CURRICULUM VITAE ET STUDIORUM

Name: ***Mirco*** Family name: ***Dindo***
Place and date of birth: *Isola della Scala (VR, Italy) 22 March 1988*
Address: Via Frate Egidio 2, 06063, Agello, Perugia, Italy
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EDUCATION

- **30th May 2022 - To Date** Assistant Professor, Department of Medicine and Surgery, Section of Biochemistry, University of Perugia, Perugia, Italy

- **October 2021 – 27th May 2022** Staff Scientist at the Okinawa Institute of Science and Technology Graduate University (OIST), Okinawa, Japan.

- **October 2019 – September 2021** JSPS (Japan Society for the Promotion of Science) Postdoctoral fellow at the Okinawa Institute of Science and Technology Graduate University (OIST), Okinawa, Japan.

- **March 2019 – September 2019** Post-doctoral scholar at the Okinawa Institute of Science and Technology, Protein Engineering and Evolution Unit, Okinawa, Japan

- **2018 – February 2019** Post-Doc at the Department of Experimental Medicine, University of Perugia. Project: **"*Development of a small-molecule therapy for PH1 based on the combined administration of B6 vitamers and pharmacological chaperones*"**;

- **2017** Post-Doc at the Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona. Project name:**"*Molecular approaches for the studying of rare disease involving PLP dependent enzymes*"***;*

- **January 2014 - December 2016** Ph.D. in Biomolecular Medicine at the University of Verona (29th September 2017) PhD Thesis: "***Molecular analysis of dimerization and aggregation processes of human alanine:glyoxylate aminotransferase and effect of mutations leading to Primary Hyperoxaluria Type I***";

  - **February-June 2015: visiting student** at the Weizmann Institute of Science in Israel (supervisor: Prof. Dan S Tawfik).

- **July - December 2013** Research fellow at the University of Verona, Department of Life and Reproduction Sciences, Section of Biological Chemistry. Project title "***Biochemical approaches for the development of new treatment strategies for the Primary Hyperoxaluria type I****";*

- **March 2013** Master degree in Bioinformatic and Medical Biotechnology at the University of Verona;

- **2010** Undergraduate in Medical Laboratory Scientist at the University of Verona;

- **2007** High-school diploma of "Chemical-biological laboratory technician" at Technical College "E. Fermi" of Verona.

Scientific activity

The research activity of Dr. Dindo is mainly focused on the study of the functional properties of pyridoxal 5'-phosphate dependent enzymes whose deficiency causes autosomal recessive disorders. He contributes to the characterization of several pathogenic variants by a combination of computational and biochemical analyses on the purified recombinant proteins paired with cell biology studies. In particular his research is focused on the study of:

- **Human AGT or alanine:glyoxylate aminotransferase**, a PLP dependent enzyme involved in the glyoxylate detoxification. Deficit of AGT leads to primary Hyperoxaluria Type I. Dr Dindo and his colleagues made important contribution in defining the effects of many AGT point mutations and in the development of new therapeutic approaches for the disease, less invasive and more specific than those currently available.
- **Human DDC or Dopa decarboxylase,** a PLP dependent enzyme that catalyzes the production of dopamine and serotonine. DDC is involved in Parkinson's disease and in a neurometabolic disorder named aromatic amino acid decarboxylase deficiency (AADC deficiency) as well. Dr Dindo and his colleagues made important contributions to the elucidation of the pathogenesis of AADC deficiency.
- **Biochemistry of Vitamin B6 in fungi metabolism,** Aspergillus fumigatus is an opportunistic fungus directly responsible for lethal invasive infections. Amino acid metabolism can regulate the fungus-host interaction and an important role is played by enzymes involved in the catabolism of L-tryptophan. Among them, AroH encodes a putative pyridoxal 5'-phosphate-dependent aminotransferase. Dr Dindo has analyzed the biochemical features of recombinant purified AroH by spectroscopic, kinetic and in silico analyses.

In the meantime, Dr Dindo has also focused his attention on the study of enzyme behavior in synthetic protocells using the liquid-liquid phase separation (LLPS). Cells organize many of their biochemical reactions in liquid membrane-less compartments that form by phase separation from the cytoplasm. However, the understanding of how enzymes behave from a structural and kinetic point of view inside this liquid liquid phase separated compartments is still a challenge. To study enzymes behavior, Dr Dindo in Laurino's lab with collaborators have developed a model of membrane-less protocell able to partition enzymes in a crowded protein environment thus mimicking the cells cytoplasm (as reported in the **Nat Commun 12, 6293, 2021**).

Dr. Dindo is a young member of the Italian Society of Biochemistry and Molecular Biology (SIB)

PUBLICATIONS

. **Dindo M**, Pascarelli S, Chiasserini D, Grottelli S, Costantini C, Uechi GI, Giardina G, Laurino P and Cellini B. "*Structural dynamics shape the fitness window of alanine:glyoxylate aminotransferase"*. **Protein Science** 2022, 31, e4303. https://onlinelibrary.wiley.com/doi/10.1002/pro.4303

. Testa A*, **Dindo M*,** Rebane AA, Nasouri B, Style RW, Golestanian R, Dufresne ER and Laurino P. *"Sustained Enzymatic Activity and Flow in Crowded Protein Droplets"* **Nature Comm** 12, 6293 (2021). (*These authors contributed equally to this work)

. **Dindo M***, Ambrosini G*, Oppici E, Pey A.L, O'Toole P.J, Marrison J.L, Morrison I.E.G, Butturini E, Grottelli S, Costantini C and Cellini B. "*Dimerization Drives Proper Folding of Human Alanine:Glyoxylate Aminotransferase But Is Dispensable for Peroxisomal Targeting*." **J. Pers. Med**. 2021

. Danielson E, **Dindo M**, Porkovich AJ, Kumar K, Wang Z, Jain P, Mete T, Ziadi Z, Kikkeri R, Laurino P and Sowwan M. "*Non-enzymatic and highly sensitive lactose detection utilizing graphene field-effect transistors".* **Biosensors and Bioelectronics,** 2020

. **Dindo M**, Mandrile G, Conter C, Montone R, Giachino D, Pelle A, Costantini C, Cellini B. *"The ILE56 mutation on different genetic backgrounds of alanine: Glyoxylate aminotransferase: Clinical features and biochemical characterization* **Mol Genet Metab**. 2020

. Cellini B, Zelante T, **Dindo M**, Bellet MM, Renga G, Romani L, Costantini C. *"Pyridoxal 5'-Phosphate-Dependent Enzymes at the Crossroads of Host-Microbe Tryptophan Metabolism"* **Int J Mol Sci**. 2020

. Montioli R, Bisello G, **Dindo M**, Rossignoli G, Voltattorni CB, Bertoldi M. *"New variants of AADC deficiency expand the knowledge of enzymatic phenotypes"* **Arch Biochem Biophys**. 2020

. **Dindo M**, Grottelli S, Annunziato G, Giardina G, Pieroni M, Pampalone G, Faccini A, Cutruzzolà F, Laurino P, Costantino G, Cellini B. "*Cycloserine enantiomers are reversible inhibitors of human alanine:glyoxylate aminotransferase: implications for Primary Hyperoxaluria type 1*" **Biochem J**. 2019

. Jaeger M, Pinelli M, Borghi M, Constantini C, **Dindo M**, van Emst L, Puccetti M, Pariano M, Ricaño-Ponce I, Büll C, Gresnigt MS, Wang X, Gutierrez Achury J, Jacobs CWM, Xu N, Oosting M, Arts P, Joosten LAB, van de Veerdonk FL, Veltman JA, Ten Oever J, Kullberg BJ, Feng M, Adema GJ, Wijmenga C, Kumar V, Sobel J, Gilissen C, Romani L, Netea MG." *A systems genomics approach identifies SIGLEC15 as a susceptibility factor in recurrent vulvovaginal candidiasis*" **Science Transl Med**. 2019

. **Dindo M,** Costanzi E, Pieroni M, Costantini C, Annunziato G, Bruno A, Romani L, Zelante T and Cellini B. "*Biochemical characterization of Aspergillus fumigatus AroH a putative aromatic amino acid aminotransferase*". **Frontiers Molec. Biosc** 2018.

. Conter C*, Oppici E*, **Dindo M,** Rossi L, Magnani M and Cellini B. *"Biochemical properties and oxalate-degrading activity of oxalate decarboxylase from Bacillus subtilis at neutral pH"*. ***IUBMB Life** 2018.*

. **Dindo M***, Conter C*, Oppici E, Ceccarelli V, Marinucci L, Cellini B. "*Molecular basis of Primary Hyperoxaluria: clues to Innovative treatments"* ***Urolithiasis. 2018.***

. Kaltenbach M*, Burke JR*, **Dindo M**, Pabis A, Munsberg FS, Rabin A, Kamerlin SCL, Noel JP, Tawfik DS. *"Evolution of chalcone isomerase from a noncatalytic ancestor"* ***Nature Chem Biol***. 2018.

. **Dindo M*,** Oppici E*, Dell'Orco D, Montone R, Cellini B, "*Correlation between the molecular effects of mutations at the dimer interface of alanine:glyoxylate aminotransferase leading to primary hyperoxaluria type I and the cellular response to vitamin B_6*" ***Journal of Inherited Metabolic Disease*** 2018.

. Oppici E*, **Dindo M***, Conter C, Borri Voltattorni C, Cellini B. *"Folding defects leading to Primary Hyperoxaluria"*. ***Handb Exp Pharmacol***. 2018 (*These authors contributed equally to this work)

. **Dindo M**, Conter C, Cellini B. "*Electrostatic interactions drive native-like aggregation of human alanine:glyoxylate aminotransferase*". ***FEBS J.*** 2017

. Dindo M, Montioli R, Busato M, Giorgetti A, Cellini B, Borri Voltattorni C. "*Effects of interface mutations on the dimerization of alanine glyoxylate aminotransferase and implications in the mistargeting of the pathogenic variants F152I and I244T"* ***Biochimie.*** 2016.

. Montioli R, Paiardini A, Kurian MA, **Dindo M**, Rossignoli G, Heales SJ, Pope S, Voltattorni CB, Bertoldi M. "*The novel R347G pathogenic mutation of aromatic amino acid decarboxylase provides additional molecular insights into enzyme catalysis and deficiency*." ***Biochim Biophys Acta.*** 2016

. Oppici E*****, Montioli R*****, **Dindo M**, Cellini B. "*Natural and unnatural compounds rescue folding defects of human alanine:glyoxylate aminotransferase leading to Primary Hyperoxaluria Type I*" ***Curr Drug Targets***. 2016.

. Oppici E, Montioli R, **Dindo M**, Maccari L, Porcari V, Lorenzetto A, Chellini S, Voltattorni CB, Cellini B. "*The Chaperoning Activity of Amino-oxyacetic Acid on Folding-Defective Variants of Human Alanine:Glyoxylate Aminotransferase Causing Primary Hyperoxaluria Type I*"***ACS Chem Biol.*** 2015.

. Montioli R*****, Oppici E*****, **Dindo M**, Roncador A, Gotte G, Cellini B, Borri Voltattorni C. "*Misfolding caused by the pathogenic mutation G47R on the minor allele of alanine:glyoxylate aminotransferase and chaperoning activity of pyridoxine*" ***Biochim Biophys Acta***. 2015 (*These authors contributed equally to this work)

. Montioli R, **Dindo M**, Giorgetti A, Piccoli S, Cellini B, Voltattorni CB. "*A comprehensive picture of the mutations associated with aromatic amino acid decarboxylase deficiency: from molecular mechanisms to therapy implications*". ***Hum Mol Genet.*** 2014

. R. Montioli, B. Cellini, **M. Dindo**, E. Oppici and C.B. Voltattorni"*Interaction of Human Dopa Decarboxylase with L-Dopa: Spectroscopic and Kinetic Studies as a Function of pH,"* ***Biomed Res Int.*** 2013.

. R. Montioli, E. Oppici, B. Cellini, A. Roncador, **M. Dindo**, C.B. Voltattorni *"S250F variant associated with aromatic amino acid decarboxylase deficiency: molecular defects and intracellular rescue by pyridoxine."* ***Hum Mol Genet*** 2013

INTERNATIONAL AND NATIONAL CONFERENCES

. Dindo M, Testa A, Rebane AA, Nasouri B, Style RW, Golestanian R, Dufresne ER and Laurino P. *"Sustained Enzymatic Activity and Flow in Crowded Protein Droplets". SIB Conference (Congresso Nazionale SIB, online), 23-24 September 2021*

. **Dindo M,** Testa A, Rebane AA, Nasouri B, Style RW, Golestanian R, Dufresne ER and Laurino P. *"Sustained Enzymatic Activity and Flow in Crowded Protein Droplets". Molecular Origins of Life, online 25-27 August 2021*

. Pampalone G, Grottelli S, Annunziato G, Pieroni M, **Dindo M**, Costantino G and Cellini B"*Identification of pharmacological chaperones for human alanine:glyoxylate aminotransferase as therapeutic strategy for Primary Hyperoxaluria Type I*" The 45th FEBS virtual congress, 3-8 July 2021.

. **Dindo M**, Giardina G, Pascarelli S, Chiasserini D, Grottelli S, Uechi GI, Costantini C, Pampalone G, Spizzichino S, Laurino P and B. Cellini. "*Intrinsically disordered regions of alanine:glyoxylate aminotransferase shape its fitness and function*" WebPro, Proteins on the Web, 20-21 maggio 2021

.**Dindo M**, Oppici E, Ambrosini G, Pey AL, Marrison J, O'Toole P and Cellini B. "*Effects of oligomerization on peroxisomal import and stability of human alanine:glyoxylate aminotransferase".* FISV 2018, Rome 18-21 Semptember

.**Dindo M**, Oppici E, Ambrosini G, Pey AL, Marrison J, O'Toole P and Cellini B. "*Effects of oligomerization on peroxisomal import and stability of human alanine:glyoxylate aminotransferase".* Proteine 2018, Verona 28-30 May

. Conter C, **Dindo M** and Cellini B. "*Electrostatic interactions drive native-like aggregation of human alanine:glyoxylate aminotransferase".* Proteine 2018, Verona 28-30 May 2018

. Conter C, Oppici E, Montioli R, **Dindo M**, Rossi L, Magnani M and Cellini B. "*Erythrocytes as carriers of oxalate decarboxylase: an innovative approach for the treatment of hyperoxaluria*" 12 International Primary Hyperoxaluria Workshop. Tenerife 14-16 July 2017.

. **Dindo M**, Oppici E, Bianchi A and Cellini B. "*Molecular and cellular effects of interfacial mutations of human alanine:glyoxylate aminotransferase leading to Primary Hyperoxaluria Type I and response to coenzyme administration*". ICC05, Unazuki, Toyama, Japan 4-8 September 2016.

. C. Conter, E. Oppici, R. Montioli, **M. Dindo**, L. Rossi, M. Magnani and B. Cellini."*Oxalate Decarboxylase as new therapeutic agent for the treatment of hyperoxaluria*" Proteins Conference 2016, Bologna (Italia) 30 march-01 april 2016

. Rossignoli G, Montioli R, Paiardini A, Kurian MA, **Dindo M**, Voltattorni CB, Bertoldi M. "*The novel R347G pathogenic mutation of Dopa Decarboxylase: additional insights into enzyme catalysis and deficiency*" Proteins Conference 2016, Bologna (Italia) 30 March-01 April 2016

. M. Kaltenbach, JR. Burke, **M. Dindo**, JP. Noel, DS Tawfik. "Emergence of enzymatic function in a non-catalytic ancestor: The plant CHI family" Annual meeting of the Society for Molecular Biology and Evolution, Vienna, July 12-16, 2015.

. R. Montioli, **M. Dindo**, A. Giorgetti, S. Piccoli, B. Cellini and Carla Borri Voltattorni. "*A comprehensive picture of the mutations associated with aromatic amino acid decarboxylase deficiency: from molecular mechanism to therapy implications" ICC-04 The Fourth International Conference on Cofactors*, 25-28 August 2014, Casa Della Musica, University of Parma, Parma, Italy

. R. Montioli, A. Roncador, E. Oppici, G. Mandrile, D.F. Giachino, **M. Dindo**, C. Borri Voltattorni and B. Cellini "*S81L and G170R mutations causing Primary Hyperoxaluria Type I in homozygosis and heterozygosis. A positive interallelic complementation*" Proteine 2014, Padova 31 March- 1 April 2014,

. **M. Dindo**, R. Montioli and C. Borri Voltattorni "*Pathogenic variants of residues belonging to loop1 of human dopa decarboxylase share common spectroscopic and catalytic features*" 57° National Meeting of the Italian society of Biochemistry and Molecular Biology (SIB) Ferrara 18-20 September 2013.

. E. Oppici, R. Montioli, A. Roncador, **M. Dindo**, B. Cellini and C. Voltattorni "*The molecular defects of the S250F variant of Dopa Decarboxylase associated with AADC deficiency syndrome*" SW02.W10–15 38th FEBS 06-11 July 2013 Saint Petersburg.

RESEARCH SUPPORTS

- **JSPS GRANT, KAKENHI EARLY CAREER SCIENTIST, 2022.** Study of enzymes inside liquid-liquid phase separated crowded droplets.
  Role: PI
  01/04/2022-31/03/2024
- **JSPS POST-DOCTORAL FELLOWSHIP.** Received by the Japan Society for the Promotion of science (Grant-in-Aid for JSPS research fellow, KAKENHI). Fellowship number: P19764
  01/10/2019-30/09/2021
- **OXALOSIS AND HYPEROXALURIA FOUNDATION**. Development of a small-molecule therapy for Primary Hyperoxaluria Type I based on the combined administration of B6 vitamers and pharmacological chaperones

Role: Active member
01/10/2017-30/09/2019

- **ITALIAN MINISTRY OF UNIVERSITY AND RESEARCH (SIR project).** Erythrocytes as carriers of oxalate-degrading enzymes: an innovative approach for the treatment of Hyperoxaluria
  Role: Active member
  23/09/2015-22/09/2019
- **UNIVERSITY OF VERONA, JOINT PROJECTS**. Biosynthetic activity of trophectoderm: new tools for embryo selection techniques in vitro
  Role: Active member
  01/01/2014-30/06/2016
- **COOPERINT 2015** (February-June 2015) obtained from University of Verona. Project title: "CHI evolution".
  01/02/2015-01/06/2015
- **OXALOSIS AND HYPEROXALURIA FOUNDATION**. A combined biochemical and cell biology approach to improve the pharmacological treatment of PH1: from pyridoxine derivatives to proteostasis regulators.
  Role: Active member
  01/10/2012-31/03/2015

ORAL PRESENTATIONS

- *07 September 2016*

Selected presentation in the fifth International Conference on Cofactors and Active Enzyme Molecule (ICC05) entitled: "*Molecular and cellular effects of interfacial mutations of human alanine:glyoxylate aminotransferase leading to Primary Hyperoxaluria Type I and response to coenzyme administration"*

- *29 January 2016*

PhD Day University of Verona Selected student for the PhD program in Biomolecular Medicine with the presentation entitled: "*Engineering of a soluble monomeric form of human alanine:glyoxylate aminotransferase*"

AWARDS

- *April 2021*

"Heritage pride 2020" received by SIB (Italian Society of Biochemistry and Molecular Biology) for the selected publication: "**Dindo M**, Grottelli S, Annunziato G, Giardina G, Pieroni M, Pampalone G, Faccini A, Cutruzzolà F, Laurino P, Costantino G, Cellini B. "*Cycloserine enantiomers are reversible inhibitors of human alanine:glyoxylate aminotransferase: implications for Primary Hyperoxaluria type 1*" **Biochem J**. 2019".

- *September 2016*

Travel Award received at the fifth International Conference on Cofactors and Active Enzyme Molecule (ICC05).

EDITORIAL BOARD MEMBER

- *Editor for the Special Issue "Protein Conformational Plasticity as a Link between Function and Genetics, Environmental and Evolutionary Factors", Frontiers in Biosciences*

REVIEWER ACTIVITIES

- *Frontiers in Molecular Biosciences, Protein Chemistry and Enzymology*
- *Frontiers in Plant Science, Plant Proteomics*
- *Frontiers in Bioengineering and Biotechnology, Bioprocess Engineering*

DIDACTIC ACTIVITIES

- 2018 "Teaching Assistant**"** of Biochemistry, Degree Course in Sport Sciences and Degree Course in Nursery, University of Perugia

I have read the Informative note and I authorize the treatment of my personal data (Law 196/03, Italy).

Dr Mirco Dindo