

BIOGRAPHICAL SKETCH

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NAME: Mirko Cortese

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

POSITION TITLE: Associate Professor – University of Campania Luigi Vanvitelli

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 Naples, Italy	B.Sc.	2006	Molecular Biotechnology
University of Naples, Italy	M.Sc.	2008	Molecular Biotechnology
University of Bologna, Italy	Ph.D.	2013	Molecular and cellular biology
University of Heidelberg, Germany	Postdoc	2021	Molecular Virology

A. Personal Statement

The overarching theme of my research is to decipher the network of interactions between viruses and their host, by analyzing the impact of viral infections on cellular organelle morphology and function. I developed a keen interest in virology and host-pathogen interactions during my Ph.D. and I have decided to further hone this interest during my post-doctoral training in the department of molecular virology at the University of Heidelberg, where I worked on positive-sense single-stranded RNA (+ssRNA) viruses. As a PI, I started my own independent research group at the Telethon Institute of Genetics and Medicine (TIGEM) in Italy where I have established a research program aimed to define the molecular and structural mechanisms regulating viral infections and virus interaction with the host cell. The research group has also been established thanks to a generous one million/five years grant received by the Human Technopole that, through a competitive peer-reviewed process, selected my application for the Early Career Fellowship award. In addition, I have received funding from the Italian government and other private research institutions. In my group, we combine advanced imaging, -omics techniques and molecular virology to dissect each step of the viral infection cycle, to define the viral and host factors required for infection progression and the host strategies to block them.

B. Positions, Scientific Appointments, and HonorsPositions and Employment

2013-2021 Postdoctoral Fellow, Department of Molecular Virology, University of Heidelberg, Heidelberg (DE)
2021- Assistant Investigator, Telethon Institute of Genetics and Medicine, Pozzuoli (IT)
2022- Associate Professor, Department of Environmental, Biological and Pharmaceutical Sciences and Technologies, University of Campania Luigi Vanvitelli, Caserta (IT)

Honors

2024 European Academy of Sciences Rising Star in Microbiology
2023 Italian Society of Virology Luria Award
2021 Human Technopole Early Career Fellowship
2020 Viruses 2020 Poster Award

C. Contributions to Science

1. My studies on the replication mechanisms of positive stranded RNA viruses have shed light on how SARS-CoV-2 interacts with the host cell and contributed to defining the cytopathic effects induced by viral replication on cellular organelles structure and function. Using advanced imaging approaches that combined light and electron microscopy, both at cryogenic and at room temperature, we have described how SARS-CoV-2 builds its replicative niche within the host endoplasmic reticulum, a replication organelle formed by a tubo-vesicular network of double membrane vesicles in which the virus replicates its genome. We have also set-up cellular sensors that detect in real-time viral infection to measure organelle morphodynamics during viral replication. Finally, we have devised strategies that, by altering the biogenesis of viral replication organelles, can blunt SARS-CoV-2 replication and thus block viral spread within the host.
 - a) **Cortese, M.#**, Lee, J. Y., Cerikan, B., Neufeldt, C. J., Oorschot, V. M. J., Kohrer, S., . . . Bartenschlager, R.# (2020). Integrative Imaging Reveals SARS-CoV-2-Induced Reshaping of Subcellular Morphologies. *Cell Host Microbe*, 28(6), 853-866 e855. doi:10.1016/j.chom.2020.11.003
 - b) Klein, S.*, **Cortese, M.***, Winter, S. L., Wachsmuth-Melm, M., Neufeldt, C. J., Cerikan, B., . . . Chlanda, P. (2020). SARS-CoV-2 structure and replication characterized by in situ cryo-electron tomography. *Nature communications*, 11(1), 1-10.
 - c) Pahmeier, F., Neufeldt, C. J., Cerikan, B., Prasad, V., Pape, C., Laketa, V., . . . **Cortese, M.** (2021). A versatile reporter system to monitor virus-infected cells and its application to dengue virus and SARS-CoV-2. *Journal of virology*, 95(4), e01715-01720.
 - d) Tiano, S. M. L., Landi, N., Marano, V., Ragucci, S., Bianco, G., Cacchiarelli, D., . . . **Cortese, M.** (2024). Quinoin, type 1 ribosome inactivating protein alters SARS-CoV-2 viral replication organelle restricting viral replication and spread. *Int J Biol Macromol*, 280(Pt 1), 135700. doi:10.1016/j.ijbiomac.2024.135700
2. I have contributed to the characterization of the host factors involved in Orthoflaviviruses infection, identifying potential novel targets for antiviral development. Using imaging approaches, we have described the ultrastructural alterations induced by Zika virus on the cell, showing how viral infection induces the formation of viral replication organelles within the endoplasmic reticulum membranes. We showed how viral replication and virion assembly are spatio-temporally coordinated events and, using high-content screening, we identified cellular kinases that could differentially modulate those processes.
 - a) **Cortese, M.**, Goellner, S., Acosta, E. G., Neufeldt, C. J., Oleksiuk, O., Lampe, M., . . . Bartenschlager, R. (2017). Ultrastructural Characterization of Zika Virus Replication Factories. *Cell Rep*, 18(9), 2113-2123. doi:10.1016/j.celrep.2017.02.014
 - b) **Cortese, M.**, Kumar, A., Matula, P., Kaderali, L., Scaturro, P., Erfle, H., . . . Bartenschlager, R. (2019). Reciprocal Effects of Fibroblast Growth Factor Receptor Signaling on Dengue Virus Replication and Virion Production. *Cell Rep*, 27(9), 2579-2592 e2576. doi:10.1016/j.celrep.2019.04.105
 - c) **Cortese, M.**, Mulder, K., Chatel-Chaix, L., Scaturro, P., Cerikan, B., Plaszczyca, A., . . . Bartenschlager, R. (2021). Determinants in Nonstructural Protein 4A of Dengue Virus Required for RNA Replication and Replication Organelle Biogenesis. *Journal of virology*, 95(21), e01310-01321.
3. I have contributed to the identification of novel viral functions responsible for the molecular mimicry of host Fc-binding receptors by human cytomegalovirus (hCMV). I have identified members of the UL11 family of viral proteins able to bind the Fc portion of the human immunoglobulins. I have defined binding specificities and intracellular trafficking of viral Fc-binding proteins (FcBP) upon interaction with anti-hCMV antibodies, a process aimed to block IgG-mediated immune responses. Using imaging approaches, we have dissected the intracellular route followed by the immune-complex bound to the viral FcBP, discovering a novel immune-evasion strategy put in place by HCMV that consists in the incorporation of human IgG during virus assembly to release IgG-coated virions.
 - a) **Cortese, M.**, Calò, S., D'Aurizio, R., Lilja, A., Pacchiani, N., & Merola, M. (2012). Recombinant human cytomegalovirus (HCMV) RL13 binds human immunoglobulin G Fc. *PLoS one*, 7(11), e50166.

- b) Vezzani, G., Pimazzoni, S., Ferranti, R., Calo, S., Monda, G., Amendola, D., . . . **Cortese M#** and Merola, M.# (2022). Human immunoglobulins are transported to HCMV viral envelope by viral Fc gamma receptors-dependent and independent mechanisms. *Front Microbiol*, 13, 1106401. doi:10.3389/fmicb.2022.1106401
4. I took part in several studies aimed at defining the immune cell response to viral infection. I have contributed to analyze which cellular sensor is activated by SARS-CoV-2, describing the role of the cGAS-STING pathway in virus sensing and cytokines secretion upon coronavirus infection. My role was to analyze cells activation and inflammatory response using imaging and virological assays. I have also contributed to studies that helped to define the importance of interferon lambda in controlling SARS-CoV-2 infection. I have supported the research activity aimed to define the alterations induced on the mitochondria-associated membranes (MAM), an important innate immune signaling platform, during flavivirus infection. By modulating mitochondria morphodynamics, we demonstrated that Orthoflaviviruses disrupt mitochondria-ER contact sites, thus impairing the activation of the MAVS-RIG-I pathway and escaping immune recognition. I have developed imaging assays to define, visualize and quantify membrane contact sites and innate immunity activation.
- a) Chatel-Chaix, L., **Cortese, M.**, Romero-Brey, I., Bender, S., Neufeldt, C. J., Fischl, W., . . . Bartenschlager, R. (2016). Dengue Virus Perturbs Mitochondrial Morphodynamics to Dampen Innate Immune Responses. *Cell Host Microbe*, 20(3), 342-356. doi:10.1016/j.chom.2016.07.008
- b) Neufeldt, C. J., Cerikan, B., **Cortese, M.**, Frankish, J., Lee, J. Y., Plociennikowska, A., . . . Bartenschlager, R. (2022). SARS-CoV-2 infection induces a pro-inflammatory cytokine response through cGAS-STING and NF-kappaB. *Commun Biol*, 5(1), 45. doi:10.1038/s42003-021-02983-5
- c) Stanifer, M. L., Kee, C., **Cortese, M.**, Zumaran, C. M., Triana, S., Mukenhirn, M., . . . Boulant, S. (2020). Critical role of type III interferon in controlling SARS-CoV-2 infection in human intestinal epithelial cells. *Cell reports*, 32(1), 107863.

*Equal contribution

#Co-corresponding author