

## Dr. ALAIN FILLOUX

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**Date of birth:** May 1, 1961

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### **Education:**

Université de la Méditerranée, 1997 □ Habilitation diploma.

Aix-Marseille II University (France), 1985-1988, Ph. D in Cellular and Molecular Biology and Microbiology.

Aix-Marseille II University (France), 1980-1984: Master degree in Cellular and Molecular Biology

Lycée Marseilleveyre (High school), 1979, Bachelor degree, life sciences

### **Employment:**

**Current status:** Research Director

Director of the CNRS Research Unit n° 9027 (Laboratoire d'Ingénierie des Systèmes Macromoléculaires, <http://lism.cnrs-mrs.fr/>)

Head of the research group Molecular Microbiology and Pathogenicity in Pseudomonads (<http://alainfilloux.com/>).

**January 1994-present:** Researcher position at the National Center for Scientific Research (CNRS, France).

**April 1990-December 1993:** Assistant Professor permanent position at the Utrecht University, Department of Molecular Cell Biology (The Netherlands).

**October 1988-March 1990:** Postdoctoral fellow with Pr. J. Tommassen, Utrecht University, Department of Molecular Cell Biology, The Netherlands.

### **Main research topics:**

*Pseudomonas aeruginosa* and bacterial virulence

Molecular mechanisms of protein and toxin secretion

Molecular mechanisms of bacterial adhesion and biofilm formation

Global regulatory networks, two component systems and quorum sensing

Bacterial genomics

### **Awards & events**

**“Coup d’élán 2003” from the Bettencourt-Schueller foundation** awarding our research on “*Pseudomonas aeruginosa*: a model organism for studying nosocomial infections” (<http://www.fondationsbs.org/index.htm>).

**Scientific and main organizer of the Pseudomonas 2005 meeting** in Marseille, France. A multidisciplinary exploration of current Pseudomonas research (<http://www.atout-org.com/pseudomonas2005/>)

### **Teaching:**

**Ph.D and Master degree lecturer** in Microbiology, Université de la Méditerranée

**International course and workshop** □ Trieste, Italy (2000 & 2002), Copenhagen, Denmark (2001), Naples, Italy (2003), Lausanne, Switzerland (2003), Hannover, Germany (2004).

### **Memberships and reviewing activities:**

**Scientific societies:** Société Française de Microbiologie (SFM); Société Française de Biochimie et Biologie Moléculaire (SFBBM), AAAS, American Society of Microbiology, ASM.

**Editorial board member of Journal of Bacteriology**

**Member of the scientific committee of the French cystic fibrosis foundation**

**ad hoc reviewer** for: Molecular Microbiology, Journal of Bacteriology, EMBO Journal, Science, Microbiology, Journal of Molecular Biology, Gene, Archives of Microbiology, Research in Microbiology, Biochimie, Biochemical Journal, FEBS Letters.

**Referee** for funding organisation: Biotechnology and biological sciences research council (BBSRC), Swiss National Founds, Vaincre la Mucoviscidose, Welcome Trust, CNRS, Ministère de la Recherche.

### **Currently funded projects:**

**2001-2004** European contract 5<sup>th</sup> RTD. "Quality of life and management of living resources" QLK2-CT-2001-01339. *Pseudomonas* Virulence. Coordination Arnaud Ducruix (EP2075-CNRS/ Paris).

**2002-2005** European contract 5<sup>th</sup> RTD. "Quality of life and management of living resources" QLK3-CT-2002-02086. NANOFOLDEX. Coordination Jan Tommassen (Utrecht University, Pays-Bas).

**2003-2004: French-German Program** Vaincre la Mucoviscidose/Mukoviscidoze. Coordination B. Tummler (Hannover/Germany). Attachment and cytotoxicity of *P. aeruginosa* to macrophages and bronchial epithelial cells.

**2004-2007** European contract 6<sup>th</sup> RTD. Network of Excellence (NoE) European Virtual institute for Functional Genomics of Bacterial Pathogens – EuroPathoGenomics Life Science, genomics and Biotechnology for health.

### **Most recent conferences:**

Pseudomonas 2001, Bruxelles, Palais des congrès. September 17-21, 2001.

XXI<sup>st</sup> congress of Brazilian Society Microbiology, Iguaçu, Brasil. October 21-25, 2001.

European Science Foundation Conference. Protein Targeting. Acquafrredda di Maratea, Italia. September 28- October 3, 2001.

EMBO Workshop. Prokaryotes in the third Millenium. EMBL, Heidelberg, Germany. April 26-30, 2002.

Gordon Conference. Bacterial Cell Surfaces. Colby Sawyer, New London, NH, USA. June 23-28, 2002

IUMS-Paris/Palais des congrès. July 27- August 1, 2002. The world of Microbes.

Pseudomonas 2003, Quebec, September 6-10, 2003.

Euresco Conference, biology of type IV secretion process, Giens France, September 12-17, 2003.

Juan march conferences, Finding the way out, October 20-22, 2003, Madrid.

ASM Conference on Biofilm, November 1-6, 2003, Victoria, British Columbia.

VAAM, Annual meeting of the german society for Microbiology, March 29-31, 2004, Braunschweig, Germany.

EMBO Conference on "Exploring prokaryotic diversity, April 22-26, 2004, EMBL, Heidelberg, Germany.

## Publications

- Filloux A., Joyet, P., Murgier, M. and Lazdunski, A. (1985). Cloning and expression of a *Bacillus licheniformis* a-amylase gene in *Pseudomonas aeruginosa*. *FEMS Microbiol. Lett.* 30: 203-207.
- Filloux, A., Murgier, M., Wretlind, B. and Lazdunski, A. (1987). Characterization of two *Pseudomonas aeruginosa* mutants with defective secretion of extracellular proteins and comparison with other mutants. *FEMS Microbiol. Lett.* 40: 159-163.
- Filloux, A., Bally, M., Soscia, C., Murgier, M. and Lazdunski, A. (1988). Phosphate regulation in *Pseudomonas aeruginosa*: cloning of alkaline phosphatase gene and identification of *phoB*- and *phoR*- like genes. *Mol. Gen. Genet.* 212: 510-513.
- Filloux, A., Bally, M., Murgier, M., Wretlind, B. and Lazdunski, A. (1989). Cloning of *xcp* genes located at the 55 min region of the chromosome and involved in protein secretion in *Pseudomonas aeruginosa*. *Mol. Microbiol.* 3: 261-265.
- Lazdunski, A., Guzzo, J., Filloux, A., Bally, M. and Murgier, M. (1990). Secretion of extracellular proteins by *Pseudomonas aeruginosa*. *Biochimie* 72: 147-156.
- Guzzo, J., Murgier, M., Filloux, A. and Lazdunski, A. (1990). Cloning of the *Pseudomonas aeruginosa* alkaline protease gene and secretion of the protease into the medium by *Escherichia coli*. *J. Bacteriol.* 172: 942-948.
- Filloux, A., Bally, M., Ball, G., Akrim, M., Tommassen, J. and Lazdunski, A. (1990). Protein secretion in Gram-negative bacteria: transport across the outer membrane involves common mechanisms in different bacteria. *EMBO J.* 9: 4323-4329.
- de Groot, A., Filloux, A. and Tommassen, J. (1991). Conservation of *xcp* genes, involved in the two-step protein secretion process in different *Pseudomonas* species and other Gram-negative bacteria. *Mol. Gen. Genet.* 229: 278-284.
- Bally, M., Filloux, A., Akrim, M., Ball, G., Lazdunski, A. and Tommassen, J. (1992). Protein secretion in *Pseudomonas aeruginosa*: characterization of seven *xcp* genes and processing of secretory apparatus components by preprotein peptidase. *Mol. Microbiol.* 6: 1121-1131.
- Tommassen, J., Filloux, A., Bally, M., Murgier, M. and Lazdunski, A. (1992). Protein secretion in *Pseudomonas aeruginosa*. *FEMS Microbiol. Rev.* 103: 73-90.
- Akrim, M., Bally, M., Ball, G., Tommassen, J., Teerink, H., Filloux, A. and Lazdunski, A. (1993). Xcp-mediated protein secretion in *Pseudomonas aeruginosa*: identification of two additional genes and evidence for regulation of *xcp* gene expression. *Mol. Microbiol.* 10: 431-443.
- de Groot, A., Heijnen, I., de Cock, H., Filloux, A. and Tommassen, J. (1994). Characterization of type IV pilus genes in plant growth-promoting *Pseudomonas putida* WCS358. *J. Bacteriol.* 176: 642-650.
- Braun, P., Tommassen, J. and Filloux, A. (1996) Role of the propeptide in folding and secretion of elastase of *Pseudomonas aeruginosa*. *Mol. Microbiol.* 19: 297-306.
- de Groot, A., Krijger, J. J., Filloux, A. and Tommassen, J. (1996) Characterization of type II protein secretion (*xcp*) genes in plant growth-stimulating *Pseudomonas putida*, strain WCS358. *Mol. Gen. Genet.* 250: 491-504.
- Bleves, S., Lazdunski, A. and Filloux, A. (1996) Membrane topology of three Xcp proteins involved in exoprotein transport by *Pseudomonas aeruginosa*. *J. Bacteriol.* 178: 4297-4300.
- Bleves, S., Voulhoux, R., Michel, G., Lazdunski, A., Tommassen, J. and Filloux, A. (1998) The secretion apparatus of *Pseudomonas aeruginosa*: Identification of a fifth pseudopilin, XcpX. *Mol. Microbiol.* 27: 31-40.
- Filloux, A. and Hardie, K. (1998) A systematic approach to study protein secretion in Gram-negative bacteria. Methods in Microbiology: Bacteriology pathogenicity. Vol. 27; pp 301-318.
- Filloux, A., Michel, G. and Bally, M. (1998) GSP-dependent protein secretion in Gram-negative bacteria : the Xcp system of *Pseudomonas aeruginosa*. *FEMS Microbiol. Rev.* 22 (3): 177-198.
- Michel, G., Bleves, S., Ball, G., Lazdunski, A. and Filloux, A. (1998) Mutual stabilization between XcpZ and XcpY components of the secretory apparatus in *Pseudomonas aeruginosa*. *Microbiology*. 144: 3379-3386.
- de Groot, A., Gerritse, G., Tommassen, J., Lazdunski, A. and Filloux, A. (1999) Molecular organization of the *xcp* gene cluster in *Pseudomonas putida*: absence of an *xcpX* (*gspK*) homologue. *Gene*. 226: 35-40.

- Bleves, S., Gérard-Vincent, M., Lazdunski, A. and Filloux, A. (1999) Structure-function analysis of XcpP, a component involved in GSP-dependent protein secretion in *Pseudomonas aeruginosa*. *J. Bacteriol.* 181: 4012-4019.
- Taupiac, M. P., Voulhoux, R., Filloux, A. and Beaumelle, B. (2000). Deletions within the translocation domain of exotoxin A affect both its secretion by *Pseudomonas aeruginosa* and its translocation across the target-cell intracellular membranes. *Int. J. Med. Microbiol.* 290:
- de Bentzmann, S. Polette, M., Zahm, J. M., Hinnrasky, J., Kileztky, C. Bajolet, O., Klossek, J. M., Filloux, A., Lazdunski, A. and Puchelle, E. (2000) *Pseudomonas aeruginosa* virulence factors delay airway epithelial wound repair by altering the actin cytoskeleton and inducing overactivation of epithelial MMP-2. *Lab. Invest.* 80: 1-11.
- Voulhoux, R., Taupiac, M-P, Czjcek, M., Beaumelle, B. and Filloux, A. (2000) Influence of exotoxin A domain II deletions on its extracellular secretion from *Pseudomonas aeruginosa*. *J. Bacteriol.* 182: 4051-4058.
- Voulhoux, R., Lazdunski, A. and Filloux, A. (2001) Colicin A hybrids: a genetic tool for selection of type II secretion-proficient *Pseudomonas* strains. *EMBO Reports.* 2: 49-54.
- de Groot, A., Koster, M., Gérard-Vincent, M., Gerritse, G., Lazdunski, A., Tommassen, J. and Filloux, A. (2001) Exchange of Xcp (Gsp) secretion machineries between *Pseudomonas aeruginosa* and *Pseudomonas alcaligenes*: species-specificity unrelated to substrate recognition. *J. Bacteriol.* 183: 959-967.
- Duong, F., Bonnet, E., Géli, V., Lazdunski, A., Murgier, M. and Filloux, A. (2001) The AprX protein of *Pseudomonas aeruginosa*: a new substrate for the Apr type I secretion system. *Gene* 262: 147-153.
- Vallet, I., Lory, S., Olson J. W., Lazdunski, A. and Filloux, A. (2001) The chaperone-usher pathways of *Pseudomonas aeruginosa*: identification of new fimbrial gene clusters (*cup*) and their involvement in biofilm formation. *Proc. Natl. Acad. Sci. USA.* 12: 6911-6916.
- Voulhoux, R., Ball, G., Ize, B., Vasil, M. L., Lazdunski, A., Wu, L-F. and Filloux, A. (2001) Involvement of the Twin-arginine translocation system in protein secretion via the type II pathway. *EMBO J.* 20: 6735-6741.
- Ball, G., Durand, E., Lazdunski, A. and Filloux, A. (2002) A novel type II secretion system in *Pseudomonas aeruginosa*. *Mol. Microbiol.* 43: 475-485.
- Ize, B., Gérard, F., Zhang, M., Chanal, A., Voulhoux, R., Palmer, T., Filloux, A. and Wu, L. F. (2002) In vivo dissection of the Tat translocation pathway in *Escherichia coli*. *J. Mol. Biol.* 317: 327-335.
- Gérard-Vincent, M., Robert, V., Ball, G., Bleves, S., Michel, G., Lazdunski, A. and Filloux, A. (2002) Identification of XcpP domains that confer functionality and specificity to the *Pseudomonas aeruginosa* type II secretion apparatus. *Mol. Microbiol.* 44: 1651-1665.
- Mattos Saliba, A., Filloux, A., Ball, G., Silva, A. S. V., Assis, M-C. and Plotkowski, M-C. (2002) Type III secretion-mediated killing of endothelial cells by *pseudomonas aeruginosa* is non-apoptotic. *Microbial pathogenesis.* 33: 153-166.
- Filloux, A., Voulhoux, R., Ize, B., Gérard, F., Ball, G. and Wu, L-F. (2002) Use of colicin-based genetic tools for studying bacterial protein transport. *Biochimie.* 84: 489-497.
- Filloux, A. et Vallet, I. (2003) Biofilm: mise en place et organisation d'une communauté bactérienne. *Médecine/Sciences.* 19: 77-83.
- Kurz, C.L., Chauvet, S., Andres, E., Aurouze, M., Vallet, I., Michel, G.P., Uh, M., Celli, J., Filloux, A., De Bentzmann, S., Steinmetz, I., Hoffmann, J.A., Finlay, B.B., Gorvel, J.P., Ferrandon, D. and Ewbank, J.J. (2003) Virulence factors of the human opportunistic pathogen *Serratia marcescens* identified by *in vivo* screening. *EMBO J.* 22:1451-1460.
- Durand, E., Bernadac, A., Ball, G., Lazdunski, A., Sturgis, J. N. and Filloux, A. (2003) Type II protein secretion in *Pseudomonas aeruginosa*: the pseudopilus is a multifibrillar and adhesive structure. *J. Bacteriol.* 185: 2749-2758.
- Vallet, I., Diggle, S. P., Stacey, R., Camara, M., Ventre, I., Lory, S., Lazdunski, A., Williams, P. and Filloux, A. (2004) *Pseudomonas aeruginosa* biofilm formation: the fimbrial *cup* gene clusters are controlled by the transcriptional regulator MvaT. *J. Bacteriol.* 186: 2880-2890.

**In press:**

- Barker, A. P., Vasil, A. I., Filloux, A., Ball, G., Wilderman, P. J., Vasil, M. L. (2004) A novel extracellular Phospholipase C of *Pseudomonas aeruginosa* is required for phospholipid chemotaxis. *Mol. Microbiol.*  
Filloux, A. (2004) The underlying mechanisms of type II protein secretion. *Biochem. Biophys. Acta.*

**Submitted:**

- Laabs, U., Gudovius, P., Filloux, A., Tummler, B. and de Bentzmann, S. Maintenance of high adherence capacity in *Pseudomonas aeruginosa* CF isolates during chronic infection is associated with disease severity. *J. Infect. Dis.*  
Vasseur, P., Vallet-Gely, I., Génin, S., Aaes-Jørgensen, A.S., Soscia, C., de Bentzmann, S., Molin, S. and Filloux, A. A member of the PST family involved in biofilm formation in *Pseudomonas aeruginosa* and *Ralstonia solanacearum*. *Microbiology*.  
Hemantha D. Kulasekara, Isabelle Ventre, Bridget R. Kulasekara, Andrée Lazdunski, Alain Filloux and Stephen Lory. Regulation of *cup* fimbriae of *Pseudomonas aeruginosa* by a novel three component regulatory system. *EMBO J.*

**Book chapters:**

- Filloux, A. (1999) Type II protein secretion: the main terminal branch of the general secretory pathway. In: "Transport of molecules across microbial membranes", JK broome-Smith, S Baumberg, CJ Stirling and FB Ward (Eds). *SGM Symposium volumes*, vol. 58 pp. 80-109.  
Filloux, A. and Gérard-Vincent, M. (2003) Type II protein secretion. In Protein Secretion Pathways in Bacteria. Edited by B. Oudega. Kluwer Academic Publishers, Dordrecht, Chapter 8, 304 pp.

*In press*

- Ventre, I., Filloux, A. and Lazdunski. (2004) Two-component signal transduction systems : a key to the adaptative potential of *Pseudomonas aeruginosa*. The Pseudomonads Vol.II. Virulence gene and regulation. Kluwer Eds.  
Filloux, A., Bleves, S., van Ulzen, P. and Tommassen, J. (2004) Protein secretion mechanisms in *Pseudomonas*. The Pseudomonads Vol I. Genomics, life style and molecular architecture. Kluwer Eds.  
Filloux, A., de Bentzmann, S., Aurouze, M., Lazdunski, A. and Vallet, I. (2004) Fimbrial genes in *Pseudomonas aeruginosa*. The Pseudomonads Vol. I. Genomics, life style and molecular architecture. Kluwer Eds.

**Other titles:**

- Bally, M., Filloux, A., Murgier, M., Wretlind, B. and Lazdunski, A. (1988). Cloning of *xcp* genes possibly involved in protein secretion in *Pseudomonas aeruginosa*. NATO ASI Series, Vol. H16, Edited by J. A. F. Op den Kamp pp. 439-444.  
Lazdunski, A., Murgier, M., Bally, M., Filloux, A., Guzzo, J., Akrim, M., Duong, F. and Tommassen, J. (1992). Secretion of extracellular proteins in *Pseudomonas aeruginosa*: existence of two pathways, wide spread among Gram-negative bacteria. In *Pseudomonas-1991* (Silver, S. Ed.), pp. 83-93. American Society for Microbiology, Washington, DC.  
Lazdunski, A., Filloux, A., Michel, G., Foglino, M., Murgier, M., Latifi, A., Chapon, V., Bléves, S. and Bally, M. (1996) The general secretion pathway in *Pseudomonas aeruginosa*: molecular mechanisms and regulation. In "Molecular biology of Pseudomonads" T. Nakazawa, K. Furukawa, D. Haas and S. Silver (Eds), pp 427-437. ASM Press, Washington, D. C.  
Voulhoux, R., Duché, D., Géli, V., Lazdunski, A. and Filloux, A. (1998). Development of a positive screen for the identification of suppressive mutations in secretion defective strains of *Pseudomonas aeruginosa*. In: Molecular mechanisms of lipid and protein traffic (Op den Kamp, J. A. F., Ed), NATO ASI Series, Springer Verlag, Berlin Heidelberg, Subseries H, Vol. 106, pp219-229.  
Filloux, A. and Lazdunski, A. (1998) La sécrétion des protéines chez les bactéries. *Biofutur* 184: 68-72.  
Filloux, A. (2001) *Pseudomonas aeruginosa* un modèle pour l'étude des interactions bactérie/hôte. Lettre BIO. 91: 7.