

BIOGRAPHICAL SKETCH

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NAME: Krenn, Veronica

eRA COMMONS USER NAME (credential, e.g., agency login): -

POSITION TITLE: Principal Investigator

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 (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Milan-Bicocca, Milan ITALY	B.S.	10/2007	Cell biology
University of Milan-Bicocca, Milan ITALY	Diploma	11/2009	Cell biology
University of Milan, Milan ITALY	PhD	03/2014	Cell biology
Max Planck Institute for Molecular Physiology, Dortmund, Germany	Postdoctoral	03/2015	Cell biology
Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna, Austria	Postdoctoral	08/2021	Neurobiology

A. Personal Statement

I am a Junior Principal Investigator with a research focus on the molecular and cellular mechanisms underlying neurodevelopmental disorders. My expertise spans cell biology, neurodevelopmental biology, and infection biology, with specialized training in human pluripotent stem cell and brain organoid research. These highly tractable models simulate human brain development and disease, allowing detailed exploration of the cellular basis of neurological conditions. During my postdoctoral training in Jürgen Knoblich's lab, a leading center for brain organoid research, I pioneered the use of brain organoid models to study neuroimmune interactions and helped establish brain organoids as transformative tools in neuroscience. Following a career break in 2021 for family obligations, I resumed my research promptly and secured funding through the prestigious Human Technopole Early Career Fellowship. As Principal Investigator, I am advancing brain organoid models to more accurately replicate in vivo development while engineering immune-competent organoids to study neuroimmune processes. Our current research focuses on generating microglia-enriched organoids, providing a powerful platform to investigate the origins of autism spectrum disorders. Additionally, we are refining techniques for precise environmental and genetic manipulation in organoids and leveraging advanced genomics technologies to dissect the genetic and environmental drivers of neuroimmune dysfunction in neurological disorders. With a highly skilled team, cutting-edge expertise, and state-of-the-art infrastructure, my lab is exceptionally positioned to conduct innovative research that directly aligns with and propels the objectives of this application.

Ongoing projects that I would like to highlight include:

Human Technopole Early Career Fellowship
Krenn (PI)
2022-2026
Project Title: Human Neuroimmunobiology.

The project aims at dissecting the contributions of interferon signalling and microglia phenotypes in the etiology of neurodevelopmental conditions using human brain organoids.

Academic Funding for Competitive Research

Krenn (PI)

2023-2025

Project title: A human organoid-based culture system of central nervous system-associated macrophages.

Telethon & Cariplo Foundations Alliance

Nicolis (PI), Role- Collaborator

2022-2024

Project title: A CRISPR-Cas9 high-throughput screening in human brain organoids of T-dark putative downstream effectors of Sox2.

The Foundation for AIDS Research

Herrera Carrillo (PI), Role- Collaborator

2024-2026

Project title: In vivo gene therapy: An HIV Cure in a Syringe

The project aims at testing the delivery of lipid nanoparticles (LNPs) in microglia-containing cerebral organoids for the development of an advanced HIV-targeted CRISPR-Cas strategy.

B. Positions, Scientific Appointments, and Honors

Positions & Scientific Appointments:

2024 Italian Qualification to the role of Associated Professor in Experimental Biology

2022 – present Principal Investigator and Human Technopole Early Career Fellow, Dept.

Biotechnology and Bioscience, University of Milan-Bicocca, Italy

2024 – present Member of Italian Society of Neuroscience (SINS)

2023 – present Member of Centro3R

2023 – present Member of Italian Glia Network (IGN)

2023 – present Member of BraYn Association

2022 – present Member of Milan Center of Neuroscience (NeuroMI)

2015 – 2021 Postdoctoral Fellow, Jürgen Knoblich lab, Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna, Austria

2018 – 2019 Consultant, CamBioScience, UK

2014 – 2015 Postdoctoral fellow, Andrea Musacchio lab, Max Planck Institute of Molecular Physiology, Dortmund, Germany

2010 – 2014 PhD student, Andrea Musacchio lab, European Institute of Oncology, Milan, Italy & Max Planck Institute of Molecular Physiology, Dortmund, Germany

Honors:

2021 Human Technopole Early Career Award

2021 Best Poster Award, SY-Stem Conference, IMBA, Vienna

2017 – 2019 Marie Skłodowska-Curie Actions (MSCA) Individual Postdoctoral Fellowship

2016 – 2017 EMBO Long-term Postdoctoral fellowship

2015 Otto Hahn Medal for outstanding PhD work, Max Plank Society

2014 Invitation to the 64th Lindau Nobel Laureate Meeting Physiology & Medicine, Germany

2010-213 Boehringer Ingelheim Fonds (BIF) PhD Fellowship

C. Contributions to Science

Researcher profile including publication list can be found here: <https://orcid.org/0000-0002-7416-3385>

1. Deciphering the molecular basis of chromosome segregation

My early publications focused on the molecular mechanisms governing accurate chromosome segregation, a fundamental process essential for cell proliferation and differentiation in human cells. Errors in this process can lead to severe neurodevelopmental disorders, such as microcephaly, and aneuploidy, a hallmark of cancer. These studies explored the molecular interactions between the mitotic proteins Bub1 and BubR1 and the kinetochore protein Knl1 (CASC5), a gene linked to primary microcephaly in humans. By identifying precise docking sites and interaction domains, my work elucidated the molecular basis of these interactions, offering unprecedented insights into the mechanisms underlying chromosome segregation. This research represented a significant conceptual advance in the field and was recognized with the Otto Hahn Medal in 2014, a prestigious award for outstanding contributions by young scientists during their doctoral work. In addition to my primary research, I contributed to several collaborative studies in the lab that further characterized the interactions of Knl1 with other kinetochore components. These efforts advanced our understanding of how the kinetochore mediates chromosome attachment to the mitotic spindle, solidifying the functional significance of Knl1 in maintaining genomic stability and in neurodevelopmental context.

- a. **Krenn, V.**, K. Overlack, I. Primorac, S. van Gerwen and A. Musacchio (2014). KI Motifs of Human Knl1 Enhance Assembly of Comprehensive Spindle Checkpoint Complexes around MELT Repeats. *Curr Biol.* 24:29-39. doi:10.1016/j.cub.2013.11.046
- b. **Krenn, V.***, A. Wehenkel*, X. Li*, S. Santaguida and A. Musacchio (2012). Structural analysis reveals features of the spindle checkpoint kinase Bub1-kinetochore subunit Knl1 interaction. *The Journal of cell biology*, 196:451-467, doi:10.1083/jcb.201110013 * Equal contributions
- c. Overlack, K., I. Primorac, M. Vleugel, **V. Krenn**, S. Maffini, I. Hoffmann, G.J. Kops and A. Musacchio (2015). A molecular basis for the differential roles of Bub1 and BubR1 in the spindle assembly checkpoint. *eLife (Cambridge)*, doi:10.7554/eLife.05269
- d. Huis In 't Veld, P.J., S. Jeganathan, A. Petrovic, P. Singh, J. John, **V. Krenn**, F. Weissmann, T. Bange and A. Musacchio (2016). Molecular basis of outer kinetochore assembly on CENP-T. *eLife (Cambridge)*. Dec 24;5. doi:10.7554/eLife.21007.
- e. Petrovic, A., S. Pasqualato, P. Dube, **V. Krenn***, S. Santaguida*, D. Cittaro, S. Monzani, L. Massimiliano, J. Keller, A. Tarricone, A. Maiolica, H. Stark, and A. Musacchio (2010). The MIS12 complex is a protein interaction hub for outer kinetochore assembly. *The Journal of Cell Biology*. 190:835-852, doi:10.1083/jcb.201002070. * equal contributions

2. Unravelling Neuroimmune Mechanisms in Neurodevelopmental Disorders Using Brain Organoids

Genetic and environmental factors are well-established risks for neurodevelopmental disorders, yet the underlying mechanisms remain incompletely understood. My recent research has illuminated some of these molecular pathways, particularly those related to neuroimmune dysfunction—an increasingly recognized contributor to these disorders. Focusing on congenital viral infections, a leading cause of neurological sequelae such as microcephaly, my work utilized brain organoids—three-dimensional human tissue models that mimic brain development—and mouse models to investigate virus-host interactions. These studies uncovered virus-specific mechanisms of neurodevelopmental toxicity, including differential activation of innate immune pathways in brain cells.

Importantly, my research demonstrated a virus-specific neuroprotective role for type I interferons, revealing a context-dependent function of innate immune signaling in the developing brain. This work established brain organoids as a robust model for studying virus-induced neurological damage and highlighted environmental contributions to neurodevelopmental diseases. Additionally, my publication pioneered the use of organoids to study brain disorders stemming from immune signaling dysregulation. My findings on the complex regulation of type I interferon signaling in human brain organoids have paved the way for ongoing mechanistic studies in my laboratory, where we aim to further elucidate how early-life immune challenges shape neurodevelopment and contribute to disease.

- a. **Krenn, V.**, Bosone, C., Burkard, T.R., Spanier, J., Kalinke, U., Calistri, A., Salata, C., Rilo Christoff, R., Pestana Garcez, P., Mirazimi, A., Knoblich, J.A., (2021). Organoid modeling of Zika and herpes simplex virus 1 infections reveals virus-specific responses leading to microcephaly. *Cell Stem Cell*, doi:10.1016/j.stem.2021.03.004.
- b. Christoff, R. R., Nani, J. V., Lessa, G., Rabello, T., Rossi, A. D., **Krenn, V.**, Higa, L. M., Tanuri, A., Garcez, P. P., & Hayashi, M. A. F. (2023). Assessing the role of Ndel1 oligopeptidase activity in congenital Zika syndrome: Potential predictor of congenital syndrome endophenotype and treatment response. *Journal of Neurochemistry*, 1–14. <https://doi.org/10.1111/jnc.15918>
- c. Nani J. V., **Krenn V.**, Christoff R. R., Rabello T., Garcez P. P. & Hayashi, M. A. F (2024). RNA-seq transcriptome of ZIKV-infected brain organoids reanalysis implicates Ndel1 oligopeptidase and its cytoskeleton protein binding partners in the infection pathogenesis and recovery following interferon treatment. *Brain Research*. 149371, <https://doi.org/10.1016/j.brainres.2024.149371>

3. Advancing Human Brain Organoid Models as tools for neurology research

Human brain organoids are an innovative culture system that models key aspects of human brain development from pluripotent stem cells. Since the foundational work in the Knoblich lab, organoid technology has become a cornerstone of neuroscience research. Building on this foundation, I contributed to two landmark studies that refined organoid models to better capture unique features of human brain development. The first study established a system for investigating long-range interactions and human interneuron migration (Bajaj et al., 2021), while the second recreated fronto-temporal cortical positioning to explore regional brain organization (Bosone et al., 2024). By validating these advanced models, this work has significantly expanded the toolkit for studying brain development, offering transformative opportunities for developmental biology and disease research.

- a. Bosone C., Castaldi D., Burkard T.R., Guzman S.J., Wyatt T., Cheroni C., Caporale N., Bajaj S., Bagley J.A., Li C., Sorre B., Villa C.E, Testa G. #, **Krenn V.**# and Knoblich J.A.# (2024). A polarized FGF8 source specifies frontotemporal signatures in spatially oriented cell populations of cortical assembloids. *Nature Methods*. <https://doi.org/10.1038/s41592-024-02412-5> #corresponding authors
- b. Bajaj, S., J.A. Bagley, C. Sommer, A. Vertesy, **V. Krenn**, S. N. Wong, J. Levi-Strauss and J.A. Knoblich. (2021). Neurotransmitter signaling regulates distinct phases of multimodal human interneuron migration. *EMBO J*, doi:10.15252/embj.2021108714