **2011**, *3*, 81ra35.

[5] Hayder M, Varilh M, Turrin CO, Saoudi A, Caminade AM, Poupot R & Liblau RS. Phosphorus-based dendrimer ABP treats neuroinflammation by promoting IL-10-producing CD4+ T cells. *Biomacromolecules* **2015**, *16*, 3425-3433.

[6] Fruchon S, Mouriot S, Thiollier T, Grandin C, Caminade AM, Turrin CO, Contamin H & Poupot R. Repeated intravenous injections in non-human primates demonstrate preclinical safety of an anti-inflammatory phosphorus-based dendrimer. *Nanotoxicology* **2015**, *9*, 933-941.

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SELECTED ABSTRACT 4

Role of the dendritic cell immunoreceptor (DCIR) in the immune regulation of colorectal cancer

Giulia Trimaglio [1,*,@] , Christel Devaud [2] , Anne-Francoise Tilkin-Mariame [2] , Nathalie Vergnolle [2] , Olivier Neyrolles [1] , Yoann Rombouts [1,*,@]

1 : Institute of Pharmacology and Structural Biology (IPBS) -
CNRS : UMR5089, Université Paul Sabatier-Toulouse III – UPS Toulouse - France
2 : Institut de Recherche en Santé Digestive (IRSD) -
INSERM : UMR1220, INRA : UMR1416, - ENVT,
Université Paul Sabatier-Toulouse III - UPS, TOULOUSE - France
* : Corresponding author

Abstract

The dendritic cell immunoreceptor (DCIR) is a C-type lectin receptor mostly expressed by dendritic cells (DCs), macrophages and neutrophils. Together with Dectin-2, BDCA-2, MCL and Mincle, DCIR belongs to the Dectin-2 family of CLRs (*Kerscher et al. 2013*). However, unlike all the other members of this family, DCIR contains an immunoreceptor tyrosine-based inhibition motif (ITIM) which is essential for inducing immunological tolerance, through the recruitment of phosphatases including SHP-1 and SHP-2 (*Huang et al., 2001*). Accordingly, mice deficient in Dcir1 (the closest murine homolog to the human DCIR) generally develop a stronger immune response to pathogen (*Troegler et al., 2016*) and are also more susceptible to aging-associated or experimentally induced antibody- and T cell-mediated autoimmune disorders than wild-type (WT) animals (*Fujikado et al., 2008*). In cancer, DCIR has been shown to be expressed by tumor-associated macrophages (TAMs) (*Allavena et al., 2010*) but nothing is known about the role played by this C-type lectin in regulating tumor development. We decided to study the role of DCIR within the context of colorectal cancer (CRC) which remains a major health burden being the third most common cancer in men and the second in women. To this end, we have developed an orthotopic syngenic pre-clinical mouse model of CRC and analyzed the tumor progression in Dcir1-WT and KO mice. We found that the lack of Dcir1 confers a higher susceptibility to the CRC development in mice, suggesting that Dcir1 plays a protective role during tumor development. Our preliminary FACS data show that Dcir1 is expressed mainly by TAMs but also by other myeloid cells infiltrating the tumor including DCs, inflammatory monocytes and neutrophils. Moreover, as compared to WT mice, tumor-bearing Dcir1-KO mice are characterized by a lower infiltration of a specific population of macrophages at 4 days post-tumor cells injection. At 28 days post-tumor cells injection, we observed a lower infiltration of CD8+ T-cells and higher levels of IFN-g- and IL-17-producing CD4+ cells in Dcir1-KO mice compared to WT mice. Altogether, we propose that the increased susceptibility of Dcir1-KO mice to tumor progression is due to a dysregulation of the balance existing between the tumor and both innate and adaptive immune responses.

Kerscher et al., The Dectin-2 family of C-type lectin-like receptors: an update, International immunology (2013)
Troegeler et al., C-type lectin receptor DCIR modulates immunity to tuberculosis by sustaining type I interferon signaling in dendritic cells. PNAS (2016)
Fujikado et al., Dcir deficiency causes development of autoimmune diseases in mice due to excess expansion of dendritic cells. Nature Medicine (2008)
Allavena et al., Engagement of the Mannose Receptor by Tumoral Mucins Activates an Immune Suppressive Phenotype in Human Tumor-Associated Macrophages. Clinical and Developmental Immunology (2010)

1st Symposium of the Occitanie Network on Monocytes-Macrophages

SELECTED ABSTRACT 5

The potential impact of dual IL-17A and IL-17F neutralization: Re-evaluating the role of IL-17F in immune-mediated chronic inflammation

Meryn Griffiths [1,@] , Ash Maroof [1] , Sophie Glatt [1] , Suzanna Cole [1] , Steven Shaw [1]

1 : UCB Slough

Abstract

Interleukin (IL)-17A and IL-17F are key drivers in mucosal protection, however under immune dysregulation these cytokines transform into important drivers of disease pathogenesis in autoimmune and chronic inflammatory conditions. The role of IL-17A in driving disease is exemplified, and well described, in diseases including psoriasis, psoriatic arthritis and axial spondyloarthritis. In this talk, in addition to what we know about IL-17A, we will also share with you why IL-17F might contribute to disease progression and that inhibition of both IL-17A and IL-17F may deliver greater benefit than targeting IL-17A alone. Our premise focuses on the shared biology between IL-17A and IL-17F, sharing 50% sequence homology and signalling through the IL-17 receptor complex. IL-17F although less potent is expressed by the same cell types as IL-17A and elicits similar effects. These effects, as with IL-17A, are most profoundly observed through synergising with pathological cytokines such as TNF. Learning from human translational studies we are building a greater understanding of the potential of IL-17F as well as IL-17A to play a role in the pathogenesis of autoimmune and chronic inflammatory conditions.

KEYNOTE LECTURE IV

New concepts revisiting old concepts

Jessica Quintin

Immunology of Fungal Infections, Department of Mycology, Institut Pasteur, Paris, France.

Abstract

Immunological memory has long been thought to be a privilege of adaptive immune comportment of the mammalian host responses. However, immunological memory characteristics have now been demonstrated in insects (deprived of adaptive immunity) and in innate immune cells in mammals. Non-specific protective effects against reinfection or “trained immunity” have been described following infection with Candida albicans that is primarily a human commensal of mucocutaneous surfaces. Other commensal organisms such as Escherichia coli induce tolerance towards secondary challenges. Innate immunological imprinting of either tolerance or trained immunity after an infection or vaccination determines the functional fate of monocytes and macrophages, and the susceptibility of the host to secondary infections. Altogether, the results of the past years of research on the innate immune memory further document the impact of microbial molecular patterns on the epigenome and the potential of functional reprogramming of monocytes for the design of improved therapeutic strategies.

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LECTURE IV

Mechanisms of macrophage tissue infiltration

C. Cougoule, V. Le Cabec, E. Van Goethem, R. Guiet, P. Gui, C. Lastrucci, S. Souriant, A. Labrousse, R. Poincloux, C. Verollet, I. Maridonneau-Parini

Migration and Differentiation of Phagocytes » group, https://phagocytes.weebly.com/
Institut de Pharmacologie et de Biologie Structurale, CNRS UMR5089, Université Toulouse, France

Abstract

Macrophages are immune cells able to migrate in all body tissues. In wounded and infected tissues, they are involved in bactericidal activity and tissue repair. In several pathologies including chronic inflammatory diseases and cancers, tissue infiltration of macrophages stimulates disease progression. It is therefore necessary to identify the molecular and cellular mechanisms that control this process, a step towards new pharmacological strategies.

Tissue migration takes place in constrained 3D environments. We have reported that macrophages can use two migration modes, the choice of the migration mode being dictated by the architecture of the extracellular matrix (ECM). The amoeboid mode (AM) is shared by all leukocytes is it is dependent of ROCK, it takes place in porous ECM. The mesenchymal mode (MM) requires proteases to degrade the ECM, it takes place in dense matrices and.

Podosomes are actin-rich cell structures with adhesion and proteolytic activities constitutively formed in macrophages, dendritic cells and osteoclasts. We have evidenced that podosomes play a critical role in the mesenchymal migration while they do not form during the amoeboid migration. Actually, interfering with podosome effectors specifically inhibits the MM. Podosomes are targeted by the Human Immunodeficiency Virus-1 (HIV-1), impacting the MM. Mtb is also able to control the MM in macrophages. Finally, our recent data reveal that macrophages can use the MM inside living tissues and that TAM specifically perform the MM inside a dense fibrosarcoma *in vivo* while macrophage perform the amoeboid migration in non-tumoral tissues. Therefore, mesenchymal-migration represents a promising pharmacological target to control detrimental TAM motility.

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SELECTED ABSTRACT 6

Tuberculosis boosts HIV-1 production by macrophages through IL-10/STAT3-dependent tunneling nanotube formation

Shanti Souriant [1,2,@] , Luciana Balboa [2,3] , Karine Pingris [1,2] , Denise Kviatcovsky [2,3] , Céline Cougoule [1,@] , Claire Lastrucci [1,2] , Aicha Bah [1] , Romain Gasser [4] , Renaud Poincloux [1,2] , Brigitte Raynaud-Messina [1,2] , Talal Al Saati [5] , Sandra Inwentarz [6] , Susana Poggi [6] , Eduardo Moraña [6] , Pablo González-Montaner [6] , Marcelo Corti [7] , Bernard Lagane [4] , Isabelle Vergne [1] , Carolina Allers [8] , Deepak Kaushal [8] , Marcelo Kuroda [8] , Maria Del Carmen Sasiain [2,3] , Olivier Neyrolles [1,2,*,@] , Isabelle Maridonneau-Parini [1,2,*,@] , Geanncarlo Lugo-Villarino [1,2,*,@] , Vérollet Christel [1,2,*,@]

1 : Institut de pharmacologie et de biologie structurale (IPBS)
Université Paul Sabatier - Toulouse 3, CNRS : UMR5089 Toulouse - France
2 : Laboratoire International Associé (LIA) CNRS "IM-TB/HIV" (1167), Toulouse, France, and Buenos Aires, Argentina
3 : Institute of Experimental Medicine-CONICET, National Academy of Medicine
4 : Centre de physiopathologie de Toulouse Purpan (CPTP)
Université Paul Sabatier - Toulouse 3, INSERM : U1043, CNRS : UMR5282 Toulouse - France
5 : Service d'Histopathologie, CHU Purpan *INSERM : US006/CREFRE, Université Paul Sabatier-Toulouse III, ENVT*
6 : Instituto de Tisioneumonologia « Raúl F. Vaccarezza », Universitad de Buenos Aires
7 : Division de SIDA, Hospital de Infecciosas Dr. F.J. Muñiz, Buenos Aires
8 : Tulane National Primate Research Center, Covington, LA 70433; Department of Microbiology and Immunology, School of Medicine, Tulane University, New Orleans
* : Corresponding author

Abstract

Mycobacterium tuberculosis (Mtb) and HIV-1 are known to act synergistically and impact the progression of one another in co-infected patients. Yet, the mechanisms by which Mtb exacerbates HIV-1 pathogenesis remain poorly characterized. Here, we show that Mtb infection enhances HIV-1 production in macrophages. This phenomenon does not rely on increased viral receptor-mediated entry or early replication, nor on the down-regulation of HIV restriction factors in macrophages. Instead, we report for the first time that Mtb infection triggers the formation of tunneling nanotubes (TNTs) which increase cell-to-cell viral spread. Strikingly, blocking IL-10, the IL-10/STAT3 signaling platform or TNT formation itself, fully abolished enhanced HIV-1 production by macrophages in a TB-associated microenvironment. We also found that such virus-overproducing macrophages belong to an M(IL-10) anti-inflammatory macrophage program, and are expanded in the peripheral blood of co-infected patients and in the lungs of co-infected non-human primates. Accumulation of this macrophage population correlates with disease severity. Altogether, our data identify TNTs induced during Mtb infection of macrophages as key players in the aggravation of HIV-1 pathogenesis, and as an unsuspected target to develop novel therapeutics against AIDS/TB co-morbidity.

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KEYNOTE LECTURE V

Development and functions of intestinal macrophages

Allan Mowat

Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, UK.

Abstract

The Intestinal mucosa contains one of the largest populations of macrophages in the body, where they are vital for the maintenance of gut homeostasis and have several unique properties. Unlike many other tissue resident macrophages, we have shown that those in the intestine require constant replenishment by classical Ly6Chi monocytes which begin to accumulate around the time of weaning and which continue to be recruited throughout adult life in a CCR2-dependent manner. Under steady state, the monocytes differentiate locally into anti-inflammatory macrophages producing IL10 and expressing a variety of scavenger receptors and other molecules involved in the uptake of apoptotic cells and in tissue remodelling. As a result, mature intestinal macrophages express a unique genetic signature that distinguishes them from other tissue resident macrophages, including those derived from monocytes such as dermal macrophages. The recruitment of monocytes is highly dependent on the presence of a microbiota, while their tissue specific differentiation requires signalling through the TGFß receptor. During inflammation, the full differentiation of monocytes is arrested, allowing the accumulation of early stage cells with pro-inflammatory properties. Together these results indicate that the constantly changing environment of the healthy intestine requires monitoring by monocytes that are sufficiently plastic to respond to local signals that normally ensure differentiation into anti-inflammatory macrophages with homeostatic properties.

POSTERS

Singapore Statement on Research Integrity

The value and benefits of research are vitally dependent on the integrity of research. While there can be and are national and disciplinary differences in the way research is organized and conducted, there are also principles and professional responsibilities that are fundamental to the integrity of research wherever it is undertaken.

What does DORAsay?

The San Francisco Declaration on Research Assessment (DORA), initiated at the 2012 Annual Meeting of the American Society for Cell Biology by a group of editors and publishers of scholarly journals, recognizes the need to improve the ways in which the outputs of scientific research are evaluated.

Singapore Statement on Research Integrity

Preamble. The value and benefits of research are vitally dependent on the integrity of research. While there can be and are national and disciplinary differences in the way research is organized and conducted, there are also principles and professional responsibilities that are fundamental to the integrity of research wherever it is undertaken.

PRINCIPLES

Honesty in all aspects of research
Accountability in the conduct of research
Professional courtesy and fairness in working with others
Good stewardship of research on behalf of others

RESPONSIBILITIES

1. Integrity: Researchers should take responsibility for the trustworthiness of their research.

2. Adherence to Regulations: Researchers should be aware of and adhere to regulations and policies related to research.

3. Research Methods: Researchers should employ appropriate research methods, base conclusions on critical analysis of the evidence and report findings and interpretations fully and objectively.

4. Research Records: Researchers should keep clear, accurate records of all research in ways that will allow verification and replication of their work by others.

5. Research Findings: Researchers should share data and findings openly and promptly, as soon as they have had an opportunity to establish priority and ownership claims.

6. Authorship: Researchers should take responsibility for their contributions to all publications, funding applications, reports and other representations of their research. Lists of authors should include all those and only those who meet applicable authorship criteria.

7. Publication Acknowledgement: Researchers should acknowledge in publications the names and roles of those who made significant contributions to the research, including writers, funders, sponsors, and others, but do not meet authorship criteria.

8. Peer Review: Researchers should provide fair, prompt and rigorous evaluations and respect confidentiality when reviewing others' work.

9. Conflict of Interest: Researchers should disclose financial and other conflicts of interest that could compromise the trustworthiness of their work in research

10. Public Communication: Researchers should limit professional comments to their recognized expertise when engaged in public discussions about the application and importance of research findings and clearly distinguish professional comments from opinions based on personal views.

11. Reporting Irresponsible Research Practices: Researchers should report to the appropriate authorities any suspected research misconduct, including fabrication, falsification or plagiarism, and other irresponsible research practices that undermine the trustworthiness of research, such as carelessness, improperly listing authors, failing to report conflicting data, or the use of misleading analytical methods.

12. Responding to Irresponsible Research Practices: Research institutions, as well as journals, professional organizations and agencies that have commitments to research, should have procedures for responding to allegations of misconduct and other irresponsible research practices and for protecting those who report such behavior in good faith. When misconduct or other irresponsible research practice is confirmed, appropriate actions should be taken promptly, including correcting the research record.

13. Research Environments: Research institutions should create and sustain environments that encourage integrity through education, clear policies, and reasonable standards for advancement, while fostering work environments that support research integrity.

14. Societal Considerations: Researchers and research institutions should recognize that they have an ethical

The San Francisco Declaration on Research Assessment (DORA), initiated at the 2012 Annual Meeting of the American Society for Cell Biology by a group of editors and publishers of scholarly journals, recognizes the need to improve the ways in which the outputs of scientific research are evaluated.

What does DORA say?

DORA makes one general and 17 specific recommendations.

General recommendation:
Do not use journal-based metrics, such as Journal Impact Factors (JIFs), as surrogate measures of the quality of individual research articles, to assess an individual scientist's contributions, or in hiring, promotion, or funding decisions.

For Organizations That Supply Metrics
- Be transparent
- Provide access to data
- Discourage data manipulation
- Provide different metrics for primary literature and reviews

For Publishers
- Cease to promote journals by Impact Factor; provide an array of metrics
- Focus on article-level metrics
- Identify different author contributions
- Open the bibliographic citation data
- Encourage primary literature citations

For Research Institutions
- When hiring and promoting, state that scientific content of a paper, not the JIF of the journal where it was published, is what matters
- Consider value from all outputs and outcomes generated by research

For Funding Agencies
- State that scientific content of a paper, not the JIF of the journal where it was published, is what matters
- Consider value from all outputs and outcomes generated by research

For Researchers
- Focus on content
- Cite primary literature
- Use a range of metrics to show the impact of your work
- Change the culture!

San Francisco DORA
Declaration on Research Assessment

See the full text of DORA at **www.ascb.org/SFdeclaration.html.** Sign the Declaration!

LABEL

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