

BIOGRAPHICAL SKETCH**DO NOT EXCEED FIVE PAGES.**

NAME: Michele Gabriele

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POSITION TITLE: Group Leader, SR-Tiget

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Pisa, Pisa, Italy	BS	Apr-11	Molecular Biology
University of Pisa, Pisa, Italy	MS	Oct-13	Molecular and Cellular Biology
School of European Molecular Medicine (SEMM), European Institute of Oncology (IEO), University of Milan, , Milan, Italy	PhD	Jan-19	System Medicine
Massachusetts Institute of Technology, Cambridge, MA, USA	Postdoc	May-25	Biophysics and 3D genomics

A. Personal Statement

My primary focus is on dissecting the molecular processes that regulate gene expression through enhancer-promoter interactions (EPs) and 3D genome architecture, whose dysregulation underlies a wide range of pathologies. In particular, I focus on chromatinopathies, which are syndromic neurodevelopmental disorders caused by germline mutations in chromatin regulators. Common features include intellectual disabilities, neurological and broader alterations. During my PhD, I discovered that YY1 mutations cause a pathology later named by OMIM after me and my collaborator as Gabriele-de Vries syndrome (OMIM: #617557). I led its first disease modelling in patient-derived 2D and 3D neuronal tissues. During my postdoc, I applied multidisciplinary approaches to study the 3D genome from a biophysical perspective. By combining computational approaches, 3D genome architecture, genome engineering, and 3D super-resolution live-cell imaging, we were the first to show that fully looped chromatin structures are rare and short-lived. In the last phase of my postdoc, supported by an NIH K99 Pathway to Independence Award, I established an experimental platform to study chromatin dynamics during neuronal differentiation, which enabled me to open my laboratory at the San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) in June 2025. Combining the expertise of my PhD and my postdoc, in my laboratory, we use an interdisciplinary approach to identify functional mechanisms that are responsible for neuronal differentiation, and whose dysregulation is responsible for several developmental disorders, with the long-term aim of identifying genomic regulatory targets and functional mechanisms that can be targeted to develop tissue-specific epigenetic therapies. The lab is currently composed of me, two research assistants, and one PhD student.

1. **Gabriele, M.**; Brandão, H. B.; Grosse-Holz, S.; Jha, A.; Dailey, G. M.; Cattoglio, C.; Hsieh, T.-H. S.; Mirny, L.; Zechner, C.; Hansen, A. S. Dynamics of CTCF- and Cohesin-Mediated Chromatin Looping Revealed by Live-Cell Imaging. *Science* **2022**, eabn6583. DOI: [10.1126/science.abn6583](https://doi.org/10.1126/science.abn6583) **Main Postdoc paper**
2. **Gabriele, M.**; Vulto-van Silfhout, A. T.; Germain, P.-L.; et al., . YY1 Haploinsufficiency Causes an Intellectual Disability Syndrome Featuring Transcriptional and Chromatin Dysfunction. *Am. J. Hum. Genet.* **2017**, 100 (6), 907–925. <https://doi.org/10.1016/j.ajhg.2017.05.006>. **Main PhD paper**
3. Pereira, M. F.; Finazzi, V.; Rizzuti, L.; Aprile, D.; Aiello, V.; Mollica, L.; Riva, M.; Soriani, C.; Dossena, F.; Shyti, R.; Castaldi, D.; Tenderini, E.; Carminho-Rodrigues, M. T.; Bally, J. F.; Vries, B. B. A. de; **Gabriele, M***; Vitriolo, A*; Testa, G*. YY1 Mutations Disrupt Corticogenesis through a Cell-Type Specific Rewiring of

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2025- now	Group Leader, “3D genome dynamics in differentiation and disease” Lab, SR-Tiget https://www.gabrielelab.com/
2023-2025	K99 postdoctoral fellow. Massachusetts Institute of Technology, Department of Biological Engineering, Cambridge (MA), United States of America. American-Italian Cancer Foundation (AICF) postdoctoral fellow. Massachusetts Institute of Technology, Department of Biological Engineering, Cambridge (MA), United States of America.
2021 - 2023	Co-chairs of Gene Regulatory Observatory (GRO) trainee groups “chromatin-imaging” subgroup. Broad Institute of MIT and Harvard.
2020 – 2022	Postdoctoral Associate. Massachusetts Institute of Technology, Department of Biological Engineering, Cambridge (MA), United States of America. Mentor: Anders Hansen
2020 - 2021	Research associate, AIRC fellow. Mentor: Giuseppe Testa, European Institute of Oncology, Department of Experimental Oncology, Milan, Italy
2019 -2020	Guest researcher. Radboud University, Mentor: Nael Nadif Kasri, Donders Institute for brain cognition and behavior genetics and neuroscience Nijmegen, The Netherlands
2017-2017	PhD Student. School of European Molecular Medicine (SEMM), University of Milan, European Institute of Oncology, Milan, Italy. Mentor: Giuseppe Testa, University of Milan, IEO, Milan, Italy. AIRC fellow
2014-2019	Research volunteer. Azienda ospedaliera Pisana (AOUP) Pathology (Anatomia Patologica) Pisa, Italy. Mentor: Adelaide Caligo, AOUP, University of Pisa, Pisa, Italy
2013-2014	Master thesis training. Azienda ospedaliera Pisana (AOUP) Pathology (Anatomia Patologica) Pisa, Italy. Mentors: Generoso Bevilacqua, Adelaide Caligo, AOUP, University of Pisa, Pisa, Italy.
2012-2013	Bachelor thesis training. Consiglio Nazionale delle Ricerche (CNR), Department of Biophysics, Pisa, Italy. Mentor: Giovanni Cercignani, University of Pisa, Scuola Normale Superiore, Pisa, Italy
2010-2011	

Honors

2025	ERC starting grant rank A in step 2 <i>fundable but not funded</i>
2023	K99/R00 Pathway to Independence Award (NIGMS K99GM149815, impact score: 15)
2022	American Italian Cancer Foundation (AICF) postdoctoral fellowship renewal
2021	American Italian Cancer Foundation (AICF) postdoctoral fellowship
2022	Co-organizer for social activities at the Gordon Research Seminar “Chromatin Structure and Function”, Barcelona, Spain
2022	3rd Epigenetics FUSION conference best talk (G. Cavalli & L. di Croce)
2020	Fellowship Awarded without funding due to COVID emergency - Autism Science Foundation
2019	Winner of EMBO travel grant - EMBO WORKSHOP - Chromatin and Epigenetics, Heidelberg, Germany
2018	Winner of Keystone Symposia “Future of Science” Fund scholarship, Whistler, BC, Canada
2018	Winner of Boehringer Ingelheim Fonds travel grant 2018 to attend “FENS Cajal course – Developmental Neurobiology and Pathologies”, 2018, Bordeaux Neurocampus, France.
2017	Discovery of “Gabriele-de Vries Syndrome” OMIM: # 617557
2017	Winner of EMBO 3 months short-term fellowship
2017-2019	Awarded with 3-years “AIRC for Italy” scholarship (Italian Association for Cancer Research)
2015	Best poster defense prize - 11th Course on Epigenetics - Institute Curie, Paris, France

C. Contributions to Science

1. Post-doc: I joined Prof. Hansen's as his first lab member when he opened his lab at MIT. In my first postdoctoral project, I focused on understanding the dynamics of topologically associating domains (TADs) mediated by CTCF and cohesin in living cells. Contrary to what was previously suggested by bulk and fixed-cell-based studies, we have found that TADs are highly dynamic, and the fully looped state exists in only a minority of cells. I led the experimental work and contributed to the analysis. This study represented a significant step forward in understanding the mechanisms of 3D chromatin organization and in developing methodologies to study chromatin dynamics in living cells. Indeed, we established new experimental, statistical, and imaging processing approaches available to the scientific community that set a new standard for the field. Also, I contributed to 3D genome dynamics and biophysics studies employing both microscopy and 3D genomics approaches. After completion of the CTCF- and cohesin-looping project (Gabriele et al., Science 2022), I have shifted my focus to understanding enhancer-promoter interactions and the establishment of gene expression during neuronal differentiation, funded by an NIH NIGMS K99, focusing on Foxg1 activation during differentiation.

- 1 Brandão HB*, **Gabriele M***, Hansen AS. *Tracking and interpreting long-range chromatin interactions with super-resolution live-cell imaging*. Curr Opin Cell Biol. **2021**. PMID: [PMC8364313](https://pubmed.ncbi.nlm.nih.gov/34111111/).
- 2 **Gabriele M***, Brandão HB*, Grosse-Holz S*, Jha A, Dailey GM, Cattoglio C, Hsieh TS, Mirny L, Zechner C, Hansen AS. *Dynamics of CTCF- and cohesin-mediated chromatin looping revealed by live-cell imaging*. Science. **2022** Apr 29;376(6592):496-501. doi: 10.1126/science.abn6583. Epub 2022 Apr 14. PMID: [PMC9069445](https://pubmed.ncbi.nlm.nih.gov/35811111/)
- 3 Nagano M., Hu B., Ogata K., Umemura F., Ishikura Y., Nosaka Y, Sasada H, Wang H., Kondo D., Katou Y., Mizuta K., Yabuta Y., Ohta H., de L. Vitorino F., Arima H., Majewski J., Garcia B., Ishihama Y., Suzuki S., Katsifis S., Yoshinaga M., Litos G., Nagasaka K., Tang W., Ichikawa T., **Gabriele M.**, Takeuchi O., Yoshida S., Hansen S.A., Peters JM., Saitou M. *The mitotic STAG3-cohesin shapes male germline nucleome*. **2025** Nature Structural and Molecular Biology. <https://doi.org/10.1038/s41594-025-01647-w>
- 4 Jusuf JM, Grosse-Holz S, **Gabriele M**, Mach P, Flyamer IM, Zechner C, Giorgetti L, Mirny LA, Hansen SA. *Genome-wide absolute quantification of chromatin looping*. bioRxiv. **2025**. Under revision NSMB. [PMC11812599](https://pubmed.ncbi.nlm.nih.gov/35811111/)

2. Graduate student: As a graduate student in the laboratory of Prof. Giuseppe Testa at the European Institute of Oncology, I focused my studies on the disease modeling of diseases caused by mutations in chromatin regulators. First, I contributed to understanding how YY1 mutations cause a neurodevelopmental disorder, later named Gabriele-de Vries syndrome (GADEVs, phenotype MIM number: #617557). We investigated the mutational status of patients with intellectual disabilities who lacked a molecular diagnosis and found a subset of patients with YY1 mutations. I led the molecular investigation of the impact of YY1 mutations. Here we found that patient-derived cells displayed lowered H3K27Ac at the sites with a loss of YY1, suggesting this disease to be caused by a defect in enhancer regulation. This discovery allowed us to start a follow-up of GADEVs individuals and suggested to the scientific community to look for YY1 mutational status. I am still contributing to updating the clinical features of this syndrome by volunteering as a moderator in a web-based platform where we collect the submitted clinical data of the newly identified GADEVs individuals. I also established patient-derived induced pluripotent stem cells (iPSCs) to study specific dysregulation in cortical neurons and cortical organoids (Pereira et al., 2025). In parallel, I established a patient-derived iPSCs platform to study Kabuki Syndrome (KS), caused by mutations in *KMT2D* in multiple disease-relevant tissues (Gabriele et al., 2021). Here we identified a gene regulatory network disrupted in KS disease-relevant tissues and a druggable electrophysiological phenotype in cortical neurons usable for drug discovery.

- 1 **Gabriele M**, Vulto-van Silfhout AT, Germain PL, Vitriolo A, Kumar R, Douglas E, Haan E, Kosaki K, Takenouchi T, Rauch A, Steindl K, Frengen E, Misceo D, Pedurupillay CRJ, Stromme P, Rosenfeld JA, Shao Y, Craigen WJ, Schaaf CP, Rodriguez-Buritica D, Farach L, Friedman J, Thulin P, McLean SD, Nugent KM, Morton J, Nicholl J, Andrieux J, Stray-Pedersen A, Chambon P, Patrier S, Lynch SA,

- Kjaergaard S, Tørring PM, Brasch-Andersen C, Ronan A, van Haeringen A, Anderson PJ, Powis Z, Brunner HG, Pfundt R, Schuurs-Hoeijmakers JHM, van Bon BWM, Lelieveld S, Gilissen C, Nillesen WM, Vissers LELM, Gecz J, Koolen DA, Testa G, de Vries BBA. *YY1 Haploinsufficiency Causes an Intellectual Disability Syndrome Featuring Transcriptional and Chromatin Dysfunction*. *Am J Hum Genet*. **2017** Jun 1;100(6):907–925. PMCID: [PMC5473733](#)
- 2 **Gabriele M**, Lopez Tobon A, D'Agostino G, Testa G. *The chromatin basis of neurodevelopmental disorders: Rethinking dysfunction along the molecular and temporal axes*. *Prog Neuropsychopharmacol Biol Psychiatry*. **2018** Jun 8;84(Pt B):306–327. [PMID: 29309830](#)
 - 3 Sá MJN, **Gabriele M**, Testa G, Vries BB de. *Gabriele-de Vries Syndrome*. *GeneReviews*. University of Washington, Seattle; **2019** May 30. [PMID: 31145572](#)
 - 4 *Pereira, M. F.; Finazzi, V.; Rizzuti, L.; Aprile, D.; Aiello, V.; Mollica, L.; Riva, M.; Soriani, C.; Dossena, F.; Shyti, R.; Castaldi, D.; Tenderini, E.; Carminho-Rodrigues, M. T.; Bally, J. F.; Vries, B. B. A. de; **Gabriele, M***; Vitriolo, A*; Testa, G*. *YY1 Mutations Disrupt Corticogenesis through a Cell-Type Specific Rewiring of Cell-Autonomous and Non-Cell-Autonomous Transcriptional Programs*. *Mol psychiatry* **2025**. <https://doi.org/10.1038/s41380-025-02929-x> ***Co-senior author***
3. Undergraduate: I carried out my master's thesis in the laboratory of Maria Adeliade Caligo, at the Azienda Ospedaliera Universitaria Pisana, Pisa, Italy. Using the NGS Ion Torrent, I investigated the association between germline variants in 24 genes of the DNA repair pathway and the clinical outcomes of neoadjuvant anthracycline and taxane therapy in patients with triple-negative breast cancer (TNBC). I was among the first students in Pisa to analyze clinical data with NGS. Here, we found that some variants in the selected DNA damage response genes, other than *BRCA1*, can predict the outcome of neoadjuvant therapy, opening new options for clinical management (Spugnesi, **Gabriele** et al. 2016).
- 1 Spugnesi L, **Gabriele M**, Scarpitta R, Tancredi M, Maresca L, Gambino G, Collavoli A, Aretini P, Bertolini I, Salvadori B, Landucci E, Fontana A, Rossetti E, Roncella M, Naccarato GA, Caligo MA. *Germline mutations in DNA repair genes may predict neoadjuvant therapy response in triple negative breast patients*. *Genes Chromosomes Cancer*. 2016 Dec;55(12):915-924. doi: 10.1002/gcc.22389. Epub 2016 Jul 26. PubMed [PMID: 27328445](#).
4. Collaborations: Given my expertise in epigenetics and disease modeling, I have been involved in several collaborations during my career. Here I briefly mention those ones that are either published or close to being published. In the Testa laboratory, I initiated projects focused on Helsmoortel-van der Aa syndrome (caused by mutations in *ADNP*; Rizzuti et al., *BioRxiv*, 2025, *invited for revision Nat comm*) and Weaver syndrome (caused by mutations in subunits of *PRC2*; Pezzali, Trattaro et al., *invited for revision Nat comm*), now led by other graduate students. Here, we dissected the molecular impact of the mutations of each disease, finding dysregulated druggable pathways and elucidating the mechanism by which each disease manifests. Moreover, I contributed to a drug-screening study where we used epigenetic drugs to treat an autism spectrum disorder. Here, we identified three histone deacetylase inhibitors that restore *GTF2I* expression, a master regulator of 7q11.23 duplication syndrome (Cavallo et al, 2020). Also, I contributed to benchmarking diverse cortical organoids differentiation methods to identify the one that recapitulates fetal corticogenesis (Cheroni et al., 2022). In addition, I contributed to the discovery that Koolen-de Vries syndrome (caused by mutations in *KANSL1*) affects neuronal electrophysiology by altering autophagy (Linda et al., 2022). I participated in an organoid-based disease modeling study to understand how *CHD8* mutations cause a syndromic form of autism (Villa et al., 2022). We have found that developmental trajectories are altered in *CHD8* isogenic brain organoids. In addition, I directly contributed to the formation of an international consortium (IMPACT: Identification of converging Molecular Pathways Across Chromatinopathies as Targets for Therapy) for the study of targeted therapy in neurodevelopmental disorders caused by mutations in chromatin regulators, composed of the groups of Hans van Bokhoven, Giacomo Cavalli, Gaia Novarino, Giuseppe Testa, Frank Kooy, and James Ellis.
- 1 Cheroni C, Trattaro S, Caporale N, López-Tobón A, Tenderini E, Troglio F, **Gabriele M**, Bressan RB, Pollard SM, Gibson WT, Testa G. *Benchmarking brain organoid recapitulation of fetal corticogenesis*. *Translational Psychiatry*; 2022. <https://doi.org/10.1038/s41398-022-02279-0>

- 2 Villa, C. E.; Cheroni, C.; Dotter, C. P.; López-Tóbon, A.; Oliveira, B.; Sacco, R.; Yahya, A. Ç.; Morandell, J.; **Gabriele, M.**; Tavakoli, M. R.; Lyudchik, J.; Sommer, C.; Gabitto, M.; Danzl, J. G.; Testa, G.; Novarino, G. *CHD8 Haploinsufficiency Links Autism to Transient Alterations in Excitatory and Inhibitory Trajectories*. *Cell Rep.* 2022, 39 (1). <https://doi.org/10.1016/j.celrep.2022.110615>.
- 3 Linda K, Lewerissa EI, Verboven AHA, **Gabriele M**, Frega M, Klein Gunnewiek TM, Devilee L, Ulferts E, Hommersom M, Oudakker A, Schoenmaker C, van Bokhoven H, Schubert D, Testa G, Koolen DA, de Vries BBA, Nadif Kasri N. *Imbalanced autophagy causes synaptic deficits in a human model for neurodevelopmental disorders*. *Autophagy*. 2022, PMID: 34286667; PubMed Central PMCID: [PMC8942553](https://pubmed.ncbi.nlm.nih.gov/PMC8942553/)
- 4 Cavallo F, Troglio F, Fagà G, Fancelli D, Shyti R, Trattaro S, Zanella M, D'Agostino G, Hughes JM, Cera MR, Pasi M, **Gabriele M**, Lazzarin M, Mihailovich M, Kooy F, Rosa A, Mercurio C, Varasi M, Testa G. High-throughput screening identifies histone deacetylase inhibitors that modulate GTF2I expression in 7q11.23 microduplication autism spectrum disorder patient-derived cortical neurons. *Mol Autism*. 2020 Nov 19;11(1):88. PubMed PMID: 33208191; PubMed Central PMCID: [PMC7677843](https://pubmed.ncbi.nlm.nih.gov/PMC7677843/).

Complete list of personal publications:

<https://www.ncbi.nlm.nih.gov/myncbi/michele.gabriele.1/bibliography/public/>
<https://scholar.google.it/citations?user=TrJJS78AAAAJ&hl=en>