
BIOGRAPHICAL SKETCH

NAME: Manzo Stefano Giustino

POSITION TITLE: Assistant Professor of Molecular Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Bologna, UNIBO	BS	11/2008	Molecular Biology
University of Bologna, UNIBO	MS	03/2011	Molecular Biology
University of Bologna, UNIBO	PHD	05/2015	Molecular Biology
University of California, Davis	Visiting PHD	08/2014	Genomics
University of Bologna, UNIBO	FIRC Postdoctoral Fellow	12/2017	Genomic/Molecular Biology
Netherlands Cancer Institute, Amsterdam	NKI Postdoctoral Fellow	12/2018	Genomic/Molecular Biology
Netherlands Cancer Institute, Amsterdam	MSCA-iCARE2.0 Postdoctoral Fellow	08/2020	Genomic/Molecular Biology
Netherlands Cancer Institute, Amsterdam	MSCA-IF Postdoctoral Fellow	02/2022	Genomic/Molecular Biology
University of Milan, UNIMI	Junior Assistant Professor	07/2025	Genomic/Molecular Biology
University of Milan, UNIMI	Assistant Professor	From 07/2025	Genomic/Molecular Biology

A. Personal Statement

I am an Assistant Professor of Molecular Biology, and my research is focused on the role of DNA topology in genome organization, function, and stability. I have a broad background in molecular biology, with specific training and expertise in transcription, DNA Topology, and genome organization. I am a Junior PI who reached scientific independence through a Next Generation EU research grant dedicated to MSCA Postdoctoral Fellows. As a doctoral and postdoctoral scientist, thanks to three prestigious research fellowships, I had seminal discoveries on how topoisomerase activity modulates genome stability and genome organization. These findings have laid the groundwork for an original research line focused on the link between DNA Topology, chromatin structure, and genome organization in physiological and pathological contexts. I successfully administered projects, collaborated with other international researchers, and produced several peer-reviewed publications from each project. I am a passionate scientist aware of the importance of frequent communication among project members and groups. I am proficient in designing realistic research plans, timelines, and budgets for research projects. I have the expertise, leadership, training, and motivation necessary to complete the proposed research project. The current application builds logically on my prior work. I advocate for open science, believing that scientific progress can be achieved only by complete transparency and total sharing of data and knowledge prior to publication.

Ongoing and recently completed projects that I would like to highlight include:

Three years FIRC (Fondazione Italiana per la Ricerca sul Cancro) fellowship for the project: *Role of R loop structures in Top1cc-driven genomic instability*. Grant amount: 75000 euro, success rate 36%

Three years International Cancer Research Fellowship iCARE2.0 (MSCA-IF) co-funded by the Italian Association for Cancer Research (AIRC) and the European Union under the Marie Skłodowska-Curie grant

agreement Nr 800924 (Horizon 2020) for the project: Role of DNA Topoisomerase 1 at the nuclear lamina. Grant amount: 180000 euro, score 89/100, success rate 26 %. (January 2019- August 2020)

Two years Marie Skłodowska-Curie Individual fellowship (MSCA-IF) for the project: Role of DNA Topoisomerase 1 at the nuclear lamina. Funded by the European Union (Horizon 2020). Grant amount: 175000 euro, score 95.2/100, success rate 14% (Starting date 1st September 2020)

Three years MSCA Young Researcher Grant. Co-funded by MUR and EU (Next Generation EU) Project Acronym: TOPOSCENCE. Project Title: Role of DNA Topoisomerases II in genome re-organization during Oncogene-Induced Senescence. Grant amount: 300000 euro.

PSR4 “Linea 4” UniMI research grant:..Funded by University of Milan. Project Title: Interplay of DNA Topology-dependent architectural proteins in genome organization. Grant amount: 15000 euro.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

From June 2025	Assistant Professor, Tenure-Track Researcher (RTT), Department of Biosciences, University of Milan, Italy
2022 – 2025	Junior Assistant Professor, RTDA, Department of Biosciences, University of Milan
2024 – Present	Member of Scientific Committee, Department of Biosciences, University of Milan, Italy
2025 – Present	Organizer of scientific seminar series “RiparaMi”, Italy
2018 – 2022	Postdoctoral scientist, Bas van Steensel Lab, NKI_AVL, Amsterdam, The Netherlands
2015 – 2018	Postdoctoral scientist, Capranico Lab, University of Bologna, Italy
2012 – 2015	PhD candidate, Capranico Lab, University of Bologna, Italy
2012 – 2015	PhD candidate, Capranico Lab, University of Bologna, Italy
2013 – 2014	visiting PhD candidate, Chedin Lab, UC Davis, Davis, California

Honors

2020	FIRC (Fondazione Italiana per la Ricerca sul Cancro) fellowship
2019	International Cancer Research Fellowship iCARE2.0/Marie Curie (MSCA-IF)
2018	Marie Skłodowska-Curie Individual fellowship (MSCA-IF)

C. Contributions to Science

1. My first publication as a first author came from my master's degree thesis project. It focused on the mechanism that triggers RNA polymerase II degradation following treatments with triptolide. This potent transcriptional inhibitor inhibits the ATPase activity of XPB, which is part of the TFIIH complex. I found that immediately after triptolide treatment, RNA polymerase II blocks on promoters and undergoes CDK7-mediated proteolytic degradation. This study provides mechanistic insights into the complicated regulation of RNA polymerase II at human promoters.

A. **Manzo SG***, Zhou ZL*, Wang YQ*, Marinello J, He JX, Li YC, Ding J, Capranico G, Miao ZH. **Natural product triptolide mediates cancer cell death by triggering CDK7-dependent degradation of RNA polymerase II.** *Cancer Res.* 2012 Oct 15;72(20):5363-73.

2. During my doctoral and junior postdoctoral studies, I focused on the link between transcription, DNA topology, and genome stability. I was particularly interested in the link between DNA topoisomerase and R loop structures, non-canonical DNA structures, which are important for genome stability. After visiting the Chedin Lab at UC Davis, I became proficient with the DRIPc-seq technique and mapped R loop structures genome-wide in cells depleted of DNA Topoisomerase 1. These data highlighted for the first

time how DNA topoisomerase activity is related to the chromatin context and created for the first time a connection between topoisomerases and nuclear lamina, a connection that I decided to investigate further as a senior postdoc and as a junior PI.

DRIPc-seq was also used for a parallel project to understand the connection between R loops, G quadruplex, and genome instability.

A. De Magis A*, **Manzo SG***, Russo M, Marinello J, Morigi R, Sordet O, Capranico G. **DNA damage and genome instability by G-quadruplex ligands are mediated by R loops in human cancer cells.** *Proc. Natl Acad Sci USA* 2019 Jan 15;116 (3):816-825. Doi: 10.1073/pnas.1810409116. Epub 2018 dec 27

B. **Manzo SG***, Hartono SR*, Sanz L, Marinello J De Biasi S, Cossarizza A, Capranico G, Chedin F. **DNA Topoisomerase I differentially modulates R-loops across the human genome.** *Genome Biol.* 2018 Jul 30;19(1):100. doi: 10.1186/s13059-018-1478-1.

C. Marinello J, Chillemi G, Bueno S, **Manzo SG**, Capranico G. **Antisense transcripts enhanced by camptothecin at divergent CpG-island promoters associated with bursts of topoisomerase I-DNA cleavage complex and Rloop formation.** *Nucleic Acids Res.* 2013 Dec;41(22):10110-23.

3. As a senior postdoc, I joined the Bas van Steensel lab at the Netherlands Cancer Institute, a leading lab in the genome organization field with strong expertise in chromatin-nuclear lamina interactions. Here, I obtained two MSCA individual fellowships to study the regulation of transcription in Lamina-associated domains and the role of DNA topoisomerases in controlling chromatin-nuclear lamina interactions. These studies paved the way for me to develop an original research line that I am pursuing as an independent scientist at the University of Milan.

A. **Manzo SG***, van Schaik T, de Haas M, Breda J, Magnitov M, de Wit E, Manjon AG, Medema RH, Buckle AJ, Naughton C, Gilbert N, van Steensel B. **Coordinated control of genome-nuclear lamina interactions by Topoisomerase 2B and Lamin B receptor.** (BiorXive, <https://doi.org/10.1101/2024.10.01.616012>, under revision in *Nucleic Acids Res*)

B. **Manzo SG**, Mazouzi A, Leemans C, van Schaik T, Neyazi N, van Ruiten MS, Rowland BD, Brummelkamp TR, van Steensel B. **Chromatin protein complexes involved in gene repression in lamina-associated domains.** *EMBO J.* 2024 Sep 25. doi: 10.1038/s44318-024-00214-1

C. **Manzo SG***, Dauban L*, van Steensel B. **Lamina-associated domains: tethers and looseners.** Review in *Current Opinion in Cellular Biology "Cell Nucleus Issue"* *Curr Opin Cell Biol.* 2022 Feb;74:80-87. doi: 10.1016/j.ceb.2022.01.004. Epub 2022 Feb 18. PMID: 35189475

D. **Manzo SG**, van Steensel B. **Phosphorylated Lamins in Euchromatin: New Clues to Progeria.** *Dev Cell.* 2020 Mar 23;52(6):676-678. doi: 10.1016/j.devcel.2020.03.003. PMID: 32208159

E. **Perturbations in 3D genome organization can promote acquired drug resistance.** Manjón AG, **Manzo SG**, Prekovic S, Potgeter L, van Schaik T, Liu NQ, Flach K, Peric-Hupkes D, Joosten S, Teunissen H, Friskes A, Ilic M, Hintzen D, Franceschini-Santos VH, Zwart W, de Wit E, van Steensel B, Medema RH. *Cell Rep.* 2023 Oct 31;42(10):113124. doi: 10.1016/j.celrep.2023.113124. Epub 2023 Sep 20.

F. **Dynamic chromosomal interactions and control of heterochromatin positioning by Ki67.** van Schaik T, **Manzo SG**, Vouzas AE, Gilbert DM, van Steensel B. *EMBO Rep.* 2022 Oct 17:e55782. doi: 10.15252/embr.202255782

G. ***CTCF and cohesin promote focal detachment of DNA from the nuclear lamina.*** van Schaik T, Liu NQ, **Manzo SG**, Peric-Hupkes D, de Wit E, van Steensel B . *Genome Biol.* 2022 Sep 1;23(1):185. doi: 10.1186/s13059-022-02754-3.

H. ***Genome-Wide Mapping and Microscopy Visualization of Protein–DNA Interactions by pA-DamID.*** van Schaik T, **Manzo SG**, van Steensel B. *Methods Molecular Biology, Vol. Methods Mol Biol.* 2022;2458:215-229. doi: 10.1007/978-1-0716-2140-0_12.

I. ***Impact of chromatin context on Cas9-induced DNA double-strand break repair pathway balance.*** Schep R, Brinkman EK, Leemans C, Vergara X, van der Weide RH, Morris B, van Schaik T, **Manzo SG**, Peric-Hupkes D, van den Berg J, Beijersbergen RL, Medema RH, van Steensel B. *Mol Cell.* 2021 May 20;81(10):2216-2230.e10. doi: 10.1016/j.molcel.2021.03.032. Epub 2021 Apr 12. PMID: 33848455

Complete List of Published Work in:

<https://pubmed.ncbi.nlm.nih.gov/?term=Stefano+G+Manzo>