



Curriculum Vitae

Personal information **Lorenzo Brunetti**

Work experience

Start date: November 2021

End date: Current

Position: Tenured Assistant Professor

Employer's name: Università Politecnica delle Marche

Country of employment: Italy

Main activities in the position:

- 1) Clinical management of acute myeloid and lymphoid leukemias in adult patients
- 2) Principal investigator and Investigator of several academic clinical trials in acute myeloid leukemias in adult patients
- 3) Principal investigator of the research project "Understanding the mechanisms promoting HOX expression in NPM1-mutated acute myeloid leukemia" funded by the Italian Association for Cancer Research
- 4) Principal investigator of the research project "Eltanexor in NPM1-mutated acute myeloid leukemia" funded by the Italian Ministry of Health

Start date: November 2018

End date: October 2021

Position: Non-tenured Assistant Professor

Employer's name: Università degli Studi di Perugia

Country of employment: Italy

Main activities in the position:

- 1) Clinical management of acute myeloid and lymphoid leukemias in adult patients
- 2) Investigator and sub-investigator of several academic and sponsored clinical trials in acute myeloid and lymphoid leukemias in adult patients
- 3) Principal investigator of the research project "Understanding the mechanisms promoting HOX expression in NPM1-mutated acute myeloid leukemia" funded by the Italian Association for Cancer Research

Start date: May 2015

End date: September 2018

Position: Visiting PhD/Post-doctoral Fellow

Employer's name: Baylor College of Medicine

Country of employment: USA

Main activities in the position: main research project "Exploiting CRISPR/Cas9 to reveal oncogenic dependencies in NPM1-mutated acute myeloid leukemia".

Education and training

Start date: November 2014

End date: October 2017
Degree: PhD
Institution: Università degli Studi di Perugia and Baylor College of Medicine
Country: Italy and USA
Subject: Cellular and molecular biology of acute myeloid leukemias

Start date: June 2009
End date: July 2014
Degree: Specialty, Hematology
Institution: Università degli Studi di Perugia
Country: Italy
Subject: Clinical management of cancers of the hemato-lymphopoietic system, with specific focus on acute myeloid and lymphoid leukemias

Start date: June 2002
End date: July 2008
Degree: MD
Institution: Università "Federico II" di Napoli
Country: Italy
Subject: Medicine and Surgery

Additional information

- Publications** Falini B, Cardinali V, Brunetti L, Martelli MP. NPM1-mutated AML with starry sky pattern. *Br J Haematol.* 2023 Jul;202(1):8. doi: 10.1111/bjh.18808. Epub 2023 May 8. PMID: 37153969.
- Falini B, Martelli MP, Brunetti L, Gjertsen BT, Andresen V. The NPM1 mutant defines AML irrespective of blast count. *Am J Hematol.* 2023 Jul;98(7):E187-E189. doi: 10.1002/ajh.26946. Epub 2023 Apr 29. PMID: 37119006.
- Ramabadran R, Wang JH, Reyes JM, et al. DNMT3A-coordinated splicing governs the stem state switch towards differentiation in embryonic and haematopoietic stem cells. *Nat Cell Biol.* 2023 Apr;25(4):528-539. doi: 10.1038/s41556-023-01109-9. Epub 2023 Apr 6. PMID: 37024683.
- Falini B, Martelli MP, Brunetti L. Mutant NPM1: Nuclear export and the mechanism of leukemogenesis. *Am J Hematol.* 2023 Apr;98(4):550-552. doi: 10.1002/ajh.26862. Epub 2023 Feb 6. PMID: 36695655.
- Othman J, Meggendorfer M, Tiacci E, et al. Overlapping features of therapy-related and de novo NPM1-mutated AML. *Blood.* 2023 Apr 13;141(15):1846-1857. doi: 10.1182/blood.2022018108. PMID: 36508705.
- Uckelmann HJ, Haarer EL, Takeda R, et al. Mutant NPM1 Directly Regulates Oncogenic Transcription in Acute Myeloid Leukemia. *Cancer Discov.* 2023 Mar 1;13(3):746-765. doi: 10.1158/2159-8290.CD-22-0366. PMID: 36455613; PMCID: PMC10084473.
- Pianigiani G, Gagliardi A, Mezzasoma F, et al. Prolonged XPO1 inhibition is essential for optimal antileukemic activity in NPM1-mutated AML. *Blood Adv.* 2022 Nov 22;6(22):5938-5949. doi: 10.1182/bloodadvances.2022007563. PMID: 36037515; PMCID: PMC9701620.

Ranieri R, Pianigiani G, Sciabolacci S, et al. Current status and future perspectives in targeted therapy of NPM1-mutated AML. *Leukemia*. 2022 Oct;36(10):2351-2367. doi: 10.1038/s41375-022-01666-2. Epub 2022 Aug 25. PMID: 36008542; PMCID: PMC9522592.

Pianigiani G, Rocchio F, Peruzzi S, et al. The absent/low expression of CD34 in NPM1-mutated AML is not related to cytoplasmic dislocation of NPM1 mutant protein. *Leukemia*. 2022 Jul;36(7):1931-1934. doi: 10.1038/s41375-022-01593-2. Epub 2022 May 14. PMID: 35568767; PMCID: PMC9252915.

Rogers JH, Gupta R, Reyes JM, et al. Modeling IKZF1 lesions in B-ALL reveals distinct chemosensitivity patterns and potential therapeutic vulnerabilities. *Blood Adv*. 2021 Oct 12;5(19):3876-3890. doi: 10.1182/bloodadvances.2020002408. PMID: 34492683; PMCID: PMC8679666.

Huang YH, Chen CW, et al. Systematic Profiling of *DNMT3A* Variants Reveals Protein Instability Mediated by the DCAF8 E3 Ubiquitin Ligase Adaptor. *Cancer Discov*. 2022 Jan;12(1):220-235. doi: 10.1158/2159-8290.CD-21-0560. Epub 2021 Aug 24. PMID: 34429321; PMCID: PMC8758508.

Martelli MP, Rossi R, Venanzi A, et al. Novel NPM1 exon 5 mutations and gene fusions leading to aberrant cytoplasmic nucleophosmin in AML. *Blood*. 2021 Dec 23;138(25):2696-2701. doi: 10.1182/blood.2021012732. PMID: 34343258; PMCID: PMC9037756.

Wu HC, Rérolle D, Berthier C, et al. Actinomycin D Targets NPM1c-Primed Mitochondria to Restore PML-Driven Senescence in AML Therapy. *Cancer Discov*. 2021 Dec 1;11(12):3198-3213. doi: 10.1158/2159-8290.CD-21-0177. PMID: 34301789; PMCID: PMC7612574.

Tovy A, Rosas C, Gaikwad AS, et al. Perturbed hematopoiesis in individuals with germline DNMT3A overgrowth Tatton-Brown-Rahman syndrome. *Haematologica*. 2022 Apr 1;107(4):887-898. doi: 10.3324/haematol.2021.278990. PMID: 34092059; PMCID: PMC8968878.

Falini B, Sciabolacci S, Falini L, Brunetti L, Martelli MP. Diagnostic and therapeutic pitfalls in NPM1-mutated AML: notes from the field. *Leukemia*. 2021 Nov;35(11):3113-3126. doi: 10.1038/s41375-021-01222-4. Epub 2021 Apr 20. PMID: 33879827; PMCID: PMC8056374.

Gionfriddo I, Brunetti L, Mezzasoma F, et al. Dactinomycin induces complete remission associated with nucleolar stress response in relapsed/refractory NPM1-mutated AML. *Leukemia*. 2021 Sep;35(9):2552-2562. doi: 10.1038/s41375-021-01192-7. Epub 2021 Mar 2. PMID: 33654209; PMCID: PMC8410589.

Perriello VM, Gionfriddo I, Rossi R, et al. CD123 Is Consistently Expressed on *NPM1*-Mutated AML Cells. *Cancers (Basel)*. 2021 Jan 28;13(3):496. doi: 10.3390/cancers13030496. PMID: 33525388; PMCID: PMC7865228.

Kabanova A, Gavriilaki E, Pelzer BW, Brunetti L, Maiques-Diaz A. Effect of the COVID-19 Pandemic on Laboratory and Clinical Research: A Testimony

and a Call to Action From Researchers. *Hemasphere*. 2020 Nov 24;4(6):e499. doi: 10.1097/HS9.0000000000000499. PMID: 33283169; PMCID: PMC7710232.

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Sportoletti P, Sorcini D, Guzman AG, et al. Bcor deficiency perturbs erythromegakaryopoiesis and cooperates with Dnmt3a loss in acute erythroid leukemia onset in mice. *Leukemia*. 2021 Jul;35(7):1949-1963. doi: 10.1038/s41375-020-01075-3. Epub 2020 Nov 6. PMID: 33159179; PMCID: PMC8257496.

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Basar R, Daher M, Uprety N, et al. Large-scale GMP-compliant CRISPR-Cas9-mediated deletion of the glucocorticoid receptor in multivirus-specific T cells. *Blood Adv*. 2020 Jul 28;4(14):3357-3367. doi: 10.1182/bloodadvances.2020001977. PMID: 32717029; PMCID: PMC7391161.

Tovy A, Reyes JM, Gundry MC, et al. Tissue-Biased Expansion of DNMT3A-Mutant Clones in a Mosaic Individual Is Associated with Conserved Epigenetic Erosion. *Cell Stem Cell*. 2020 Aug 6;27(2):326-335.e4. doi: 10.1016/j.stem.2020.06.018. Epub 2020 Jul 15. PMID: 32673568; PMCID: PMC7494054.

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Zanelli M, Zizzo M, Sanguedolce F, Martino G, Brunetti L, Ascani S. Prenatal diagnosis of familial hemophagocytic lymphohistiocytosis: morphological findings in the product of conception. *Ann Hematol*. 2021 Feb;100(2):585-586. doi: 10.1007/s00277-020-04108-0. Epub 2020 Jun 4. PMID: 32500225.

Pastore N, Huynh T, Herz NJ, et al. TFEB regulates murine liver cell fate during development and regeneration. *Nat Commun*. 2020 May 18;11(1):2461. doi: 10.1038/s41467-020-16300-x. PMID: 32424153; PMCID: PMC7235048.

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Gundry MC, Goodell MA, Brunetti L. It's All About MEis: Menin-MLL Inhibition Eradicates NPM1-Mutated and MLL-Rearranged Acute Leukemias in Mice. *Cancer Cell*. 2020 Mar 16;37(3):267-269. doi: 10.1016/j.ccell.2020.02.011. PMID: 32183947.

Pianigiani G, Betti C, Brunetti L. Response to: "Cytoplasmic dislocation of NPM1 and PU.1 in NPM1-mutated leukemia is obscured by paraformaldehyde fixation". *Br J Haematol*. 2020 May;189(3):577-578. doi: 10.1111/bjh.16544. Epub 2020 Mar 2. PMID: 32118285.

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Colleluori G, Aguirre L, Phadnis U, et al. Aerobic Plus Resistance Exercise in Obese Older Adults Improves Muscle Protein Synthesis and Preserves Myocellular Quality Despite Weight Loss. *Cell Metab*. 2019 Aug 6;30(2):261-273.e6. doi: 10.1016/j.cmet.2019.06.008. Epub 2019 Jul 3. PMID: 31279675; PMCID: PMC6685749.

Pastore N, Vainshtein A, Herz NJ, et al. Nutrient-sensitive transcription factors TFEB and TFE3 couple autophagy and metabolism to the peripheral clock. *EMBO J*. 2019 Jun 17;38(12):e101347. doi: 10.15252/embj.2018101347. Epub 2019 May 24. PMID: 31126958; PMCID: PMC6576167.

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Brunetti L, Gundry MC, Sorcini D, et al. Mutant NPM1 Maintains the Leukemic State through HOX Expression. *Cancer Cell*. 2018 Sep 10;34(3):499-512.e9. doi: 10.1016/j.ccell.2018.08.005. PMID: 30205049; PMCID: PMC6159911.

Brunetti L, Gundry MC, Kitano A, Nakada D, Goodell MA. Highly Efficient Gene Disruption of Murine and Human Hematopoietic Progenitor Cells by CRISPR/Cas9. *J Vis Exp*. 2018 Apr 10;(134):57278. doi: 10.3791/57278. PMID: 29708546; PMCID: PMC5933422.

Tan Q, Brunetti L, Rousseaux MWC, et al. Loss of Capicua alters early T cell development and predisposes mice to T cell lymphoblastic leukemia/lymphoma. *Proc Natl Acad Sci U S A*. 2018 Feb 13;115(7):E1511-E1519. doi: 10.1073/pnas.1716452115. Epub 2018 Jan 30. PMID: 29382756; PMCID: PMC5816173.

Huang YH, Su J, Lei Y, et al. DNA epigenome editing using CRISPR-Cas SunTag-directed DNMT3A. *Genome Biol*. 2017 Sep 18;18(1):176. doi: 10.1186/s13059-017-1306-z. PMID: 28923089; PMCID: PMC5604343.

Brunetti L, Di Battista V, Venanzi A, et al. Blastic plasmacytoid dendritic cell neoplasm and chronic myelomonocytic leukemia: a shared clonal origin. *Leukemia*. 2017 May;31(5):1238-1240. doi: 10.1038/leu.2017.38. Epub 2017 Jan 23. PMID: 28111467.

Brunetti L, Gundry MC, Goodell MA. DNMT3A in Leukemia. *Cold Spring Harb Perspect Med*. 2017 Feb 1;7(2):a030320. doi: 10.1101/cshperspect.a030320. PMID: 28003281; PMCID: PMC5287058.

Gundry MC, Brunetti L, Lin A, et al. Highly Efficient Genome Editing of Murine and Human Hematopoietic Progenitor Cells by CRISPR/Cas9. *Cell Rep.* 2016 Oct 25;17(5):1453-1461. doi: 10.1016/j.celrep.2016.09.092. PMID: 27783956; PMCID: PMC5087995.

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Falini B, Sportoletti P, Brunetti L, Martelli MP. Perspectives for therapeutic targeting of gene mutations in acute myeloid leukaemia with normal cytogenetics. *Br J Haematol.* 2015 Aug;170(3):305-22. doi: 10.1111/bjh.13409. Epub 2015 Apr 19. PMID: 25891481.

Martelli MP, Gionfriddo I, Mezzasoma F, et al. Arsenic trioxide and all-trans retinoic acid target NPM1 mutant oncoprotein levels and induce apoptosis in NPM1-mutated AML cells. *Blood.* 2015 May 28;125(22):3455-65. doi: 10.1182/blood-2014-11-611459. Epub 2015 Mar 20. PMID: 25795919.

Martelli MP, Pettirossi V, Thiede C, et al. CD34+ cells from AML with mutated NPM1 harbor cytoplasmic mutated nucleophosmin and generate leukemia in immunocompromised mice. *Blood.* 2010 Nov 11;116(19):3907-22. doi: 10.1182/blood-2009-08-238899. Epub 2010 Jul 15. PMID: 20634376.

Brunetti L, Di Noto R, Abate G, et al. CD200/OX2, a cell surface molecule with immuno-regulatory function, is consistently expressed on hairy cell leukaemia neoplastic cells. *Br J Haematol.* 2009 Jun;145(5):665-7. doi: 10.1111/j.1365-2141.2009.07644.x. Epub 2009 Mar 12. PMID: 19344398.

Projects GRANTS

2022-2025: Ricerca Finalizzata GR-2021-12372418 funded by the Italian Ministry of Health euro 450.000

2020-2024: Start-Up Grant 22895 funded by Associazione Italiana per la Ricerca sul Cancro (AIRC) euro 988.000.

PARTICIPATION IN CLINICAL TRIALS

Year: 2023

Role: Principal Investigator and Study Coordinator

Type of trial: Phase II academic interventional study on acute myeloid leukemia;

Year: 2023

Role: Local Principal Investigator

Type of trial: Phase II academic interventional study on acute myeloid leukemia

Year: 2023:

Role: Local Principal Investigator

Type of trial: Phase I interventional study on acute leukemias, lymphomas and multiple myeloma

Year 2023:

Role: Sub-Investigator
Type of trial: Phase III interventional study on acute myeloid leukemia

Year 2022:
Role: Sub-Investigator
Type of trial: Phase I interventional study on acute myeloid leukemia

Year: 2018
Role: Sub-Investigator;
Type of trial: Phase III interventional study on acute myeloid leukemia

Year: 2018
Role: Sub-Investigator
Type of trial: Phase III interventional study on acute myeloid leukemia

Year: 2017
Role: Sub-investigator
Type of trial: Phase II academic interventional study on acute myeloid leukemia

Memberships Current Executive Board Member: Specialized Working Group (SWG) on acute myeloid leukemia, European Hematology Association
Current member: European Affairs Committee, European Hematology Association
Current member: YoungEHA Committee, European Hematology Association

Other Relevant Information 2019: Clinical Research Training in Hematology scholar funded by European Hematology Association
2017: Translational Research Training in Hematology scholar funded by American Society of Hematology