Bruno Bernardo AMATI **Biosketch** for **RNA Horizons 2026**

Academic education

1985	Diploma of Biology, University of Geneva, Switzerland.
1986	Certificate of specialization (Masters) in Molecular Biology, University of Geneva.
1990	Ph.D., Swiss Institute for Experimental Cancer Research (ISREC) and University of Lausanne.

Positions Held

1986-1990	Ph.D. student, ISREC, Lausanne.
1990-1993	Post-doc, Imperial Cancer Research Fund (ICRF), London.
1994-1999	Associate Scientist (junior group leader), ISREC, Lausanne.
1999-2002	Group leader, DNAX Inc., Palo Alto (CA, USA).
2003-present	Group leader, Dept. of Experimental Oncology, European Institute of Oncology (IEO), Milan, Italy.
2011-2017	Director, Center for Genomic Science, Italian Institute of Technology (IIT), Milan.
2017-present	Scientific Director, European School of Molecular Medicine (SEMM), Milan.

SCOPUS: https://www.scopus.com/authid/detail.uri?authorId=7003826331
ORCID: https://orcid.org/0000-0002-2958-1799

Synopsis of scientific contributions

My overarching long-term commitment has been to unravel the function of the *MYC* proto-oncogene and its protein product, MYC. This took us into diverse areas of molecular and cellular biology, including cell cycle control, gene regulation, chromatin and RNA biology, genomics, transcriptomics, mouse tumor models and preclinical development. Over the years, we contributed original concepts and connections between these research areas. In particular:

As a post-doc, I focused on the role of the MYC dimerization partner MAX. I demonstrated that MYC/MAX dimers function as sequence-specific transcriptional activators *in vivo* (1) and that dimerization is essential for MYC to promote cell proliferation, apoptosis and transformation (2,3).

My group initially focused on the mechanisms by which MYC activation deregulates cell cycle progression (4,5). Along this line, we also uncovered phosphorylation-dependent degradation of p27 (6), the cyclin E2 variant (7), the phenotype of cyclin E1/E2 double-KO mice (8) and the role of CDK2 in suppressing MYC-induced senescence (9).

In 2000, with the handful of MYC-target genes identified at the time [e.g.(10)] we started to explore mechanisms of transcriptional control. We developed and published the first quantitative Chromatin Immunoprecipitation (qChIP) assay, which we used to show that MYC mediates acetylation of histone H4 on its target promoters (11), in part by recruiting the histone acetyl-transferase Tip60 (12), which we later found to act – paradoxically – as a tumor suppressor (13). Using the qChIP assay, we reported the first large-scale screen for MYC-target sites in the human genome (14) as well as their histone modification profiles (15). While pre-dating the emergence of genome-wide technologies, this work established the key concept that MYC, unlike pioneer transcription factors, depends upon an open chromatin context to access its genomic targets. From 2010 onward, we invested into genomic technologies (ChIP-seq, RNA-seq) contributing innovative insight and concepts into genome recognition and transcriptional regulation by MYC (16-23).

Following from the above, we undertook functional-genomics screens to identify MYC-effector genes in B-cell lymphoma, revealing a critical role of the mitochondrial ribosome in tumor maintenance (24). This paved the way for a new line of pre-clinical research, addressing the therapeutic potential of targeted, mechanism-based, drug combinations against MYC-driven B-cell lymphomas (25-28) including high-grade subtypes refractory to current therapies (29,30).

In this context, and given MYC's wide impact on RNA biology (17), we ran reverse-genetic screens aimed at identifying synthetic-lethal interactions between MYC and RNA-binding proteins. Among other candidates, this led to the identification of the nonsense-mediated mRNA decay (NMD) pathway as an actionable therapeutic liability in MYC-driven lymphoma. This will be presented at RNA Horizons 2026.

Selected papers

1. Amati B *et al.* 1992 *Nature* 359;423-6 https://doi.org/10.1038/359423a0
2. Amati B *et al.* 1993 *Cell* 72;233-45 https://doi.org/10.1016/0092-8674(93)90663-b
3. Amati B *et al.* 1993 *Embo J* 12;5083-7 https://doi.org/10.1002/j.1460-2075.1993.tb06202.x
4. Vlach J *et al.* 1996 *Embo J* 15;6595-604 https://doi.org/10.1002/j.1460-2075.1996.tb01050.x
5. Alevizopoulos K *et al.* 1997 *Embo J* 16;5322-33 https://doi.org/10.1093/emboj/16.17.5322
6. Vlach J *et al.* 1997 *Embo J* 16;5334-44 https://doi.org/10.1093/emboj/16.17.5334
7. Lauper N *et al.* 1998 *Oncogene* 17;2637-43 https://doi.org/10.1038/sj.onc.1202477
8. Parisi T *et al.* 2003 *Embo J* 22;4794-803 https://doi.org/10.1093/emboj/cdg482
9. Campaner S *et al.* 2010 *Nat Cell Biol* 12;54-9 https://doi.org/10.1038/ncb2004
10. Greasley PJ *et al.* 2000 *Nucleic Acids Res* 28;446-53 https://doi.org/10.1093/nar/28.2.446
11. Frank SR *et al.* 2001 *Genes Dev* 15;2069-82 https://doi.org/10.1101/gad.906601
12. Frank SR *et al.* 2003 *EMBO Rep* 4;575-80 https://doi.org/10.1038/sj.embor.embor861
13. Gorrini C *et al.* 2007 *Nature* 448;1063-7 https://doi.org/10.1038/nature06055
14. Fernandez PC *et al.* 2003 *Genes Dev* 17;1115-29 https://doi.org/10.1101/gad.1067003
15. Guccione E *et al.* 2006 *Nat Cell Biol* 8;764-70 https://doi.org/10.1038/ncb1434
16. Sabò A, Amati B. 2014 *Cold Spring Harb Perspect Med* 4;a014191 https://doi.org/10.1101/cshperspect.a014191
17. Kress TR *et al.* 2015 *Nat Rev Cancer* 15;593-607 https://doi.org/10.1038/nrc3984
18. Kress TR *et al.* 2016 *Cancer Res* 76;3463-72 https://doi.org/10.1158/0008-5472.CAN-16-0316
19. de Pretis S *et al.* 2017 *Genome Res* 27;1658-64 https://doi.org/10.1101/gr.226035.117
20. Sabò A, Amati B. 2018 *Science* 360;713-4 https://doi.org/10.1126/science.aat6664
21. Tesi A *et al.* 2019 *EMBO Rep* 20;e47987 https://doi.org/10.15252/embr.201947987
22. Bywater MJ *et al.* 2020 *Nat Commun* 11;1827 https://doi.org/10.1038/s41467-020-15552-x
23. Pellanda P *et al.* 2021 *Embo J* 40;e105464 https://doi.org/10.15252/embj.2020105464
24. D'Andrea A *et al.* 2016 *Oncotarget* 7;72415-30 https://doi.org/10.18632/oncotarget.11719
25. Ravà M *et al.* 2018 *Sci Transl Med* 10;eaan8723 https://doi.org/10.1126/scitranslmed.aan8723
26. Donati G *et al.* 2022 *Mol Oncol* 16;1132-52 https://doi.org/10.1002/1878-0261.13115
27. Donati G *et al.* 2023 *EMBO Mol Med* 15;e16910 https://doi.org/10.15252/emmm.202216910
28. Donati G *et al.* 2026 *Br J Haematol* 208;722-6 https://doi.org/10.1111/bjh.70249
29. Bisso A *et al.* 2019 *Immunol Rev* 288;178-97 https://doi.org/10.1111/imr.12734
30. Donati G, Amati B. 2022 *Mol Oncol* 16;3828-54 https://doi.org/10.1002/1878-0261.13319