

CURRICULUM VITAE

ALESSANDRO MICHIEZZI

PRESENT POSITION AND ADDRESS

Research Staff Scientist,
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BIOGRAPHICAL

Born: July 5, 1969, Rome-Italy

Citizenship: Italian

EDUCATION AND QUALIFICATIONS

- 1993 **Degree** (laurea) in Biological Science (summa cum laude):
University of Rome "La Sapienza".
Final dissertation: "Characterization of a small nucleolar RNA
(U16) encoded inside the L1 ribosomal gene protein intron in
X.Laevis".
- 1994 **Thesis's prize** from the Pasteur Institute-Cenci Bolognetti
Foundation.
- 2000 A scientific committee from the Italian National Center for
Research (C.N.R.) granted a PhD equivalent title.

AWARDS AND HONORS

- 1994 Undergraduate thesis prize from the Pasteur Institute-Fondazione
Cenci Bolognetti

- 2011 ICAR 2011 AWARD - Premio Fondazione AVIRALIA for the best scientific contribution from young researcher
- 1995-1997 Fellowship from the Pasteur Institute-Fondazione Cenci Bolognetti at the Department of Genetics and Molecular Biology c/o Centro Acidi Nucleici C.N.R at the University of Rome "La Sapienza"
- 1997-1998 A.I.D.S italian fellowship from the Istituto Superiore di Sanita' at the Department of Genetics and Molecular Biology c/o Centro Acidi Nucleici C.N.R at the University of Rome "La Sapienza"

RESEARCH EXPERIENCE

- 1991-1993 **Undergraduate Studentship:** University of Rome "La Sapienza", Department of Genetics and Molecular Biology c/o Centro Acidi Nucleici C.N.R in the Prof. Irene Bozzoni laboratory.
- 1993-1995 **Post-graduate training:** Centro Acidi Nucleici C.N.R c/o Department of Genetics and Molecular Biology in the Prof. Irene Bozzoni laboratory under the supervision of Dr. Paola Fracapane.
- 1995-1997 **Fellowship from the Pasteur Institute-Cenci Bolognetti Foundation** at the Department of Genetics and Molecular Biology c/o Centro Acidi Nucleici C.N.R at the University of Rome "La Sapienza" under the supervision of Prof. Irene Bozzoni.
- 1997-1998 **A.I.D.S italian fellowship** from the Istituto Superiore di Sanita' at the Department of Genetics and Molecular Biology c/o Centro Acidi Nucleici C.N.R at the University of Rome "La Sapienza" under the supervision of Prof. Irene Bozzoni.
- 1998-2003 **Post-doctoral fellow** at the Beckman Institute c/o City of Hope, National Medical Center in the Prof. J. J. Rossi's laboratory.
- 2003-2006 **Postdoctoral research associate**, Department Cellular Biology and Neuroscience, I.S.S., Rome, Italy. Work in the laboratory of Dr. Sandra Gessani.
- 2006-present **Research Staff Scientist**, Department of Experimental Medicine and Biochemical Science-University of Rome "Tor Vergata".

COURSES

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|-----------------------|--|
| 29 March-1 April 1994 | “RNA STRUCTURE AND FUNCTION”, ICGEB-Trieste, Italy. |
| 13-18 September 1997 | “Second Advanced Course of Gene Therapy” FEBS course-Venice, Italy. |
| 23-27 August 2002 | “Ribozymes and RNA Catalysis”
West Park Centre, University of Dundee, Scotland-UK |

INVITED SPEAKER AT MEETINGS

- Gruppo di cooperazione “Struttura molecolare ed espressione genica”
Capalbio- May 1993.
- Convegno congiunto SIBBM, ABCD e AGI, Riccione, 2-5 October 1996.
- Beckman Research Institute & City of Hope-20th Annual Advance, Lake Arrowhead, CA, USA, April 30-May 2, 2000.
- Ribosome Biogenesis & Nucleolar Function, Fifth International Conference, Granlibakken, August 17-21, 2000.
- RNA meeting 2002-Seventh Annual Meeting of the RNA Society
University of Wisconsin, Madison May 28 - June 2, 2002
- ICAR 2011 Italian Conference on AIDS and Retroviruses
Florence, Italy, 27 - 29 March 2011

PUBLICATIONS

1-“A novel small nucleolar RNA (U16) is encoded inside a ribosomal protein intron and originates by processing of the pre-mRNA”.

P. Fragapane, S. Prislei, **A. Michienzi**, E. Caffarelli and I. Bozzoni, (1993).
EMBO J, **12**, pp.2921-2928.

2-“ Two different snoRNA are encoded in introns of the L1 ribosomal protein genes of amphibia and humans”

Prislei S., **Michienzi A.**, Presutti C., Fracapane P., and Bozzoni I., (1993).
Nucleic Acid Research, **21**, pp.5834-5840.

3-“U1 snRNA-chimeric ribozymes with substrate specificity for the Rev pre-mRNA of HIV”

A.Michienzi, S. Prislei, and I. Bozzoni. (1996).
Proc. Natl. Acad. Sci., **93**, pp.7219-7224.

4-“Use of adenoviral VAI small RNA as carrier for cytoplasmic delivery of ribozymes”
S. Prislei, S.B.C. Buonomo, **A. Michienzi** and I. Bozzoni (1997).
RNA, **3**, pp.1-11.

5-“Inhibition of HIV-1 replication by nuclear chimeric anti-HIV ribozymes in a human T-lymphoblastoid cell line”.

A.Michienzi, L. Conti, B. Varano, S. Prislei, S. Gessani and I. Bozzoni (1998).
Human Gene Therapy, **9**, pp. 621-628.

6. “The Rev protein is able to transport to the cytoplasm small nucleolar RNAs containing a Rev binding element”.

S. B. C. Buonomo, **A. Michienzi**, F. G. De Angelis, and I. Bozzoni (1999).
RNA, **5**, pp. 993-1002.

7. ”A chimeric nucleolar Rev decoy inhibits the HIV replication”.

A.Michienzi, L. Cagnon, I. Bozzoni and J.J. Rossi.
Nucleic Acids Symposium Series No. 41 (1999), pp. 211-214.

8. “Ribozyme-mediated inhibition of HIV-1 suggests nucleolar trafficking of HIV-1 RNA”.

A.Michienzi, L. Cagnon, I. Bahner, and J. J. Rossi.
(2000) *Proc. Natl. Acad. Sci.*, **97**, pp.8955-8960.

9.”Intracellular Applications of Ribozymes”

Alessandro Michienzi and John J. Rossi (2001)
METHODS IN ENZYMOLOGY, **341**, pp.581-596.

10.” Ribozymes as Therapeutic Agents and Genetics Tools”

Poggi, A., **Michienzi, A.** and Rossi, J.J. (2002) In *Pharmaceutical Perspectives of Nucleic Acid-Based Therapeutics*, Taylor and Francis Publishers, London, U.K.. (2002).

11.”A nucleolar TAR decoy inhibitor of HIV-1 replication”.

A. Michienzi, S. Li, J.A.Zaia, and J. J. Rossi
Proc. Natl. Acad. Sci (2002), **99**:14047-14052.

12.” Intracellular ribozyme applications.”

Castanotto D., Li JR, **Michienzi A.** Langlois MA, Lee NS, Puymirat J, Rossi JJ.
Biochem Soc Trans. 2002 Dec;30(6):1140-5.

13. “Novel ribozyme, RNA decoy, and siRNA approaches to inhibition of HIV in a gene therapy setting”
Alessandro Michienzi, Daniela Castanotto, Nancy Lee, Shirley Li, John A. Zaia, John J. Rossi.
Clinical and Applied Immunology Reviews (2003) 3: 223-233.
14. Inhibition of HIV-1 infection by lentiviral vectors expressing Pol III-promoted anti HIV RNAs.
Ming-Jie Li, Gerhard Bauer, **Alessandro Michienzi**, Jiing-Kuan Yee, Nan-Sook Lee, James Kim, Shirley Li, Daniela Castanotto, John Zaia and John J. Rossi. (2003)
Molecular Therapy, 8:196-206
15. “RNA-mediated inhibition of HIV in a gene therapy settings”.
Michienzi A, Castanotto D, Lee N, Li S, Zaia JA, Rossi JJ. (2003) *Ann N Y Acad Sci.*, 1002:63-71.
16. A nucleolar localizing Rev binding element inhibits HIV replication.
Michienzi A, DeAngelis F, Bozzoni I, Rossi J *AIDS Research and Therapy*, 2006 3:13.
17. CCL2 down-modulation by selected TLR agonist combinations contributes to Th1 polarization in human dendritic cells.
Del Corno M*, **Michienzi A***, Masotti A, Da Sacco L, Bottazzo GF, Belardelli F, Gessani S. (2009) *Blood*. Jul 23;114(4):796-806. Epub 2009 May 22.
*The authors contributed equally to this work.
18. EDITING OF HIV-1 RNA BY THE DOUBLE-STRANDED RNA DEAMINASE ADAR1 STIMULATES VIRAL INFECTION.
Margherita Doria, Francesca Neri, Angela Gallo, Maria Giulia Farace and **Alessandro Michienzi**.
Nucleic Acids Res. 2009 Aug 3. [Epub ahead of print].
19. ADAR2 editing enzyme is a novel human immunodeficiency virus-1 proviral factor.
Doria M, Tomaselli S, Neri F, Ciafrè SA, Farace MG, **Michienzi A***, Gallo A*.
*The authors contributed equally to this work. *J Gen Virol.* 2011 May;92(Pt 5):1228-32.
Epub 2011 Feb 2.
20. The HIV-1 Tat protein modulates CD4 expression in human T cells through the induction of miR-222. Orecchini E, Doria M, **Michienzi A**, Giuliani E, Vassena L, Ciafrè SA, Farace MG, Galardi S. *RNA Biol.* 2014;11(4):334-8
21. HIV-1 infection causes a down-regulation of genes involved in ribosome biogenesis.
Kleinman CL, Doria M, Orecchini E, Giuliani E, Galardi S, De Jay N, **Michienzi A**.
PLoS One. 2014 Dec 2;9(12):e113908.

22. The ADAR1 editing enzyme is encapsidated into HIV-1 virions. Orecchini E, Federico M, Doria M, Arenaccio C, Giuliani E, Ciafrè SA, **Michienzi A**. *Virology*. 2015 Nov;485:475-80.
23. CPEB1 restrains proliferation of Glioblastoma cells through the regulation of p27(Kip1) mRNA translation. Galardi S, Petretich M, Pinna G, D'Amico S, Loreni F, **Michienzi A**, Groisman I, Ciafrè SA. *Sci Rep*. 2016 May 4;6:25219.
24. ADAR1 restricts LINE-1 retrotransposition. Orecchini E, Doria M, Antonioni A, Galardi S, Ciafrè SA, Frassinelli L, Mancone C, Montaldo C, Tripodi M, **Michienzi A**. *Nucleic Acids Res*. 2017 Sep 21. pii: gkw834.
25. Novel HBsAg mutations correlate with hepatocellular carcinoma, hamper HBsAg secretion and promote cell proliferation in vitro. Salpini R, Surdo M, Warner N, Cortese MF, Colledge D, Soppe S, Bellocchi MC, Armenia D, Carioti L, Continenza F, Di Carlo D, Saccomandi P, Mirabelli C, Pollicita M, Longo R, Romano S, Cappiello G, Spanò A, Trimoulet P, Fleury H, Vecchiet J, Iapadre N, Barlattani A, Bertoli A, Mari T, Pasquazzi C, Missale G, Sarrecchia C, Orecchini E, **Michienzi A**, Andreoni M, Francioso S, Angelico M, Verheyen J, Ceccherini-Silberstein F, Locarnini S, Perno CF, Svicher V. *Oncotarget*. 2017 Feb 28;8(9):15704-15715. doi: 10.18632/oncotarget.14944.
26. "Resetting cancer stem cell regulatory nodes upon MYC inhibition". Silvia Galardi, Mauro Savino, Fiorella Scagnoli, Serena Pellegatta, Federica Pisati, Federico Zambelli, Barbara Illi, Daniela Annibali, Sara Beji, Elisa Orecchini, Maria Adele Alberelli, Clara Apicella, Rosaria Fontanella, **Alessandro Michienzi**, Gaetano Finocchiaro, Maria Farace, Giulio Pavesi, Silvia Ciafrè, and Sergio Nasi *EMBO REPORT* - 2016 Dec;17(12):1872-1889.
27. Orecchini E, Frassinelli L, Michienzi A (2017). Restricting retrotransposons: ADAR1 is another guardian of the human genome. *RNA BIOLOGY*, vol. 14, p. 1485-1491, ISSN: 1547-6286, doi: 0.1080/15476286.2017.1341033.
28. Post-transcriptional regulation of LINE-1 retrotransposition by AID/APOBEC and ADAR deaminases. Orecchini E, Frassinelli L, Galardi S, Ciafrè SA, **Michienzi A**. *Chromosome Res*. 2018 Mar;26(1-2):45-59. doi: 10.1007/s10577-018-9572-5. Epub 2018 Feb 2. Review.
29. The lncRNA H19 positively affects the tumorigenic properties of glioblastoma cells and contributes to NKD1 repression through the recruitment of EZH2 on its promoter. Fazi B, Garbo S, Toschi N, Mangiola A, Lombardi M, Sicari D, Battistelli C, Galardi S, **Michienzi A**, Trevisi G, Harari-Steinfeld R, Cicchini C, Ciafrè SA. *Oncotarget*. 2018 Feb 14;9(21):15512-15525. doi: 10.18632/oncotarget.24496. eCollection 2018 Mar 20.

PATENTS

Patent number: RM97A000150

title: Molecole chimeriche ribozima-scRNA ad attività catalitica per RNA a localizzazione citoplasmatica

inventors: Irene Bozzoni Silvia Prislei Sara C.B. Buonomo Alessandro Michienzi

Date: March 17 1997

Patent number: RM99A000126

title: Molecole chimeriche di RNA a localizzazione nucleolare e in grado di legare la proteina Rev di HIV

inventors: Irene Bozzoni Alessandro Michienzi Sara C.B. Buonomo

Date: February 24, 1999.

Patent number: US Patent 6995258

Title: Nucleolar Targeting of Therapeutics Against HIV

Inventors: John Rossi, Alessandro Michienzi

Date: February 7, 2006

CLINICAL TRIAL

The nucleolar TAR decoy (to sequester HIV-1 Tat protein in the nucleolus) designed and tested by Alessandro Michienzi has been included together with other antiviral genes in a Pilot Study of the Safety and Feasibility of Stem Cell Therapy for AIDS Lymphoma using Stem Cells Treated with a Lentiviral Vector-encoding the Multiple anti-HIV RNA's that is a fully recruited and patient monitoring ongoing at the City of Hope in Duarte, California. This is an important study as it is the first human clinical trial using lentiviral vector transduction of haematopoietic stem cells (HSCs). It is also the first human trial with expressed RNA interference trigger (shRNA) and the first triple gene therapy combination trial for HIV/AIDS.

Due to the success seen in the initial pilot study planning is well advanced for the next human study expected to commence in late 2010 after manufacture of clinical trial material and further process development work.

This consortium program involves six collaborative partners, namely:

- i. Beckman Research Institute, COH (BRICOH, Duarte CA);
- ii. Benitec company
- iii. Colorado State University (CSU, Fort Collins, CO);
- iv. Fred Hutchinson Cancer Research Centre (FHCRC/WU, Seattle WA)
- v. International Therapeutics Inc (ITI, Seattle, WA);
- vi. University of Pennsylvania (UPENN, Philadelphia, PA).

This program is a multi-project effort centred at COH to investigate HIV-based vector delivery of anti-HIV RNA

(initially pHIV7-shI-TAR-CCR5RZ) to CD4+ peripheral blood T-cells (as opposed to the CD34+ stem cells targeted in the clinical pilot study above) as a clinical modality.