

BIOGRAPHICAL SKETCH

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NAME: Montanaro Lorenzo

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eRA COMMONS USER NAME: LORENZO.MONTANARO

POSITION TITLE: Full Professor of Clinical Pathology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Bologna University (Italy)	MD	1989-1994	Medicine
Bologna University (Italy)	PhD	1995-2000	Experimental Pathology
Bologna University (Italy)	Residency	2000-2004	Clinical Pathology

A. Personal Statement

I am a Full Professor of Clinical Pathology with a long-standing research focus on the molecular mechanisms underlying human disease, particularly alterations of the protein synthesis machinery in pathological conditions, with a specific emphasis on human cancer. My work aims to elucidate how dysregulation of translational control contributes to disease initiation and progression, and to identify molecular vulnerabilities with potential diagnostic and therapeutic relevance.

I have a broad background in laboratory medicine, supported by extensive training and expertise in molecular biology and RNA biology. This interdisciplinary profile allows me to integrate clinical pathology with mechanistic and translational research approaches, bridging fundamental molecular insights with clinically relevant questions.

As Principal Investigator or co-Investigator on multiple national and international competitive grants, I have established and coordinated independent research programs in this field. These activities have provided the scientific, technical, and organizational foundations for the research proposed here. The current application builds directly and logically on my prior work, leveraging established expertise, validated experimental platforms, and ongoing collaborations to address novel and timely research questions.

Ongoing completed projects that I would like to highlight include:

Ongoing

PI - Grant from Italian Ministry of University (MUR) Years 2023-2025 “snoRNA retaining transcripts (snoRTs) as post-transcriptional determinants of breast cancer cells phenotype” (Prot. PRIN 2022R8L3RB).

PI - Grant from “Associazione Italiana per la Ricerca sul Cancro” (AIRC). Years 2025-2029. Title: “Comprehensive characterization of snoRNA retaining transcripts in human cancer” Grant no. IG30616

Completed

PI - Grant from the Association for International Cancer Research (AICR) Years: 2009-2012 Title: “Role of dyskerin as a tumour suppressor” Grant no: 09-0083

Co-PI - Grant from Italian Ministry for Education and University: PRIN project 2010-11 entitled: Role of the translational apparatus in the control of cell growth and tumorigenesis (Grant no. 20104AE23N_002).

PI - Grant from “Associazione Italiana per la Ricerca sul Cancro” (AIRC). Years 2012-2014 Title: “Role of JHDM1B in Breast Cancer Development and Progression” Grant no: IG11416

PI - Grant from Telethon Foundation: Exploratory project 2016: "Defining the molecular pathogenesis of the ribosomopathy cartilage hair hypoplasia" Grant no: GEP15019.

PI - Grant from “Associazione Italiana per la Ricerca sul Cancro” (AIRC). Years 2016-2018. Title: Mechanisms contributing to cancer in cells lacking proper function of the pseudouridine synthase dyskerin - Grant no: IG16962

PI - Grant from “Associazione Italiana per la Ricerca sul Cancro” (AIRC). Years 2019-2023 “Role and impact of the alterations of H/ACA box snoRNAs in breast cancer” dalla “Associazione Italiana per la Ricerca sul Cancro” (AIRC). (Prot. AIRC IG - 16962).

B. Positions, Scientific Appointments, and Honors

Positions

2000-2007: Assistant faculty member, Department of experimental Pathology, Bologna University (leave of absence from 2003 to 2004)

2003-2004 Memorial Sloan Kettering Cancer Center (NY USA) – Post-Doctoral Research Fellow, Department of Pathology (Pier Paolo Pandolfi's Lab)

2007-2020: Associate Professor, Department of experimental Pathology / Department of Experimental, Diagnostic and Specialty medicine, Bologna University

2020-now: Full Professor, Department of Experimental, Diagnostic and Specialty medicine / Medical and Surgical Sciences Bologna University

Appointments

2012- now: Member of the American association of Cancer Research (AACR)

2019- now: Member of the RNA Society

2015-2021: University of Bologna — Academic Quality Assurance Board

Coordinator, Research Quality Assurance Committee (2018–2021)

2024 Chair of panel for the University Cooperation grant - Nordforsk

2024 Discovery Research Expert review panel member – Cancer UK (CRUK)

2024-now Member of the Editorial Board of NAR Cancer

2025 Ribomod2025 - Tools and Methods for the Annotation and Study of snoRNA-Mediated Ribosomal RNA Modifications (Bologna 12-13/6/2026), Member of the organizing Committee and local host

Honors

Stanford University / Elsevier – World's Top 2% Scientists

Citation-based distinction (single-year impact, citation year 2023; 2024 edition)

C. Contributions to Science

My research focuses on defining how alterations in ribosome biogenesis and mRNA translation contribute to human disorders and, in particular, to cancer initiation and progression. I have contributed to establishing deregulated mRNA translation as a causal driver of tumorigenesis rather than a secondary consequence of malignant transformation. My work integrates mechanistic studies with translational relevance, with the goal of identifying novel therapeutic vulnerabilities in cancer.

Early in my career, I helped define the oncogenic role of the translation initiation factor eIF4E. Using in vivo models, I demonstrated that eIF4E overexpression can overcome c-Myc–induced apoptosis, providing the first direct in vivo evidence that altered mRNA translation is sufficient to induce cancer (Nature Medicine, 2004). This work contributed to a conceptual shift recognizing translational control as a critical component of cancer biology.

I subsequently pioneered studies on the role of the pseudouridine synthase dyskerin in human tumors. I demonstrated that reduced dyskerin expression in breast cancer alters rRNA pseudouridylation, impairs telomerase activity, and correlates with poor prognosis (Journal of Pathology, 2006; Cellular Oncology, 2008).

Further work from my laboratory showed that dyskerin deficiency causes selective translational defects affecting key cancer-related mRNAs, including p53 and VEGF, through intrinsic ribosomal dysfunction (Cancer Research, 2010; Nucleic Acids Research, 2013). To directly test ribosome function, I developed a novel method for the characterization of purified ribosomes, later disseminated through Nature Protocols. In addition my group was the first to characterize the site specific alterations in rRNA pseudouridylation in human breast cancer (NAR Cancer 2023).

More recently, I identified and characterized snoRNA-retaining transcripts (snoRTs), a novel class of non-coding RNAs involved in post-transcriptional regulation of hormone receptor signaling in breast cancer (Genome Biology, 2022, Noncoding RNA Research, 2025). Together, these studies have advanced understanding of ribosome-centered mechanisms in cancer and position me to lead studies targeting translational and metabolic vulnerabilities in tumors.

Original publications relevant to the present proposal:

Ruggero D, **Montanaro L**, Ma L, Xu W, Londei P, Cordon-Cardo C, Pandolfi PP. The translation factor eIF-4E promotes tumor formation and cooperates with c-Myc in lymphomagenesis. **Nature Medicine**, **10:484-486**, **2004**

Montanaro L, Brigotti M, Clohessy J, Barbieri S, Ceccarelli C, Santini D, Taffurelli M, Calienni M, Teruya-Feldstein J, Treré D, Pandolfi PP, Derenzini M. Dyskerin expression influences the level of ribosomal RNA pseudo-uridylation and telomerase RNA component in human breast cancer. **Journal of Pathology**, **210:10-18**, **2006**.

Montanaro L, Calienni M, Ceccarelli C, Santini D, Taffurelli M, Pileri S, Treré D, Derenzini M. Relationship between dyskerin expression and telomerase activity in human breast cancer. **Cellular Oncology**, **30:483-490**, **2008**

Montanaro L, Calienni M, Bertoni S, Rocchi L, Sansone P, Storci G, Santini D, Ceccarelli C, Taffurelli M, Carnicelli D, Brigotti M, Bonafé M, Treré D, Derenzini M. Novel dyskerin-mediated mechanism of p53 inactivation through defective mRNA translation. **Cancer Research**, **70:4767-77**, **2010**

Rocchi L, Pacilli A, Sethi R, Penzo M, Schneider RJ, Treré D, Brigotti M, **Montanaro L**. Dyskerin depletion increases VEGF mRNA internal ribosome entry site-mediated translation. **Nucleic Acids Research**, **41: 8308-8318**, **2013**.

Penzo M, Rocchi L, Brugiére S, Carnicelli D, Onofrillo C, Couté Y, Brigotti M, **Montanaro L**. Human ribosomes from cells with reduced dyskerin levels are intrinsically altered in translation. **FASEB Journal**, **29:3472-82**, **2015**.

Penzo M, Carnicelli D, **Montanaro L**, Brigotti M. A reconstituted cell-free assay for the evaluation of the intrinsic activity of purified human ribosomes. co-corresponding author **Nature Protocols**, **11:1309-25**, **2016**.

Zacchini F, Venturi G, De Sanctis V, Bertorelli R, Ceccarelli C, Santini D, Taffurelli M, Penzo M, Treré D, Inga A, Dassi E, **Montanaro L**. Human dyskerin binds to cytoplasmic H/ACA-box-containing transcripts affecting nuclear hormone receptor dependence. **Genome Biol**, **23(1):177**, **2022**

Barozzi C, Zacchini F, Corradini AG, Morara M, Serra M, De Sanctis V, Bertorelli R, Dassi E, **Montanaro L**. Alterations of ribosomal RNA pseudouridylation in human breast cancer. **NAR Cancer**, **5:zcad026**, **2023**

Rambaldelli G, Asghar S, Venturi G, Zacchini F, Serra M, Giovannini C, Gramantieri L, Bernini M, Inga A, Dassi E, **Montanaro L**. Characterization of small nucleolar RNA retaining transcripts in human normal and cancer cells. **Noncoding RNA Res**, **13:153-161**, **2025**