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Biography

Flavia Marinelli graduated at Rome with a Laurea in Biology focusing on Industrial Microbiology and Fermentation Chemistry in 1986; she got her PhD in Chemistry at Scuola Normale Superiore di Pisa in 1991. Her studies focused on the cultivation of microbes and plant cells and on the chemistry and genetics of their secondary metabolites. She did post-doc period at the Freiburg University in Germany, working on secondary metabolism enzymes in plant suspension cultures, then she joined the Lepetit Antinfective Research Center of the pharmaceutical firm Marion Merrell Dow, as Researcher devoted to the genetic improvement of antibiotic producing microbes. In the 1995, she was appointed as Director of the Microbial Isolation and Fermentation Group first for Lepetit, then for Biosearch Italia and later on for Vicuron Pharmaceuticals. For thirteen years she had worked in pharmaceutical companies on the industrial microbiology and the genetics of filamentous microorganisms, mainly actinomycetes, producing new antibiotics and other bioactive secondary metabolites. She was also responsible of the Microbial Collection and of the Fermentation Pilot Plant. In the 1996, she was one of the eight founders of Biosearch Italia, the first Italian biotechnology company quoted at Nuovo Mercato, Italy and then at Nasdaq, USA, and member of the first Board of Directors. In the 2003-2004 she was appointed as Contractor Professor of Chemistry and Biotechnology of Fermentation at Insubria University. At the end of 2004 she was appointed as Associate Professor of Chemistry and Biotechnology of Fermentation at the Department of Biotechnology and Molecular Sciences at Insubria University, where she is leading the Microbial Biotechnology Laboratories and Fermentation Unit. The group is associated with the Interuniversity center "The Protein Factory", Università dell'Insubria and Politecnico di Milano. In this last decade, Flavia Marinelli has built many national and international research co-operations, getting funds from regional, national, European institutions and private companies. Her group hosts many students, PhD students and Post docs. She has written 66 papers; she is co-inventor of four patents and has presented more than 150 lectures, abstracts, posters to national and international congresses.

Qualifications and awards

Member of: -Società Italiana di Microbiologia Generale e Biotecnologie Microbiche (SIMGBM), -Society for Industrial Microbiology (SIM), USA, -American Society for Microbiology (ASM), USA, -World Federation of Culture Collections, - European

Federation of Biotechnology (EFB). Twice she has been called by EC as Expert for evaluation of research and development projects in biotechnological productions. She has been nominated by the Belgian Science Policy Office as foreign Expert for the evaluation of "Belgian Coordinated Collection of Microorganisms".

Research interests

Currently ongoing research projects deals with the biotechnological exploitation of uncommon and /or newly isolated and /or industrially relevant microorganisms, with a particular focus on actinomycetes. Production of bioactive secondary metabolites, peptides and proteins is studied, improved and optimized by combining molecular biology tools and fermentation process skills. Novel metabolic pathways, products and resistance mechanisms are being discovered in actinomycetes and their elucidation together with the development of manipulation procedures, cultivation methods and fermentation protocols represents a main interest of the lab. Some examples are the production of glycopeptides (teicoplanin and A40926), polyketides and lantibiotics. Novel species of actinomycetes have been recently employed to perform specific bioconversion of industrial interest, mainly regio-stereo specificity modification of complex antibiotic molecules such as lipoglycopeptides and depsipeptides. Heterologous expression of valuable peptides and proteins is ongoing comparing classical hosts (i.e. *E.coli*) with non conventional ones (*Streptomyces* spp.). The labs are fully equipped to perform 3L parallel computer batch and fed-batch fermentations controlled by the bidirectional software BioExpert. Scaling up is possible in larger reactors coupled with dedicated downstream systems for the recovery of the products. Medium and fermentation parameters are optimised by statistical design using StatGraphicsPlus software.

Teaching experience and appointments

Flavia Marinelli currently holds the following courses:

- Chemistry and Biotechnology of Fermentations for Biotechnologists -I level 5CFU
- Microbial Biotechnology for Biotechnologists -II level 6CFU
- Biotechnology of Microbial Processes for Biotechnologists -II level 5CFU

She actively collaborates to the activities of the commissions devoted to the biotechnology courses (first and master degrees)

Flavia Marinelli joins the Professor College for PhD fellows in Analysis, Management and Protection of Biodiversity.

She has been the supervisor of many graduate and PhD students, participating also as international referee in PhD dissertations at Ghent, Liege, Wageningen, Cape Town and Trondheim universities.

She is member of the Faculty team of the Summer School in Applied Molecular Microbiology Inter-University Centre (IUC) and John Innes Center.

She participates to the EU Cost Action CM0804 Chemical Biology with Natural Products and to the EU consortium Metaexplore: metagenomics for bioexploration – tools and application.

Representative publications

Selected publications from 2005:

F. Gaspari, Y. Paitan, M. Mainini, D. Losi, E. Z. Ron, F. Marinelli (2005) Myxobacteria isolated in Israel as potential source of new anti-infectives. *Journal of Applied Microbiology* 98: 429-439

F.Molinari, D.Romano, R.Gandolfi, R.M. Kroppenstedt, F.Marinelli (2005) Newly isolated *Streptomyces* spp. as enantioselective biocatalysts: hydrolysis of 1,2-O-isopropylidene glycerol racemic esters. *Journal of Applied Microbiology* 99: 960-967

M.Brunati , A.Bava, F.Marinelli, G.Lancini (2005) Influence of leucine and valine on ramoplanin production by *Actinoplanes* sp.ATCC 33076. *Journal of Antibiotics (Tokyo)* 58: 473-478

S.Jovetic, F.Marinelli, J. Tramper (2006) Continuous biotransformation of glycopeptide antibiotic A40926 in a cascade of three airlift bioreactors using immobilized *Actinoplanes teichomyceticus* cells. *Enzyme and Microbial Technology* 38:34-39

F.Beltrametti, R.Rossi, E.Selva, F.Marinelli (2006) Antibiotic production improvement in the rare actinomycete *Planobsipora rosea* by selection of resistance mutations to the aminoglycosides streptomycin and gentamycin and to rifamycin. *Journal of Industrial Microbiology and Biotechnology* 33:283-288

L.Brandi, A. Lazzarini, L. Cavaletti, M. Abbondi, E.Corti, I. Ciciliato, L. Gastaldo, A. Marazzi, M. Feroggio, A. Fabbretti, A. Maio, L.Colombo, S. Donadio, F. Marinelli, D.Losi, C. O.Gualerzi, E. Selva (2006) Novel tetrapeptide inhibitors of bacterial protein synthesis produced by a *Streptomyces* sp. *Biochemistry* 45:3700-3710

A Taton, S. Grubisic, D. Ertz, D. A. Hodgson, R. Piccardi, N. Biondi, M.Tredici, M.Mainini, D. Losi, F. Marinelli, A. Wilmotte (2006) Polyphasic study of Antarctic cyanobacterial strains. *Journal of Phycology* 42:1257-1270

F.Beltrametti, A.Consolandi, L.Carrano, F.Bagatin, R.Rossi, L.Leoni, E.Zennaro, E.Selva, F.Marinelli (2007) Resistance to glycopeptide antibiotics in the teicoplanin producer is mediated by *van*-gene homologue expression directing the synthesis of a modified cell wall peptidoglycan. *Antimicrobial Agents and Chemotherapy* 51: 1135-1141

S.Di Palo, R.Gandolfi, S.Jovetic, F.Marinelli,D.Romano, F.Molinari (2007) A new bacterial mannosidase for the selective modification of ramoplanin and its derivatives, *Enzyme and Microbial Technology* 41: 806-811

R.Gandolfi, S.Jovetic, F.Marinelli, F.Molinari (2007) Biotransformations of lipoglycopeptides to obtain novel antibiotics, *Journal of Antibiotics (Tokyo)* 60:265-271

F.Beltrametti, D.Barucco, R.Rossi, E.Selva, F.Marinelli (2007) Protoplast fusion

and gene recombination in the uncommon actinomycete *Planobispora rosea* producing GE2270, *Journal of antibiotics (Tokyo)* 60: 447-454

F.Castiglione, L.Cavaletti, D.Losi, A.Lazzarini, L.Carrano, M.Feroggio, I.Ciciliato, E.Corti, G.Candiani, F.Marinelli, E.Selva. (2007) A novel lantibiotic acting on bacterial cell wall synthesis produced by the uncommon actinomycete *Planomonospora* sp., *Biochemistry*, 46:5884-95

F.Castiglione, A.Lazzarini, L.Carrano, E.Corti, I.Ciciliato, L.Gastaldo, P.Candiani, D. Losi, F.Marinelli, E.Selva, F.Parenti (2008) Determining the structure and mode of action of microbisporicin, a potent lantibiotic active against multiresistant pathogens, *Chemistry & Biology* 15:22-31

N.Biondi, M.Tredici, A Taton, A. Wilmotte, D.Hodgson, D. Losi, F. Marinelli (2008) Cyanobacteria from benthic mats of Antarctic lakes as a source of new bioactivities, *Journal of Applied Microbiology* 105:105-15

F.Volontè, F. Marinelli, L. Gastaldo, S. Sacchi, M.S. Pilone, L.Pollegioni, G. Molla (2008) Optimization of glutaryl-7-aminocephalosporanic acid acylase expression in *E. coli*. *Protein Expression Purification* 61:131-7

S.Jovetic, M. Feroggio, F. Marinelli, G.Lancini (2008) Factors influencing cell fatty acid composition and A40926 antibiotic complex production in *Nonomuraea* sp. ATCC 39727. *Journal of Industrial Microbiology and Biotechnology* 35:1131-8

R.Gandolfi, R. Villa, S.Jovetic, F. Marinelli, F. Molinari (2008) Use of biocatalysis in pharmaceutical manufacturing. *Bioforum Europe*12:10-12

f.Marinelli(2009) **Antibiotics and *Streptomyces*: the future of antibiotic discovery.** *Microbiology Today* 36:20-23

F.Marinelli (2009) **Chapter 2. From microbial products to novel drugs that target a multitude of disease indications.** *Methods in Enzymology* 458:29-58

J.L.Rojas, J.Martín, J.R.Tormo, F.Vicente, M.Brunati, I.Ciciliato,, D.Losi, S.Van Trappen, J. Mergaert, J.Swings, F. Marinelli, O. Genilloud (2009) Bacterial diversity from benthic mats of Antarctic lakes as a source of new bioactive metabolites. *Marine Genomics* 2:33-41

M.Brunati, J.LRojas, F.Sponga, I.Ciciliato, D.Losi, E.Göttlich, S.de Hoog, O.Genilloud, F. Marinelli (2009) Diversity and pharmaceutical screening of fungi from benthic mats of Antarctic lakes. *Marine Genomics* 2:43-50

D.Romano, G.Molla, L.Pollegioni , F.Marinelli (2009) **Optimization of human d-amino acid oxidase expression in *Escherichia coli*.** *Protein Expression Purification* 68:72-8

G.L.Marcone, L.Carrano, F.Marinelli, F. Beltrametti. (2010). Protoplast preparation and reversion to the normal filamentous growth in antibiotic-producing uncommon

actinomycetes. *Journal of Antibiotics (Tokyo)* 63:83-8

F.Volontè, L.Pollegioni, G.Molla, L.Frattini, F.Marinelli, L.Piubelli (2010) Production of recombinant cholesterol oxidase containing covalently bound FAD in *Escherichia coli*. *BMC Biotechnology* 10:33

G.L.Marccone, F.Beltrametti, E.Binda., L.Carrano, L.Foulston ,A.Hesketh , M.Bibb, F.Marinelli (2010). Novel mechanism of glycopeptide resistance in the A40926 producer *Nonomuraea* sp. ATCC 39727. *Antimicrobial Agents and Chemotherapy* 54:2465-72

G.L.Marccone, L.Foulston, E.Binda., F.Marinelli, M.Bibb, F.Beltrametti (2010). Methods for genetic manipulation of *Nonomuraea* sp. ATCC 39727. *Journal of Industrial Microbiology and Biotechnology* 37:1097-110

S.Jovetic, Y.Zhu, G.L.Marccone, F.Marinelli, J.Tramper (2010). β -lactams and glycopeptide antibiotics: first and last line of defence? *Trends in Biotechnology* 28:596-604

F.Marinelli, A.Tomasz (2010). Antimicrobials, Editorial overview. *Current Opinion in Microbiology* 13:1-4