

BIOGRAPHICAL SKETCH

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NAME: Marco Nardini

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Full professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Genoa (Genoa, Italy)	Laurea	12/1993	Physics
University of Groningen (Groningen, The Netherlands)	Ph.D.	06/2000	Biophysical Chemistry
Advanced Biotechnology Center (Genoa, Italy)	Postdoc	04/2001	Structural Biology
University of Genoa (Genoa, Italy)	postdoc	12/2002	Biophysics and Structural Biology

A. Personal Statement

Prof. Marco Nardini (ORCID: 0000-0002-3718-2165) has been working in the field of structural biology and biophysics since 1993. Over the years, the Nardini's lab has been deeply involved in the development of research networks with research groups in Italy and abroad to integrate synergistically structural biology with other more functional approaches. Molecular biology, biophysics, X-ray crystallography, together with simulative methods (dynamics, modeling, and docking) and, more recently, cryo-EM, build the core of all Nardini lab's projects, which are based on medium-throughput approaches to protein production, biochemical and biophysical characterization, and crystallographic, SAXS, and cryo-EM analyses. Current research activities are focused on proteins and enzymes (flavoenzymes¹, hemoproteins², cold-adapted proteins³), and DNA-protein complexes (transcription factors)^{4,5} related to basic questions in biology and to biomed/biotech applications, including protein function, inhibition, and drug development.

References:

1. Molla, G. *et al.* Structure and kinetic properties of human D-aspartate oxidase, the enzyme-controlling D-aspartate levels in brain. *The FASEB J.* (2020) 34:1182-1197. doi:10.1096/fj.20190 1703R.
2. De Henau, S. *et al.* A redox signalling globin is essential for reproduction in *Caenorhabditis elegans*. *Nature Communications* (2015) Dec 1;6:8782. doi: 10.1038/ncomms9782.
3. Gourlay, L.J. *et al.* Structural determinants of cold activity and glucose tolerance of a family 1 glycoside hydrolase (GH1) from Antarctic *Marinomonas* sp. ef1. *FEBS J.* (2024) Jul;291(13):2897-2917. doi: 10.1111/febs.17096.
4. Nardini, M. *et al.* Sequence-specific transcription factor NF-Y displays histone-like DNA binding and H2B-like ubiquitination. *Cell* (2013) Jan 17;152(1-2):132-43. DOI: 10.1016/j.cell.2012.11.047
5. Tiberi, M. *et al.* Structural basis of Nuclear Factor 1-X DNA recognition provides prototypic insight into the NFI family. *Nature Communications* (2025) Nov 19;16(1):10170. doi: 10.1038/s41467-025-65186-0.

You can access the full list of Marco Nardini's publications on PubMed through his lab page:
<https://nardini-lab.unimi.it/people/marco-nardini/> → PubMed

Grants:

In the last 15 years Marco Nardini has secured more than 600 k€ for his research:
- PI of Seed4Innovation 2024 grant (University of Milan)

- PI of the preclinical research contract for research institutes "X-ray crystallography studies on neurotrophins and their ligands", in collaboration with Dompe farmaceutici S.p.A. (2022)
- Responsible of Unit (University of Milan) for the project PRIN2022 (2022K9SJ27) "Oligomerization of zinc-finger MucR protein as a key for bacterial genomic DNA structuring" (Italian Ministry of Education and Research)
- Responsible of Unit (University of Milan) for the project PRIN2020 (2020K53E57) "Biochemical modulation of D-aspartate metabolism in brain functions" (Italian Ministry of Education and Research)
- PI of the AIRC INVESTIGATOR GRANT - IG 2014 (Rif 15267) "Structural based inhibition of the NF- κ B transcription factor involved in cell transformation and in tumorigenesis" (Italian Cancer Research Association)
- Responsible of Unit (University of Milan) for the project CARIPLO FOUNDATION, 2010 (2010-0652), "Outer membrane biogenesis in Gram-negative bacteria as a target for innovative antibacterial drugs"(CARIPLO foundation)

Statistics:

H-index: 38 (SCOPUS, January 2026)

Total number of publications 115 (16 first author, 22 corresponding author) (SCOPUS, January 2026)

Total citations: 5321 (SCOPUS, January 2026)

1 European patent, 1 Italian patent request

13 invited oral presentations and 55 poster communications at national and international meetings

93 protein structure depositions at the Protein Data Bank (<http://www.rcsb.org/pdb>).

B. Positions, Scientific Appointments, and Honors

Academic

- 2022 –2025: Deputy Deen of the Dept. of Biosciences, University of Milan (Italy)
- 2022-present: Member of the Scientific Committee of UNITECH-NOLIMITS, University of Milan (Italy) (<https://www.unimi.it/en/research/places-organizations-and -infrastrutture/unitech/nolimits-unitech>)
- 2017 – 2023: President of the "Teaching Committee of Industrial Biotechnology" of the University of Milan
- 2017 – 2023: Coordinator of the international Master programme of "Molecular Biotechnology and Bioinformatics", University of Milan (Italy)
- Since 2017: Full Professor of Biochemistry, Dept of Biosciences, University of Milan, Italy
- 2014 – 2023: Member of the Faculty Committee of Science and Technology, University of Milan (Italy)
- 2014 – 2015: Member of the National Committee for the Italian Professional Biologist qualification, University of Milan (Italy)
- 2013 – present: Member of the Ph.D. School in Molecular and Cellular Biology at the University of Milan (Italy)
- 2010 – 2017: Associate Professor in Biochemistry, Dept. of Biosciences, University of Milan, Italy
- 2005 – 2010: Assistant Professor in Biochemistry, Dept of Biomolecular Sciences and Biotechnology, University of Milan, Italy
- 2002 – 2005: Research Associate, National Institute for the Physics of Matter (INFN), Dept. of Physics, University of Genoa, Italy

On 30/07/2002, I was awarded the European Doctorate in Biotechnology by the European Association for Higher Education in Biotechnology.

Editorial

- 2021-2025: Member of the editorial board of Frontiers in Molecular Biosciences
- 2021-2022: Guest Editor of Frontiers in Molecular Biosciences (Research topic: "Integration of Structural Biology Data in Lead Drug Discovery and Optimization" (<https://www.frontiersin.org/researchtopics/20517/integration-of-structuralbiology- data-in-lead-drug-discovery-and-optimization>))

Scientific memberships

- Since 2018: Member of the Italian Society of Biochemistry and Molecular Biology (SIB)
- 2017 – 2024: Member of the Italian Society of the Crystallography (AIC)

Referee for the following scientific journals

“Academia Biology” (ISSN:2837-4010); “Andrology” (ISSN: 2047-2927); “BBA-Proteins and Proteomics” (ISSN:1570-9639); “Biomolecules” (EISSN: 2218-273X); “Biopolymers” (ISSN: 1097-0282); “Chemical Biology” (ISSN: 1554-8929), “Crystals” (ISSN 2073-4352), “FEBS J.” (ISSN: 1742-464X); “Frontiers in Molecular Sciences” (ISSN:2296-889X), “IUBMB Life” (ISSN: 1521-6551); “Journal of Structural Biology” (ISSN:1047-8477); “The Plant Cell” (ISSN: 1040-4651); “Nature Communications” (ISSN 2041-1723).

Referee for the following grant institution

- Since 2017: Member of REPRISE (Register of Expert Peer-Reviewers for Italian Scientific Evaluation, Italian Ministry of Education, University and Research - MIUR)
- Since 2022: Member of the Independent Review Board for Instruct-ERIC
- 2014: Grant Reviewer, Scientific Independence of young Researchers (SIR) program 2014, Italian Ministry of Education, University and Research - MIUR
- 2012: Grant Reviewer, ECHO programme-Chemistry in Relation to Biological and Medical Sciences 2012 CW, Netherlands Organisation for Scientific Research (The Netherlands)
- 2010: Grant Reviewer, Contrats doctoraux, Université Franco-Italienne (Italy/France)

Organisation of scientific national and international meetings

- 2026: Member of the Scientific Committee of the Congress “Biotech2026-Frontiers in Italian Biotechnology”, which will take place in Verona, June 24–26, 2026
- 2024: Chair of the microsimposium on “Nucleic acid-protein interactions” at the 34th European Crystallography Congress (ECM34), Padua 26/08/2024-02/09/2024
- 2017: Member or the Organizing Committee of the PhD Workshop “Experimental methods applied to biological systems. Biology and physics working together”, Milan, September 12-14, 2017
- 2016: Member of the Scientific Committee of the XIX International Conference “Oxygen Binding and Sensing Proteins (O2BIP)”, Hamburg, September 12-16, 2016
- 2014: Member or the Organizing Committee of the PhD Workshop “Frontiers in structural biology”, Milan, November 24-25, 2014

C. Contributions to Science

1. Early scientific work (1999-2007)

The first part of my career (Ph.D. at the University of Groningen, The Netherlands) focused on X-ray crystallographic studies of lipolytic enzymes, particularly members of the α/β -hydrolase fold family, including lipases, esterases, and epoxide hydrolases. The aim was to elucidate their structure–function relationships and explore their potential biotechnological applications. Among other publications, this line of research resulted in one of the most cited reviews in the field: Nardini M. & Dijkstra B., *Curr Opin Struct Biol* 1999, 9(6):732-7, cited 778 in Scopus.

Main publications

1. Tiesinga, J.J. *et al.* Structural basis of phospholipase activity of *Staphylococcus hyicus* lipase. *J Mol Biol.* (2007) Aug 10;371(2):447-56. doi: 10.1016/j.jmb.2007.05.041
2. Nardini, M. *et al.* Crystal structure of *Pseudomonas aeruginosa* lipase in the open conformation. The prototype for family I.1 of bacterial lipases. *J Biol Chem.* (2000) Oct 6;275(40):31219-25. doi: 10.1074/jbc.M003903200
3. Nardini, M. *et al.* The X-ray structure of epoxide hydrolase from *Agrobacterium radiobacter* AD1. An enzyme to detoxify harmful epoxides. *J Biol Chem.* (1999) May 21;274(21):14579-86. doi: 10.1074/jbc.274.21.14579
4. Nardini, M. & Dijkstra, B.W. α/β hydrolase fold enzymes: the family keeps growing. *Curr Opin Struct Biol.* (1999) Dec;9(6):732-7. doi: 10.1016/S0959-440X(99)00037-8
5. Rink, R. *et al.* Mutation of tyrosine residues involved in the alkylation half reaction of epoxide hydrolase from *Agrobacterium radiobacter* AD1 results in improved enantioselectivity. *J Am Chem Soc.* (1999) 121:7417-7418. doi: 10.1021/ja990501o

2. Hemoproteins (1993-present)

One of my main research lines has consistently focused on the structural analysis of the function and adaptation/evolution of hemoproteins, particularly globins. My work has concentrated on globins with unusual structures and/or distinctive functional properties, including truncated hemoglobins, neuroglobins, cytoglobins, protoglobins, and globin-coupled sensors. To date, I have published more than 50 scientific papers on this topic.

Main publications

1. Pesce, A. *et al.* Structural and dynamic characterization of the hexa-coordinated globin from *Spisula solidissima*. *J Inorg Biochem.* (2023) Sep;246:112289. doi: 10.1016/j.jinorgbio.2023.112289
2. Germani, F. *et al.* Structural and functional characterization of the globin-coupled sensors of *Azotobacter vinelandii* and *Bordetella pertussis*. *Antioxid Redox Signal.* (2020) Feb 20;32(6):378-395. doi: 10.1089/ars.2018.7690
3. Pesce, A. *et al.*, The N-terminal pre-A region of *Mycobacterium tuberculosis* 2/2HbN promotes NO-dioxygenase activity. *FEBS J.* (2016) Jan;283(2):305-22. doi: 10.1111/febs.13571
4. De Henau, S. *et al.* A redox signalling globin is essential for reproduction in *Caenorhabditis elegans*. *Nature Communications* (2015) Dec 1;6:8782. doi: 10.1038/ncomms9782
5. Nardini, M. *et al.* Archaeal protoglobins structure indicates new ligand diffusion paths and modulation of haem-reactivity. *EMBO Rep.* (2008) Feb;9(2):157-63. doi: 10.1038/sj.embor.7401153

3. Cold adapted proteins (2015-present)

The aim of this work is to shed light on the molecular strategies by which cold-adapted proteins enhance their flexibility while maintaining sufficient stability for biological function. To date, in my lab we have solved the structures of several psychrophilic proteins and enzymes from diverse origins, including a truncated hemoglobin, a cytoglobin, an acyl aminoacyl peptidase, a β -galactosidase, and a glycoside hydrolase. Within this research line, we also determined the structure, at atomic resolution (0.84 Å), of an antifreeze protein capable of protecting organisms from freezing damage under permanent sub-zero conditions or seasonal temperature drops. Owing to these properties, antifreeze proteins have attracted considerable interest for potential applications in food processing, cryopreservation, cryosurgery, fisheries and agriculture, as well as in the development of anti-icing materials.

Main publications

1. Gourlay, L.J. *et al.* Structural determinants of cold activity and glucose tolerance of a family 1 glycoside hydrolase (GH1) from Antarctic *Marinomonas* sp. ef1. *FEBS J.* (2024) Jul;291(13):2897-2917. doi: 10.1111/febs.17096
2. Mangiagalli, M. *et al.* The co-existence of cold activity and thermal stability in an Antarctic GH42 β -galactosidase relies on its hexameric quaternary arrangement. *FEBS J.* (2021) Jan;288(2):546-565. doi: 10.1111/febs.15354
3. Mangiagalli, M. *et al.* Structure of a bacterial ice binding protein with two faces of interaction with ice. *FEBS J.* (2018) May;285(9):1653-1666. doi: 10.1111/febs.14434
4. Brocca, S. *et al.* A bacterial acyl aminoacyl peptidase couples flexibility and stability as a result of cold adaptation. *FEBS J.* (2016) Dec;283(23):4310-4324. doi: 10.1111/febs.13925
5. Giordano, D. *et al.* Structural flexibility of the heme cavity in the cold-adapted truncated hemoglobin from the Antarctic marine bacterium *Pseudoalteromonas haloplanktis* TAC125. *FEBS J.* (2015) Aug;282(15):2948-65. doi: 10.1111/febs.13335

Flavoenzymes (2012-present)

In my lab, we study flavoproteins and other enzymes involved in human pathologies, as well as wild-type and engineered variants with biotechnological potential. Recently, our work has focused on FAD-dependent enzymes catalyzing L- and D-amino acid oxidation, particularly on the structural characterization of D-aspartate oxidase. This enzyme degrades D-aspartate, a neuromodulator crucial for brain development and neurotransmission, and plays an important role in regulating its levels, with implications for neural function and disorders such as schizophrenia and neurodegeneration.

Main publications

1. Molla, G. *et al.* Structure and kinetic properties of human D-aspartate oxidase, the enzyme-controlling d-aspartate levels in brain. *The FASEB J.* (2020) 34:1182-1197. doi: 10.1096/fj.201901703R
2. Motta, P. *et al.* 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. doi: 10.1074/jbc.M115.703819
3. Molla, G. *et al.* Aminoacetone oxidase from *Streptococcus oligofermentans* belongs to a new three-domain family of bacterial flavoproteins. *Biochem J.* (2014) Dec 15;464(3):387-99. doi: 10.1042/BJ20140972
4. Hopkins, S.C. *et al.* Structural, kinetic, and pharmacodynamic mechanisms of D-amino acid oxidase inhibition by small molecules. *J Med Chem.* (2013) May 9;56(9):3710-24. doi: 10.1021/jm4002583
5. Caldinelli, L. *et al.* Characterization of human DAAO variants potentially related to an increased risk of schizophrenia. *Biochim Biophys Acta (BBA)-Molecular Basis of Disease* (2013) Mar;1832(3):400-10. doi: 10.1016/j.bbadis.2012.11.019

Transcription factors (2002-present)

My research over the past 25 years has focused on the structural analysis of DNA-binding proteins, particularly transcription factors (TFs), in complex with their cognate DNA, using X-ray crystallography and cryo-EM. Four major achievements stand out. In 2003 I solved the crystal structure of CtBP/BARS, a dual-function protein involved in transcription co-repression and Golgi membrane fission. In 2013, I solved the crystal structure of the histone-fold TF NF-Y, which binds CCAAT boxes in promoters and regulates genes involved in cell cycle

control, metabolism, and development. The structure revealed the molecular mechanisms of DNA binding and ubiquitination. Since then, we have published six additional studies on NF-Y biology, including post-translational modifications, inhibition, interactions with partner TFs (by cryo-EM), and the structure of plant NF-Y homologs. In 2024, in my lab we determined the structure of MucR, a bacterial transcriptional regulator acting as a global repressor of genes involved in virulence, stress response, and symbiosis. Using cryo-EM and NMR, we uncovered the mechanism of its functional oligomerization required for DNA bridging. In 2025, we solved the structure of Nuclear Factor I-X (NFI), a TF essential for neural stem cell biology, hematopoiesis, muscle development, and oncogenesis. Combining X-ray crystallography and cryo-EM, we identified key structural determinants of activity, providing a framework for interpreting NFI family function and guiding drug design.

Main publications

1. Tiberi, M. *et al.* Structural basis of Nuclear Factor 1-X DNA recognition provides prototypic insight into the NFI family. *Nature Communications* (2025) Nov 19;16(1):10170. doi: 10.1038/s41467-025-65186-0.
2. Chaves-Sanjuan, A. *et al.* Circular oligomeric particles formed by Ros/MucR family members mediate DNA organization in α -proteobacteria. *Nucleic Acids Res.* (2024) Nov 26:gkae1104. doi: 10.1093/nar/gkae1104.
3. Chaves-Sanjuan, A. *et al.* Structural determinants for NF-Y subunit organization and NF-Y/DNA association in plants. *Plant J.* (2021) Jan;105(1):49-61. doi: 10.1111/tpj.15038
4. Nardini, M. *et al.* Sequence-specific transcription factor NF-Y displays histone-like DNA binding and H2B-like ubiquitination. *Cell* (2013) Jan 17;152(1-2):132-43. DOI: 10.1016/j.cell.2012.11.047
5. Nardini, M. *et al.* CtBP/BARS: a dual-function protein involved in transcription co-repression and Golgi membrane fission. *EMBO J.* (2003) 22(12):3122-30. doi: 10.1093/emboj/cdg283