BIOSKETCH

NAME: Laura Lentini

POSITION TITLE: Associated Professor (Genetics; 05 BIOS-14/A) at the University of Palermo, Italy

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Department of Cellular and Developmental Biology "A Monroy", Section of Genetics, University of Palermo, Italy.	Master's Degree in Biological Sciences (110/110)	07/1999	Cell and Molecular Biology.
Department of Cellular and Developmental Biology "A Monroy", Section of Genetics, University of Palermo, Italy.	PhD in " Cellular and Developmental Biology "	03/2003	Cancer Genetics, Molecular Genetics: Study on Retinoblastoma and AURKA proteins in cancer.
Department of Cellular and Developmental Biology "A Monroy", Section of Genetics, University of Palermo, Italy.	Postdoctoral Researcher (BIO/18) Sector: Academic and Research	11/2003 11/2007	Cancer genetics- Involvement of the alteration of mitotic tumor suppressors in chromosome instability induction in human cells.
Faculty of Medicine and Surgery - Department of Pathobiology and Biomedical Methodology, Italy. University of Palermo, Italy	Awarded the Specialization in Clinical Pathology.	11/2003 11/2007	Cancer genetics- Study of the role of AURKA protein overexpression in different stages of human colon cancer.
Centro di Oncobiologia sperimentale (COBS), Palermo, Italy.	Awarded the Fellowship funded by AIRC (Associazione Italiana Ricerca sul Cancro) grant (2007).	11/2007 11/2008	Cancer genetics- Identification of mechanism underlying chromosomal instability in human cells by DNA microarrays and siRNA.
STEMBIO Department Section of Physiology, University of Palermo.	Awarded the Post-doc Fellowship.	11/2008 01/2010	Gene expression- Analysis of molecular mechanisms that control gastrointestinal mobility in physiological and pathological conditions.

STEBICEF Department Section of Genetics, University of Palermo.	Researcher (RTI) Genetics-BIO/18 Permanent position	10/2012 10/2016	Cancer genetics- Identification of mechanism underlying chromosomal instability in human cells by DNA microarrays and siRNA.
STEBICEF Department Section of Genetics, University of Palermo.	Associated professor (PA) Genetics-BIO/18 Permanent position	10/2016 current	Genetics: Rare disease and precision medicine research in cystic fibrosis, Duchenne Muscular dystrophy (DMD), and PIRDs fields.
STEBICEF Department Section of Genetics, University of Palermo.	National qualification as Full Professor in Genetics	11/2023	Genetics: Rare disease and precision medicine research in cystic fibrosis, Duchenne Muscular dystrophy (DMD), and PIRDs fields.

A. Personal Statement

The applicant is the Head of the Molecular Genetics lab at the University of Palermo and has dedicated the past 13 years to research in the field of rare diseases, focusing on therapeutic strategies centered around the design and validation of small molecules to address nonsense mutations in cystic fibrosis and other human genetic disorders, such as Shwachman-Diamond syndrome and Primary Immune Regulatory Disorders (PIRD) (Lentini et al., Mol. Pharm., 2014; Pibiri et al., Int. J. Mol. Sci., 2020; Bezzerri et al., Biomedicines, 2022; Corrao et al., Biomed. Pharmacother., 2022; Fiduccia et al., Mol. Ther., 2024, in press). Specifically, the applicant was the Principal Investigator for three projects (FFC#1/2014; FFC#3/2017; FFC#6/2020) funded by the Italian Cystic Fibrosis Foundation and as a co-investigator for three additional projects (FFC#2/2011; FFC#5/2019) sponsored by the same foundation and by Terzo Pilastro International Foundation in recent years. Furthermore, the applicant is credited as one of the inventors of three patents aimed at mitigating the effects of nonsense mutations (Italian Patent RBI15083-IT "Derivati ossadiazolici per il trattamento di patologie genetiche dovute a mutazioni nonsenso," Owners: University of Palermo and Italian Foundation for Cystic Fibrosis Research; International patent PCT/EP2018/081850 Ref. RBW15083-PCT "Oxadiazole Derivatives For The Treatment Of Genetic Diseases Due To Nonsense Mutations," publ. WO2019101709, Owners: University of Palermo and Italian Foundation for Cystic Fibrosis Research). The research team comprises researchers with longstanding expertise in Organic Chemistry, Pharmaceutical Chemistry, and Molecular Biology, with two PhD students currently in their second year of the program, along with numerous national and international collaborations worldwide.

B. Positions, Scientific Appointments, and Honors

Positions:

2018– current:

Associated Professor of Genetics (05 BIOS-14/A (ex BIO/18)
STEBICEF Department, University of Palermo, Italy (https://www.unipa.it/persone/docenti/l/laura.lentini).
Main duties/responsibilities: Research, mentoring, and teaching, Department referent for disabled students.
Sector: Academic sector

-Research projects international reviewer for the following institutions:
-*Agence Nationale de La Reserche* (ANR-France)
-*Foundation For Rare Diseases* (Fondation Maladies Rares) (France)

2018-2021:
Teaching at The International Summer School on Advanced Biotechnology”

University of Palermo and Biotechnet Switzerland (partnership of the Swiss Universities of Applied Sciences active in the field of biotechnology).
Main duties/responsibilities: Teaching
Sector: Academic

2017-Current:
Member of the Board of Professors for the PhD in Technologies and Science for Human Health.
University of Palermo, Palermo Italy.
Main duties/responsibilities: Organization and mentoring.
Sector: Academic

2013-2016:
Member of the Board of Professors for the PhD in Molecular Medicine and Biotechnology.
University of Palermo, Palermo Italy.
Main duties/responsibilities: Organization and mentoring.
Sector: Academic

2012-2018:
Assistant Professor (BIO/18)
University of Palermo, Palermo, Italy
Main duties/responsibilities: Research, mentoring and teaching
Sector: Academic

2007-2009:
Post-DOC Fellow (BIO/09)
University of Palermo, Palermo, Italy
Main duties/responsibilities: Research, mentoring, and lecturer
Sector: Academic and Research

2003-2007:
Post-DOC Fellow (BIO/18)
University of Palermo, Palermo, Italy
Main duties/responsibilities: Research, mentoring, and lecturer
Sector: Academic and Research

B. Scientific Appointments:

•Principal Investigator in the following research projects:

2020-2022:
Principal Investigator -FFC#6/2020, grant funded by Fondazione Italiana per la ricerca sulla Fibrosi Cistica
Title: Validation of the distribution and activity of new optimized leads in mouse model and other CF model systems.
90.000 €

2018-2019:
Principal Investigator -Fondazione III Pilastro International, grant funded by Fondazione III Pilastro International Title: "Identification of molecules with readthrough activity towards premature termination codons (PTCs) to rescue the genic function of CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) in murine and human model cell system".
50.000 €

2018-2019:

Principal Investigator FFR_2018_160876
1.200 €

2017-2019:
Principal Investigator PJ_RIC_FFABR_2017_160876
3000 €

2017-2019:
Principal Investigator -FFC#3/2017, grant funded by Fondazione Italiana per la ricerca sulla Fibrosi Cistica (PI)
Title: "Optimization of a new lead promoting the readthrough of nonsense mutations for the CFTR rescue in human CF cells".
57.000 €

2014-2016:
Principal Investigator -FFC#1/2014 grant funded by Fondazione Italiana per la ricerca sulla Fibrosi Cistica (PI).
Title: "Identification and validation of new molecules obtained by computational and Experimental integrated approaches, for the readthrough of PTCs in CF cells".
38.000 €

Co-investigator in the following research projects:

2024-2026: Co-Investigator in PNRR-POC-2023-12378248 Project- "Rescuing eyes from nonsense: a precision medicine approach to rescue stop mutation in hereditary ocular diseases by translational readthrough inducing drugs (TRIDs)" PNRR M6/C2 2023.
950.000 €

2023-2025:
Co-Investigator in PRIN 2022 Project - INNOVATIVE THERAPIES FOR THE TREATMENT OF RARE GENETIC DISEASES CHARACTERIZED BY NONSENSE MUTATIONS - Macrosettore LS Life Sciences – Settore LS2 – Integrative Biology: from Genes and Genomes to Systems.
163.969,00€

2022-2026:
Co-Investigator in-HEAL ITALIA Partnership - Spoke 5 Next-Gen Therapeutics WP 1: Targeting tricks: innovative approaches for selective and specific therapeutic targeting-Task 1.1: TRIDS that make the Tricks – Design, synthesis, and validation of Translational Readthrough Inducing Drugs (TRIDS) to overcome nonsense mutations.

2011-2013
FFC#2/2011, grant funded by Fondazione Fibrosi Cistica Italiana (co-investigator).
Title: PTC124 derivatives as a new approach to boost the readthrough of premature termination codons in the CFTR gene"
40.000 €

2007-2010
2007-ATE-0233. Title: "Identificazione dei meccanismi di
instabilità cromosomica in cellule umane in coltura N. ORPA07E94Y.
1700 €

2006-2009
2006-ATE-0582 Title: "Identificazione dei meccanismi di instabilità cromosomica in cellule umane in coltura" N. ORPA06T8WC
2500 €

Honors:
2016-current
Italian Genetic Association Membership (AGI).
2011-2024
Italian Cystic Fibrosis Foundation FFC Researcher (https://www.fibrosicisticaricerca.it/ricercatore/lentini-laura/.

C. Contributions to Science

The principal and important contribution to science was the role in the study of new small molecules for a particular class of genetic mutations known as stop mutations. The applicant's contribution, relative to all the biological aspects of the research in recent years, was decisive both in terms of ideas and from the point of view of acquiring grants. The following products as inventors are the important result of this research:
•IT Patent: RBI15083-IT "Derivati ossadiazolici per il trattamento di patologie genetiche dovute a mutazioni nonsenso." Owners: University of Palermo and Italian Foundation for Cystic Fibrosis Research.
•International patents:
USA: n.US20210002238A1 "Oxadiazole Derivatives for the treatment of genetic diseases due to nonsense mutations. Owners: University of Palermo and Italian Foundation for Cystic Fibrosis Research.
UE: EP3713934B1 "OXADIAZOLE DERIVATIVES FOR THE TREATMENT OF GENETIC DISEASES DUE TO NONSENSE MUTATIONS". Owners: University of Palermo and Italian Foundation for Cystic Fibrosis Research.

Commercialization of the patent family on 'Oxadiazolic Derivatives for Overcoming Premature Stop Codons (readthrough)' relating to the international patents described in the preceding points.
Institutions involved in the option contract: University of Palermo and Cystic Fibrosis Foundation.

D. Relevant Publications

Bibliometric Indicators:
Publications: 40; # Citations: 965; H index: 20.

1. Corrao F. et al. Nonsense codons suppression. An acute toxicity study of three optimized TRIDs in murine model, safety and tolerability evaluation Biomedicine and Pharmacotherapy., 2023, 156, 113886.
2.V. Bezzerri et al. "Novel translational read-through–inducing drugs as a therapeutic option for Shwachman-Diamond syndrome" Biomedicines, 2022, 10, 886-900. DOI: 10.3390/biomedicines10040886.
3.M. Tutone et al. "Pharmacophore-Based Design of New Chemical Scaffolds as Translational Readthrough-Inducing Drugs (TRIDs)" ACS Med. Chem. Lett. 2020, 11(5), 747-753. DOI: 10.1021/acsmedchemlett.9b00609.
4. Melfi R., et al. (2020) Investigating REPAIRv2 as a Tool to Edit CFTR mRNA with Premature Stop Codon. International Journal of Molecular Sciences, vol. 21, p. 4781-4796, ISSN: 1422-0067, doi: 10.3390/ijms21134781L.
5. Lentini L. et al. "Caffeine boosts Ataluren's readthrough activity" Heliyon 2019, 5, e01963. DOI: 10.1016/j. heliyon.2019.e01963.
6. Tutone M. et al. "Deciphering the Nonsense Readthrough Mechanism of Action of Ataluren: An in Silico Compared Study" ACS Med. Chem. Lett. 2019, 10, 522−527. DOI: 10.1021/acsmedchemlett.8b00558.
7. Pibiri I. et al. "Rescuing the CFTR protein function: Introducing 1,3,4-oxadiazoles as translational readthrough inducing drugs" European Journal of Medicinal Chemistry, 2018, 159, 126-142. DOI: 10.1016/j.ejmech.2018.09.057.

8. Pibiri I. et al. “Exploring the readthrough of nonsense mutations by non-acidic Ataluren analogues selected by ligand-based virtual screening” European Journal of Medicinal Chemistry, 2016, 122, 429-435. DOI: 10.1016/j.ejmech.2016.06.048.
9. Pibiri I. et al. “Enhancement of premature stop codon readthrough in the CFTR gene by Ataluren (PTC124) derivatives” European Journal of Medicinal Chemistry, 2015, 101, 236-244. DOI: 10.1016/j.ejmech.2015.06.038.
10. Lentini L. et al. “Toward a Rationale for the PTC124 (Ataluren) Promoted Readthrough of Premature Stop Codons: A Computational Approach and GFP-Reporter Cell-Based Assay”. Molecular Pharmaceutics, 2014, 11 (3), 653−664. DOI: 10.1021/mp400230.

F. to Laura Lentini