

# EDUCATIONAL SYMPOSIUM

14<sup>th</sup> September 2014, Vinci Congress center, Tours, France



# ORGANIZED BY THE FRENCH DENDRITIC CELL SOCIETY













Club Francophone des Cellules Dendritiques

French DC Society



The French DC society was created in 1999 to promote research on dendritic cells (DC), and favor exchanges within the DC community through the organization of meetings and workshops, such as the international plasmacytoid DC symposium organized every two years in Paris.

It also helps young researchers to attend international meetings by offering travel grants.

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The CFCD organizing committee warmly thanks the following companies and regional councils for their support to the "CFCD EDUCATIONAL SYMPOSIUM" of DC2014

















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# Welcome address by CFCD

# Dear participants,

The organizers, the CFCD (Club Francophone des Cellules Dendritiques) and the DC2014 team, wish to welcome you to this educational symposium. This is an original satellite event to the DC2014 meeting, aiming at approaching important DC biology questions in an educational, conceptual, and/or historical manner, three aspects often underrepresented in regular research talks. We decided to limit the number of presentations and participants, in order to leave time for open discussions and promote interactions between speakers and participants in a friendly atmosphere.

We would like to warmly thank all the speakers who accepted to contribute original presentations in the spirit of the symposium.

We would also like to acknowledge the support from our partners, which made this event possible: Miltenyi Biotec, The Région Centre, FeRI Infectiologie, Université of Tours and DC2014 organizing committee.

We wish all participants and speakers a very nice and enriching symposium.

Bertrand Dubois (president) and Vassili Soumelis (vice-president)



# Welcome address by Pr Lesigne, Vice-President of the FRANCOIS-RABELAIS UNIVERSITY of TOURS

On behalf of the President of the University François-Rabelais of Tours, Pr. L. Vaillant, it is my pleasure to welcome you at the DC 2014 congress.

The DC congress will feature an exciting line-up of expert speakers including researchers from all around the world. These areas are of great interest in view of the development of the many diseases that obliterate the lives of our contemporaries and developments of new promising techniques in the domain of immune modulation of DC functions.

It gives me a nice opportunity to talk to you about the research in Biology and Health Sciences at the University of Tours. The François-Rabelais University of Tours has established an ambitious policy for developing its research, based on major centers that group together research units, research organizations and companies. In our university, the Life and Health field is particularly dynamic, and organized in 10 research units. The thematic "Dendritic cell" is particularly present in 3 teams of these teams: 1) Animal immunology research in infectious diseases (INRA-University U1282 "Infectiologie et Santé Publique"), 2) The unit of "Immunologie Parasitaire et Vaccination" of the Chemistry University, 3) The human immunotherapy in organ grafts (Cellules Dendritiques, Immunomodulation et Greffes, (CDG)), covering the interest of DC both in vaccination and immunity modulation. The research laboratory CDG together with several clinical departments is involved in a multi-university research consortium focusing on improving organ transplantation.

It is a great opportunity and an honor for the French scientific community that the DC2014 has chosen France and especially Tours, to organize its congress. We welcome you in Tours and wish you an amazing congress.

Pr. E Lesigne



# **CERTICATE OF ATTENDANCE**

The CFCD organizing committee certifies that:	
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# Attended:

The «CFCD EDUCATIONAL SYMPOSIUM» of DC2014,

Which was held at the Vinci Congress Center in Tours, France, 14<sup>th</sup> September 2014.

The CFCD Secretary Dr Sandrine HENRI secretariat@cfcd.fr



# **PROGRAM** Programme

8h15	Opening of the registration desk Ouverture de l'accueil
8h30	Welcome coffee Café de Bienvenue
9h15	Workshop Introduction by Vassili Soumelis (CFCD Vice-President) Message d'introduction du workshop par Vassili Soumelis (Vice-Président du CFCD)
9h25	Welcome address by Pr. E. Lesigne (VP Research University of Tours) Message de Bienvenue par le Pr. E. Lesigne (Vice-Président Recherche de l'Université de Tours)

# **SESSION I**

Chairpersons Modérateurs: Vassili Soumelis & Fabienne Anjuère

9h30-10h30	Miriam Merad, New York, USA Revisiting the Mononuclear Phagocytic System in Steady State & Inflammation
10h30-11h30	<b>Federica Sallusto</b> , Bellinzona, Switzerland The Long and Winding Road of Monocyte-Derived Dendritic Cells

11h30-12h30 Ken Shortman, Melbourne, Australia
My Convoluted Developmental Pathway to DCs & Vaccines

12h30-13h30 Lunch Déjeuner

# **SESSION II**

Chairpersons Modérateurs: Bertrand Dubois & Elodie Segura

13h30-14h30 Nir Hacohen, Cambrigde, USA

How to Reconstruct Molecular Networks of Dendritic Cells

14h30-15h30 Ana-Maria Lennon-Duménil, Paris, France

Dendritic Cells in motion

15h30 Concluding Remarks Conclusions

# **MIRIAM MERAD**



Miriam Merad, M.D. Ph.D. is a Professor of Oncological science, Medicine (Hem/Onc division) and Immunology and a Member of the Immunology Institute and The Tisch Cancer Institute at the Mount Sinai School of Medicine in New York. Dr. Merad obtained her MD at the University of Algiers, Algeria. She did her residency in Hematology and Oncology in Paris, France and obtained her PhD in immunology in collaboration between Stanford University and University of Paris VII. She was recruited to Mount Sinai School of Medicine in 2004 and was promoted to the rank of Associate Professor with Tenure in 2007 and to Full Professor in 2010.

In 2010 Dr. Merad became the program leader of the Cancer immunology immunotherapy group at The Tisch Cancer Institute and the director of the Human Immunomonitoring center. Dr. Merad also serves as the Associate Director for the MD PhD program at Mount Sinai Medical School.

Dr. Merad's laboratory studies the mechanisms that regulate the development and function of the mononuclear phagocyte lineage including dendritic cells, Langerhans cells and macrophages. Her laboratory has extensively studied the mechanisms that control dendritic cells and macrophage homeostasis and function in barrier tissues such as the skin, lung and gut. Dr. Merad has also made seminal discoveries in Langerhans cells and macrophage biology revealing their embryonic origin and their local maintenance in situ. Dr. Merad's belongs to the Immgen consortia to help decipher the transcriptional regulation of the tissue dendritic cell and macrophage lineage. Currently, one of the major goals of her laboratory is to identify the contribution of phagocytes to disease outcome including cancer and microbial immunity.

# **Selected Publications**

- Agudo J, Ruzo A, Tung N, Salmon H, Leboeuf M, Hashimoto D, Becker C, Garrett-Sinha L-A, Baccarini A, Merad M, Brown BD. 2014. The miR-126-VEGFR2 axis controls the innate response to pathogenassociated nucleic acids. Nat. Immunol. 15:54–62.
- Idoyaga J, Fiorese C, Zbytnuik L, Lubkin A, Miller J, Malissen B, Mucida D, Merad M, Steinman RM. 2013. Specialized role of migratory dendritic cells in peripheral tolerance induction. J. Clin. Invest. 123:844–854.
- Miller JC, Brown BD, Shay T, Gautier EL, Jojic V, Cohain A, Pandey G, Leboeuf M, Elpek KG, Helft J, Hashimoto D, Chow A, Price J, Greter M, Bogunovic M, Bellemare-Pelletier A, Frenette PS, Randolph GJ, Turley SJ, Merad M, Immunological Genome Consortium. 2012. Deciphering the transcriptional network of the dendritic cell lineage. Nat. Immunol. 13:888–899.
- Hashimoto D, Miller J, Merad M. 2011. Dendritic cell and macrophage heterogeneity in vivo. Immunity 35:323–335.
- Helft J, Manicassamy B, Guermonprez P, Hashimoto D, Silvin A, Agudo J, Brown BD, Schmolke M, Miller JC, Leboeuf M, Murphy KM, García-Sastre A, Merad M. 2012. Cross-presenting CD103+ dendritic cells are protected from influenza virus infection. J. Clin. Invest. 122:4037–4047.
- Geissmann F, Manz MG, Jung S, Sieweke MH, Merad M, Ley K. 2010. Development of monocytes, macrophages, and dendritic cells. Science 327:656–661.
- Bogunovic M, Ginhoux F, Helft J, Shang L, Hashimoto D, Greter M, Liu K, Jakubzick C, Ingersoll MA, Leboeuf M, Stanley ER, Nussenzweig M, Lira SA, Randolph GJ, Merad M. 2009. Origin of the lamina propria dendritic cell network. Immunity 31:513–525.
- Ginhoux F, Merad M. 2010. Ontogeny and homeostasis of Langerhans cells. Immunol. Cell Biol. 88:387–392.
- Ginhoux F, Liu K, Helft J, Bogunovic M, Greter M, Hashimoto D, Price J, Yin N, Bromberg J, Lira SA, Stanley ER, Nussenzweig M, Merad M. 2009. The origin and development of nonlymphoid tissue CD103+ DCs. J. Exp. Med. 206:3115–3130.
- Merad M, Manz MG. 2009. Dendritic cell homeostasis. Blood 113:3418–3427.



# Frederica SALLUSTO

Federica Sallusto is an expert in the field of human cellular immunology. Her research is focused on dendritic cell and T cell traffic, mechanisms of T cell differentiation and immunological memory. Her studies revealed a differential expression of chemokine receptors in Th1 and Th2 cells and led to the characterization of "central memory" and "effector memory" T cells as memory subsets with distinct migratory capacity and effector function.

Among her recent contributions is the discovery of Th22 cells, the identification of surface markers of Th17 cells, and the characterization of two distinct types of pathogen-specific Th17 cells that produce IFN-γ or IL-10. In the mouse system her work has focused on leukocyte traffic in lymph nodes and brain. She showed that NK cells, T helper cells, and cytotoxic T cells can migrate to inflamed lymph nodes, where they profoundly modulate T cell responses, that pioneer CCR6-positive Th17 cells enter the CNS through the choroid plexus, which in turn allows other cells to enter and cause autoimmunity, and that persistent antigen and germinal centre B cells sustain Tfh cell responses and phenotype.

For her scientific achievements, she received the Pharmacia Allergy Research Foundation Award in 1999, the Behring Lecture Prize in 2009, and was elected member of the German Academy of Science Leopoldina in 2009 and of EMBO in 2011. She is currently President of the Swiss Society for Allergology and Immunology.

# **Selected Publications**

- Sallusto F. 2013. DCs: a dual bridge to protective immunity. Nat. Immunol. 14:890–891.
- Sallusto F, Impellizzieri D, Basso C, Laroni A, Uccelli A, Lanzavecchia A, Engelhardt B. 2012. T-cell trafficking in the central nervous system. Immunol. Rev. 248:216–227.
- Zielinski CE, Mele F, Aschenbrenner D, Jarrossay D, Ronchi F, Gattorno M, Monticelli S, Lanzavecchia A, Sallusto F. 2012. Pathogen-induced human TH17 cells produce IFN-γ or IL-10 and are regulated by IL-1β. Nature 484:514–518.
- Sallusto F, Lanzavecchia A. 2010. Monocytes join the dendritic cell family. Cell 143:339–340.
- Acosta-Rodriguez EV, Napolitani G, Lanzavecchia A, Sallusto F. 2007. Interleukins 1beta and 6 but not transforming growth factor-beta are essential for the differentiation of interleukin 17-producing human T helper cells. Nat. Immunol. 8:942–949.
- Macagno A, Napolitani G, Lanzavecchia A, Sallusto F. 2007. Duration, combination and timing: the signal integration model of dendritic cell activation. Trends Immunol. 28:227–233.
- Langenkamp A, Casorati G, Garavaglia C, Dellabona P, Lanzavecchia A, Sallusto F. 2002. T cell priming by dendritic cells: thresholds for proliferation, differentiation and death and intraclonal functional diversification. Eur. J. Immunol. 32:2046–2054.
- Lanzavecchia A, Sallusto F. 2001. The instructive role of dendritic cells on T cell responses: lineages, plasticity and kinetics. Curr. Opin. Immunol. 13:291–298.
- Langenkamp A, Messi M, Lanzavecchia A, Sallusto F. 2000. Kinetics of dendritic cell activation: impact on priming of TH1, TH2 and nonpolarized T cells. Nat. Immunol. 1:311–316.
- Sallusto F, Lenig D, Förster R, Lipp M, Lanzavecchia A. 2014. Pillars article: two subsets of memory T lymphocytes with distinct homing potentials and effector functions. Nature. 1999. 401: 708-712. J. Immunol. Baltim. Md 1950 192:840–844.

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# Ken SHORTMAN

Prof Ken Shortman is a Laboratory Head in the Immunology Division of The Walter and Eliza Hall Institute. He was Head of this Division from 1997 to 2005. He was elected Fellow of the Australian Academy of Science in 1999. He is awaiting acceptance of his 340th scientific publication.

Ken Shortman obtained his science degree from Sydney University, originally training as a plant biochemist. He obtained his PhD with Gordon Ada at WEHI when Burnet was Director, then had post-doctoral training with Slonimsky at Gif-sur-Yvette, France, and with Kornberg and Lehman at Stanford University; he was then a molecular biologist, before the term was invented.

Ken Shortman's research at WEHI was initially in the field of biophysics, developing procedures for immune cell isolation. These techniques were then applied to the field of cellular immunology. Immune cell development became his major research theme; his work on mapping the pathway of T cell development in the thymus with Roland Scollay and Li Wu being especially notable. In 1990 his attention shifted to dendritic cells (DC) and he is probably best known now for his studies on DC development and on DC subset separation and function. This basic information on DC biology is now being applied to vaccine development in his research with Irene Caminschi and Mireille Lahoud at the Burnet Institute on modulating immune responses by targeting antigens to DC surface molecules in situ.

# **Selected Publications**

- Sathe, Priyanka, et al., and Ken Shortman. "Lymphoid Tissue and Plasmacytoid Dendritic Cells and Macrophages Do Not Share a Common Macrophage-Dendritic Cell-Restricted Progenitor." Immunity 41, no. 1 (July 17, 2014): 104–15.
- Sathe, Priyanka et al., and Ken Shortman. "Convergent Differentiation: Myeloid and Lymphoid Pathways to Murine Plasmacytoid Dendritic Cells." *Blood* 121, no. 1 (January 3, 2013): 11–19.
- Caminschi, Irina, and Ken Shortman. "Boosting Antibody Responses by Targeting Antigens to Dendritic Cells." *Trends in Immunology* 33, no. 2 (February 2012): 71–77.
- Zhang, Jian-Guo, et al., and Ken Shortman "The Dendritic Cell Receptor Clec9A Binds Damaged Cells via Exposed Actin Filaments." *Immunity* 36, no. 4 (April 20, 2012): 646–57.
  - Dresch, Christiane, et al., and Ken Shortman. "Development of Antigen Cross-Presentation Capacity in Dendritic Cells." Trends in Immunology 33, no. 8 (August 2012): 381–88.
  - Lahoud, Mireille H., et al. and Ken Shortman "DEC-205 Is a Cell Surface Receptor for CpG Oligonucleotides." *PNAS* 109, no. 40 (October 2, 2012): 16270–75.
  - Shortman, Ken, and William R. Heath. "The CD8+ Dendritic Cell Subset." *Immunological Reviews* 234, no. 1 (March 2010): 18–31.
  - Shortman, Ken, and Priyanka Sathe. "Another Heritage for Plasmacytoid Dendritic Cells." *Immunity* 38, no. 5 (May 23, 2013): 845–46.
  - Villadangos, Jose A., and Ken Shortman. "Found in Translation: The Human Equivalent of Mouse CD8+ Dendritic Cells." *The Journal of Experimental Medicine* 207, no. 6 (June 7, 2010): 1131–34.
  - Bedoui, Sammy, et al., and Ken Shortman "Cross-Presentation of Viral and Self Antigens by Skin-Derived CD103+ Dendritic Cells." Nature Immunology 10, no. 5 (May 2009): 488–95.
  - Naik, Shalin H., et al., and Ken Shortman "Development of Plasmacytoid and Conventional Dendritic Cell Subtypes from Single Precursor Cells Derived in Vitro and in Vivo." Nature Immunology 8, no. 11 (November 2007): 1217–26.



# Nir HACOHEN

Dr. Hacohen is an immunologist, geneticist and systems biologist focused on dissecting the basic mechanisms of immunity, developing and applying genetic technologies that accelerate the study of the immune system, and deciphering and treating human diseases -- including cancer and immune disorders -- based on genomic approaches. Dr. Hacohen is a founding member of the Broad Institute<sup>TM</sup>s RNAi Consortium -- a public-private partnership that has built genome-wide RNA interference libraries to silence every gene in mice and humans -- and a founding director of the Broad Immune Circuits Initiative. These efforts have put RNAi technologies in the hands of the community to address numerous biological and immunological questions.

Projects in the laboratory focus on innate immunity and dendritic cells, as well as technology development, and include: (I) developing methods for network reconstruction of pathogensensing pathways in mice and humans, with a focus on viral and bacterial sensing pathways; (II) dissecting how DNA is sensed by the immune system, including the role of nucleases in clearance of self DNA; (III) analyzing mechanisms underlying autoimmunity in lupus patients; (IV) uncovering interactions between tumors and the immune system; (V) testing a new generation of personalized tumor vaccines (together with Dr. Catherine Wu, DFCI).

# **Selected Publications**

- Ponichtera HE, Shainheit MG, Liu BC, Raychowdhury R, Larkin BM, Russo JM, Salantes DB, Lai C-Q, Parnell LD, Yun TJ, Cheong C, Bunnell SC, Hacohen N, Stadecker MJ. 2014. CD209a expression on dendritic cells is critical for the development of pathogenic Th17 cell responses in murine schistosomiasis. J. Immunol. Baltim. Md 1950 192:4655–4665.
- Arazi A, Pendergraft WF, Ribeiro RM, Perelson AS, Hacohen N. 2013. Human systems immunology: hypothesis-based modeling and unbiased data-driven approaches. Semin. Immunol. 25:193–200.
- Shapira SD, Hacohen N. 2011. Systems biology approaches to dissect mammalian innate immunity. Curr. Opin. Immunol. 23:71–77.
- Garg S, Sharma M, Ung C, Tuli A, Barral DC, Hava DL, Veerapen N, Besra GS, Hacohen N, Brenner MB. 2011. Lysosomal trafficking, antigen presentation, and microbial killing are controlled by the Arf-like GTPase Arl8b. Immunity 35:182–193.
- Amit I, Regev A, Hacohen N. 2011. Strategies to discover regulatory circuits of the mammalian immune system. Nat. Rev. Immunol. 11:873–880.
- Colvin RA, Means TK, Diefenbach TJ, Moita LF, Friday RP, Sever S, Campanella GSV, Abrazinski T, Manice LA, Moita C, Andrews NW, Wu D, Hacohen N, Luster AD. 2010. Synaptotagmin-mediated vesicle fusion regulates cell migration. Nat. Immunol. 11:495–502.
- Huang Q, Liu D, Majewski P, Schulte LC, Korn JM, Young RA, Lander ES, Hacohen N. 2001. The plasticity of dendritic cell responses to pathogens and their components. Science 294:870–875.
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# Ana-Maria LENNON-DUMENIL

Ana-Maria Lennon-Duménil is an expert in the field of cell migration and antigen presentation. She uses an original interdisciplinary approach at the interface of Immunology, Cell Biology and Biophysics to unravel the fundamental mechanisms used by dendritic cells and B lymphocytes to achieve their immune function. Her studies revealed the key role of cell polarity and lysosome secretion in the uptake and presentation of surface-tethered antigens by B lymphocytes. They further provided the first evidence for the existence of a molecular mechanism that couples cell function with cell migration, allowing their coordination in time and space. Using this mechanism, dendritic cells adopt an intermittent search migration pattern that optimizes their tissue patrolling function. For her scientific achievements, she received the Awards "Olga Sain" and "Gaston Rousseau" from the French Academy of Science. She is actually a group leader in the Curie Institute in Paris.

# **Selected Publications**

- Bretou M, Jouannot O, Fanget I, Pierobon P, Larochette N, Gestraud P, Guillon M, Emiliani V, Gasman S, Desnos C, Lennon-Duménil AM, Darchen F. Cdc42 controls the dilation of the exocytotic fusion pore by regulating membrane tension. Mol Biol Cell. 2014 Aug 20. pii: mbc.E14-07-1229
- Lamsoul I, Métais A, Gouot E, Heuzé ML, Lennon-Duménil AM, Moog-Lutz C, Lutz PG. ASB2α regulates migration of immature dendritic cells. Blood. 2013 Jul 25;122(4):533-41.
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- Yuseff MI, Reversat A, Lankar D, Diaz J, Fanget I, Pierobon P, Randrian V, Larochette N, Vascotto F, Desdouets C, Jauffred B, Bellaiche Y, Gasman S, Darchen F, Desnos C and Lennon-Duménil AM. Polarized Secretion of Lysosomes at the B Cell Synapse Couples Antigen Extraction to Processing and Presentation. Immunity (2011) 35(3):361-74.
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- Faure-André G, Vargas P, Yuseff MI, Heuzé M, Diaz J, Lankar D, Steri V, Manry J, Hugues S, Vascotto F, Boulanger J, Raposo G, Bono MR, Rosemblatt M, Piel M and Lennon-Duménil AM. Regulation of Dendritic Cell Migration by CD74, the MHC class II associated Invariant Chain. Science (2008) 322(5908):1705.
- Le Roux D, Lankar D, Yuseff MI, Vascotto F, Yokozeki T, Faure-André G, Mougneau E, Manoury B, Bonnerot C and Lennon-Duménil AM. Sykdependent Actin Dynamics controls regulates endocytic trafficking and processing of Antigens internalized through the B cell Receptor. Molecular Biology of the Cell (2007) 9(18):3651.





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- Recombinant cytokines



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# DC Differentiation and Maturation

- DendriMACS™GMP Medium\*
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# Analysis Tools

- MACSQuant<sup>®</sup> Flow Cytometers (RUO)
- MACS Antibodies (RUO)



# Downstream Analysis

- Cryopreservation
- CryoMACS® Freezing Bags
   CryoMACS DMSO 10 (RUO, EP, USP)



RUO=Research Use Only EP=European Pharmacopoeia USP=United States Pharmacopoeia \*MACS GMP Products are for research use only and for exvivo cell culture processing only.

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