
BIOGRAPHICAL SKETCH (EN)

NAME	POSIZIONE E TITOLO		
Gianluca Molla	Associate Professor, Dip. di Biotecnologia e Scienze della Vita, Università dell'Insubria (Varese, Italia)		
EDUCATION			
INSTITUTION (PLACE)	TITLE	YEARS(S)	FIELD
Università degli Studi di Milano (Italia)	Degree 5 years (110 e Lode)	1994	Biology
Università degli Studi di Milano (Italia)	Internship	1995	Enzymology
Università degli Studi di Milano (Italia)	PhD	1999	Evolutionary and Developmental Biology
Università degli Studi dell'Insubria Varese (Italia)	Post-Doc	2000-2002	Enzymology

Professional positions:

1998 "Visiting Researcher" in Structural Biochemistry, Konstanz University (Germany)

1999-2007 Consultant for various pharmaceutical companies (ACS DOBFAR SpA, Antibioticos SpA Farmaopera SpA Ingenza Ltd, UK)

2000-2002 Research grant holder at the University of Insubria, Varese (Italy)

2002-2004 Researcher, Dept. of Structural and Functional Biology, University of Insubria, Varese (Italy)

2004 - 2015 Researcher, Dept. of Biotechnology and Life Sciences, University of Insubria, Varese (Italy)

2016 - Present Associate Professor (BIO10, Biochemistry), Dept. of Biotechnology and Life Sciences, University of Insubria, Varese (Italy)

2019 - present President of the Degree Course in Molecular and Industrial Biotechnology

Investments in companies / committees:

2000-present Member of the Organizing Committee of several national and international symposiums (The National Symposium "Protein 2000", The 52nd National Symposium of the Italian Society of Biochemistry and Molecular Biology -2007-, XI Biotechnology National Congress -2012-, 10th International Conference on Protein Stabilization -2014)

2004-present He has collaborated as a "referee" with scientific journals: Analytical Biochemistry, Biotechnology Progress, Computational Biology and Chemistry, FEMS Microbiology Letters, Journal of Chemical Technology and Biotechnology, PLOS ONE.

2004 Member of the Organizing Committee of the "School on Rapid Kinetics Techniques"

2005 Member of the Organizing Committee of the "School on Enzyme Engineering"

2005-present Member of the Italian Society of Biochemistry and Molecular Biology (SIB)

2006 Member of the "Society of Chemical Industry" (SCI)

2006-present Member of the Italian Association for Biocatalysis and Bioseparations "(AIBB)

2010 Member of the Organizing Committee of the "School on Protein Engineering"

2010 Winner of the "Mario Ripa" Prize awarded by the Italian Society of Biochemistry and Molecular Biology to the best national research project in the field of biochemistry. Project: A new mechanism of glyphosate tolerance by means of protein engineering

2010-present Member of the Teaching Committee of the PhD in Analysis, Protection and Management of Biodiversity - University of Insubria, Varese (Italy)

2012 Member of the editorial board of the IRSN Biotechnology magazine

2013-present Member of the Teaching Body of the Doctoral Program in Biotechnology, Biosciences and Surgical Technologies - University of Insubria, Varese (Italy)

2014-2018 Website Management of the Italian Society of Biochemistry and Molecular Biology

2015 Member of the Organizing Committee of the "International School on Enzyme Discovery"

2015 Member of the "New York Academy of Science"

2016 Review editor of the international scientific magazine "Frontiers in Cell and Developmental Biology and Molecular Biosciences".

2017 Guest Editor of the international scientific journal BBA - Proteins and Proteomics

Scientific interests:

The research activity of prof. Gianluca Molla regards:

- the study of the relationship between structure and function of enzymes, in particular of flavoproteins oxidase. These enzymes have been studied by means of multidisciplinary approaches: kinetic studies (at steady-state and performance status), structural studies (eg X-ray crystallography), computational and protein engineering approaches. In particular the prof. Molla was involved in the characterization of numerous wild-type and i-type enzymes of industrial interest (eg DAAO from different organisms, L-amino acid deaminase and cholesterol oxidase bacterial, glycine oxidase from *Bacillus* (GO), cephalosporin acylase from *Pseudomonas* (VAC), etc.) or ii) of human origin (eg proteins D-aspartate oxidase, proline oxidase, DAAO and pLG72). Some of these proteins, involved in the regulation of the concentration of neuromodulators at the level of the central nervous system, are implicated in important pathologies including schizophrenia, ALS, etc.

- the in vitro evolution (through rational mutagenesis and "random mutagenesis") of new enzymatic activities not present in nature (VAC, DAAO from yeast, GO and proteolytic enzymes) in order to obtain enzymes for the realization of biosensors or for the use as biocatalysts in synthesis or deracemization reactions. More recently, Dr. Molla has been involved in the identification and characterization of L-amino acid oxidase and microbial deaminases in order to obtain new biocatalysts of biotechnological interest. Several flavoenzymes produced through these approaches have been used for the production of biosensors for the analytical determination of D-amino acids and for biocatalysis reactions. These studies have been supported by computational approaches such as the study of the interaction between proteins and ligands through automatic docking and innovative molecular dynamics approaches. Eg., Molecular docking studies conducted in silico have allowed the development of new inhibitors of human D-amino acid oxidase.

- development of heterologous expression systems (prokaryotes and eukaryotes) in order to obtain recombinant proteins in an appreciable quantity for applications on an industrial scale.

- Computational approaches applied to the study of proteins (in silico studies) such as the study of the interaction between macromolecules and ligands through molecular docking; the study of oxygen diffusion modality within flavoproteins oxidase (in particular of D-amino acid oxidase); the study of protein dynamics by classical molecular dynamics, Steered MD and Scaled MD.

- the study of the biotechnological use of enzymes (as biocatalysts) to produce antibiotic intermediates and other biomedical compounds or as biological elements of biosensors.

Participation in funded projects

The professor. Gianluca Molla has participated in 11 projects (9 as "principal investigator") of various agencies (MIUR, Lombardy Region, Cariplo Foundation, etc.). He has also been a consultant for several biotechnology companies: ACS DOBFAR, Antibioticos, Farmaopera, Ingenza, UK. He also held 4 research contracts (2017-2018).

Participation in congresses

The professor. Molla has participated in more than 25 conferences, with 15 oral presentations (of which 9 as invited speaker).

Publications

Prof. Molla is the author of more than 75 publications in major international journals in the fields of biochemistry, molecular and structural biology and biotechnology. Overall H-index equal to 29 (2259 total citations, source: Web of Science, January 2019). Considering the last 10 years (2008-2017), the H-index is equal to 16, a value that is positioned in the top 15% of the publications of associate professors belonging to the BIO / 10 Disciplinary Scientific Sector.

Furthermore, prof. Molla is the author of 1 patent and more than 150 communications at national and international conferences.

20 selected publications (in chronological order)

1. Umhau S, Pollegioni L, Molla G, Diederichs K, Welte W, Pilone MS, Ghisla S. The x-ray structure of D-amino acid oxidase at very high resolution identifies the chemical mechanism of flavin dependent substrate dehydrogenation Proc. Natl. Acad. Sci. USA, **2000**;97:12463-8.
2. Pollegioni L, Diederichs K, Molla G, Umhau S, Welte W, Ghisla S, Pilone MS. Yeast D-amino acid oxidase: structural basis of its catalytic properties. J. Mol. Biol. 2002;324:535-46.
3. Sacchi S, Lorenzi S., Molla G., Pilone MS., Rossetti C, Pollegioni L. Engineering the substrate specificity of D-amino-acid oxidase J. Biol. Chem. **2002**;277:27510-6
4. Molla G, Motteran L, Job V, Pilone MS, Pollegioni L. Kinetic mechanisms of glycine oxidase from *Bacillus subtilis*. Eur J Biochem. 2003;270(7):1474-82.
5. Mortl M, Diederichs K, Welte W, Molla G, Motteran L, Andriolo G, Pilone MS, Pollegioni L. Structure-function correlation in glycine oxidase from *bacillus subtilis*. J. Biol. Chem. **2004**;279(28):29718-27
6. Caligiuri A, D'Arrigo P, Rosini E, Tessaro D, Molla G, Servi S, Pollegioni L. Enzymatic conversion of unnatural amino acids by yeast D-amino acid oxidase. Advanced Synthesis and Catalysis 2006;348(15):2183-2190
7. Pollegioni L, Piubelli L, Sacchi S, Pilone MS, Molla G. Physiological functions of D-amino acid oxidases: from yeast to humans. Cell Mol Life Sci. **2007**;64(11):1373-94. Review.
8. Sacchi S, Bernasconi M, Martineau M, Mothet JP, Ruzzene M, Pilone MS, Pollegioni L, Molla G. pLG72 modulates intracellular D-serine levels through its interaction with D-amino acid oxidase: Effect on schizophrenia susceptibility. J Biol Chem. **2008**;283(32):22244-56.
9. Pedotti M, Rosini E, Molla G, Moschetti T, Savino C, Vallone B, Pollegioni L. Glyphosate resistance by engineering the flavoenzyme glycine oxidase. J Biol Chem. **2009** 284(52):36415-23.
10. Saam J, Rosini E, Molla G, Schulten K, Pollegioni L, Ghisla S. O₂ reactivity of flavoproteins: dynamic access of dioxygen to the active site and role of a H⁺ relay system in D-amino acid oxidase. J Biol Chem. **2010**;285(32):24439-46.
11. Pollegioni L, Molla G. New biotech applications from evolved D-amino acid oxidases. Trends Biotechnol. 2011 Jun;29(6):276-83. Review.

12. Sacchi S, Caldinelli L, Cappelletti P, Pollegioni L, Molla G. Structure-function relationships in human D-amino acid oxidase. *Amino Acids*. 2012;43(5):1833-50. Review.
13. Golden E, Paterson R, Tie WJ, Anandan A, Flematti G, Molla G, Rosini E, Pollegioni L, Vrielink A. Structure of a class III engineered cephalosporin acylase: comparisons with class I acylase and implications for differences in substrate specificity and catalytic activity. *Biochem J*. 2013 Apr 15; 451(2):217-26.
14. Hopkins SC, Heffernan ML, Saraswat LD, Bowen CA, Melnick L, Hardy LW, Orsini MA, Allen MS, Koch P, Spear KL, Foglesong RJ, Soukri M, Chytil M, Fang QK, Jones SW, Varney MA, Panatier A, Oliet SH, Pollegioni L, Piubelli L, Molla G, Nardini M, Large TH. Structural, Kinetic, and Pharmacodynamic Mechanisms of d-Amino Acid Oxidase Inhibition by Small Molecules. *J Med Chem*. 2013 May 9;56(9):3710-24.
15. Molla G, Nardini M, Motta P, D'Arrigo P, Panzeri W, Pollegioni L. Aminoacetone oxidase from *Streptococcus oligofermentans* belongs to a new three-domain family of bacterial flavoproteins. *Biochem J*. 2014 Dec 15;464(3):387-99.
16. Rosini E, Piubelli L, Molla G, Frattini L, Valentino M, Varriale A, D'Auria S, Pollegioni L. Novel biosensors based on optimized glycine oxidase. *FEBS J*. 2014;281(15):3460-72.
17. Motta P, Molla G, Pollegioni L, Nardini M. Structure-Function Relationships in L-Amino Acid Deaminase, a Flavoprotein Belonging to a Novel Class of Biotechnologically Relevant Enzymes. *J Biol Chem*. 2016 May 13;291(20):10457-75.
18. Molla G, Melis R, Pollegioni L. Breaking the mirror: L-Amino acid deaminase, a novel stereoselective biocatalyst. *BIOTECHNOLOGY ADVANCES*. 2017; 35(6): 657-668
19. Molla G. Competitive Inhibitors Unveil Structure/Function Relationships in Human D-Amino Acid Oxidase. *FRONTIERS IN MOLECULAR BIOSCIENCES*. 2017; 4. DOI: 10.3389/fmolb.2017.00080
20. Melis R, Rosini E, Pirillo V, et al. In vitro evolution of an L-amino acid deaminase active on L-1-naphthylalanine. *CATALYSIS SCIENCE & TECHNOLOGY* 2018; 8(20):5359-5367

Patents

1. Pollegioni L., Pitone M., Molla G., Cucchetti E., Verga R., Cabri W. And Antibioticos SpA. US2005158818: Enzymes with cephalosporin C acylase activity obtained by site-directed, random or "site-saturation" mutagenesis of a native sequence optimized for expression in *E. coli*. July, 2005

Varese, 18 July 2019

Prof. Gianluca Molla

