

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 studying the molecular and cellular mechanisms underlying neurodevelopmental disorders. My expertise integrates molecular and cell biology, neurodevelopment, and infection biology, with specialized training in human pluripotent stem cell and brain organoid research. These advanced models allow us to simulate human brain development and disease, enabling detailed investigation 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 organoids to study prenatal immune stress as a risk factor for neurodevelopmental disabilities, helping to establish brain organoids as transformative tools in neuroscience.

After a career break in 2021 for family obligations, I promptly resumed my research and secured funding through the prestigious Human Technopole Early Career Fellowship. As a Principal Investigator, my research focuses on how prenatal immune stress- in particular viral infections and prenatal interferon exposure- disrupts neurodevelopmental trajectories. We are leveraging and advancing brain organoid models to more accurately replicate in vivo development and immune responses, with particular emphasis on generating microglia-enriched organoids to investigate microglia's contributions. In parallel, we are refining approaches for precise environmental and genetic manipulation in organoids and molecular studies, and applying advanced genomics technologies to uncover the mechanisms underlying immune-driven pathogenesis. With a skilled team, cutting-edge expertise, and access to state-of-the-art infrastructure, my lab is uniquely positioned to deliver innovative research that directly advances the objectives of this application.

Ongoing projects that I would like to highlight include:

Human Technopole Early Career Award
Role: PI

2022-2026

Project Title: *Human Neuroimmunobiology*

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

GEDi HT National Facility (24-GEDM-Pilot, Project No.1990387)

PI: Krenn

Project Title: *Dissecting TGF- β 1 Signaling and Microglia-Organoid Co-Culture Dynamics Using TGFB2-Knockout hPSCs*

The project aims at generating TGFB2-Knockout hPSCs to prove the requirement of TGFB receptor signalling in microglia-containing organoids

The Foundation for AIDS Research

Role: Collaborator; PI: Herrera Carrillo Elena, UMC Amsterdam

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 as 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 Planck Society
2014 Invitation to the 64th Lindau Nobel Laureate Meeting Physiology & Medicine, Germany
2010-2013 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. 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. Molecular mechanisms underlying the etiology of neurodevelopmental disorders

Genetic and environmental factors are well-established risks for neurodevelopmental disorders, yet the molecular mechanisms remain incompletely understood. My recent work has shed light on these pathways, with a focus on prenatal immune stress as an emerging contributor. Using brain organoids—three-dimensional human tissue models that recapitulate key features of brain development—together with mouse models, I investigated the impact of congenital TORCH infections, a leading cause of neurological sequelae such as microcephaly. These studies identified radial glia, the main neural stem cells of the developing brain, as primary viral targets and revealed molecular pathways underlying virus-specific neurodevelopmental toxicity, alongside a limited capacity of these cells to mount innate immune responses. Importantly, my research uncovered a neuroprotective role for the antiviral cytokines type I interferons during infection-driven neurodevelopmental injury. My work not only established brain organoids as a powerful model for studying virus-induced neurological damage but also pioneered their application in dissecting immune signaling dysregulation in neurodevelopmental disease. By linking cytokine responses to developmental outcomes, my studies opened a new avenue for understanding how prenatal immune challenges shape brain development. Building on this foundation, my laboratory is now investigating how transient cytokine exposure during pregnancy may leave lasting molecular “memories” that alter neurodevelopmental trajectories.

- 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 in vitro models as tools for neural stem cell research

Human brain organoids are an innovative culture system that models fundamental aspects of human brain development from pluripotent stem cells. Since their inception in the Knoblich lab, organoid technology has become a cornerstone of modern neuroscience. Building on this foundation, I played a key role in two landmark studies that refined organoid models to better capture defining features of development and human neural stem cell behavior. In the first, I helped establish a system to investigate long-range interactions and human interneuron migration (Bajaj et al., 2021). In the second, I contributed to recreating fronto-temporal cortical positioning, enabling the study of regional organization of neural stem cells (Bosone et al., 2024). More recently, I contributed to a collaborative work (Xu et al. accepted) leveraging both 2D and 3D hPSC-derived neural progenitor cultures to identify a novel gene responsible for microcephaly. By leading the validation of these models and refining their application, I have significantly expanded the toolkit available for probing brain development. This work provides transformative opportunities not only for basic developmental biology but also for uncovering the mechanisms of neurological disease.

- 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
- c. Xu, Mao, Liu, Jiang, Wong, Liu, Wang, Zhan, Liu, Yu, Yuan, **V. Krenn**, Bai, Huang, Xie, Kirchhoff, Wang, Guo, Bian. CETN3 Deficiency Induces Microcephaly by Disrupting NPC Cell Fate through Impaired Centrosome Assembly and RNA Splicing (accepted at EMBO Molecular Medicine).