

**BIOGRAPHICAL SKETCH****NAME: Giorgio Milazzo, PhD****POSITION TITLE: Associate 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<br>(if applicable) | Start Date<br>MM/YYYY | Completion<br>Date<br>MM/YYYY | FIELD OF STUDY                     |
|------------------------------|---------------------------|-----------------------|-------------------------------|------------------------------------|
| University of Palermo, Italy | <b>BSc</b>                | 10/2003               | 10/2008                       | Biological sciences                |
| University of Palermo, Italy | <b>MSc</b>                | 11/2008               | 10/2011                       | Molecular and cellular biology     |
| University of Bologna, Italy | <b>PhD</b>                | 01/2012               | 04/2015                       | Molecular genetics and epigenetics |
| University of Bologna, Italy | <b>Research fellow</b>    | 02/2012               | 12/2015                       | Genetics and epigenetics of cancer |
| University of Bologna, Italy | <b>Research fellow</b>    | 01/2016               | 12/2018                       | Genetics and epigenetics of cancer |

**A. Personal Statement**

The research of my laboratory focuses on understanding transcriptional mechanisms mediated by HDAC-containing epigenetic protein complexes, with the goal of identifying novel therapeutic vulnerabilities in pediatric cancers.

Our research strategy centers on the identification of critical nuclear targets involved in complex transcriptional regulatory networks. Specifically, we aim to: **1.** systematically define the molecular composition of epigenetic complexes; **2.** biochemically characterize their enzymatic activities in vitro through the purification of individual complexes; **3.** determine the impact of their depletion on tumor cell biology; and **4.** rigorously assess their transcriptional output using genome-wide approaches, including RNA-seq and ChIP-seq.

In recent years, our work has focused on elucidating the role of CoREST epigenetic complexes in the establishment and maintenance of enhancers and super-enhancers in pediatric cancers.

**B. Positions, Scientific Appointments and Honors**

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|--------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2025-present | <b>Invited Professor</b> , University of Gent, Belgium                                                                                                                                                                        |
| 2025-present | <b>Associate Professor</b> , University of Bologna, Italy                                                                                                                                                                     |
| 2022-2025    | <b>Senior Assistant Professor</b> , University of Bologna, Italy                                                                                                                                                              |
| 2019-2022    | <b>Young Assistant Professor</b> , University of Bologna, Italy                                                                                                                                                               |
| 2022         | <b>Genes 2022 Best Paper Rank 1 Award</b> , Histone Deacetylases (HDACs): Evolution, Specificity, Role in Transcriptional Complexes, and Pharmacological Actionability. (doi:10.3390/genes11050556) By Giorgio Milazzo et al. |

**C. Contributions to Science**

My expertise lies in genome architecture and transcriptional regulation. My research to date has been strongly committed to childhood cancer research, with a particular focus on transcriptional control mediated by epigenetic mechanisms driven by large nuclear histone-modifying complexes in neuroblastoma (NB).

I contributed to the characterization of the first two NB-specific long non-coding RNAs, IncUSMycN and IncNB1, and investigated how histone modifiers including LSD1, WDR5, DOT1L, and JMJD6 regulate MYCN-

driven transcription. I also served as co-first author in the identification of a RUNX1T1 point mutation in neuroblastoma that fully blocks MYCN-driven tumorigenesis in NB mouse models.

Over the past five years, my research has focused on the epigenetic CoREST nuclear complex family (CoREST1, CoREST2, and CoREST3) in MYCN-driven neuroblastoma. CoREST complexes are primarily composed of one RCOR protein (RCOR1, RCOR2, or RCOR3) and two enzymatic components, HDAC1/2 and LSD1. These complexes exhibit histone deacetylation and demethylation activities and have been traditionally associated with transcriptional repression.

Despite the high structural conservation among RCOR proteins, specific domains distinguish individual family members, including N-terminal coiled-coil domains and the proline-rich "PPPLI" motif unique to RCOR2 and RCOR3. By integrating multiple genome-wide approaches (ChIP-seq, ATAC-seq, RNA-seq, and HiChIP), we demonstrated that RCOR2 plays a non-canonical activating role by promoting chromatin looping between CRTF-bound enhancers and target promoters, thereby sustaining oncogenic transcriptional programs in neuroblastoma.

The results of this work were recently published in Cell Reports:

**"Non-canonical activating roles of RCOR2 sustain transcription in adrenergic neuroblastoma."**

Recent relevant publications:

- a. Aloisi S., Santulli M., Russo M., Zadrán S.K., Rigamonti A., Chin D.H., Palombo M., Cimadam L., Scrofani L., Bernardoni R., Capranico G., Gryder B.E., Perini G., **Milazzo G.**

**Non-canonical activating roles of RCOR2 sustain transcription in adrenergic neuroblastoma.**

Cell reports, 2025.

- b. Murray J.E.\* , Valli E.\* , **Milazzo G.\***, Mayoh C., Gifford A.J., Fletcher J.I., Xue C., Jayatilake N., Salehzadeh F., Gamble L.D., Rouaen J.R.C., Carter D.R., Forgham H., Sekyere E.O., Keating J., Eden G., Allan S., Alfred S., Kusuma F.K., Clark A., Webber H., Russell A.J., de Weck A., Kile B.T., Santulli M., De Rosa P., Fleuren E.D.G., Gao W., Wilkinson-White L., Low J.K.K., Mackay J.P., Marshall G.M., Hilton D.J., Giorgi F.M., Koster J., Perini G., Haber M., Norris M.D.

**The transcriptional co-repressor Runx1t1 is essential for MYCN-driven neuroblastoma tumorigenesis.**

Nature communication, 2024. \* Co-First authors

- c. Pandher R., Xue C., Gamble L.D., **Milazzo G.**, Giacomo S.D., Murray J., Cheung L., Ferrucci F., Palombo M., Purgato S., Burkhart C.A., Fedtsova N., Gleiberman A.S., Purmal A.A., Korotchikina L., Nikiforov M.A., Makarov S.S., Telfer T.J., Codd R., Marshall G.M., Scott D.A., Osterman A.L., Gudkov A.V., Perini G., Haber M., Norris M.D.

**The cell-permeable iron chelator M606 inhibits MYCN-driven neuroblastoma via an E2F3-mediated response**

Proc Natl Acad Sci U S A, 2025.

- d. Zadrán S.K., Facchinello N., De Rosa P., Saporetti R., Costantini P.E., Ulfo L., Nigro M., Petrosino A., Pappagallo L., Aloisi S., **Milazzo G.**, Din Z.A., Rigamonti A., Flora L., Santulli M., Cimadam L., Zuccheri G., Zangoli M., Sante M.D., Giosia M.D., Maria F.D., Bernardoni R., Barbieri E., Calvaresi M., Danielli A., Perini G.

**Systematic Targeting of GD2-Positive Neuroblastoma Tumors With a Photooncolytic Phage Nanovector Platform.**

Advanced Science, 2025.