



Sophie UGOLINI, PhD

Innate lymphoid cells and Neural Regulation of Immunity

- Research Director (DR), Institut National de la Santé et de la Recherche Médicale (INSERM)
- Group leader: Neural regulation of Immunity

Background and scientific interests

I am interested in the molecular and cellular mechanisms that control inflammation and regulate the balance between immunity and tolerance. I began by studying different aspects of the adaptive immune response to pathogens. My research interests then shifted to the analysis of innate immunity to pathogens and tumors, from single molecules to the systemic level. These studies led me to focus on neuroimmune interactions and to dissect the regulatory role of the nervous system in immunity.

Education

1998: PhD in Immunology, Aix-Marseille University, Marseille, France

Research

- 2015-present: Principal investigator of the ERC consolidator project "Neural Regulation of Immunity", Centre d'immunologie de Marseille-Luminy (CIML), Marseille, France
- 2015: Visiting Scientist at the Walter and Elisa Hall Institute (WEHI) and the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia.
- 2013: Visiting Scientist, laboratory of Jean-Laurent Casanova, The Rockefeller University, New York, USA.
- 2012: Appointed Research Director (DR2, INSERM)
- 2010-2015: Co-management, with Eric Vivier, of the NK Cells and Innate Immunity laboratory, CIML.
- 2006: Visiting scientist, laboratory of Bruce Beutler, The Scripps Research Institute, La Jolla, California, USA.
- 2006: Appointed senior scientist (CR1, INSERM)
- 2001-2006: Junior scientist (CR2, INSERM), NK Cells and Innate Immunity laboratory, CIML, France.
- 2000-2001: Postdoctoral position, laboratory of Nicolas Glaichenhaus, Institut de pharmacologie moléculaire et cellulaire, Sophia Antipolis, Nice, France.
- 1998-2000: Postdoctoral position, Laboratory of Eric Vivier, CIML, France.
- 1995-1998: PhD student, laboratory of Quentin Sattentau, CIML, France.



Teaching

- 2013: Co-organizer of a Master program (M2), Aix-Marseille University
- 2007-2011: Co-organizer of a Master program (M1) at Marseille Medical School
- 2005-2013: Immunology teaching for Masters programs (M2), Aix-Marseille University
- 2002: Immunology teaching, Universités du Monde, Ougadougou, Burkina Faso.
- 1995-1998: Cell biology tutor, Aix-Marseille University.

Awards

- ERC (European Research Council) Consolidator grant (2015)
- Prix Duquesne (Duquesne Award) from la Ligue Nationale contre le Cancer, shared with Eric Vivier (2013)
- Prix Recherche de l'INSERM (Research award from INSERM) (2012)
- Prime d'excellence scientifique (Scientific excellence award, INSERM) (2012-present)
- Dandrimont-Bénicourt Award from the Institut de France (2011)
- Thesis award from Aix-Marseille University (1998)

Membership and responsibilities

- Member of the scientific advisory board of the "Office parlementaire d'évaluation des choix scientifiques et technologiques" (OPECST, 2016-2019)
- Member of the scientific advisory board of INSERM (2012-2017)
- Member of the scientific committee (# 1) of the Association pour la Recherche sur le Cancer (ARC), France (2009-2014)
- Expert for the ANR (Agence Nationale de la Recherche), Member of a scientific committee (2018)
- Expert for the FRS-FNRS (Fonds de la Recherche Scientifique), Belgium and for the Austrian Science Fund (FWF)
- Organization of internal seminars at CIML (2002-2015)
- Jury member for the Masters 2 course in Development and Immunology, Aix-Marseille University (2009-2010)
- Referee for Nature, Science Translational Medicine, Blood, PNAS, J. Immunol., FASEB J., Eur.J. Immunol, Int. Immunol., Scientific Report...
- Associate Editor, Frontiers in NK Cell Biology
- Editor, Immunology Letters

Selected grants (as a principal investigator)

- European Research Council (ERC) Consolidator grant (2015-2020)
- Fondation ARC (Programme ARC: 2014-2017)
- Agence Nationale de la Recherche (ANR programme blanc: 2014-2019)
- Projet exploratoire région PACA (2014-2016)
- Ligue Nationale contre le Cancer, SensorImmune (2014-2016)
- Agence Nationale de la Recherche (ANR Jeune Chercheur: 2007-2011)
- Agence Nationale de la Recherche (ANR-ERC starting grant: 2008-2012)

Main achievements

Over the last 15 years, we have used natural killer (NK) cells as a model system for exploring the regulation of the balance between immunity and tolerance. We have shown that NK cells and macrophages cooperate in innate responses to pathogens (PNAS, 2005). Our studies have demonstrated that NK cells adapt their reactivity to their environment within the host through the engagement of inhibitory and activating receptors, to promote both responsiveness and tolerance (Immunity, 2006; Science Signaling, 2011; Science, 2012; Nature Commun. 2014).

We have also performed genetic and functional studies based on N-ethyl N-nitrosourea (ENU) mutagenesis to decipher innate immune responses in infection and tumor models and showed that:

- Neutrophils are involved in NK cell maturation, function, and homeostasis (J. Exp. Med. 2012)
- The tuning of NK cell reactivity helps to shape T-cell immune responses (Science, 2012)
- The Bcl2 gene is involved in NK cell survival and homeostasis (J. Exp. Med. 2017a).

Through a collaboration with the biotech company "Innate Pharma", we have validated the use of inhibitory receptors (KIR) blockade as a promising therapeutic strategy in a mouse preclinical model (PNAS, 2009; Blood, 2014). Our lab is also involved in a clinical trial based on the use of natural killer cells as anticancer agents.

More recently, I was awarded an ERC consolidator grant to address challenging questions in the field of neuroimmunology. My laboratory aims to identify new regulatory mechanisms affecting the immune response, by investigating the role of the nervous system in immunity. The team has already identified a neuroendocrine-immune pathway playing a crucial role in host protection against immunopathology in a model of septic shock (J. Exp. Med. 2017b). In particular, we found that host resistance to endotoxic shock requires the regulation of group 1 innate lymphoid cell function by the glucocorticoid receptor. In parallel, the lab is also dissecting the role of sensory neurons in the activation and recruitment of immune cells in the skin after tissue damage, inflammation or infection, and in the generation of adaptive immune responses.

Selected publications

Original publications

- Ugolini S, I. Mondor, P. Parren, D. Burton, S Tiley, P.J. Klasse, and Q.J. Sattentau. Inhibition of virus-cell binding is a major mechanism of HIV-1 neutralization. **J. Exp. Med.** 1997, 186: 1287-98
- Ugolini S, C. Arpin, N. Anfossi, T. Walzer, A. Cambiaggi, R. Forster, M. Lipp, R.E.M. Toes, C. Melief, J. Marvel, E. Vivier. Involvement of inhibitory NKRs in the survival of a subset of memory-phenotype CD8⁺ T cells. **Nature Immunol.** 2001, 2: 430-435
- Filippi C, Hugues S, Cazareth J, Julia V, Glaichenhaus N, Ugolini S. CD4⁺ T cell polarization in mice is modulated by strain-specific major histocompatibility complex-independent differences within dendritic cells. **J. Exp. Med.** 2003, 198: 201-9
- Baratin M, Roetyneck S, Lepolard C, Falk C, Sawadogo S, Uematsu S, Akira S, Ryffel B, Tiraby JG, Alexopoulou L, Kirschning CJ, Gysin J, Vivier E, Ugolini S. Natural killer cell and macrophage cooperation in MyD88-dependent innate responses to Plasmodium falciparum. **Proc Natl Acad Sci USA.** 2005, 102:14747-52
- Anfossi N, André P, Guia S, Falk C, Stewart C A, Bresó V, Roetyneck S, Frassati C, Reviron D, Middleton D, Romagné F, Ugolini S*, Vivier E*. Human NK cell education by inhibitory receptors for MHC class I. **Immunity.** 2006; 25: 331-342
- Zhang SY, Jouanguy E, Ugolini S, Smahi A, Elain G, Sancho-Shimizu V, Lorenzo L, Puel A, Picard C, Chapgier A, Plancoulaine S, Cognet C, Casrouge A, Zhang XX, Barreiro L, Titeux M, Hamilton C, Lebon P, Héron B, Vallée L, Quintana-Murci L, Hovnanian A, Rozenberg F, Vivier E, Geissmann F, Tardieu M, Abel L and Casanova JL. Herpes simplex encephalitis in human TLR3 deficiency. **Science**, 2007, 317, 1522
- Sola C., André P., Lemmers C., Fuseri N., Bonnafous C., Bléry M., Wagtmann N.R., Romagné F., Vivier E., Ugolini S. Genetic and antibody-mediated reprogramming of natural killer cell missing-self recognition *in vivo*. **Proc. Natl. Acad. Sci. USA.** 2009. 106: 12879-12884
- Guia S., Jaeger B.N., Piatek S., Mailfert S., Trombik T., Fenis A., Chevrier N., Walzer T., Kerdiles Y.M., Marguet D., Vivier E., Ugolini S. Activating receptor confinement at the plasma membrane controls natural killer cell tolerance. **Science Signaling**, 2011, 4(167):ra21
- Narni-Mancinelli E, Jaeger BN, Bernat C, Fenis A, Kung S, De Gassart A, Mahmood S, Gut M, Heath SC, Estellé J, Bertosio E, Vely F, Gastinel LN, Beutler B, Malissen B, Malissen M, Gut IG, Vivier E and Ugolini S. Tuning of natural killer cell reactivity by NKp46 and Helios calibrates T cell responses. **Science**, 2012, 335:344-8
- Jaeger, B, Donadieu, J, Cognet, C, Bernat, D Ordoñez-Rueda, V Barlogis, N Malhaoui, A Fenis, B Beaupain, C Bellanné-Chantelot, M Bajénoff, B Malissen, M Malissen, Vivier E and Ugolini S. Neutrophil depletion impairs natural killer cell maturation, function and homeostasis. **J. Exp. Med.**, 2012, 209:565-80

- Viant C, Fenis A, Chicanne G, Payrastra B, Ugolini S*, Vivier E*. SHP-1-mediated inhibitory signals promote responsiveness and anti-tumour functions of natural killer cells. **Nat Commun.** 2014, 30; 5:5108
- Viant C, Guia S, Bernat C, Delconte R, Roger M, Simon V, Goh W, Jiao Y, Grabow S, Kile B, Strasser A, Gray D, Belz GT, Beutler B, Vivier E, Ugolini S*, Huntington ND*. Cell cycle progression dictates requirement for BCL2 in Natural Killer cell survival. **J. Exp. Med.** 2017 Feb;214(2):491-510
- Quatrini L, Wieduwild E, Guia S, Bernat C, Glaichenhaus N, Vivier E and Ugolini S. Host resistance to endotoxic shock requires the neuro-endocrine regulation of group 1 innate lymphoid cells. **J. Exp. Med.** 2017 Dec 4;214(12):3531-3541

*: equal contribution and co-corresponding authors

Selected Reviews/News and views

- Ugolini S, Mondor I, Sattentau QJ. HIV-1 attachment: another look. **Trends Microbiol.** 1999; 7:144-9
- Ugolini S, Vivier E. Regulation of T cell function by NK cell receptors for classical MHC class I molecules. **Curr Opin Immunol.** 2000, 12: 295-300
- Ugolini S, Vivier E. Multifaceted roles of MHC class I and MHC class I-like molecules in T cell activation. **Nature Immunology.** 2001; 2:198-200
- Anfossi N, Pascal V, Vivier E, Ugolini S. Biology of T memory type 1 cells. **Immunol Rev.** 2001, 181: 269-78.
- Roetyneck S, Baratin M, Johansson S, Lemmers C, Vivier E, Ugolini S. Natural killer cells and malaria. **Immunol. Rev.** 2006; 214: 251-263
- Vivier E, Tomasello E, Walzer T, Ugolini S. The functions of natural killer cells. **Nature Immunology.** 2008; 9: 503-10
- Ugolini S, Vivier E. Natural killer cells remember. **Nature** 2009. 457: 544-545
- Vivier E. and Ugolini S. Regulatory natural killer cells: new players in the IL-10 anti-inflammatory response. **Cell Host and Microbe**, 2009, 6: 493-5
- Vivier E., Raulet D.H., Moretta A., Caligiuri M.A., Zitvogel L., Lanier L.L., Yokoyama W.M., Ugolini S. Innate or adaptive immunity? The example of natural killer cells. **Science.** 2011, 331:44-9
- Quatrini L, Ugolini S. Disarming the Killers: Brain Strikes on NK Cells. **Immunity.** 2017 46(3):340-342.