

BIOGRAPHICAL SKETCH

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NAME: **Fabio Martelli**

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: **Director, Molecular Cardiology Laboratory, IRCCS-Policlinico San Donato, Milan, Italy**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Dana Farber Cancer Institute-Harvard Medical School, Boston, MA, USA, D.M. Livingston laboratory	Post-doctoral fellow in medicine	1995	2000	Molecular Oncology
Sapienza University, Rome, Italy. A. Felsani laboratory	PhD	1994	1994	Molecular Biology
Biology Board Certification		1993	1993	Molecular Biology
Sapienza University, Rome, Italy. A. Felsani laboratory	MSc	1991	1991	Molecular Biology

A. Personal Statement

My research focuses on understanding how RNA dysregulation contributes to human disease, with a long-standing and sustained commitment to **myotonic dystrophy type 1 (DM1)** and, more broadly, to non-coding RNA-mediated regulation in muscle and cardiovascular pathophysiology. Over the past two decades, my laboratory has investigated the role of non-coding RNAs, alternative splicing, circular RNAs, and RNA-based regulatory networks in DM1, combining patient-derived models, human muscle biopsies, and *in vivo* systems with transcriptomic and functional approaches.

A central unresolved question in DM1 concerns how RNA chemical modifications contribute to transcriptome complexity, splicing defects, and disease-relevant gene regulation. Particularly, involvement of **N⁶-methyladenosine (m⁶A)** in DM1 pathogenesis has not yet been addressed, despite strong evidence for its role in regulating RNA stability, splicing, and translation. To tackle this gap, my group has established a unique and well-controlled experimental framework, incorporating **isogenic DM1 patient-derived cells with CTG-expanded alleles and their CTG-excised counterparts**, pharmacological modulation of the m⁶A machinery (including METTL3 and m⁶A eraser inhibition, with appropriate controls), and **skeletal muscle biopsies (*vastus lateralis*) from DM1 patients and healthy individuals**. Within this context, **Direct RNA sequencing represents an enabling technology**: access to it will allow extending my group's capacities and expertise in RNA regulation beyond short-read-based approaches and well into modification-aware, full-length RNA analyses.

My expertise in RNA biology is rooted in my extensive work in cardiovascular diseases, where, until today, my laboratory is leading and contributing to large-scale transcriptomic studies, non-coding RNA discovery, and translational biomarker development. There is reciprocal relationship between the two fields: concepts, analytical frameworks, and technologies developed in cardiovascular research directly inform our investigation of DM1 transcriptomic dysregulation. This complementary molecular and technological expertise provides a strong foundation for the proposed work, ensuring rigorous experimental design, robust data interpretation, and maximal exploitation of Direct RNA sequencing. I am committed to dedicating the necessary time and resources to this proof-of-concept project and to establish feasibility and generate novel insights into DM1 with translational potential.

B. Positions, Scientific Appointments and Honors

INSTITUTION AND LOCATION	POSITIONS	YEAR(s)
Molecular Cardiology Laboratory, IRCCS-Policlinico San Donato, Milan, Italy	Director, tenured	2012-to date
Molecular Cardiology Laboratory, IRCCS-Policlinico San Donato, Milan, Italy	Head/senior consultant	2007-2012
Vascular Pathology Laboratory, IDI-IRCCS, Rome	Senior Scientist-Tenured	2003-2012
Vascular Pathology Laboratory, IDI-IRCCS, Rome	Scientist	2000-03

Scientific Societies

2006-to date American Heart Association Professional Member, Basic Cardiovascular Sciences Council

2015-to date European Society of Cardiology - Working Group on Atherosclerosis and Vascular Biology

2018-to date European Society of Cardiology - Working Group on Myocardial Function

2022-to date European Society of Cardiology - Working Group on Cellular Biology of the Heart

2023-to date European Society of Cardiology - Heart Failure Association

Editorial activity

- Academic Editor of PLoS ONE (from 8/2010 to 9/2022, 76 final dispositions)
- Associate Editor of Frontiers in Cardiovascular Medicine-Cardiovascular Biologics and Regenerative Medicine (from Sept 12th, 2016 to date, 6 final dispositions)
- Editorial board member of International Journal of Molecular Sciences (from 2020, 16 final dispositions)
- Guest Editor of the FORUM ISSUE on "Hypoxamirs" of Antioxidants & Redox Signaling (Sept. 2014)
- Guest Editor of the FORUM ISSUE on "NON-CODING RNAs AND EPIGENETICS" of Antioxidants & Redox Signaling (Sept 2018)
- Guest Editor for the special issue of the International Journal of Molecular Sciences "RNAs in Cardiovascular Diseases - CardioRNA EU-COST Action." (Nov 2019)

Ad hoc reviewer for more than **230 manuscripts submitted to peer reviewed journals** and **180 applications to research funding societies**.

Research Fellowships

- Leukemia and Lymphoma Society Special Fellowship (1998–2001)
- Human Frontier Science Program (HFSP) Long-Term Fellowship (1995–1997)
- Telethon Fellowship for Research Abroad (1995)
- AIRC Fellowship (1992–1994)

C. Contributions to Science

Bibliometric indicators

Number of papers: 165; H index: 66; H index last 5 years: 41; Scopus: 59

Google Scholar page: <https://scholar.google.it/citations?user=wAPKO9wAAAAJ&hl=it&oi=ao>

ResearchGate Profile: https://www.researchgate.net/profile/Fabio_Martelli

ORCID: 0000-0002-8624-7738; Scopus ID: 7102826282; Web of Science ResearcherID: AAL-3788-2020

Selection of relevant publications

1. Baci D, Tastsoglou S, Provenzano C, Perfetti A, Izzo M, Lisanti M, Frolova S, Voellenkle C, Tascini AS, Cardani R, Cardinali B, Meola G, Falcone G, **Martelli M**. circARHGAP10 as a candidate biomarker and therapeutic target in myotonic dystrophy type 1. *Mol Ther Nucleic Acids*. 2025 Sep 9;36(3):102646.
2. Marinescu-Colan CI, Nastase-Rusu EG, Neculachi CA, **Martelli F**, Cherry L, Preda MB, Burlacu A. From cancer to heart fibrosis - GLIPR1 highlights a subset of myofibroblasts responsive to mesenchymal stem cell therapy after myocardial infarction. *Biomed Pharmacother*. 2025 Jun;187:118087.
3. Izzo M, Battistini J, Golini E, Voellenkle C, Provenzano C, Orsini T, Strimpakos G, Scavizzi F, Raspa M, Baci D, Frolova S, Tastsoglou S, Zaccagnini G, Garcia-Manteiga JM, Gourdon G, Mandillo S, Cardinali B, **Martelli F**, Falcone G. Muscle-specific gene editing improves molecular and phenotypic defects in a mouse model of myotonic dystrophy type 1. *Clin Transl Med*. 2025 Feb;15(2):e70227. Shares corresponding authorship.
4. Devaux Y, Zhang L, Lumley AI, Karaduzovic-Hadziabdic K, Mooser V, Rousseau S, Shoaib M, Satagopam V, Adilovic M, Srivastava PK, Emanuelli C, **Martelli F**, Greco S, Badimon L, Padro T, Lustrek M, Scholz M,

- Rosolowski M, Jordan M, Brandenburger T, Benczik B, Agg B, Ferdinandy P, Vehreschild JJ, Lorenz-Depiereux B, Dörr M, Witzke O, Sanchez G, Kul S, Baker AH, Fagherazzi G, Ollert M, Wereski R, Mills NL, Firat H. Development of a long noncoding RNA-based machine learning model to predict COVID-19 in-hospital mortality. *Nat Commun.* 2024 May 20;15(1):4259.
5. Garoffolo G, Casaburo M, Amadeo F, Salvi M, Bernava G, Piacentini L, Chimenti I, Zaccagnini G, Milcovich G, Zuccolo E, Agrifoglio M, Ragazzini S, Baasansuren O, Cozzolino C, Chiesa M, Ferrari S, Carbonaro D, Santoro R, Manzoni M, Casalis L, Raucci A, Molinari F, Menicanti L, Pagano F, Ohashi T, **Martelli F**, Massai D, Colombo GI, Messina E, Morbiducci U, Pesce M. Reduction of Cardiac Fibrosis by Interference With YAP-Dependent Transactivation. *Circ Res.* 2022 Jun 30;101161CIRCRESAHA121319373.
6. Cardinali B, Provenzano C, Izzo M, Voellenkle C, Battistini J, Strimpakos G, Golini E, Mandillo S, Scavizzi F, Raspa M, Perfetti A, Baci D, Lazarevic D, Garcia-Manteiga JM, Gourdon G, **Martelli F**. Time-controlled and muscle-specific CRISPR/Cas9-mediated deletion of CTG-repeat expansion in the DMPK gene. *Mol Ther Nucleic Acids.* 2022 Mar 8;27:184–99.
7. Zaccagnini G, Greco S, Voellenkle C, Gaetano C, **Martelli F**. miR-210 hypoxamiR in angiogenesis and diabetes. *Antioxid Redox Signal.* 2021 24 Dec.
8. Zaccagnini G, Greco S, Longo M, Maimone B, Voellenkle C, Fuschi P, Carrara M, Creo P, Maselli D, Tirone M, Mazzone M, Gaetano C, Spinetti G, **Martelli F**. Hypoxia-induced miR-210 modulates the inflammatory response and fibrosis upon acute ischemia. *Cell Death Dis.* 2021 May 1;12(5):435.
9. Voellenkle C, Perfetti A, Carrara M, Fuschi P, Renna LV, Longo M, Sain SB, Cardani R, Valaperta R, Silvestri G, Legnini I, Bozzoni I, Furling D, Gaetano C, Falcone G, Meola G, **Martelli F**. Dysregulation of Circular RNAs in Myotonic Dystrophy Type 1. *Int J Mol Sci.* 2019 Apr 19;20(8):1938.
10. Besnier M, Gasparino S, Vono R, Sangalli E, Facoetti A, Bollati V, Cantone L, Zaccagnini G, Maimone B, Fuschi P, Da Silva D, Schiavulli M, Aday S, Caputo M, Madeddu P, Emanuelli C, **Martelli F***, Spinetti G*. miR-210 Enhances the Therapeutic Potential of Bone-Marrow-Derived Circulating Proangiogenic Cells in the Setting of Limb Ischemia. *Mol Ther.* 2018 Jun 13. * Corresponding author.
11. Perfetti A, Greco S, Cardani R, Fossati B, Cuomo G, Valaperta R, Ambrogi F, Cortese A, Botta A, Mignarri A, Santoro M, Gaetano C, Costa E, Dotti MT, Silvestri G, Massa R, Meola G, **Martelli F**. Validation of plasma microRNAs as biomarkers for myotonic dystrophy type 1. *Sci Rep.* 2016 Dec 1;6:38174.
12. Cardinali B, Cappella M, Provenzano C, Garcia-Manteiga JM, Lazarevic D, Cittaro D, **Martelli F**, Falcone G. MicroRNA-222 regulates muscle alternative splicing through Rbm24 during differentiation of skeletal muscle cells. *Cell Death Dis.* 2016 Feb 4;7:e2086. Shares corresponding authorship.
13. Zaccagnini G, Palmisano A, Canu T, Maimone B, Lo Russo FM, Ambrogi F, Gaetano C, De Cobelli F, Del Maschio A, Esposito A, **Martelli F**. Magnetic Resonance Imaging Allows the Evaluation of Tissue Damage and Regeneration in a Mouse Model of Critical Limb Ischemia. *PLoS One.* 2015 Nov 10;10(11):e0142111.
14. Biferi MG, Nicoletti C, Falcone G, Puggioni EM, Passaro N, Mazzola A, Pajalunga D, Zaccagnini G, Rizzuto E, Auricchio A, Zentilin L, De Luca G, Giacca M, **Martelli F**, Musio A, Musarò A, Crescenzi M. Proliferation of multiple cell types in the skeletal muscle tissue elicited by acute p21 suppression. *Mol Ther.* 2015 Feb 11.
15. Falcone G, Perfetti A, Cardinali B, **Martelli F**. Noncoding RNAs: Emerging Players in Muscular Dystrophies. *Biomed Res Int.* 2014;2014:503634.
16. Perfetti A, Greco S, Fasanaro P, Bugiardini E, Cardani R, Garcia-Manteiga JM, Riba M, Cittaro D, Stupka E, Meola G, **Martelli F**. Genome wide identification of aberrant alternative splicing events in myotonic dystrophy type 2. *PLoS One.* 2014;9(4):e93983.
17. Perfetti P, S Greco S, Bugiardini E, Cardani R, Gaia P, Gaetano C, Meola G, **Martelli F**. Plasma microRNAs as biomarkers for myotonic dystrophy type 1. *Neuromuscular Disorders*, 2014, (6):509-15.
18. Cicchillitti L, Di Stefano V, Isaia E, Crimaldi L, Fasanaro P, Ambrosino V, Antonini A, Capogrossi MC, Gaetano C, Piaggio G, **Martelli F**. Hypoxia Inducible Factor 1- alpha induces miR-210 in normoxic differentiating myoblasts. *J. Biol. Chem.* 2012 Dec 28;287(53):44761-71
19. Greco S, Perfetti A, Fasanaro P, Cardani R, Capogrossi MC, Meola G, **Martelli F**. Deregulated microRNAs in myotonic dystrophy type 2. *PLoS One.* 2012;7(6):e39732.
20. Perbellini R, Greco S, Sarra-Ferraris G, Cardani R, Capogrossi MC, Meola G, **Martelli F**. Dysregulation and cellular mislocalization of specific miRNAs in myotonic dystrophy type 1. *Neuromuscul Disord NMD.* 2011 Feb;21(2):81–8.
21. Greco S, De Simone M, Colussi C, Zaccagnini G, Fasanaro P, Pescatori M, Cardani R, Perbellini R, Isaia E, Sale P, Meola G, Capogrossi MC, Gaetano C, **Martelli F**. Common micro-RNA signature in skeletal

- muscle damage and regeneration induced by Duchenne muscular dystrophy and acute ischemia. *FASEB J Off Publ Fed Am Soc Exp Biol.* 2009 Oct;23(10):3335–46.
22. Fasanaro, P., Greco, S., Lorenzi, M., Pescatori, M., Brioschi, M., Kulshreshtha, R., Banfi, C., Stubbs, A., Calin, G. A., Ivan, M., Capogrossi, M. C., and **Martelli, F.**, An integrated approach for experimental target identification of hypoxia-induced miR-210, *J Biol Chem*, 284, 35134 (2009).
 23. Cardinali, B., Castellani, L., Fasanaro, P., Basso, A., Alema, S., **Martelli, F.**, and Falcone, G., MicroRNA-221 and microRNA-222 modulate differentiation and maturation of skeletal muscle cells, *PLoS One*, 4, e7607 (2009).
 24. Colussi C, Mozzetta C, Gurtner A, Illi B, Rosati J, Straino S, Ragone G, Pescatori M, Zaccagnini G, Antonini A, Minetti G, **Martelli F**, Piaggio G, Gallinari P, Steinkuhler C, Clementi E, Dell'Aversana C, Altucci L, Mai A, Capogrossi MC, Puri PL, Gaetano G. HDAC2 blockade by nitric oxide and histone deacetylase inhibitors reveals a common target in Duchenne muscular dystrophy treatment. *Proc Natl Acad Sci U S A.* 2008 Dec 9;105(49):19183–7.
 25. Zaccagnini, G., **Martelli, F.***, Magenta, A., Cencioni, C., Fasanaro, P., Nicoletti, C., Biglioli, P., Pelicci, P. G., and Capogrossi, M. C., p66(ShcA) and oxidative stress modulate myogenic differentiation and skeletal muscle regeneration after hind limb ischemia, *J Biol Chem.*, 282, 31453 (2007). *Corresponding author; shares first authorship.
 26. Straino, S., Germani, A., Di Carlo, A., Porcelli, D., De Mori, R., Mangoni, A., Napolitano, M., **Martelli, F.**, Biglioli, P., and Capogrossi, M. C., Enhanced arteriogenesis and wound repair in dystrophin-deficient mdx mice, *Circulation*, 110, 3341 (2004).
 27. Di Carlo, A., De Mori, R., **Martelli, F.**, Pompilio, G., Capogrossi, M. C., and Germani, A., Hypoxia inhibits myogenic differentiation through accelerated MyoD degradation, *J Biol Chem.*, 279, 16332 (2004).
 28. **Martelli, F.**, Cenciarelli, C., Santarelli, G., Polikar, B., Felsani, A., and Caruso, M., MyoD induces retinoblastoma gene expression during myogenic differentiation, *Oncogene*, 9, 3579 (1994).

D. Scholastic Performance

Ongoing research support

2025-26 FMM – Fondazione Malattie Miotoniche (Myotonic Diseases Foundation). Project coordinator. “Myotonic Dystrophy Type 1 at Single-Nucleus Resolution: Dissecting Differential Gene Expression Across Whole-Genome and Cellular Transcriptomes” €50 000.

2025-29 COST ACTION CardioPharmaGENET CA24165. MC member. Network for Cardiovascular Pharmacogenomics and Precision Medicine.

2024-26 Ministero della Salute (Ministry of Health) PNRR. PI. “Mechanically regulated long non-coding RNAs in cardiac fibroblasts as new markers and effectors of cardiac fibrosis” €200 000.

2023-26 Ministero della Salute (Ministry of Health) PNRR. Project coordinator. “Cell specific targeting of hypoxia-induced miR-210 to modulate inflammation and fibrosis in the ischemic heart”. €399 850.

2023-27 Ministero della Salute (Ministry of Health). Co-PI. “CALabria HUB for Innovative and Advanced Research (CAL.HUB.RIA)”. €759 863.

2022-26 COST ACTION AtheroNET CA21153. MC member. “Network for implementing multiomics approaches in atherosclerotic cardiovascular disease prevention and research”.

Completed research support

2023-24 FMM – Fondazione Malattie Miotoniche (Myotonic Diseases Foundation). Project coordinator. “Deregulation and function of m6A RNA methylation and circularRNAs in Myotonic Dystrophy type 1” €50 000.

2022 Italian Cardiology Network. CoPI. “Atherosclerosis and Ischemic Heart Disease”. €97 750.

2021 Italian Cardiology Network. CoPI. “Post-COVID19: cardiovascular manifestations”. €92 000.

2021-2024 Ministero della Salute (Ministry of Health) RF2019. Project coordinator. “Role of the BACE1AS/BACE1/beta-amyloid pathway in Heart Failure”. €269 900.

2020-22 Horizon 2020 Framework Programme. PI. “A diagnostic test to improve surveillance and care of COVID-19 patients - COVIRNA”. Grant agreement 101016072; €174.388.

2020-22 AFM Telethon: “Circular RNA role in Myotonic Dystrophy type 1”. Project coordinator. €58 000. “

2020 Ministero della Salute (Ministry of Health) 5x1000-2019. Project coordinator. “microRNA role in macrophage response to pro-fibrotic stimuli”. €92 500.

2020-21 I-VASC research grant. Project coordinator. “New IVASC technology: safety evaluation of the device” €5 790.

2019-21 Telethon Foundation. PI. “Gene editing in Myotonic Dystrophy type 1: assessment of efficiency, safety and therapeutic effect of CTG-repeat deletion in a mouse model of disease” €190 000.

2019 I-VASC research grant. Project coordinator. “New IVASC technology: histological and immune-histochemical evaluation of efficacy” €16 230.

2018-22 COST ACTION cardioRNA CA17129. PI. “Catalysing transcriptomics research in cardiovascular disease”, leader of the WG1 “Regulatory function of the transcriptome”. MC member.

2018-19 Ministero della Salute (Ministry of Health) 5x1000-2015. Project coordinator. “Assessment of the potential as therapeutic targets of BACE1-AS, BACE1 e β -amyloid using mouse models of heart failure” €134 360.

2016-17 Ministero della Salute (Ministry of Health) 5x1000-2013-14. Project coordinator. “Advanced imaging techniques for miR-210 validation as a therapeutic target in myocardial infarction and heart failure” €85 000

2015-17 Association Française contre les Myopathies (AFM): “microRNA function and use as biomarkers in Myotonic Dystrophy type 1”. €46 400

2015 (for 2017) Ministero della Salute (Ministry of Health) 5x1000: “Advanced imaging techniques for miR-210 validation as a therapeutic target in myocardial infarction and heart failure” €42500

2014-18 Telethon Foundation: “Skeletal muscle and circulating microRNAs in Myotonic Dystrophy Type 1”. €220 000.

2014-18 Ministero della Salute (Ministry of Health) RF2011-12: “Epigenome wide profiling of dysfunctional endothelial progenitor cells in diabetic patients”. €146 000.

2014-18 Ministero della Salute (Ministry of Health) RF2011-12: “Enhanced cell therapy: novel strategies to improve transplanted cell survival and engraftment by protection from oxidative stress”. €118 000.

2014 Ministero della Salute (Ministry of Health) 5x1000: “Evaluation by MRI of tissue damage and regeneration in a mouse model of peripheral ischemia” €42000

2014-16 Fondazione Cariplo grant “Role of miR-210 hypoxamiR in peripheral ischemia”. €219 000

2012-14 AIRC Investigator grant “Angiogenesis regulation by hypoxia-induced miRNA-210”. €300 000.

2012-13 Ministero della Salute (Ministry of Health) 5x1000: “Role of noncoding RNAs in tissue response to ischemia” € 73000

2008-10 Ministero della Salute (Ministry of Health) RF2007: “Pathogenesis and therapy of heart failure: innovative approaches in the post-genomic era”. €64 000.

2007-11 Ministero della Salute (Ministry of Health) RF2007: “Molecular characterization of melanoma cancer stem cells”, €251 600.

2007-08 Istituto Superiore di Sanità (National Institute of Health): “Innovative strategies for regenerative therapy using stem cells”, €30 000.

2006-08 Ministero della Salute (Ministry of Health) RF2005: “Innovative therapeutic strategies for ischemic disease using cell therapy”, €48 400.

2005-07 Ministero della Salute (Ministry of Health) RF2005: “Development of new therapies for ischemic tissue revascularization”, €23 000.

2002-04 Ministero della Salute (Ministry of Health) RF2002: “Interactions between adhesion molecules and vascular growth factor receptors: new strategies for melanoma therapy”, €62 200.

2001-02 Sigma-Tau research grant, “Development of a stable transfectant” €40 300.

2001-02 CNR-Agenzia 2000, “Transcriptional control of cell division: E2F1 role”, €10 300.