

## CURRICULUM VITAE

**NAME :** CAVAILLON Jean-Marc  
**Born :** May 28<sup>th</sup>, 1952; Paris, France - Married, 3 children  
**Address :** Unit "Cytokines & inflammation"  
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### EDUCATION :

Maîtrise-ès-Sciences	June 1974 (University Orsay-Paris XI)
Diplôme d'Immunologie Approfondie (Master)	June 1975 (Institut Pasteur)
Doctorat de 3e cycle (PhD)	Jan. 1977 (University Paris VII)
Doctorat ès-Sciences Naturelles (Dr.Sc.)	Dec. 1980 (University Paris VI)

### POSITION AT INSTITUT PASTEUR AND ABROAD

Nov. 1976 / Aug. 1977	Fellow of Roux Foundation (Inst. Pasteur)
Sept. 1977 / July 1979	Fellow of the Medical Research Council of Canada (Immunology Dept., University of Toronto)
Aug. 1979 / Dec. 1980	Fellow of Roux Foundation (Inst. Pasteur)
Jan. 1981 / Dec. 1983	Assistant
June / August 1993	Sabatical term at the New England Medical Center, Boston
Jan. 1984 / Dec. 1990	Chargé de Recherche (Assistant-Professor)
Since Jan. 1991	Chef de Laboratoire (Associate-Professor)
July 2001 / Jan 2006	Head of Provisional Unit
Since Feb. 2006	Head of Unit

### RESPONSABILITIES WITHIN THE INSTITUT PASTEUR

Member of the "Commission Consultative de Valorisation"	1995 - 1998
Member of the "Scientific Council of Hybridolab"	1996 - 1997
Member of the "Scientific Evaluation Committee"	Elected en 1994, 2001 & 2003
Co-secretary	1994/96 & 2001/02
Chairman sub-committee #3	2001/02
Vice-president	2003
Member "Jurys de Qualification"	Elected in 1984, 1990, 1996
Member of the "Immunology Department Council"	Elected in 1982
Member of the "Physiopathology Department Council"	Elected in 1994 & 1997
Member of the "l'Assemblée de l'Institut Pasteur"	1993 - 2005
Scientific Director "Euroconferences"	2002 - 2006
Member of the "Scientific Evaluation Committee" for 5 Pasteur Institutes of the Network ( <i>Sénégal, République Centrafricaine,     Cameroun, Madagascar, Cambodge</i> )	since 2005
President	since 2006
Director of the Department "Infection and Epidemiology"	since April 2006

## JOURNALS

Member of the Editorial Board	"Journal of Endotoxin Research"	since 1994
Member of the Editorial Board	"Shock"	since 1999
Member of the Editorial Board	"Sepsis"	1999 - 2002
Member of the Editorial Board	"European Cytokine Network "	since 2002
Member of the Editorial Board	"Journal of Infectious Diseases"	since 2004
Member of the Editorial Board	"American Journal of Surgery"	since 2006
Associate-Editor	"Cytokine"	since 2002

## REFEREE

Referee for the "Association Française de Lutte contre la Mucoviscidose"	since 1996
Referee "Délégation à la Recherche Clinique Assistance Publique Hôpitaux de Paris"	1998 - 2000
Member of the Scientific Council of Cantacuzene Institute (Bucharest, Romania)	since 1999
Referee for the scientific evaluation department of INSERM	2001 - 2002
Expert for the Deutsche Forschungsgemeinschaft (Germany)	2003 - 2006
Expert for the National Science Foundation (Belgium)	2005
Expert for the Canadian Cystic Fibrosis Foundation (Canada)	since 2005

## Ad'hoc REVIEWER (2001-2007)

Fondazione Cenci Bolognetti (Roma) ; Health Research Board of Ireland ; Programme Emergence de la Région Rhône-Alpes BUPA Foundation (London) ; Conseil Régional de Bourgogne ; Laboratoire Français du Fractionnement ; Hospice civils de Lyon ; Wellcome Trust (London) ; Swiss National Science Foundation; Programme Hospitalier de la Recherche Clinique – National Medical Research Council of Singapore.

### For journals

*American Journal of Physiology ; American Journal of Respiratory and Critical Care Medicine; Blood ; Cellular Microbiology ; Clinical and Experimental Immunology ; Critical Care Medicine ; European Journal of Biochemistry ; European Journal of Immunology; Immunology ; Infection and Immunity ; Intensive Care Medicine ; Journal of Clinical Investigation ; Journal of Immunology ; Journal of Antimicrobial Chemotherapy ; Journal of Leukocyte Biology ; Microbes & Infections ; Journal of Thoracic and Cardiovascular Surgery ; Microbes and Infection ; Pediatric Research ; Scandinavian Journal of Infectious Diseases.*

## SOCIETIES

Member of the board of the European Cytokine Network	1997 - 1998	
Member of the board of the "European Research Network on Surgical Infection"	1996 - 1999	
Member of	Société Française d'Immunologie	since 1980
	European Shock Society	1991 - 2000
	Association des Enseignants d'Immunologie	1993 - 2002
	International Cytokine Society	since 1995
	International Shock Society	since 1999
Honorary Member	Association des Anciens Élèves de	
l'Institut Pasteur	since 2007	
	<b>International Endotoxin Society</b>	since 1988
	(Now : "International Endotoxin and Innate Immunity Society")	
	President-elect	1996 - 1998
	President	1998 - 2000
	Chairman Nominating Committee	2000 – 2004
	Member of the Committee for the Bang Award	since 2000

## MEETING ORGANISATION (Member of scientific committees)

- 1<sup>st</sup> and 2<sup>nd</sup> International Autumnal Meeting on Sepsis (Deauville, 1994, 1995)
- 9<sup>th</sup> Annual Meeting of the Surgical Society Europe (Paris, May 1996)
- EuroConference Institut Pasteur "Cytokines : Tools and targets for tomorrow's therapies" (Paris, oct. 1997)
- 9<sup>th</sup> International Conference on "Clinical Concept in Infectious Diseases" (Davos, Feb. 2000)
- 5<sup>th</sup> European Winter Conference in Immunity "Innate Immunity" (St Sorlin, France, Jan. 2001)
- Euroconference on "Interactions between innate and adaptive immunity in mammalian defense against bacterial infections" (Mecklenburg, Germany, 5 - 8 juin 2002)
- 7<sup>th</sup> Conference of the International Endotoxin Society (Bethesda, USA, 18 - 21 juil. 2002)

## TEACHING ACTIVITIES

### "General Immunology" course of Institut Pasteur

*The "General Immunology" course of Institut Pasteur was the first course of Immunology to be hold in Europe when created by Prof. M. Faure in 1950.*

Head of practical works	1987 - 1994
Deputy-Director	1994 - 1997
Director	1997 - 2002

### Institut Pasteur (given courses)

Cours d'Immunologie Générale	1993 - 2002
Cours de Bactériologie	1993 & 1996
Cours de Virologie Médicale	1993 - 1997
Stages REGAIN de l'Association des Anciens Elèves de l'Institut Pasteur	1993, 1997 & 2006
Formation Permanente : "Bases Fondamentales de l'Immunologie"	1993 & 1997
Cours de Microbiologie Tropicale	1994
Hôpital de l'Institut Pasteur	1995 - 2000
Cours de Virologie Systématique	2002, 2004 & 2006
Cours de Virologie Fondamentale	since 2004
École Pasteurienne de Santé Publique	since 2004

Committee member : DEA "Cellule Normale et Pathologique" (University Paris V) 1997 - 2002

Committee member : DEA "Immunologie Approfondie" (University Paris VI & VII) 1998 - 2002

### Courses given in DEA / master (since 1993)

DEA Structure et Fonctionnement des Systèmes Biologies Intégrés (Paris XI, Orsay)	1993 - 1994
DEA de Physiologie et Physiopathologie des Appareils Respiratoires et Circulatoires	1993 - 1996
DEA de Biologie Cutanée (Institut Fournier)	1994 & 1996
DEA "Équilibre de la fonction circulatoire et ses modifications en anesthésie-réanimation	1995
DEA de Pharmacologie et Pharmacochimie (Illkirch / Strasbourg)	1996
DEA "Méthodes Expérimentales et Cliniques d'Évaluation des Agents Anti-Infectieux"	1996 & 1997
DEA Microbiologie, Enzymologie & Nutrition (Nancy)	2001
DEA "Biomolécules et dynamique cellulaire" (Reims)	2000 - 2001
DEA Relations Hôtes-Parasites (Institut Pasteur, Paris)	1993 - 1998
DEA d'Immunologie et Immunopathologie (Toulouse)	1995 - 2001
DEA des Maladies Infectieuses (Lille)	1999 - 2001
DEA Biologie de la Cellule Normale et Pathologique (UFR Biomédicale des St-Pères)	1994 - 2002
DEA de Physiologie Cellulaire et Moléculaire (Faculté de Médecine Saint-Antoine)	1996 - 2003
DEA de Microbiologie (Chatenay-Malabry)	2002 - 2004
Master "Biologie Intégrative et Physiologie" - "Physiopathologie pulmonaire" (Paris 6)	since 2004
Master "Parasitologie/mycologie Fondamentale et Médicale" (Paris 6)	since 2004
Master "Biologie et Thérapies Innovantes des Grandes Fonctions" (Paris 11 & 12)	since 2004
Master "Communication cellulaires intra et interspécifique" (Ecole Normale Supérieure)	since 2005

Master de Sciences et Technologies, UE : Médiateurs de l'Inflammation (Paris 6)	since 2005
Master "Biologie et pharmacologie cutanée" (Paris 7)	2005
Master 1, Faculté des Sciences d'Orsay (Paris XI)	2006

### Other courses

Capacité d'Allergologie (Hôpital Sainte-Marguerite, Marseille)	1995
Capacité d'Allergologie, DU d'Immuno-allergologie appliqué, (Besançon)	1996
École Normale Supérieure de Cachan (Formation Continue)	1996 & 1997
Cours de Microbiologie des Écosystèmes (Institut Pasteur de Lille)	1997 - 2000
Diplôme Universitaire de Biologie Clinique Oncologique (Centre René Huguenin)	1998 - 2000
Maîtrise, Université de Paris XI (Orsay)	1998, 2004 - 2006
Diplôme Inter-Universitaire de Pneumologie Pédiatrique (Hôp. Trousseau, Paris)	2001 - 2002
PCEM2, Faculté de Médecine (CHU Broussais - Hôtel-Dieu)	1997 - 2004
DU "Thérapeutiques Immunologiques" (Hôp. Broussais)	1999 - 2002
Cours Annuel de la Société Française d'Immunologie (Annecy)	1998 & 2003
Enseignement Post-Universitaire, Service de Rhumatologie du CHU Bichat	2003
DESC Maladies Infectieuses et Transmissibles	2004 & 2006

### International Teaching

Universidad de Chile (INTA, Santiago)	Nov., 1992
"Post-Graduate courses" Federal University of Rio de Janeiro (Brasil)	August, 1995
Institut Territorial de Recherches Médicales Louis Malardé (Tahiti)	Feb., 1996
Mexican Society of Allergology (Mexico City)	April, 1998
Guadalajara University (Mexico)	April, 1998
1 <sup>st</sup> Prince of Songkla University, Faculty of Medicine, Hat Yai, Thailand	Sept., 2002
Université Saint-Joseph, Faculté de Médecine, Certificat des Sciences Biologiques et Médicales (Beyrouth, Lebanon)	April, 2003
Université Saint-Joseph, Faculté de Médecine, Certificat d'Immunologie (Beyrouth, Lebanon)	Oct. 2003, & Oct. 2004
Cantacuzène Institute, Bucarest, Romania "Immunophysiology of infections"	May 2006
Institute of Hygiene, School of Medicine, University of Uruguay, Montevideo, Uruguay - "Innate immunity against pathogens"	May 2006
Khon Kaen University, (Khon Kaen International Teaching Platform), Thailand "Effect of Natural Product on CancerCell and Cytokine production"	July 2006

### Board of thesis and habilitation committees (1993 - 2007)

60 boards of which 41 times main reviewer

## INTERNATIONAL INVITED LECTURES (since 1999)

- 1999** Surgery Department (Dr. W. Haupt), University of Erlangen-Nuremberg, Germany  
*Immunomodulation of the inflammatory response by IL-10*
- Round Table Conference "The Immune Response in Critically Ill" Bruxelles  
*The proinflammatory cascade*
- 19th International Symposium on Intensive Care and Emergency Medicine, Bruxelles  
- *Pro- and anti-inflammatory cytokines*  
- *Ex vivo cytokine production to monitor immunodepression*
- Symposium " Expression and action of anti-inflammatory cytokines in the brain", Arcachon,  
*Anti-inflammatory cytokines : myth or reality ?*
- 4th International Shock Congress, Philadelphia, USA  
*Overview of the concept of endotoxin tolerance*
- 4th World Congress on Inflammation, Paris  
*The paradoxical cytokine production in human sepsis*
- The Margaux Conference on Critical Illness (Margaux)  
*Modulation of tissue factor expression by cytokines and cell-cell interactions*
- Symposium "Immunologie", Institut Cantacuzène, Bucarest  
*Modulation par les cytokines anti-inflammatoires de la production de cytokines induites par les endotoxines : du dogme au paradoxe.*  
*Les cytokines : marqueurs pour suivre le processus inflammatoire et l'immunodépression associés au sepsis*
- 2000** 9th International Conference "Concepts in infectious diseases", Davos, Switzerland  
*Septic Shock : New developments*
- 5th World Congress on Trauma, Shock, Inflammation and Sepsis, Munich  
*Some paradoxical properties of IL-10*
- 20th International Symposium on Intensive Care and Emergency Medicine, Bruxelles  
**Opening session** : *Pro- versus anti-inflammatory cytokines*; Tutorials: *Sepsis mediators*
- Joint Seminar of Pasteur Institutes of Iran and Paris (Teheran)  
*Immune depression associated to sepsis and critical illness.*
- Joint meeting of Surgical Infection Society (Europe) and European Shock Society, Nijmegen (Nederland)  
*Intracellular cytokines*
- Conference of the Siberian Division of the Russian Academy of Medical Sciences on "Chronic Inflammation" (Novosibirsk, Sibérie)  
*Dichotomy pro- versus anti-inflammatory cytokines : myth or reality ?*
- 2001** 5<sup>th</sup> European Winter Conference on Immunity (St Sorlin)  
*Immune depression associated with exacerbated innate immunity*
- 21<sup>st</sup> International Symposium on Intensive Care and Emergency Medicine (Bruxelles)  
*Immunoactivation versus immunosuppression : the compartmentalization story*
- Workshop "Anti-Inflammatory cytokines - Biological and Medical Aspects (Cracovie)  
*Adherence influences monocytes responsiveness to interleukin-10*
- Burn and Shock Trauma Institute, Loyola University (Prof. M. Sayeed) - Chicago  
*Paradoxical cytokine production in systemic inflammatory response syndrome*
- Intensive Care Society - State of the Art Meeting - London  
*Immunoparalysis - the pathophysiology*

- 2002** 22<sup>nd</sup> International Symposium on Intensive Care and Emergency Medicine, Bruxelles  
*Cytokine response in sepsis*
- Euroconference "Interactions between innate and adaptative immunity in mammalian defense against bacterial infections" Göhre-Lebbin, Germany  
*Soluble mediators as coordinators of an anti-bacterial response : introduction*
- 7<sup>th</sup> Conference of the International Endotoxin Society, Washington, DC  
*Similarities and differences between endotoxin tolerance and immune dysfunction observed in sepsis and in patients with systemic inflammation.*
- 1ère Journée Scientifique de la Société Tunisienne d'Immunologie (Tunis, 2 nov. 2002)  
*Cytokines : actualités*
- 2003** 23<sup>rd</sup> International Symposium on Intensive Care and Emergency Medicine (Bruxelles)  
 - *Endotoxin tolerance : any clinical relevance ?* -  
*Altered immune response*  
 - *Pathogens associated molecular patterns and their host receptors* - *Sepsis Mediators*
- NOBEL SYMPOSIUM "Septicemia and shock: pathogenesis and novel therapeutic strategies (Stockholm)  
*Cytokine cascade*
- Istituto Nazionale Neurologico "Carlo Besta", Milano, Italy  
*Pro- versus anti-inflammatory cytokines : myth or reality*
- 16<sup>th</sup> Annual Meeting of the Surgical Infection Society Europe (Cernobbio, Italy)  
**SEMMELEWEISS LECTURE** : *Immunodysregulation associated with systemic inflammation*
- 26<sup>th</sup> Annual Conference of the American Shock Society (Phoenix, Arizona)  
*Endotoxin tolerance : Is there clinical relevance ?*
- Yomiuri Health Forum (Tokyo, Japan)  
*The revival of innate immunity, one century after Metchnikoff*
- Institute for Surgical Research (Prof. A.O. Aasen, Director), Rikshospitalet (Oslo, Norway)  
*Immunodysregulation associated with systemic inflammation*
- 2004** 6th World Congress on Trauma, Shock, Inflammation and Sepsis, Munich  
 - *Stress-induced reprogramming of circulating cells*  
 - *Overcoming Toll-like receptor induced tolerance*
- 24<sup>th</sup> International Symposium on Intensive Care and Emergency Medicine, Bruxelles  
 - *Immune dysregulation*  
 - *The mediator cascade*  
 - *Endotoxin Tolerance*
- 3<sup>rd</sup> International Course on Critical Care Nephrology, Vicenza (Italy)  
*Mechanisms of immunodysregulation in sepsis*
- 6<sup>th</sup> European Congress of Trauma and Emergency Surgery, (Rotterdam, Nederland)  
*Compartmentalisation of the inflammatory response.*
- 8<sup>th</sup> biennial meeting of the International Endotoxin Society, (Kyoto, Japan)  
*Reprogramming of circulatory cells in sepsis and SIRS*
- Réunion du Conseil Scientifique, Institut Cantacuzène, (Bucarest, Roumanie)  
*Leukocyte reprogramming following severe inflammation*
- 2005** 25<sup>th</sup> International Symposium on Intensive Care and Emergency Medicine (Brussels)  
 - *The leukocyte response in sepsis*  
 - *Old and new sepsis mediators : endotoxin*  
 - *The sepsis network of mediators*
- VI International Meeting on Sepsis (Valladolid, Spain)*

- *Mediators in sepsis*                      - *Leukocyte reprogramming*
- 2006** Novartis Foundation Symposium "Sepsis – new insights, new therapies" London
  - Discussant -
- 26<sup>th</sup> International Symposium on Intensive Care and Emergency Medicine (Bruxelles)
  - *Immune deactivation – The mechanisms*
  - *Compartmentalization in sepsis*
  - *The host response to infection*
- 2007** Universidad de Guadalajara (Mexico), Jan. 2007
  - *"Inflammatory response and leukocyte reprogramming during sepsis"*
- 7th World Congress on Trauma, Shock, Inflammation and Sepsis, Munich, (Germany), March 2007
  - **Opening session** : *Early events in innate immunity in the recognition of microbial pathogens*
  - *What is the rationale to target endotoxin*
- 26<sup>th</sup> International Symposium on Intensive Care and Emergency Medicine (Bruxelles), March 2007
  - *What is new in the world of mediators? - Synergy is the word*
  - *Pathophysiology of sepsis*
  - *How pathogens counteract the host response*
  - *Molecular mechanisms of immunosuppression*
- 16<sup>th</sup> International Course on Critical Care Nephrology, Vicenza (Italy), May 2007
  - *Determining the degree of immunodysregulation in sepsis*
- World Conference of stress, Budapest (Hungary), August 2007
  - *Leukocyte reprogramming after endotoxin encounter*
- International Sepsis Forum, Paris, Sept. 2007
  - *Cytokines*

## INVITED LECTURES IN FRANCE (since 1999)

- 1999** Journées Parisiennes d'Allergie (Paris)
  - Cycle de Conférences de Pathologie Infectieuse Moléculaire, Inst. Pasteur
  - 41<sup>e</sup> Congrès National d'Anesthésie et de Réanimation (Paris)
  - Séminaire Annuel de la Société Française d'Anatomie Pathologique Vétérinaire (Alfortville)
- 2000** Conférence d'Immunologie (Université Claude Bernard, Lyon)
  - Société Française du Cancer - Réunion du Club Facteur de Croissance, Paris
  - Académie Nationale de Pharmacie : Séance Thématique (Paris)
  - Journée Thématique "Anticorps" (Institut Pasteur)
  - XX<sup>e</sup> Conférence de Consensus en Réanimation et Médecine d'Urgence (Caen)
  - Réunions hebdomadaires de Réanimation de l'Hôpital Bichat-Claude Bernard, Paris
  - Journées Internationales de Biologie (Paris-La-Défense)
  - Congrès annuel de la Société Française d'Immunologie (Paris-UNESCO)
  - 3<sup>e</sup> Journées Francophones de Nutrition (Tours)
- 2001** Réunions interdisciplinaires de Pathologie Infectieuse (Hôp. Avicenne, Bobigny)
  - 9<sup>èmes</sup> Rencontres en Toxinologie (Paris)
  - 16<sup>ème</sup> Séminaire Fondamental de Microbiologie Clinique (Noisy-Le-Grand)
- 2002** Laboratoires L.F.B. (Les Ulis)
  - IFR 100 "Épidémiologie et Biologie de l'athérome et du Cancer" (Dijon)
  - Conférence Aventis-Pasteur (Marcy-l'Étoile)
  - 11<sup>e</sup> Réunion Conjointe Comité d'interface INSERM / Société Française de Biologie Clinique (Paris)
  - 2<sup>e</sup> Réunion d'interface INSERM / Société Française d'Anesthésie et de Réanimation / Société de Réanimation de Langue Française (Paris)

- 2003** Club Réa-Ouest, Hôpital Raymond Poincaré (Garches)  
 Journée Clinique du Département de Médecine Moléculaire (Institut Pasteur)  
 4<sup>èmes</sup> Journées Nationales d'Infectiologie (Lille)  
 Centre Hospitalier de Versailles (Dr. Ghnassia)  
 Service de Rhumatologie, Hôp. Bichat (Prof. O. Meyer)
- 2004** Séminaires des Anciens Scientifiques Pasteuriens  
 Actualités et Rencontres d'Immuno-Allergologie, Centre Médical Institut Pasteur
- 2005** Séminaire de l'IFR65, Hôpital Saint-Antoine, Paris
- 2006** Service des Maladies Infectieuses et Tropicales, Hôpital Necker, Paris.  
 Assemblée Générale Association Anciens Élèves de l'Institut Pasteur, Confolens  
 Colloque Pasteur – Bio-Rad, Paris.  
 Unité Inserm U570 – Pathogénèse des infections systémiques – Hôpital Necker, Paris.  
 Université Inter-Âge de Versailles

## **SUPERVISION and WELCOME**

### **Students [14 DEA (masters), 3 PhD thesis]**

Laurent Vidard (DEA, Paris VII; 1987); Luchino Cohen (DEA Paris XI; 1990)  
 André Cabié, MD (DEA Paris VII; 1991) ; Claire Marty (DEA, Paris XI; 1992)  
 Fabienne Tamion, MD (DEA, Paris VII; 1993) ; Eric Maury, MD (DEA Paris VII; 1994)  
 Christelle Marie (DEA, Paris XI; 1994; Thesis Paris XI; 1997) ; Jane Muret, MD (DEA, Paris VII; 1996)  
 Naïma Rayhane (Thesis Paris V; 2000); Anne-France Petit (DEA, Paris V, 1999, Thesis Paris V; 2003)  
 Karim Assenhoune, MD (DEA Paris XI; 2001) ; Virginie Maxime, MD (DEA Paris VI; 2003)  
 Ronan Kapetanovic (DEA Paris 7; 2004, Thesis) ; Nassima Redjimi (Master Paris XI, 2005) :  
 François Phillipart, MD (Master, Paris 5, 2006)

### **Trainees**

#### **Scientists**

Laszlo Czirjak, MD (Hungary) (Oct. - Dec. 1986)	Christine Aznar, Pharm. (Oct. 1987 - Oct. 1989)
Carlos Muñoz, MS (Chili) (Sept. 1989- Aug 1990)	Riad Fadel, MD (Algeria) (June 1987 - June 1989)
Ravin Agah, MD, PhD (USA) (Apr. - June 1993)	Heide Müller-Alouf, MD, PhD (1993 - 1995)
Sean Near, PhD (UK) (June- July 1995)	Christina Pitton, PhD (Sept. 92 - Dec. 1995)
Pedro Elsas, PhD (Brasil) (Jan. - Feb. 1997)	Suman Dhawan, PhD (India) (Oct. 1997 - Dec. 1998)
Jutta Riese, PhD (Germany) (April - May 1999)	Catherine Blondin, PhD (June - Dec. 1999)
Martin Yordanov, PhD (Bulgaria) (March-May 2006)	Cristina Ciornei, PhD (Sweden) (April 2006 - July 07)
Oh Yoen Kim, PhD (South Korea) (Dec.2006 – Dec. 2007)	

#### **Technicians and students**

Corinne Vioux (BTS, Oct. 1993 - Jan. 94)	Marcello Lopez (Techn. Chili, Sept. - Oct. 1994)
Dorothee Rosenberg (BTS, June - July. 1995)	Angélique Giselbrecht (MS, July - Aug 1996)
Caroline Soulas (Licence, July - Aug 1998)	Michael Ozanon (BTS, June - July 1999)
Homer Venter (MD, USA, June 2000 & June 2001)	Carolynn Ismain (Apr. – May 2002)
Emilie Hue (DEUG, June – July 2003)	Xavier Ladonne (BTS, May - June 2004)
Anke Buman (Techn. Germany; June-Jul. 2005)	Maren Wittermann (Techn. Germany; June-Jul. 2005)

#### **Sabatical**

Prof. E. Rietschel (Borstel, Germany, Sept. – Dec. 1999)  
 Prof. S. Warren (Boston, USA, Sept. 2002 – July 2003)



## GRANTS

- 1995 Contrat CNRS "Interface Chimie-Biologie"  
**Co-investigator**
- 1995-1996 Réseau Nord-Sud Inserm (with Brazilian & Chilian colleagues)  
**Co-investigator**
- 1996-1997 Action de Recherche – Centre National de Recherche Scientifique  
*"Interaction between LPS and its CD14 receptor. Structural and functional characterization"*  
**Co-investigator**
- 1998 Comité Consultatif de la Valorisation (Inst. Pasteur)  
*Setting of an IL-1Ra ELISA*  
**Principal investigator**
- 1998-2000 Association Française de lutte contre la Mucoviscidose  
*Mechanisms involved in the airway inflammation and infection in cystic fibrosis,*  
*pharmacological strategies*  
**Co-investigator**
- 1999-2000 Recherche Clinique (Inst. Pasteur)  
*Systemic inflammatory diseases and immunodepression*  
**Principal investigator**
- 2001-2002 Association Contre la Mucoviscidose  
*Influence of adherence of leukocytes on the properties of interleukin-10*  
**Principal investigator**
- 2002-2003 Association Contre la Mucoviscidose  
*Interaction between neutrophils and respiratory epithelial cells in cystic fibrosis : control of apoptosis and pro- and anti-inflammatory cytokine production*  
**Co-investigator**
- 2002-2004 Interdisciplinary Research Program #94 (Inst. Pasteur)  
*The role of Toll-like receptors and Nod proteins in innate immunity : recognition and responses generted by whole microbes versus distinct microbial products*  
**Co-investigator**
- 2004-2005 Association Contre la Mucoviscidose  
*Neutrophils and inflammation in cystic fibrosis*  
**Co-investigator**
- 2004-2005 Interdisciplinary Research Program #150 (Inst. Pasteur)  
*Toll-like receptors and B lymphocytes*  
**Co-investigator**
- 2004-2005 Interdisciplinary Research Program #155 (Inst. Pasteur)  
*Influence of digestive commensal bacterial flora on the immune system: attempts to characterize and enrich the implantation flora used y laboratory animal breeders*  
**Co-investigator**
- 2005-2007 Biotox  
*Genetic determinism of mouse susceptibility to plague*  
**Co-investigator** (Principal Investigator : Dr. E. Carniel Inst. Pasteur)
- 2005-2006 Legs Poix (Chancellerie des Universités)

*Study on compartmentalization of the immuno-inflammatory response in severe sepsis: systemic and lung pro- and anti-inflammatory responses.*

**Principal investigator**

2005 - 2007            Actions Concertées Inter-Pasteuriennes (ACIP) : Joint project with Stephan Angelov

Institute, Sofia, and Cantacuzino Institute, Bucarest (Institut Pasteur Network):  
*Macrophage-dependent immunoprotective action of Candida albicans DNA*

**Co-investigateur** (Principal Investigator: Dr. Nina Ivanovska, Sofia)

2005 - 2007    Agence de Biomédecine (previously "Etablissement Français des Greffes")  
*Cerebral death: inflammatory syndrome, apoptosis and endotoxin tolerance*

**Co-investigateur** (Principal Investigator: Dr. Christophe Adrie, Hôpital Saint-Denis)

2005 - 2007    Association Vaincre la Mucoviscidose

*Involvement of phagocytosis in the induction of inflammatory cytokines by Staphylococcus aureus & Pseudomonas aeruginosa*

**Principal investigator**

2005 - 2009    NIH grant 1 R01 AI 59010-01A1

*Mouse model for sepsis: why are normal mice so resistant to bacterial toxins?*

**Co-investigateur** (Principal Investigator: Prof. Shaw Warren, Boston)

## PRICES

Prix "Allergie 2000" (May 1990)

Prix de Thèse GREMI for Christelle Marie (1999)

## PATENTS

- Monoclonal anti-IL-1 $\alpha$  (Pharmingen)

- "Inflammatory-inhibitory serum factors and uses thereof"

Warren Shaw, Cavaillon Jean-Marc, 2005

(ref. Massachusetts General Hospital : MGH 2310 ; ref. Pasteur : DI 2005-30)

## PUBLICATIONS

I am the author of 122 papers published (or in press) in peer-reviewed journals, 63 reviews, and 36 invited chapters in books. In addition, I am the author of the first book in French on cytokines ("Les Cytokines" 1<sup>st</sup> Ed. 1993 ; 2<sup>nd</sup> Ed. 1996). I have been invited by Wiley VCH Verlag, (Germany) to organize a book on "Sepsis and Non-infectious Systemic Inflammation" (2008)

### Bibliometry / Citation Index

Total number of citations :	4968
Number of articles cited > 50 fold & < 100 fold	21
Number of articles cited more than 100 fold	10
Most frequently cited paper ( <i>J.Clin.Invest.</i> 1991, 88, 1747)	317 x
H factor = 40	

## SUMMARY

When I joined the Institut Pasteur as a student, 33 years ago, Prof. Anne-Marie Staub, a well-known immunochemist in the 70's, introduced me to the endotoxins. These intriguing molecules led me to be fascinated by the interaction between microbial agents and immune cells, far before innate immunity was fashionable ! I spent my post-doctoral term in Prof. Bernard Cinader's lab (Toronto), internationally recognized in the field of cellular immunology in the 80's, and I showed that B-lymphocytes help T-lymphocytes to proliferate in response to mitogens. Back in Paris, I investigated the structure/function relationship of endotoxins in terms of cytokine induction, and particularly interleukin-1 (IL-1) production. We showed that the inner core region of the lipopolysaccharide (LPS) was involved in the specific binding of the molecule to monocytes/macrophages and involved in the signaling leading to IL-1 release. We studied many compounds that interfere with LPS-induced cytokine production and showed that plasma factors could either amplify (e.g. C5a), or inhibit (e.g. lipoproteins) the release of IL-1. In Prof. Joseph Alouf's lab, I worked with exotoxins from *Streptococcus pyogenes*, when they were not yet known as superantigens. I was the first to demonstrate their capacity to induce cytokine production, namely interferon- $\gamma$ . Addressing a wider panel of cytokines (i.e. TNF, lymphotoxin- $\alpha$ , IL-1Ra, IL-3, IL-4, IL-6, IL-8, IL-10, TGF- $\beta$ ), I showed that the nature of the cells, the timing of the events, the nature of the activators, the sequence of the signals, or even the adherence of monocytes have a profound effect on cytokine production. Our findings illustrated that the frontiers between pro- and anti-inflammatory cytokines are not so clear-cut. My interest for this universal language of the cells led me to write the first book in French on cytokines in 1993.

With the motivation to contribute to studies on human diseases, I joined Prof. Bernard David's lab in 1984, where I started to work on allergy. I studied chronic hemodialyzed patients who suffered severe allergic reactions. With the help of physicians, we set up new parameters of hemodialysis sessions that dramatically reduced the occurrence of allergic reactions. We were the first to show that IL-1 was induced during the hemodialysis session. I showed that the presence of circulating IL-6 in these patients illustrated the inflammatory process. Then, thanks to a Chilean post-doctoral fellow, Carlos Muñoz, and Dr. Jean Carlet, head of the intensive Care Unit of Hôp. St Joseph, we initiated our series of studies on sepsis patients. We showed that high plasma levels of IL-6 and IL-8 correlate with poor outcome. We established the usefulness of measuring cell-associated cytokines. We investigated *ex vivo* cytokines production by monocytes and were the first to demonstrate a reduced responsiveness in terms of IL-1 $\alpha$ , IL-1 $\beta$ , IL-6 and TNF upon stimulation by LPS. Then, we extended our study to cytokine production by T lymphocytes and neutrophils and included patients with non-infectious systemic inflammatory response syndrome (surgery, trauma, resuscitated cardiac arrest). The alteration of the cytokine production appeared reminiscent of the endotoxin tolerance phenomenon. We illustrated this concept by studies that addressed the molecular signaling, such as the activation of NF- $\kappa$ B. In addition to the signaling pathways initiated by endotoxins, we study those initiated by the different ligands of Toll-like receptors and intracellular receptors Nod1 and Nod2. Altogether, our investigations contribute to the understanding of the cellular and molecular events that take place during innate immune response initiated during bacterial infections.

**PEER REVIEWED SCIENTIFIC PUBLICATIONS**

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