BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Renato Brandimarti	Assistant Professor of Molecular Virology
eRA COMMONS USER NAME RBRANDI	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Bologna, Italy	Science Dr	1988	Biology
University of Bologna, Italy	PhD	1993	Cell Biology and Physiology
University of Chicago, IL	Postdoc	1993-1999	Molecular Virology

Teaching

Since 1999, I've been teaching in different Programs at the University of Bologna.

URL to teaching activity at the University of Bologna: https://www.unibo.it/sitoweb/renato.brandimarti/didattica

A. Personal Statement

Over the years, I've been interested in several aspects and mechanistic features of viral molecules involved in viral infection, with a specific focus on understanding their impact on the functions of cellular molecules in the context of the infected environment. My specific interests were driven by a particular notion: the central role that virus-cell interactions play in viral replication and virus-dependent host pathologies through alteration/repurposing of cellular activities.

Since my early studies as a PhD student at the University of Bologna, in Italy, and the subsequent post-doctoral training at the University of Chicago, in the US, I've been working with neurotropic viruses, such as Herpes Simplex Virus (HSV) and Human Immunodeficiency Virus (HIV). This specific research interest was further developed as an independent researcher at the University of Bologna, with a main focus on developing molecular tools tailored to define the role of specific players in cellular pathways involved in cognitive dysfunction and neurodegeneration.

Virus-host interactions are obligate and uniquely intimate, and can be investigated from multiple perspectives: they can be seen as a way to identify therapeutical targets, or as manageable tools to understand cellular functions, or as exploitable options to modify molecular activities. These complementary perspectives are ingrained into my research activities and brought me to focus on the molecular mechanisms leading to cognitive decline and neurodegeneration, with viruses as possible etiological agents (such as in HIV Associated Neurocognitive disorder: HAND), or as unique tools to control molecular pathways (as we are investigating with Alzheimer's Disease: AD). To this end, I have maintained an active and continuous collaboration with Dr. Meucci, and have regularly visited her laboratory at Drexel University College of Medicine in Philadelphia for the last 20 years. Our complementary backgrounds, combined with a shared interest in understanding the molecular basis of neuronal mechanisms represent the solid basis of a long-standing productive interaction.

The approach to science I just outlined is also evident in the following sections of the Contribution to Science paragraph, where I tried to make clear the different components of my research activity from a more virus-focused to a more virus-supporting cell-focused research. Ongoing and completed projects that I would like to highlight include:

NIH grant: Effects of opiates on neurons and their impact on HIV neuropathology. R01 DA32444. 2019-2024.
PI: Olimpia Meucci
Role: co-investigator

NIH grant: Effects of HIV-1 neurotoxins on lipid rafts-associated proteins. 1R21DA040519-01A1. 2016-2018.

PI: Olimpia Meucci
Role: co-Investigator
RFO Grants – University of Bologna. 2012-2014. Brandimarti, Renato (PI)
Molecular basis of virus-independent US9 transport activity.
Role: PI
Pallotti Foundation 2007-2008. Brandimarti, Renato (PI)
Role of cks1 in cell cycle progression and cell proliferation control.
Role: PI
RFO Grants – University of Bologna. 2007-2008. Brandimarti, Renato (PI)
Role of cks1 in cell cycle progression and cell proliferation control.
Role: PI
1R01-DA15014-01. 2001-2006. Olimpia Meucci (PI)
Role of chemokine receptors in neuronal survival
Role: co-investigator
RFO Grants – University of Bologna. 2002-2004. (PI)
Post-translational modifications and localization of US9 protein of Herpes Simplex Virus 1.
Role: PI
RFO Grants – University of Bologna. 2005-2007. Hochkoeppler, Alejandro (PI)
Transcriptional regulation of cks1 expression in yeast.
Role: co-investigator
Young scientists Grants– University of Bologna. 2001. (PI)
Analysis of localization of a US9-gfp chimaeric protein of Herpes Simplex Virus 1.
Role: PI

URL to Publications list in PubMed: https://www.ncbi.nlm.nih.gov/pubmed/?term=brandimarti+r

B. Positions, Scientific Appointments and Honors

Positions and Employment

1993-1995	University of Chicago, Chicago, IL. Dept. of Molecular Genetics and Cellular Biology. *Research Associate (AIDS Research Fellow)*
1995-1998	University of Chicago, Chicago, IL. Dept. of Molecular Genetics and Cellular Biology. *Research Associate*
1998-1999	University of Chicago, Chicago, IL. Dept. of Molecular Genetics and Cellular Biology. *Research Associate-Instructor*
1999-present	University of Bologna, Italy. Department of Experimental Pathology - Department of Pharmacy and Biotechnology, *Assistant Professor*
2001-present	Drexel University College of Medicine (formerly MCP-Hahnemann University), Philadelphia PA Department of Pharmacology and Physiology, *Visiting Researcher*
2011-2014	University of Bologna, Italy. *Member of the Academic Senate*.

C) Contribution to science

My interest in understanding the effects and the molecular basis of the several functional changes associated with Alzheimer's Disease (AD) and AD-Related Dementias (ADRD) developed over several years of research. This specific focus did not diverge from previous activities that were more oriented on investigating signaling mechanisms in the Central Nervous System (CNS), and on defining the contribution of individual viral proteins on the infectious process. Indeed, beside providing solid technical and rational basis, these different efforts well integrate into a research strategy that takes advantage of these complimentary perspectives.

1) Control of AD-related proteins behavior through repurposed US9-based molecular tools.

HSV is a neurotropic virus able to establish a life-long latency in the nervous system. This specific property requires specialized functionalities that can support an effective transport of the virion inside the long neuronal processes. We contributed to establish the viral protein US9 as the HSV anterograde transport protein in

axons. Furthermore, we were able to demonstrate that US9 transport properties were not dependent on other viral functions, and that it could be loaded with functional cargos that would localize in specific subcellular compartments. Finally, we showed that by modifying US9 with APP-related proteins, APP processing and AD-related proteins can be altered. This research establishes US9 as a novel tool to study AD-related molecular changes and possibly identify individual steps leading to the disease.

1. **BRANDIMARTI R**, IROLLO E, MEUCCI O. The US9-Derived Protein gPTB9TM Modulates APP Processing Without Targeting Secretase Activities. *Mol. Neurobiol. 2023*; Apr;60(4):1811-1825. doi: 10.1007/s12035-022-03153-2. PMID: 36576708 PMCID: PMC9984340
2. **BRANDIMARTI R**, HILL GS, GEIGER JD, MEUCCI O**.** The lipid raft-dwelling protein US9 can be manipulated to target APP compartmentalization, APP processing, and neurodegenerative disease pathogenesis. *Sci Rep. 2017*; 7(1):15103. doi: 10.1038/s41598-017-15128-8.
3. PEDRAZZI M, NASH B, MEUCCI O, **BRANDIMARTI R**. Molecular features contributing to virus-independent intracellular localization and dynamic behavior of the herpesvirus transport protein US9. *PLoS One. 2014*; 9(8):e104634. doi: 10.1371/journal.pone.0104634.
4. LAVAIL JH, TAUSCHER AN, SUCHER A, HARRABI O, **BRANDIMARTI R**. Viral regulation of the long distance axonal transport of herpes simplex virus nucleocapsid. *Neuroscience. 2007***;** 146(3):974-85.

2) Interplay between chemokine signaling and cell-cycle proteins in the brain

Neurons are post-mitotic cells, with cell-cycle proteins not expected to play a canonical role. Our interest in defining the effect that chemokines, namely CXCL12, have in neurons brought us to investigate changes induced by the presence of the chemokine. This series of studies contributed to our understanding of the neuroprotective activity of CXCL12 and its importance for neuronal survival and function, also providing some details on the induced molecular changes.

1. KHAN MZ, **BRANDIMARTI R**, SHIMIZU S, NICOLAI J, CROWE E, MEUCCI O.The chemokine CXCL12 promotes survival of postmitotic neurons by regulating Rb protein. *Cell Death Differ. 2008*. 15(10):1663-72.
2. KHAN MZ, SHIMIZU S, PATEL JP, NELSON A, LE MT, MULLEN-PRZEWORSKI A, **BRANDIMARTI R**, FATATIS A, MEUCCI O. Regulation of neuronal P53 activity by CXCR 4. *Mol Cell Neurosci. 2005*;30(1):58-66.
3. KHAN, M.Z., **BRANDIMARTI, R**., PATEL, J., HUYNH,N., WANG, J.,HUANG, Z., FATATIS, A., and MEUCCI, O. Apoptotic and Antiapoptotic Effects of CXCR4: Is It a Matter of Intrinsic Efficacy? Implications for HIV Neuropathogenesis. *AIDS Research and Human Retroviruses. 2004*; 20(10): 1063-71.
4. **BRANDIMARTI, R.**, KHAN, M.Z., MUSSER, B.J., RESUE, D.M., FATATIS, A., and O.MEUCCI. Regulation of celle cycle proteins by chemokine receptors: a novel pathway in HIV pathogenesis? *J Neurovirol. 2004;*10 Suppl 1:108-12.
5. KHAN, M.Z., **BRANDIMARTI, R.**, MUSSER, B.J., RESUE, D.M., FATATIS, A., and O. MEUCCI. The chemokine receptor CXCR4 regulates cell cycle proteins in neurons. *J Neurovirol. Jun;9(3)*:300-14. 2003.

3) Role of viral proteins in the HSV infectious cycle

HSV is a large DNA virus that impacts cellular functionalities at several stages during its replication cycle. Our studies significantly contributed to the understanding of the initial steps of the infection, providing findings that allowed the identification of the individual role played by viral proteins present on the HSV envelope in the attachment and penetration steps. Furthermore, we studied the fine tuning of cellular protein synthesis during viral infection. These studies were instrumental in defining the role played by specific viral proteins in establishing a productive viral infection, and are essential part of the rational background for the design and generation of oncolytic viruses currently used.

1. HE, B., CHOU, J., **BRANDIMARTI, R.**, MOHR, J., GLUZMAN, Y., and ROIZMAN, B. Suppression of the phenotype of $\gamma_1$34.5- herpes simplex virus 1: failure of activated RNA-dependent protein kinase to shut off protein synthesis is associated with a deletion in the domain of the α47 gene. *J. Virol., 71:6049-54, 1997*.
2. **BRANDIMARTI, R.**, HUANG, T., ROIZMAN, B., and CAMPADELLI FIUME, G., Mapping of Herpes Simplex Virus 1 genes with mutations which overcome host restrictions to infection. *Proc. Natl. Acad. Sci. USA, 91:5406-5410, 1994.*
3. VAN GENDEREN, I.L., **BRANDIMARTI, R.**, TORRISI, M.R., CAMPADELLI, G., and VAN MEER, G., The phospholipid composition of extracellular herpes simplex virions differs from that of host cell nuclei. *Virology, 200:831-836, 1994*.

4. CAMPADELLI, G., **BRANDIMARTI, R.**, DI LAZZARO, C., WARD, P.L., ROIZMAN, B., and TORRISI, R., Fragmentation and dispersal of Golgi proteins and redistribution of Glycoproteins and glycolipids processed through the Golgi apparatus after infection with herpes simplex virus. *Proc. Natl. Acad. Sci. USA, 90:2798-2802, 1993*.

Peer reviewed publications

IROLLO, E., NASH, B., LUCHETTA, J. BRANDIMARTI, R, MEUCCI, O. The Endolysosomal Transporter DMT1 is Required for Morphine Regulation of Neuronal Ferritin Heavy Chain. ***J Neuroimmune Pharmacol*. 2023.** 18, 495–508. https://doi-org.ezproxy.unibo.it/10.1007/s11481-023-10082-x

BRANDIMARTI R, IROLLO E, MEUCCI O. The US9-Derived Protein gPTB9TM Modulates APP Processing Without Targeting Secretase Activities. **Mol. Neurobiol. 2023**; Apr;60(4):1811-1825. doi: 10.1007/s12035-022-03153-2. PMID: 36576708 PMCID: PMC9984340

NASH B, IROLLO E, BRANDIMARTI R, MEUCCI O. Opioid Modulation of Neuronal Iron and Potential Contributions to NeuroHIV. **Methods Mol Biol. 2021**;2201:139-162. doi: 10.1007/978-1-0716-0884-5_13. PMID: 32975796; PMCID: PMC7641316.

BORSETTI F, DAL PIAZ F, D'ALESSIO F, STEFAN A, BRANDIMARTI R, SARKAR A, DATTA A, MONTÓN SILVA A, DEN BLAAUWEN T, ALBERTO M, SPISNI E, HOCHKOEPPLER A. Manganese is a Deinococcus radiodurans growth limiting factor in rich culture medium. **Microbiology**. **2018** 164(10):1266-1275. doi: 10.1099/mic.0.000698.

BRANDIMARTI R, HILL GS, GEIGER JD, MEUCCI O**.** The lipid raft-dwelling protein US9 can be manipulated to target APP compartmentalization, APP processing, and neurodegenerative disease pathogenesis. **Sci Rep. 2017**; 7(1):15103. doi: 10.1038/s41598-017-15128-8.

LAPENTA F, MONTÓN SILVA A, BRANDIMARTI R, LANZI M, GRATANI FL, VELLOSILLO GONZALEZ P, PERTICARARI S, HOCHKOEPPLER A. Escherichia coli DnaE Polymerase Couples Pyrophosphatase Activity to DNA Replication. **PLoS One. 2016**; 11(4):e0152915. doi: 10.1371/journal.pone.0152915

PEDRAZZI M, NASH B, MEUCCI O, BRANDIMARTI R. Molecular features contributing to virus-independent intracellular localization and dynamic behavior of the herpesvirus transport protein US9. **PLoS One. 2014**; 9(8):e104634. doi: 10.1371/journal.pone.0104634.

KHAN MZ, BRANDIMARTI R, SHIMIZU S, NICOLAI J, CROWE E, MEUCCI O.The chemokine CXCL12 promotes survival of postmitotic neurons by regulating Rb protein. **Cell Death Differ. 2008. 15(10):1663-72**.

LAVAIL JH, TAUSCHER AN, SUCHER A, HARRABI O, BRANDIMARTI R. Viral regulation of the long distance axonal transport of herpes simplex virus nucleocapsid. **Neuroscience. 2007; 146(3):974-85.**

KHAN MZ, SHIMIZU S, PATEL JP, NELSON A, LE MT, MULLEN-PRZEWORSKI A, BRANDIMARTI R, FATATIS A, MEUCCI O. Regulation of neuronal P53 activity by CXCR 4. **Mol Cell Neurosci. 2005;30(1):58-66.**

KHAN, M.Z., BRANDIMARTI, R., PATEL, J., HUYNH,N., WANG, J.,HUANG, Z., FATATIS, A., and MEUCCI, O. Apoptotic and Antiapoptotic Effects of CXCR4: Is It a Matter of Intrinsic Efficacy? Implications for HIV Neuropathogenesis. **AIDS Research and Human Retroviruses. 2004; 20(10): 1063-71.**

BRANDIMARTI, R., KHAN, M.Z., MUSSER, B.J., RESUE, D.M., FATATIS, A., and O.MEUCCI. Regulation of celle cycle proteins by chemokine receptors: a novel pathway in HIV pathogenesis? **J Neurovirol. 2004;10 Suppl 1:108-12.** .

KHAN, M.Z., BRANDIMARTI, R., MUSSER, B.J., RESUE, D.M., FATATIS, A., and O. MEUCCI. The chemokine receptor CXCR4 regulates cell cycle proteins in neurons. **J Neurovirol. Jun;9(3):300-14. 2003.**

GALVAN, V., BRANDIMARTI, R., MUNGER, J., and B. ROIZMAN. Bcl-2 blocks a caspase-dependent pathway of apoptosis activated by herpes simplex virus 1 infection in HEp-2 cells. **J Virol. 74:1931-8, 2000.**

ADVANI, S.J., BRANDIMARTI, R., WEICHSELBAUM, R.R., and B. ROIZMAN. The disappearance of cyclins A and B and the increase in activity of the G(2)/M-phase cellular kinase cdc2 in herpes simplex virus 1-infected cells require expression of the alpha22/U(S)1.5 and U(L)13 viral genes. **J Virol. 74:8-15, 2000.**

GALVAN, V., BRANDIMARTI, R., and B. ROIZMAN. Herpes simplex virus 1 blocks caspase-3-independent and caspase-dependent pathways to cell death. **J Virol. 73:3219-26,1999.**

BRANDIMARTI, R., and B. ROIZMAN. Us9, a stable lysine-less herpes simplex virus 1 protein, is ubiquitinated prior to packaging into virions, and associates with proteasomes. **Proc. Natl. Acad. Sci. USA, 94:13973-13978, 1997**.

HE, B., CHOU, J., BRANDIMARTI, R., MOHR, J., GLUZMAN, Y., and ROIZMAN, B. Suppression of the phenotype of ã134.5- herpes simplex virus 1: failure of activated RNA-dependent protein kinase to shut off protein synthesis is associated with a deletion in the domain of the α47 gene. **J. Virol., 71:6049-54, 1997**.

BRANDIMARTI, R., HUANG, T., ROIZMAN, B., and CAMPADELLI FIUME, G., Mapping of Herpes Simplex Virus 1 genes with mutations which overcome host restrictions to infection. **Proc. Natl. Acad. Sci. USA, 91:5406-5410, 1994**.

VAN GENDEREN, I.L., BRANDIMARTI, R., TORRISI, M.R., CAMPADELLI, G., and VAN MEER, G., The phospholipid composition of extracellular herpes simplex virions differs from that of host cell nuclei. **Virology, 200:831-836, 1994**.

CAMPADELLI, G., BRANDIMARTI, R., DI LAZZARO, C., WARD, P.L., ROIZMAN, B., and TORRISI, R., Fragmentation and dispersal of Golgi proteins and redistribution of Glycoproteins and glycolipids processed through the Golgi apparatus after infection with herpes simplex virus. **Proc. Natl. Acad. Sci. USA, 90:2798-2802, 1993**.