

BIOGRAPHICAL SKETCH

NAME: **DAVIDE RONCARATI**

POSITION TITLE: Associate Professor of Molecular Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Bologna, Bologna, Italy	M.Sc	10/2003	Biotechnology
University of Bologna, Bologna, Italy and Novartis Vaccines and Diagnostics, Siena, Italy	PhD	05/2007	Molecular Biology and Genetics of Microorganisms
University of Bologna, Bologna, Italy	PostDoc	10/2008	Molecular Biology and Genetics of Microorganisms
University of Oxford, Department of Biochemistry, Oxford, United Kingdom	Visiting Research Assistant	07/2010	Host-Pathogen Interaction

A. Personal Statement

As a molecular microbiologist, my research centers on understanding bacterial pathogenesis and the molecular mechanisms that regulate host-pathogen interactions. I am particularly interested in the role of non-coding RNAs and other post-transcriptional regulators in mediating bacterial virulence. This aligns closely with the objectives of this project, which aims to elucidate the RNAome of *Helicobacter pylori* outer membrane vesicles (OMVs) and their impact on host gene expression.

Over the years, I have developed a multidisciplinary skillset that integrates molecular biology, biochemistry, and advanced -omics techniques. My lab has contributed to optimizing pipelines for OMV isolation and RNA purification, addressing critical challenges in studying OMV-associated RNA. These efforts have positioned us to make significant strides in characterizing OMV-RNAs and their roles in pathogenesis.

This project builds directly on my expertise in RNA biology and bacterial stress responses, as well as my longstanding collaboration with bioinformatics experts to analyze complex datasets. My lab's preliminary findings, showing the enrichment of specific RNAs in OMVs under stress conditions, provide a strong foundation for the proposed research.

Through this work, I aim not only to deepen our understanding of *H. pylori* pathogenesis but also to lay the groundwork for innovative therapeutic strategies targeting OMV-mediated host-pathogen communication. My commitment to advancing molecular microbiology and mentoring future scientists will ensure the success and broader impact of this project.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2004 – 2007 PhD fellow - University of Bologna (UniBO), Bologna, Italy / Novartis Vaccines and Diagnostics, Siena, Italy.
2008 - 2009 post-doctoral fellow - University of Bologna (UniBO), Bologna, Italy

2009 – 2010	Visiting Research Assistant - University of Oxford, Department of Biochemistry, Oxford, United Kingdom.
2008 – 2019	Assistant Professor - Faculty of Science, University of Bologna, (UniBO), Bologna, Italy.
2019 – present	Associate Professor in Molecular Biology - Department of Pharmacy and Biotechnology – Alma Mater Studiorum University of Bologna (UniBO). Bologna, Italy

Other experience and professional memberships

2019 - Associate Editor, Biochemistry and Biophysics Reports
 2019 - Ad hoc reviewer, National Science Centre (Narodowe Centrum Nauki – NCN), Poland.
 2020 - Special Guest Editor, “Genomics of Host-Pathogen Interaction”, Genes.
 2020 - Ad hoc reviewer, ETH Zurich, Switzerland.
 2021 - Special Guest Editor, "Regulation of Gene Expression in Response to Environmental Changes in Bacterial Pathogens", Microorganisms.
 2022 – Guest Editor, “Transcriptional Regulators in Prokaryotes: Mechanisms of Action, Physiological Importance and their Use as Therapeutic Targets”, Frontiers in Cellular and Infection Microbiology
 2022 – Associate Editor, Frontiers in Cellular and Infection Microbiology

Membership of Scientific Societies

Italian Society of General Microbiology and Microbial Biotechnology (SIMGBM) and of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).

Ad hoc reviewer in Scientific Journals

Frontiers in Microbiology, BMC Microbiology, Microorganisms, Nucleic Acids Research, Scientific Reports, Nature Communications, Biochimie, Pathogens, Toxins, Cancers, International Journal of Molecular Sciences.

C. Contributions to Science

1. One of the key research areas I have pursued since the start of my career focuses on uncovering the molecular mechanisms that major pathogenic bacteria use to adapt to diverse environmental stresses. My work has shed light on the critical roles of stress-responsive transcriptional regulators, such as HrcA and HspR, in orchestrating the precise expression of genes encoding chaperones and heat-shock proteins in prominent pathogens like *Helicobacter pylori* and *Campylobacter jejuni*.

This line of research has led to the publication of 11 scientific articles, 4 review papers, and 1 book chapter, alongside multiple oral presentations at international conferences.

- **Roncarati D**, Vannini A, Scarlato V. Temperature sensing and virulence regulation in pathogenic bacteria. *Trends Microbiol.* 2024 Aug 19:S0966-842X(24)00180-X. doi: 10.1016/j.tim.2024.07.009.
- Versace G, Palombo M, Menon A, Scarlato V, **Roncarati D**. Feeling the Heat: The *Campylobacter jejuni* HrcA Transcriptional Repressor Is an Intrinsic Protein Thermosensor. *Biomolecules.* 2021 Sep 27;11(10):1413. doi: 10.3390/biom11101413.
- Pepe S, Pinatel E, Fiore E, Puccio S, Peano C, Brignoli T, Vannini A, Danielli A, Scarlato V, **Roncarati D**. The *Helicobacter pylori* Heat-Shock Repressor HspR: Definition of Its Direct Regulon and Characterization of the Cooperative DNA-Binding Mechanism on Its Own Promoter. *Front Microbiol.* 2018 Aug 14;9:1887. doi: 10.3389/fmicb.2018.01887.
- **Roncarati D**, Danielli A, Scarlato V. The HrcA repressor is the thermosensor of the heat-shock regulatory circuit in the human pathogen *Helicobacter pylori*. *Mol Microbiol.* 2014 Jun;92(5):910-20. doi: 10.1111/mmi.12600.
- **Roncarati D**, Danielli A, Spohn G, Delany I, Scarlato V. Transcriptional regulation of stress response and motility functions in *Helicobacter pylori* is mediated by HspR and HrcA. *J Bacteriol.* 2007 Oct;189(20):7234-43. doi: 10.1128/JB.00626-07.

2. An important project I was involved in during my time at the research center of Novartis Vaccines and Diagnostics focused on studying the regulatory mechanisms of crucial virulence factors and vaccine candidates in the major human pathogen *Neisseria meningitidis*. My work was part of a collaborative network of research

teams united in the mission to develop an effective vaccine against *Meningococcus B*. This collective effort culminated in the creation of Bexsero, a vaccine that is now successfully available on the market.

- Metruccio MM, Pigozzi E, **Roncarati D**, Berlanda Scorza F, Norais N, Hill SA, Scarlato V, Delany I. A novel phase variation mechanism in the meningococcus driven by a ligand-responsive repressor and differential spacing of distal promoter elements. *PLoS Pathog.* 2009 Dec;5(12):e1000710. doi: 10.1371/journal.ppat.1000710
- Metruccio MM, Fantappiè L, Serruto D, Muzzi A, **Roncarati D**, Donati C, Scarlato V, Delany I. The Hfq-dependent small noncoding RNA NrrF directly mediates Fur-dependent positive regulation of succinate dehydrogenase in *Neisseria meningitidis*. *J Bacteriol.* 2009 Feb;191(4):1330-42. doi: 10.1128/JB.00849-08
- Ieva R, **Roncarati D**, Metruccio MM, Seib KL, Scarlato V, Delany I. OxyR tightly regulates catalase expression in *Neisseria meningitidis* through both repression and activation mechanisms. *Mol Microbiol.* 2008 Dec;70(5):1152-65. doi: 10.1111/j.1365-2958.2008.06468.x

3. Throughout my career, I have been deeply engaged in unraveling the intricacies of metal-dependent regulation in the pathogenic bacterium *Helicobacter pylori*. This research addresses a critical aspect of *H. pylori* pathogenesis, focusing on two master regulators, Fur and NikR, which orchestrate the expression of numerous target genes through partially overlapping and interconnected regulons.

To decode these complex regulatory networks, I combined advanced molecular techniques with cutting-edge functional genomics approaches, including RNA-sequencing and ChIP-sequencing, enabling a genome-wide exploration of Fur- and NikR-mediated regulation. This body of work has culminated in the publication of 8 scientific articles and 1 review paper.

- Vannini A, Pinatel E, Costantini PE, Pellicciari S, **Roncarati D**, Puccio S, De Bellis G, Scarlato V, Peano C, Danielli A. (Re)-definition of the holo- and apo-Fur direct regulons of *Helicobacter pylori*. *J Mol Biol.* 2024 May 15;436(10):168573. doi: 10.1016/j.jmb.2024.168573
- Vannini A, Pinatel E, Costantini PE, Pellicciari S, **Roncarati D**, Puccio S, De Bellis G, Peano C, Danielli A. Comprehensive mapping of the *Helicobacter pylori* NikR regulon provides new insights in bacterial nickel responses. *Sci Rep.* 2017 Apr 10;7:45458. doi: 10.1038/srep45458
- **Roncarati D**, Pellicciari S, Doniselli N, Maggi S, Vannini A, Valzania L, Mazzei L, Zambelli B, Rivetti C, Danielli A. Metal-responsive promoter DNA compaction by the ferric uptake regulator. *Nat Commun.* 2016 Aug 25;7:12593. doi: 10.1038/ncomms12593
- Agriesti F, **Roncarati D**, Musiani F, Del Campo C, Iurlaro M, Sparla F, Ciurli S, Danielli A, Scarlato V. FeON-FeOFF: the *Helicobacter pylori* Fur regulator commutates iron-responsive transcription by discriminative readout of opposed DNA grooves. *Nucleic Acids Res.* 2014 Mar;42(5):3138-51. doi: 10.1093/nar/gkt1258
- Danielli A, **Roncarati D**, Delany I, Chiarini V, Rappuoli R, Scarlato V. In vivo dissection of the *Helicobacter pylori* Fur regulatory circuit by genome-wide location analysis. *J Bacteriol.* 2006 Jul;188(13):4654-62. doi: 10.1128/JB.00120-06

4. The study of the HP1043 transcriptional regulator in *Helicobacter pylori* has spanned the past decade, serving as an excellent example of how fundamental research can transition into applied science. As an essential protein for the pathogen, HP1043 presented unique challenges for characterization. The journey began with the development of a genome-wide approach (Chromatin Immunoprecipitation), which enabled us to define HP1043's pivotal role as a transcriptional regulator in *H. pylori*. Building on these insights, we delved into molecular and structural studies, uncovering the intricate details of HP1043's interaction with DNA. This foundational work paved the way for interdisciplinary collaborations, leading to the identification and optimization of molecules designed to target HP1043, thereby compromising bacterial fitness. This research exemplifies the seamless transition from fundamental science to translational applications, adding a dynamic and impactful dimension to my work.

- Fiore C, Antoniciello F, **Roncarati D**, Scarlato V, Grepioni F, Braga D. Levofloxacin and Ciprofloxacin Co-Crystals with Flavonoids: Solid-State Investigation for a Multitarget Strategy against *Helicobacter pylori*. *Pharmaceutics.* 2024 Jan 30;16(2):203. doi: 10.3390/pharmaceutics16020203

- Antoniciello F, **Roncarati D**, Zannoni A, Chiti E, Scarlato V, Chiappori F. Targeting the Essential Transcription Factor HP1043 of *Helicobacter pylori*: A Drug Repositioning Study. *Front Mol Biosci*. 2022 May 11;9:887564. doi: 10.3389/fmolb.2022.887564
- Zannoni A, Pellicciari S, Musiani F, Chiappori F, **Roncarati D**, Scarlato V. Definition of the Binding Architecture to a Target Promoter of HP1043, the Essential Master Regulator of *Helicobacter pylori*. *Int J Mol Sci*. 2021 Jul 22;22(15):7848. doi: 10.3390/ijms22157848
- Pellicciari S, Pinatel E, Vannini A, Peano C, Puccio S, De Bellis G, Danielli A, Scarlato V, **Roncarati D**. Insight into the essential role of the *Helicobacter pylori* HP1043 orphan response regulator: genome-wide identification and characterization of the DNA-binding sites. *Sci Rep*. 2017 Jan 23;7:41063. doi: 10.1038/srep41063

5. Throughout my career, the study of gene expression regulation by non-coding RNAs has complemented my work on the characterization of protein transcriptional regulators. The research projects I have been involved in have shed light on several important regulatory RNAs in major human pathogens such as *Neisseria meningitidis* and *Helicobacter pylori*. This area of research, driven by advancements in various “omics” technologies, has increasingly become a central focus of my scientific interests in recent years.

- D'Agostino F, Pinatel E, Meynhardt A, Scarlato V, Vannini A, **Roncarati D**. RNase Y Mediates Posttranscriptional Control of the Virulence-Associated CncR1 small-RNA in *Helicobacter pylori*. *iScience* 2025 (in press)
- Vannini A, **Roncarati D**, Danielli A. The cag-pathogenicity island encoded CncR1 sRNA oppositely modulates *Helicobacter pylori* motility and adhesion to host cells. *Cell Mol Life Sci*. 2016 Aug;73(16):3151-68. doi: 10.1007/s00018-016-2151-z
- Metruccio MM, Fantappiè L, Serruto D, Muzzi A, **Roncarati D**, Donati C, Scarlato V, Delany I. The Hfq-dependent small noncoding RNA NrrF directly mediates Fur-dependent positive regulation of succinate dehydrogenase in *Neisseria meningitidis*. *J Bacteriol*. 2009 Feb;191(4):1330-42. doi: 10.1128/JB.00849-08

Complete List of Published Work in PubMed:

<https://pubmed.ncbi.nlm.nih.gov/?term=roncarati%20d&sort=date>

D. Research Support

Current support:

PRIN2022

Title: NORA: a sequencing-based approach to define NucleOid structural Alterations in *Helicobacter pylori* dormancy.

Agency/Founder: Italian Ministry of Education and Research

Principal Investigator and Responsible of the research unit: Davide Roncarati

Period: 28/09/2023 to 28/09/2025

Relevant past funding

Title: The essential transcriptional regulator HP1043 of *Helicobacter pylori*: a new target for the design of a new antibacterial drug.

Agency/Founder: ESCMID - European Society of Clinical Microbiology and Infectious Diseases.

Principal Investigator and Scientific Coordinator: Davide Roncarati.

Period: 01/03/2018 to 31/03/2020.

Title: Identification of new antibacterial molecules against *Campylobacter jejuni* infections.

Agency/Founder: CARISBO – Fondazione Casa di Risparmio di Bologna.

Principal Investigator: Davide Roncarati.

Period: 01/01/2019 to 30/06/2020.