

BIOGRAPHICAL SKETCH

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NAME: Francesca Valetti

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

POSITION TITLE: Associate Professor of Biochemistry

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 Torino (Italy)	MSc	11/1992	Biology
University of Torino (Italy)	PhD	07/1997	Protein Chemistry
Imperial College London (UK)	Postdoctoral	12/1998	Redox Protein Engineering

A. Personal Statement

I am an Associate Professor of Biochemistry, and my research is focused on studying and enhancing the performances of enzyme catalysts for energy production, green processes and bioremediation. The applied strategies are enzymology, protein engineering, protein design and modelling by site directed mutagenesis and by novel directed evolution techniques (iterative site saturation mutagenesis). A particular emphasis, starting from 2008, is given to the study of [FeFe]-hydrogenases for molecular hydrogen production, by producing recombinant variants and thus evolving natural bio-catalysts for artificial devices and solar driven bioelectrodes. The research includes interfacing of enzymes to innovative materials such as semiconductors and light-activated materials. Another applicative perspective is focused to the bio-production of specific chemicals and building blocks by enzyme-driven reactions, in order to propose innovative and sustainable bio-based industrial processes.

Track-record

Author of 34 publications, 4 reviews, 3 conference papers and 2 editorial in international journals
ISI 1 patent. H-index:19, i10-index:27, 867 citations (source: Scopus). Participating in 14 international and 13 national congresses. Invited speaker at 7 congresses and 2 residential PhD Schools.

Ongoing and recently completed projects (participation and direction -last 5 years-) that I would like to highlight include:

- 2023-ongoing National Coordinator of PRIN project MORF “Molecular determinants of Oxygen Resistance in a unique [FeFe]-hydrogenase” (€ 111403)
- 2023-ongoing Local coordinator for UNITO unit of PRIN PNRR project SMARFeS “Small

- Molecule Activation by Redesigned iron-sulfur (FeS) proteins” (€ 60000)
- 2022- ongoing Local co-coordinator for UNITO project PERCIVAL (€ 279653) PON Ricerca Industriale e Sviluppo Sperimentale nelle 12 aree di specializzazione individuate dal PNR 2015 – 2020, di cui al Decreto Direttoriale del 13 luglio 2017, n. 1735. (Chimica Verde), approvato dal CIPE.
- 2022- PI for Ex-Post 2020 funding scheme di Fondazione San Paolo (€ 59358) “Generation of Renewable Fuel with Enzyme based Photo Electrochemical Cells-GOPHORCELL”
- 2019-2022 PI for DBIOS, Università di Torino (€ 158760) project SATURNO "Scarti organici e Anidride carbonica Trasformati in carbURanti, fertilizzanti e prodotti chimici; applicazione concreta dell'ecoNomia circolare" finanziato da POR FESR 2014-2020 EU Structural Funds, competitive call su Piattaforma Bioeconomia Regione Piemonte
- 2019-2021 PI Ex-Post funding scheme di Fondazione San Paolo (€ 51380) "A sustainable hybrid platform for enzyme-based biofuel production synergically managing waste"

B. Positions, Scientific Appointments, and Honors

2023-present: Faculty of PhD program of Innovation for the Circular Economy

2022-present: Associate Professor in Biochemistry at University of Torino.

2018-present: Associate Editor for Biotechnology and Applied Biochemistry (Ed. Wiley)

2015-present: Member of The Protein Society

2013-present: Member of the American Chemical Society – ACS

2004–2021: Senior Lecturer in Biochemistry at University of Torino

2001-present: Member of S.B.I.C. Society of Biological Inorganic Chemistry

1999-2004: Permanent staff as research assistant at University of Torino.

1997-1999: Post-doctoral research associate at Biochemistry Department Imperial College London (UK) with an EC sponsored fellowship within the Biotech program

1993-present: Member of the Italian Biochemical Society SIB

C. Contributions to Science

- 1) A new line of research has been initiated at the biochemistry group of the Department of Life Sciences and Systems Biology, directed toward the study of hydrogen-producing enzymes, both for applications in the field of bioenergy and to investigate the details of some aspects of the fine catalytic mechanism of cluster H, peculiar to this enzyme class. The research has been carried out since late 2008, with the participation, in collaboration with Imperial College London (Prof. J. Barber /Prof. Gilardi) in a European project (SOLHYDROMICS project EC program FP7-Energy, Collaborative project 227192-2, coordinated by the Politecnico di Torino) dedicated to the study of the so-called nano-leaf, for couplings of photoactivated systems to hydrogen-producing enzymes. Subsequent developments have involved both more biotechnological aspects, such as the coupling of [FeFe]hydrogenases to electrodes and semiconductor materials, including photoactivatable metal oxides, and the optimization of conditions for hydrogen production from waste biomass, as well as aspects of fundamental biochemistry, including elucidation of the details of the proton transport pathway by site-saturation mutagenesis and characterization of a new enzyme in the class with a mechanism of protection against damage by oxygen, unique reported for this class of enzymes. In the laboratories, equipment and methods have been set up and fine-tuned to express in recombinant form in *E. coli* and work under anaerobic conditions on [FeFe]-sensitive oxygen hydrogenases from *Clostridium acetobutylicum* and from *Chlamydomonas reinhardtii*, to measure their catalytic activity in both consumption and hydrogen production (with a dedicated GC line) and to characterize their redox states by FTIR (defining the method on the equipment already available in the research group). Important national and international scientific

collaborations on this topic have also been initiated with various research groups and innovative companies engaged in the application of biotechnology to renewable energy production.

In detail:

Academic collaboration

- Dr. P.W. King, NREL, Golden, CO, USA (co-author of 3 papers)
- Prof. Elio Giamello e Prof. Mario Chiesa, Dipartimento di Chimica, Università di Torino, Italy (co-authors of 2 papers)
- Prof. Thomas Happe, RUHR-UNIVERSITÄT BOCHUM, Germany (co-author of 1 paper in Nature Comm)
- Prof. Christophe Leger, CNRS, Marseille, France co-author of 1 paper in Nature Comm)
- Prof. Vincent Artero, CEA, Grenoble, France
- Prof. Gustav Berggren, Dept. of Chemistry – Ångström Laboratory Uppsala University, Uppsala, Sweden
- Prof. Maria Lodovica Gullino, DISAFA e Agroinnova, Università di Torino (co-author of 2 papers)

Industrial collaboration

- Dr. Toby Meyer, Solaronix, Aubonne, Switzerland (co-author of 1 paper)
- Dr. Ing. Paola Zitella, Environment Park, Torino, Italy (co-author of 2 papers)
- Prof. Massimo Pugliese, AgriNewTech, Grugliasco, Italy (co-author of 2 papers).

The research resulted in 15 publications of which 11 as corresponding author. 2 regional projects (BIOH2 and HyStrEM), 2 feasibility studies (BIOTHYTAN and COMPIDRO) on EU POR-FESR funds have been funded on this topic and 1 project is ongoing funded by PRIN 2022 national Italian funding Additional supporting funds were obtained on this topic from Compagnia di San Paolo, Torino, Fondazione CRT Lagrange project, DAAD, Erasmus Traineeship.

Currently, research is also expanding to enzymes related to hydrogenases and involved in the reductive conversion of CO₂ to formate, with an additional POR-FESR-funded project 2019-2023 (SATURNO), and a collaboration on this topic with Prof. Golbeck of Penn State University, USA, has been initiated in January 2020.

Relevant papers

Mazzoli, R., Pescarolo, S., Gilli, G., Gilardi, G., **Valetti, F***. Hydrogen production pathways in Clostridia and their improvement by metabolic engineering *Biotechnology Advances*, 73, 108379, 2024, 2

Gasteazoro, F., Catucci, G., Barbieri, L., Gilardi, G., **Valetti, F***. Cascade reactions with two non-physiological partners for NAD(P)H regeneration via renewable hydrogen *Biotechnology Journal*, 19(4), 2300567, 2024, 1

Valetti, F*, Morra, S., Barbieri, L., Sadeghi, S.J., Gilardi, G. Oxygen-resistant [FeFe]hydrogenases: new biocatalysis tools for clean energy and cascade reactions, *Faraday Discussions*, 252, pp. 223–240, 2024

Arizzi M, Morra S, Gilardi G, Pugliese M, Gullino ML, **Valetti F***. Improving sustainable hydrogen production from green waste: [FeFe]-hydrogenases quantitative gene expression RT-qPCR analysis in presence of autochthonous consortia *BIOTECHNOLOGY FOR BIOFUELS* (2021) Volume: 14 Issue 1 Article number 182

Winkler M, Duan J, Rutz A., Felbek C, Scholtysek L, Lampret O, Jaenecke J, Apfel, Gilardi G, **Valetti F**, Fourmond V, Hofmann E, Léger C, Happe T. A safety cap protects hydrogenase from oxygen attack Nature Communications Open Access Volume 12, Issue 1 December 2021 Article number 756

Morra, Simone; Arizzi, Mariaconcetta; **Valetti, Francesca***; Gilardi Gianfranco* Oxygen Stability in the New [FeFe]-Hydrogenase from *Clostridium beijerinckii* SM10 (CbA5H). BIOCHEMISTRY (2016) Volume: 55 Issue: 42 Pages: 5897-5900

Arizzi M, Morra S, Pugliese M, Gullino ML, Gilardi G, **Valetti F***. Biohydrogen and biomethane production sustained by untreated matrices and alternative application of compost waste WASTE MANAGEMENT (2016) Volume: 56 Pages: 151-157

Polliotto V, Morra S, Livraghi S, **Valetti F**, Gilardi G, Giamello E. Electron transfer and H₂ evolution in hybrid systems based on [FeFe]-hydrogenase anchored on modified TiO₂. INTERNATIONAL JOURNAL OF HYDROGEN ENERGY (2016) vol. 41, p. 10547-10556, ISSN: 0360-3199, doi:10.1016/j.ijhydene.2016.05.002

Morra S, Maurelli S, Chiesa M, Mulder DW, Ratzloff MW, Giamello E, King PW, Gilardi G, **Valetti F***. The effect of a C298D mutation in CaHydA [FeFe]-hydrogenase: Insights into the protein-metal cluster interaction by EPR and FTIR spectroscopic investigation. Biochim Biophys Acta. (2015) Oct 16. pii: S0005-2728(15)00212-1. doi: 10.1016/j.bbabo.2015.10.005.

Morra S, Cordara A, Gilardi G, **Valetti F***. Atypical effect of temperature tuning on the insertion of the catalytic iron-sulfur center in a recombinant [FeFe]-hydrogenase. Protein Sci. (2015) Sep 12. doi: 10.1002/pro.2805.

Morra S, **Valetti F**, Sarasso V, Castrignanò S, Sadeghi SJ, Gilardi G. Hydrogen production at high Faradaic efficiency by a bio-electrode based on TiO₂ adsorption of a new [FeFe]-hydrogenase from *Clostridium perfringens*. Bioelectrochemistry (2015) 106(Pt B): 258-62.

Morra S, Mongili B, Maurelli S, Gilardi G, **Valetti F***. Isolation and characterisation of a new [FeFe]-hydrogenase from *Clostridium perfringens*. Biotechnol. Appl. Biochem. (2015) doi: 10.1002/bab.1382.

Morra S, Arizzi, M, Allegra P, La Licata B, Sagnelli F, Zitella P, Gilardi G, **Valetti F***. Expression of different types of [FeFe]-hydrogenase genes in bacteria isolated from a population of a bio-hydrogen pilot-scale plant. Int. J. Hydrogen Energy (2014) 39, 9018-9027.

Morra S, Giraudo A, Di Nardo G, King PW, Gilardi G, **Valetti F***. Site Saturation Mutagenesis Demonstrates a Central Role for Cysteine 298 as Proton Donor to the Catalytic Site in CaHydA [FeFe]-Hydrogenase. PLoS ONE (2012) 7(10): e48400.

Morra S, **Valetti F**, Sadeghi SJ, King PW, Meyer T, Gilardi G. Direct electrochemistry of an [FeFe]-hydrogenase on a TiO₂ electrode. Chem Commun (Camb). (2011) 47(38):10566-8.

2) Study of catechol dioxygenase and related metabolic pathway for applications in biocatalysis and bioremediation

Research has led to the recombinant production of a bacterial catechol 1,2-dioxygenase from *A. radioresistens* S13 that does not require reduction equivalents for molecular oxygen activation and subsequent dearomatization of catechol and its derivatives. Both site-specific mutagenesis results with details of the fine structure-function relationship and its modulation

by certain amino acids have been published, as well as application-related results related to the stabilization of the enzyme for biocatalysis (conversion of catechol to muconic acid for sustainable production of adipic acid) and for bioremediation (degradation of chlorinated derivatives). In addition, studies have also been carried out on the other oxygenase enzymes in the same organism that are metabolically related to the degradation and conversion of toxic aromatic compounds. Groups from other departments of the University of Torino and other Italian universities were involved (Prof. Stefano Bruno, Prof. Andrea Mozzarelli, University of Parma, Prof. Menico Rizzi, University of Piemonte Orientale, Prof. Loredano Pollegioni, Univ. Insubria). The research topic has led to the publication of 10 papers (including 1 as a corresponding author) In addition, an Italian patent has been filed for the encapsulation and stabilization of the enzyme catechol 1,2-dioxygenase WT and its mutants in silica/hormosil gels and their use for bioremediation of materials contaminated with catechols and their derivatives.

Relevant Papers

Elisa Vignali, Loredano Pollegioni, Giovanna Di Nardo, **Francesca Valetti**, Silvia Gazzola, Gianfranco Gilardi, Elena Rosini. Multi-Enzymatic Cascade Reactions for the Synthesis of cis,cis-Muconic Acid Advanced Synthesis & Catalysis, First published: 23 September 2021, DOI: (10.1002/adsc.202100849)

Micalella C, Bruno, S, Mozzarelli A, Caglio R, **Valetti F**, Pessione E, Giunta C. Ormosil gels doped with engineered catechol 1,2 dioxygenases for chlorocatechols bioremediation. Biotechnol. Appl. Biochem. (2014) 61, 297-303.

Caglio, R., Pessione, E., **Valetti**, F., Giunta, C., Ghibaudi, E. An EPR and thermostability investigation of wt and mutant forms of catechol 1,2 dioxygenase from *Acinetobacter radioresistens* S13. Biometals (2013) 26(1):75-84.

Valetti F, Fantuzzi A, Sadeghi SJ, Gilardi G. Iron-based redox centres of reductase and oxygenase components of phenol hydroxylase from *A. radioresistens*: a redox chain working at highly positive redox potentials. Metallomics. (2012) Jan;4(1):72-7.

Micalella C, Martignon S, Bruno S, Pioselli B, Caglio R, **Valetti F**, Pessione E, Giunta C, Rizzi M. X-ray crystallography, mass spectrometry and single crystal microspectrophotometry: A multidisciplinary characterization of catechol 1,2 dioxygenase. Biochim Biophys Acta. (2011) Jun;1814(6):817-23.

Di Nardo G, Roggero C, Campolongo S, **Valetti F**, Trotta F, Gilardi G. Catalytic properties of catechol 1,2-dioxygenase from *Acinetobacter radioresistens* S13 immobilized on nanosponges. Dalton Trans. (2009) Sep 7;(33):6507-12.

Caglio R, **Valetti F***, Caposio P, Gribaudo G, Pessione E, Giunta C. Fine-Tuning of Catalytic Properties of Catechol 1,2-Dioxygenase by Active Site Tailoring. Chembiochem. (2009) 10: 1015-1024

Complete List of Published Work at:

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