

Name:

Vincenzo Ciminale

Current Position:

Associate Professor of General Pathology, University of Padova Medical School.

Previous Positions & Qualification:

1987-1988. Postdoctoral Fellow, Institute of Oncology, University of Padova.

1989-1992. Postdoctoral Fellow, Human Retrovirus Section, Molecular Mechanisms of Carcinogenesis Laboratory, ABL-Basic Research Program, NCI-Frederick Cancer Research and Development Center, Frederick, Maryland.

M.D., University of Padova Medical School (1987), with maximum score and honours (110/110 e lode); Specialty in Oncology (1991) earned with maximum score (70/70) at the University of Padova; United States Medical Licensing Examination certification (steps 1 and 2).

Current Teaching duties.

Oncology in the Medical School

General Pathology in the Nursing School.

Previous Teaching duties.

Pathophysiology in the 3-year degree program for biomedical lab technicians (University of Padova)

Recombinant DNA in the 3-year degree program for biomedical lab technicians (University of Padova).

Current international collaborations.

- Prof. Charles Bangham, Imperial College, London.
- Dr. Genoveffa Franchini, NCI, Bethesda.
- Prof. Pierre Jalinot, Ecole normale supérieure de Lyon
- Dr. Andrea Kress, University of Erlangen.

Funding

- Progetti di ricerca- Università' di Padova - Bando 1998 - Analisi molecolari e funzionali del gene MEN1 in neoplasie poliendocrine umane ereditarie
- Progetti di ricerca- Università' di Padova - Bando 2001 - Nuovi approcci diagnostici ed analisi funzionali per lo studio del gene MEN1 in neoplasie endocrine familiari e sporadiche

- PRIN 2005: IDENTIFICAZIONE DI NUOVI TARGET DI TERAPIE ANTINEOPLASTICHE ATTRAVERSO LO STUDIO DI PROTEINE SEGNALE CELLULARI E VIRALI E STUDIO DI INIBITORI SPECIFICI
- PRIN 2007: BERSAGLI MOLECOLARI PER NUOVE TERAPIE ANTINEOPLASTICHE ATTRAVERSO LO STUDIO DI PROTEINE-SEGNALE CELLULARI E VIRALI E DI INIBITORI SPECIFICI
- ISS - II, III, IV, V, VI Programmi nazionali di ricerca sull'AIDS 1998-2007 - Analisi genetiche e funzionali delle proteine regolatorie di HIV e retrovirus Correlati
- European Union FP6-2004-LIFESCIHEALTH-5: The role of chronic Infections in the development of CAncer
- AIRC investigator grant 2008 (progetto #5996): Functional dissection of virus-cell interactions involved in human lymphomagenesis
- AIRC investigator grant 2005 (progetto #1452): Functional dissection of virus-cell interactions involved in human lymphomagenesis
- AIRC investigator grant 2004 (progetto #1452): Functional dissection of virus-cell interactions involved in human lymphomagenesis
- NIH/FIC 2002-2005 (grant R03 TW05705-02): Studies of p30II and p13II in HTLV-1 infection.

Research interests:

As a medical student, I conducted experiments on the immunosuppressive properties of UV-inactivated human immunodeficiency virus (HIV) and B-cell activation in HIV-infected patients. As a post-doctoral fellow at NCI-FCRDC, studied the expression strategies of the human oncoretroviruses HTLV-1 and HTLV-2.

Over the past 20 years my studies have focused on understanding the molecular mechanisms underlying the persistence in the host and oncogenic properties of HTLVs. Studies on the alternative splicing pattern of viral mRNAs led to the discovery of novel proteins coded by both HTLV-1 and HTLV-1 and revealed differences in their expression kinetics. To follow up on these findings, I initiated a series of studies aimed at investigating the function of some of these novel viral gene products. My lab demonstrated that the p13 protein of HTLV-1 is targeted to the mitochondrial inner membrane where it triggers K⁺ influx, leading to production of reactive oxygen species (ROS). Interestingly, in the context of in primary T-cells, these effects resulted in their ROS-dependent activation, while in leukemic T-cells p13 was pro-apoptotic. These findings suggest that p13 may have a distinct impact on cell turnover depending on the inherent ROS levels and that it might represent the first example of a “viral tumor suppressor”. In the context of the HTLV-1 propagation strategy, p13 could increase the pool of “normal” infected cells while culling cells acquiring a transformed phenotype, thus favoring lifelong persistence of the virus in the host.

Building on these findings, current studies are aimed at exploiting HTLV-1 as a model to gain insight into the general mechanisms of T-cell transformation and to develop tumor-specific therapies that exploit the higher ROS set-point of tumor cells to target pediatric T-ALL (T-acute lymphoblastic leukemia), which is not linked to a virus. As 25% of T-ALL patients respond poorly to current therapies and have a dismal prognosis, new effective therapies against these neoplasms are needed. Initial studies are investigating the possibility of translating into clinical application drug treatments that mimic the anticancer properties of p13.

Publications

1. Silic-Benussi M, Scattolin G, Cavallari I, Minuzzo S, del Bianco P, Francescato S, Basso G, Indraccolo S, D'Agostino DM and Ciminale V. Selective killing of human T-ALL cells: an integrated approach targeting redox homeostasis and the OMA1/OPA1 axis. *Cell Death and Disease*, 2018, *in press*.
2. Pinazza M, Ghisi M, Minuzzo S, Agnusdei V, Fossati G, Ciminale V, Pezzè L, Ciribilli Y, Pilotto G, Venturoli C, Amadori A, Indraccolo S. Histone deacetylase 6 controls Notch3 trafficking and degradation in T-cell acute lymphoblastic leukemia cells. *Oncogene*. 2018 Apr 12. doi: 10.1038/s41388-018-0234-z. PMID:29643474
3. Cavallari I, Scattolin G, Silic-Benussi M, Raimondi V, D'Agostino DM, Ciminale V. Mitochondrial Proteins Coded by Human Tumor Viruses. *Front Microbiol*. 2018 Feb 6;9:81. doi: 10.3389/fmicb.2018.00081. eCollection 2018. Review. PMID:29467726
4. Ciccarese F, Ciminale V. Escaping Death: Mitochondrial Redox Homeostasis in Cancer Cells. *Front Oncol*. 2017 Jun 9;7:117. doi: 10.3389/fonc.2017.00117. eCollection 2017. Review. PMID:28649560
5. Urso L, Cavallari I, Silic-Benussi M, Biasini L, Zago G, Calabrese F, Conte PF, Ciminale V, Pasello G. Synergistic targeting of malignant pleural mesothelioma cells by MDM2 inhibitors and TRAIL agonists. *Oncotarget*. 2017 Jul 4;8(27):44232-44241. doi: 10.18632/oncotarget.17790. PMID: 28562336
6. Manicone M, Rende F, Cavallari I, Thoma-Kress AK, Ciminale V. Expression of HTLV-1 Genes in T-Cells Using RNA Electroporation. *Methods Mol Biol*. 2017;1582:155-170. doi: 10.1007/978-1-4939-6872-5_12. PMID:28357669
7. Raimondi V, Minuzzo S, Ciminale V, D'Agostino DM. STR Profiling of HTLV-1-Infected Cell Lines. *Methods Mol Biol*. 2017;1582:143-154. doi: 10.1007/978-1-4939-6872-5_11. PMID:28357668
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9. Desbats MA, Morbidoni V, Silic-Benussi M, Doimo M, Ciminale V, Cassina M, Sacconi S, Hirano M, Basso G, Pierrel F, Navas P, Salviati L, Trevisson E. The COQ2 genotype predicts the severity of coenzyme Q10 deficiency. *Hum Mol Genet*. 2016 Aug 4. pii: ddw257. PMID:27493029
10. Pizzuto MS, Silic-Benussi M, Ciminale V, Elderfield RA, Capua I, Barclay WS. An engineered avian-origin influenza A virus for pancreatic ductal adenocarcinoma virotherapy. *J Gen Virol*. 2016 Sep;97(9):2166-79. doi: 10.1099/jgv.0.000549. PMID: 27417501

11. Sharova E, Grassi A, Marcer A, Ruggero K, Pinto F, Bassi P, Zanovello P, Zattoni F, D'Agostino DM, Iafrate M, Ciminale V. A circulating miRNA assay as a first-line test for prostate cancer screening. *Br J Cancer*. 2016 Jun 14;114(12):1362-6. doi: 10.1038/bjc.2016.151. PMID:27228285
12. Cavallari I, Rende F, Bona MK, Sztuba-Solinska J, Silic-Benussi M, Tognon M, LeGrice SF, Franchini G, D'Agostino DM, Ciminale V. Expression of Alternatively Spliced Human T-Cell Leukemia Virus Type 1 mRNAs Is Influenced by Mitosis and by a Novel cis-Acting Regulatory Sequence. *J Virol*. 2015 Nov 18;90(3):1486-98. doi: 10.1128/JVI.02298-15. PMID:26581997.
13. Pasello G, Urso L, Mencoboni M, Grosso F, Ceresoli GL, Lunardi F, Vuljan SE, Bertorelle R, Sacchetto V, Ciminale V, Rea F, Favaretto A, Conte P, Calabrese F. MDM2 and HIF1alpha expression levels in different histologic subtypes of malignant pleural mesothelioma: correlation with pathological and clinical data. *Oncotarget*. 2015 Dec 8;6(39):42053-66. doi: 10.18632/oncotarget.5974. PMID:26544728
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17. Pasello G, Urso L, Silic-Benussi M, Schiavon M, Cavallari I, Marulli G, Nannini N, Rea F, Ciminale V, Favaretto A. Synergistic antitumor activity of recombinant human Apo2L/tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) in combination with carboplatin and pemetrexed in malignant pleural mesothelioma. *J Thorac Oncol*. 2014 Jul;9(7):1008-17. doi: 10.1097/JTO.000000000000198. PMID:24922007
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22. Cavallari I, Rende F, Bender C, Romanelli MG, D'Agostino DM, Ciminale V. Fine tuning of the temporal expression of HTLV-1 and HTLV-2. *Front Microbiol.* 2013 4:235.
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25. Mocquet V, Neusiedler J, Rende F, Cluet D, Robin JP, Terme JM, Duc Dodon M, Wittmann J, Morris C, Le Hir H, Ciminale V, and Jalinot P. (2012) The Human T-Lymphotropic Virus Type 1 Tax Protein Inhibits Nonsense-Mediated mRNA Decay by Interacting with INT6/EIF3E and UPF1. *J Virol.* Jul;86(14):7530-43. *IF JCR 2011 = 5.402.*
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28. Rende F, Cavallari I, Corradin A, Silic-Benussi M, Toulza F, Toffolo GM, Tanaka Y, Jacobson S, Taylor GP, D'Agostino DM, Bangham CR, and Ciminale V. (2011) Kinetics and intracellular compartmentalization of HTLV-1 gene expression: nuclear retention of HBZ mRNA. *Blood.* 117(18):4855-9. *IF JCR 2011 = 9.898.*
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32. Silic-Benussi M, Cavallari I, Vajente N, Vidali S, Chieco-Bianchi L, Di Lisa F, Saggiaro D, D'Agostino DM and Ciminale V. (2010) Redox regulation of T-cell turnover by the p13 protein of human T-cell leukemia virus type 1: distinct effects in primary vs. transformed cells. *Blood*, 116:54-62. *IF JCR 2011 = 9.898.*
33. Silic-Benussi M, Biasiotto R, Andresen V, Franchini G, D'Agostino DM, and Ciminale V. (2010) HTLV-1 p13, a small protein with a busy agenda. *Mol Aspects Med.* 31(5):350-8. *IF JCR 2011 = 9.970.*
34. Biasiotto R, Aguiari P, Rizzuto R, Pinton P, D'Agostino DM, and Ciminale V. (2010) The p13 protein of human T cell leukemia virus type 1 (HTLV-1) modulates mitochondrial membrane potential and calcium uptake. *Biochim Biophys Acta-Bioenergetics.* 1797:945-951. *IF JCR 2011 = 4.483.*
35. Silic-Benussi M, Marin O, Biasiotto R, D'Agostino DM, and Ciminale V. (2010) Effects of human T-cell leukemia virus type 1 (HTLV-1) p13 on mitochondrial K(+) permeability: A new member of the viroporin family? *FEBS Lett.* 584:2070–2075. *IF JCR 2011 = 3.538.*
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37. Silic-Benussi M, Cannizzaro E, Venerando A, Cavallari I, Petronilli V, La Rocca N, Marin O, Chieco-Bianchi L, Di Lisa F, D'Agostino DM, Bernardi P, and Ciminale V. (2009) Modulation of mitochondrial K(+) permeability and reactive oxygen species production by the p13 protein of human T-cell leukemia virus type 1. *Biochim Biophys Acta-Bioenergetics.* 1787:947-54. *IF JCR 2011 = 4.483.*
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