



Gianluca Molla

 UNIVERSITY OF INSUBRIA



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Biography

Gianluca Molla was born in Varese, Italy, in 1969.

He studied Biological Sciences at the University of Milan where he received his Degree in 1994. In 1996 he joined the research group directed by Prof. M. Pilone and L. Pollegioni in Varese (Functional Post-Genomics and Protein Engineering Laboratory) at the Dept. of Structural and Functional Biology of the University of Insubria, where he currently works.

In 1999 Gianluca Molla received his Ph.D. in Developmental and Evolutionary Biology. During his Ph.D. research activity, in 1998, he spent several months as a research fellow in the laboratories directed by Prof. S. Ghisla (Flavoproteins Biochemistry) and by Prof. W. Welte (Protein Crystallography) at the University of Konstanz (Germany).

From 2000 to 2002 Gianluca Molla carried out his research activity as a Post-Doc fellow.

Since 2002 Gianluca Molla has been employed as an Assistant Professor at the University of Insubria:

- from 2002 to 2004 at the Dept. of Structural and Functional Biology;
- in 2004 he moved, as a co-founder, to the newly established Dept. of Biotechnology and Molecular Sciences still in Varese.

Gianluca Molla was a member of the organizing committee of the School on Rapid Kinetics Techniques (in 2004), the School on Enzyme Engineering (in 2005) and the National Symposium "Proteine 2000" for the Italian Society of Biochemistry and Molecular Biology.

He is a referee for the Journal of Chemical Technology & Biotechnology

Qualifications and awards

1999 Ph.D. in Developmental and Evolutionary Biology, Università degli Studi di Milano, Italy, Thesis title: "3D structure and site directed mutagenesis of the *Rhodotorula gracilis* D-amino acid oxidase: evolutive comparison with other D-amino acid oxidases" (in Italian).

1994 Degree in Biological Sciences, Università degli Studi di Milano,

Italy, Thesis title: "Cloning of the cDNA coding for the D-amino acid oxidase from *R. gracilis*" (in Italian).

Since 2005 Member of the Italian Society of Biochemistry and Molecular Biology

Research interests

The scientific career of Gianluca Molla focused, as a general topic, on the structure-function relationships in enzymatic proteins, as FAD-dependent oxidases (namely D-amino acid oxidase, cholesterol oxidase and glycine oxidase).

The functional and structural properties of the enzyme D-amino acid oxidase (DAAO) from microorganisms, a model protein in enzyme biochemistry, has been investigated by using a multidisciplinary methodological approach: kinetic studies (steady state and pre-steady state kinetics), reaction mechanism studies (substrate specificity, chemical modification and site-directed mutagenesis), structural studies (X-ray crystallography, limited proteolysis), flavin reactivity and protein stability on heating and denaturing agents.

Gianluca Molla has acquired a wide experience on the fundamental aspects of functional and structural properties of flavooxidases and on the functional role of the covalent link of the flavin coenzyme. In the past few years, the experience in structural and functional biology of Gianluca Molla has been widely exploited in the field of protein biotechnology: DAAO (participation to contracts with the pharmaceutical companies Antibioticos and ACS Dobfar), acylases (contract with Antibioticos, 2002-2004) have been employed as biocatalysts. The same enzymatic reaction has been used for the production of a prototype biosensor for the analytical determination of D-amino acids.

In last five years, Gianluca Molla specialised in the evolution of enzymatic activities by using rational (site-directed mutagenesis) and directed evolution (random and site-saturation mutagenesis) methods. These investigations allowed the production of a new enzymatic activity in the bioconversion of cephalosporin C (contract with Antibioticos and patent pending), and a new DAAO activity which is able to oxidise both neutral and acidic D-amino acids.

As a complementary approach to his biochemical studies, Gianluca Molla is also interested in computational techniques for the analysis of protein 3D structure and the building of protein 3D models; he is also interested in in silico methods for the automated docking of small ligands to macromolecules.

Teaching experience and appointments

Teaching activities:
Enzymology
Applied Biochemistry
Industrial Biochemistry

Lecturer for the School on Rapid Kinetics Techniques (in 2004) and on Enzyme Engineering (in 2005) organized by the Italian Society of Biochemistry and Molecular Biology.

Representative publications

1: Pollegioni L, Lorenzi S, Rosini E, Marcone GL, Molla G, Verga R, Cabri W, Pilone MS.

Evolution of an acylase active on cephalosporin C.
Protein Sci. 2005 Oct 31;

2: Molla G, Bernasconi M, Sacchi S, Pilone MS, Pollegioni L.
Expression in *Escherichia coli* and in vitro refolding of the human protein pLG72.
Protein Expr Purif. 2005 Sep 22;

3: Caldinelli L, Iametti S, Barbiroli A, Bonomi F, Fessas D, Molla G, Pilone MS, Pollegioni L.
Dissecting the structural determinants of the stability of cholesterol oxidase containing covalently bound flavin.
J Biol Chem. 2005 Jun 17;280(24):22572-81.

4: Boselli A, Piubelli L, Molla G, Sacchi S, Pilone MS, Ghisla S, Pollegioni L.
On the mechanism of *Rhodotorula gracilis* D-amino acid oxidase: role of the active site serine 335.
Biochim Biophys Acta. 2004 Oct 1;1702(1):19-32.

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 Jul 9;279(28):29718-27.

6: Sacchi S, Rosini E, Molla G, Pilone MS, Pollegioni L.
Modulating D-amino acid oxidase substrate specificity: production of an enzyme for analytical determination of all D-amino acids by directed evolution.
Protein Eng Des Sel. 2004 Jun;17(6):517-25.

8: Pollegioni L, Caldinelli L, Molla G, Sacchi S, Pilone MS.
Catalytic properties of D-amino acid oxidase in cephalosporin C bioconversion: a comparison between proteins from different sources.
Biotechnol Prog. 2004 Mar-Apr;20(2):467-73.

9: Piubelli L, Molla G, Caldinelli L, Pilone MS, Pollegioni L.
Dissection of the structural determinants involved in formation of the dimeric form of D-amino acid oxidase from *Rhodotorula gracilis*: role of the size of the betaF5-betaF6 loop.
Protein Eng. 2003 Dec;16(12):1063-9.

10: Molla G, Motteran L, Piubelli L, Pilone MS, Pollegioni L.
Regulation of D-amino acid oxidase expression in the yeast *Rhodotorula gracilis*.
Yeast. 2003 Sep;20(12):1061-9.

11: Molla G, Motteran L, Job V, Pilone MS, Pollegioni L.
Kinetic mechanisms of glycine oxidase from *Bacillus subtilis*.
Eur J Biochem. 2003 Apr;270(7):1474-82.

12: 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 Nov 29;324(3):535-46.

13: Piubelli L, Caldinelli L, Molla G, Pilone MS, Pollegioni L.

Conversion of the dimeric D-amino acid oxidase from *Rhodotorula gracilis* to a monomeric form. A rational mutagenesis approach. *FEBS Lett.* 2002 Aug 28;526(1-3):43-8.

14: 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 Jul 26;277(30):27510-6.

15: Job V, Molla G, Pilone MS, Pollegioni L.

Overexpression of a recombinant wild-type and His-tagged *Bacillus subtilis* glycine oxidase in *Escherichia coli*. *Eur J Biochem.* 2002 Mar;269(5):1456-63.

16: Pollegioni L, Harris CM, Molla G, Pilone MS, Ghisla S.

Identification and role of ionizing functional groups at the active center of *Rhodotorula gracilis* D-amino acid oxidase. *FEBS Lett.* 2001 Nov 2;507(3):323-6.

17: Motteran L, Pilone MS, Molla G, Ghisla S, Pollegioni L.

Cholesterol oxidase from *Brevibacterium sterolicum*. The relationship between covalent flavinylation and redox properties. *J Biol Chem.* 2001 May 25;276(21):18024-30

18: 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 U S A.* 2000 Nov 7;97(23):12463-8.

19: Pollegioni L, Porrini D, Molla G, Pilone MS.

Redox potentials and their pH dependence of D-amino acid oxidase of *Rhodotorula gracilis* and *Trigonopsis variabilis*. *Eur J Biochem.* 2000 Nov;267(22):6624-32.

20: Molla G, Porrini D, Job V, Motteran L, Vegezzi C, Campaner S, Pilone MS, Pollegioni L.

Role of arginine 285 in the active site of *Rhodotorula gracilis* D-amino acid oxidase. A site-directed mutagenesis study. *J Biol Chem.* 2000 Aug 11;275(32):24715-21.

21: Harris CM, Molla G, Pilone MS, Pollegioni L.

Studies on the reaction mechanism of *Rhodotorula gracilis* D-amino acid oxidase. Role of the highly conserved Tyr-223 on substrate binding and catalysis. *J Biol Chem.* 1999 Dec 17;274(51):36233-40.

22: Molla G, Vegezzi C, Pilone MS, Pollegioni L.

Overexpression in *Escherichia coli* of a recombinant chimeric

Rhodotorula gracilis d-amino acid oxidase.
Protein Expr Purif. 1998 Nov;14(2):289-94.

23: Pollegioni L, Molla G, Campaner S, Martegani E, Pitone MS.
Cloning, sequencing and expression in *E. coli* of a D-amino acid
oxidase cDNA from *Rhodotorula gracilis* active on cephalosporin C.
J Biotechnol. 1997 Oct 17;58(2):115-23.