

Chiara Ambrogio, PhD

Education

2004-2008: Ph.D. in Immunology and Cellular Biology at the Department of Biomedical Sciences and Human Oncology, University of Torino

1999-2004: BS/MS Degree in Medical Biotechnology at University of Torino. Graduated summa cum laude

Current position

December 2019-present: Assistant Professor, Department of Molecular Biotechnology and Health Sciences, University of Torino

Scientific training

April 2016-December 2019: Senior Scientist, Dr Jänne Laboratory Medical Oncology Department, Dana Farber Cancer Institute, Boston, USA

November 2009 – March 2016: Postdoc, Dr Barbacid Laboratory, Experimental Oncology Department, CNIO, Madrid, Spain

December 2008 - November 2009: Post Doctoral Fellow in Prof R. Chiarle laboratory, CeRMS (Center of Research in Experimental Medicine), University of Torino, Italy

2004-2008: PhD training in Prof R. Chiarle laboratory, CeRMS (Center of Research in Experimental Medicine), University of Torino, Italy

Publications

- 1) **Ambrogio C**, Voena C, ..., Chiarle R. p130Cas mediates the transforming properties of the anaplastic lymphoma kinase. *Blood*. 2005
- 2) Piva R, Chiarle R, Manazza AD, Taulli R, Simmons W, **Ambrogio C**, ..., Inghirami G. Ablation of oncogenic ALK is a viable therapeutic approach for anaplastic large-cell lymphomas. *Blood*. 2006
- 3) Voena C, Conte C, **Ambrogio C**, ..., Chiarle R. The tyrosine phosphatase Shp2 interacts with NPM-ALK and regulates anaplastic lymphoma cell growth and migration. *Cancer Res*. 2007
- 4) Berto G, Camera P, Fusco C, Imarisio S, **Ambrogio C**, ..., Di Cunto F. The Down syndrome critical region protein TTC3 inhibits neuronal differentiation via RhoA and Citron kinase. *J Cell Sci*. 2007
- 5) Costa C, Barberis L, **Ambrogio C**, ..., Hirsch E. Constitutive elevation of phosphoinositide 3-Kinase γ activity in mice does not increase tumor susceptibility but reveals a negative feedback loop regulating Rac during leukocyte chemotaxis. *PNAS* 2007
- 6) Chiarle R, Voena C, **Ambrogio C**, Piva R, Inghirami G. The anaplastic lymphoma kinase in the pathogenesis of cancer. *Nat Rev Cancer*. 2008
- 7) Chiarle R, Martinengo C, Mastini C, **Ambrogio C**, ..., Inghirami G. Anaplastic Lymphoma Kinase is an effective oncoantigen for lymphoma vaccination. *Nat Med* 2008
- 8) Crosetto N, Bienko M, Hibbert RG, Perica T, **Ambrogio C**, ..., Dikic I. Human WRNIP1 is localized in replication factories in a UBZ-dependent manner. *J Biol Chem*. 2008
- 9) **Ambrogio C**, Voena C, ... Chiarle R. Anaplastic Lymphoma Kinase controls cell shape and growth of Anaplastic Large Cell Lymphoma through Cdc42. *Cancer Res* 2008
- 10) Barberis L, Pasquali C, Bertschy-Meier D, Cuccurullo A, Costa C, **Ambrogio C**, ..., Hirsch E. Leukocyte transmigration is modulated by chemokine-mediated, PI3K γ -dependent phosphorylation of vimentin. *European Journal of Immunology* 2009
- 11) Gonzalo P, Guadamillas MC, Hernández-Riquer MV, Pollán A, Grande-García A, Bartolomé RA, Vasanji A, **Ambrogio C**, ... Arroyo AG. Membrane type 1-matrix metalloproteinase contributes to macrophage fusion through the regulation of the Rac1 signaling pathway. *Dev Cell*. 2010
- 12) **Ambrogio C**, Martinengo C, ..., Chiarle R. NPM-ALK oncogenic tyrosine kinase controls T cell identity by transcriptional and epigenetic silencing in lymphoma cells. *Cancer Res* 2009
- 13) Riera L, Lasorsa E, **Ambrogio C**, ..., Chiarle R. Involvement of Grb2 adaptor protein in nucleophosmin-anaplastic lymphoma kinase (NPM-ALK)-mediated signaling and anaplastic large cell lymphoma growth. *J Biol Chem*. 2010
- 14) Boselli D, Ragimbeau J, Orlando L, Cappello P, Capello M, **Ambrogio C**, ..., Novelli F. Expression of IFN γ R2

mutated in a dileucine internalization motif reinstates IFN γ signaling and apoptosis in human T lymphocytes. *Immunol Lett.* 2010 2010

- 15) **Di Paolo D***, **Ambrogio C***, Pastorino F, ..., Perri P. Selective Therapeutic Targeting of the Anaplastic Lymphoma Kinase With Liposomal siRNA Induces Apoptosis and Inhibits Angiogenesis in Neuroblastoma. *Mol Ther.* 2011. ***equally contributed**
- 16) Bosio Y, Berto G, Camera P, Bianchi F, **Ambrogio C**, Claus P, Di Cunto F. PPP4R2 regulates neuronal cell differentiation and survival, functionally cooperating with SMN. *Eur J Cell Biol.* 2012
- 17) Voena C, Di Giacomo F, Panizza E, D'Amico L, Boccalatte FE, Pellegrino E, Todaro M, Recupero D, Tabbò F, **Ambrogio C**, ..., Inghirami G. The EGFR family members sustain the neoplastic phenotype of ALK+ lung adenocarcinoma via EGR1. *Oncogenesis.* 2013
- 18) Piazza R, Magistroni V, Mogavero A, Andreoni F, **Ambrogio C**, ..., Gambacorti-Passerini C. Epigenetic silencing of the proapoptotic gene BIM in anaplastic large cell lymphoma through an MeCP2/SIN3a deacetylating complex. *Neoplasia.* 2013
- 19) Martinengo C, Poggio T, Menotti M, Scalzo MS, Mastini C, **Ambrogio C**, ..., Chiarle R. ALK-Dependent Control of Hypoxia-Inducible Factors Mediates Tumor Growth and Metastasis. *Cancer Res.* 2014
- 20) **Ambrogio C**, Carmona FJ, ..., Villanueva A. Modeling Lung Cancer Evolution and Preclinical Response by Orthotopic Mouse Allografts. *Cancer Res.* 2014
- 21) **Ambrogio C**, Stern P, Scuoppo C, Kranz H, Barbacid M, Santamaría D. Lentiviral-based approach for the validation of cancer therapeutic targets in vivo. *Biotechniques.* 2014
- 22) Blasco RB, Karaca E, **Ambrogio C**, ..., Chiarle R. Simple and rapid in vivo generation of chromosomal rearrangements using CRISPR/Cas9 technology. *Cell Rep.* 2014
- 23) Lopez-Contreras AJ, Specks J, Barlow JH, **Ambrogio C**, ..., Fernandez-Capetillo O. Increased Rrm2 gene dosage reduces fragile site breakage and prolongs survival of ATR mutant mice. *Genes Dev.* 2015
- 24) García-Beccaria M, Martínez P, Méndez-Pertuz M, Martínez S, Blanco-Aparicio C, Cañamero M, Mulero F, **Ambrogio C**, ..., Blasco MA. Therapeutic inhibition of TRF1 impairs the growth of p53-deficient K-RasG12V-induced lung cancer by induction of telomeric DNA damage. *EMBO Mol Med.* 2015
- 25) Voena C, Menotti M, Mastini C, Di Giacomo F, Longo DL, Castella B, Merlo ME, **Ambrogio C**, ..., Chiarle R. Efficacy of a Cancer Vaccine against ALK-Rearranged Lung Tumors. *Cancer Immunol Res.* 2015
- 26) **Ambrogio C**, Cámara JA, Nieto P, Santamaría D, Mulero F. Analysis of Murine Lung Tumors by Micro PET-CT Imaging. *Bio-protocol*, 2015
- 27) Ceccon M, Merlo ME, Mologni L, Poggio T, Varesio LM, Menotti M, Bombelli S, Rigolio R, Manazza AD, Di Giacomo F, **Ambrogio C**, ..., Voena C. Excess of NPM-ALK oncogenic signaling promotes cellular apoptosis and drug dependency. *Oncogene.* 2016
- 28) Choudhari R, Minero VG, ..., **Ambrogio C***, Chiarle R*. Redundant and non-redundant roles for Cdc42 and Rac1 in lymphomas developed in NPM-ALK transgenic mice. *Blood.* 2016. ***Co-last author**
- 29) **Ambrogio C***, Gómez-López G, ..., Barbacid M*. Combined inhibition of Ddr1 and Notch signaling as an effective therapeutic strategy for K-Ras-driven/p53-null lung adenocarcinomas. *Nat Med.* 2016. ***Co-corresponding author**
- 30) **Ambrogio C***, Nadal E, ..., Santamaría D. KRAS-driven lung adenocarcinoma: combined DDR1/Notch inhibition as an effective therapy. *ESMO Open.* 2016. ***Corresponding author**
- 31) **Ambrogio C***, Barbacid M, Santamaría D*. In vivo oncogenic conflict triggered by co-existing KRAS and EGFR activating mutations in lung adenocarcinoma. *Oncogene.* 2016. ***Co-corresponding author**
- 32) **Ambrogio C**, Santamaria D. DDR1 and Notch: a multifaceted synergy. *Translational Cancer Research.* 2016
- 33) Compagno M, Wang Q, Pighi C, Cheong TC, Meng FL, Poggio T, Yeap LS, Karaca E, Blasco RB, Langellotto F, **Ambrogio C**, ..., Chiarle R. Phosphatidylinositol 3-kinase δ blockade increases genomic instability in B cells. *Nature.* 2017
- 34) Kohler J, Catalano M, **Ambrogio C**. Back to the bench? MEK and ERK inhibitors for the treatment of KRAS mutant lung adenocarcinoma. *Curr Med Chemistry.* 2017
- 35) Zeng M, Lu J, Li L, Feru F, Quan C, Gero TW, Ficarro SB, Xiong Y, **Ambrogio C**, ..., Gray NS. Potent and Selective Covalent Quinazoline Inhibitors of KRAS G12C. *Cell Chem Biol.* 2017
- 36) Nieto P, **Ambrogio C**, ..., Santamaría D. A B-Raf kinase inactive mutant induces lung adenocarcinoma. *Nature.* 2017
- 37) **Ambrogio C***, Köhler J, ..., Jänne PA*. KRAS dimerization impacts MEK inhibitor sensitivity and oncogenic activity of mutant KRAS. *Cell.* 2018. ***Co-corresponding author**
- 38) **Ambrogio C**, Darbo E, Lee SW, Santamaria D. A putative role for Discoidin Domain Receptor 1 in cancer chemoresistance. *Cell Adhesion & Migration*, 2018

- 39) Abravanel DL, Nishino M, Sholl LM, **Ambrogio C**, Awad MM. An acquired NRAS Q61K mutation in BRAF V600E-mutant lung adenocarcinoma resistant to dabrafenib plus trametinib. *J Thorac Oncol*. 2018
- 40) Li S, Liu S, Deng J, Akbay EA, Hai J, **Ambrogio C**, ..., Wong KK. Assessing Therapeutic Efficacy of MEK Inhibition in a KRAS G12C-Driven Mouse Model of Lung Cancer. *Clin Cancer Res*. 2018
- 41) Kobayashi Y, **Ambrogio C**, Mitsudomi T. Ground-glass nodules of the lung in never-smokers and smokers: clinical and genetic insights. *Transl Lung Cancer Res* 2018
- 42) Dagogo-Jack I, Martinez P, Yeap BY, **Ambrogio C**, ..., Awad MM. Impact of BRAF Mutation Class on Disease Characteristics and Clinical Outcomes in BRAF-Mutant Lung Cancer. *Clin Cancer Res*. 2018
- 43) Menotti M, **Ambrogio C**, ..., Chiarle R. Wiskott–Aldrich syndrome protein (WASP) is a tumor suppressor in T cell lymphoma. *Nat Med*. 2018
- 44) Wang H, Lv Q, ..., **Ambrogio C*** and Köhler J*. An integrative pharmacogenomics analysis identifies CK2 alpha as a promising therapeutic target in KRAS(G12C) mutant lung cancer. *EBioMedicine*. 2019. ***Co-last author**
- 45) **Zhou Z***, **Ambrogio C***, Bera AK, ..., Westover KD. KRASQ61H signals through MAPK in a RAF dimer-dependent manner in non-small cell lung cancer. *Cancer Res*. 2020. ***equally contributed**
- 46) Nokin MJ, Darbo E, ..., **Ambrogio C**. Inhibition of DDR1 enhances in vivo chemosensitivity in KRAS-mutant lung adenocarcinoma. *JCI Insight*. 2020
- 47) Marmarelis ME, Chiarle, **Ambrogio C*** and Aggarwal C*. A LIBRETTO to orchestrate targeted therapy. *Nature Cancer*, 2020. ***Co-last author**
- 48) Nokin MJ, **Ambrogio C**, Nadal E, Santamaria D. Targeting Infrequent Driver Alterations in Non-Small Cell Lung Cancer. *Trends in Cancer*, 2020
- 49) Kramer-Drauberg M and **Ambrogio C**. Discoveries in the redox regulation of KRAS. *The International Journal of Biochemistry & Cell Biology*, 2020
- 50) Köhler J, Zhao Y, Li J, Gokhale PC, Tiv HL, Knott AR, Wilkens MK, Soroko KM, Lin M, **Ambrogio C**, ..., Janne PA. ERK inhibitor LY3214996-based treatment strategies for RAS-driven lung cancer. *Mol Cancer Ther*. 2021
- 51) Mysore VP*, Zhou Z*, **Ambrogio C***, Wang Q, Okoro J, Janne PA, Westover KD, Shan Y, Shaw DE. Structural model of a Ras-Raf signalosome. *Nature Structural and Molecular Biology*, in press. ***equally contributed**

Meetings and Communications (speaker, last 5 years)

- 1) CNIO-Frontiers Meeting: “NEW TRENDS IN ANTICANCER DRUG DEVELOPMENT”, Madrid, Spain, (March 22-25, 2015). *Oral presentation*.
- 2) EACR-AACR-SIC 2015 Conference, “From cancer biology to the clinic”, Firenze, Italy, (June 20-23, 2015). *Oral presentation*.
- 3) ESMO 2016 Personalized Medicine Symposium, “Signaling Pathways in Cancer”, Barcelona, Spain, (March 4-5, 2016). *Invited speaker*.
- 4) Tongji University, Shanghai, School of Life Science and Technology Program, Shanghai, China, (September 12-13, 2016). *Invited speaker*.
- 5) ESMO 2017-EACR, Madrid, Spain (September 8-12, 2017). *Oral presentation*.
- 6) 2017 NCI RAS Initiative Symposium, Frederick, USA (December 6-8, 2017). *Oral presentation*.
- 7) 2018 AACR RAS Meeting, San Diego, USA (December 9-12, 2018). *Invited speaker*.
- 8) 2019 RAS Symposium, Santander, Spain (May 16-18, 2019). *Invited speaker*.
- 9) RAS Initiative, NIH, Frederick, (July 18, 2019). *Invited speaker*.
- 10) “Rising Stars seminar series”, NIH Bethesda, (July 19, 2019). *Invited speaker*.
- 11) HansonWade RAS-Targeted Drug Discovery Summit, Boston, (September 16-19, 2019). *Invited speaker*.
- 12) University of Copenhagen, (November 7, 2019). *Invited speaker*.
- 13) Sixth AACR-IASLC International Joint Conference: Lung Cancer Translational Science from the Bench to the Clinic, San Diego, USA (January 11 - 14, 2020). *Invited speaker*.
- 14) University of Zurich, (February 12, 2020). *Invited speaker*.
- 15) HansonWade, 2nd RAS-Targeted Drug Discovery Summit (Virtual), Boston, (September 14-16, 2020). *Invited speaker*.
- 16) 9th Annual PREDiCT Tumor Models Meeting (Virtual), London, December 1-3, 2020. *Invited speaker*.
- 17) Precision Medicine for RAS pathway mutations in cancer (Virtual), Manchester, (December 8-9, 2020). *Keynote lecture*.
- 18) IASLC 2020 World Conference on Lung Cancer (Virtual), Singapore, (January 28-31, 2021), *Invited speaker*.
- 19) INSIDE - The dark side of the cell (Virtual), Vienna, (February 11-12, 2021), *Invited speaker*.
- 20) UNITO-POLITO CONFERENCE SERIES IN CANCER, Nanoscience in Cancer Immunotherapy, (March 9-11, 2021).

Virtual Event, *Invited speaker*.

- 21) UCSF, San Francisco, "10 years in the RAS-MAPK field, from genetic mouse models to translational oncology", (April 27, 2021), Virtual Event, *Invited speaker*.
- 22) Non-Small Cell Lung Cancer Drug Development Summit, (July 13-15, 2021), Virtual Event, *Invited Speaker*.
- 23) ESMO 2021-EACR, Paris, France (September 16-19, 2021). *Invited Speaker*.

Awards

2020: Award "Marcellina Gilli" for Entrepreneur Women in Italy

2020: Listed in the 2020 "40 under 40" by Fortune (Italy)

2019: Award "Premio Chianello" for Oncology Research

2019: Award "Fondazione Lorini" for under-40 young scientists in cancer research

2018: Scientific Merit Award from the Lung Cancer Research Foundation (LCRF)

2014: Award Com.It.Es (Organization of Italians abroad), category "University and Research".

2014: Best Poster presentation award EACR-23 meeting, "From Basic Research to Personalized Cancer Treatment", Munich, Germany, (July 5-8, 2014).

2012: Proffered Paper Award EACR-22, Barcelona, Spain, (July 7-10).

2012: AECC (Spanish Association Against Cancer) Postdoctoral Award, personally conferred by the Queen of Spain

2009: Award "Silvia Fiocco" for Lymphoma and Leukemia Research, Accademia dei Lincei-Roma, personally conferred by the Italian President Giorgio Napolitano

2008: Award "Fondazione Costa" for cancer research

2007: SIBBM Prize (Italian Society of Biophysics and Molecular Biology) (please see <http://www.sibbm.org/premio2007.php>)

Projects and Funding

2021-2026: ERC Consolidator Grant, funded budget €2.000.000.

2021-2022: SRA (Scientific Research Agreement) Revolution Medicine, \$ 300.000.

2020-2023: Harvard-Armenise Career Development Grant, funded budget \$1.000.000.

2020-2023: "Ramon y Cajal" Excellence Grant, Ministry of Health and Innovation (Spain), 500.000 euros (declined).

2018-2020: Principal Investigator, Lung Cancer Research Foundation (LCRF) grant, funded budget \$150.000.

2017-2018: Principal Investigator of the Wong Funds in Translational Oncology (DFCI, Boston), funded budget \$150.000.

2016-2018: Stand Up To Cancer, Lung Cancer Dream Team.

2012-2017: AECC (Spanish Association Against Cancer) Postdoctoral Fellowship (5 years).

2009-2011: CNIO-Caja Navarra International Postdoctoral Program

2009-2012: Principal Investigator of the **MFAG-2009** funded by AIRC (Italian Association for Cancer Research), funded budget for the project: €150.000.