EUROPEAN CURRICULUM VITAE

PERSONAL INFORMATIONS

Name	**MICHELE MANNELLI**
Address	
Telephone number	
Mobile phone	
E-mail	
Nationality	ITALIAN
Date of birth	

WORK EXPERIENCE

• Date	**2022-2025**
• Position	Post-Doc Research Fellow
• Research project title	Characterization of metabolic changes induced by gold complexes in ovarian cancer cell lines
• Scientific supervisor	Prof. Tania Fiaschi, University of Florence

• Date	**2018 – 2021**
• Position	PhD student
• Title	PhD student in Biochemistry and Molecular Biology BIBIM 2.0. – XXXIV cycle
• Name and address of the institution	University of SIENA - Department of Biotechnology, Chemistry and Pharmacy - 53100 SIENA
• Hosting institution	Department of Experimental and Clinical Biochemical Sciences "Mario Serio" Viale Morgagni 50 Florence
• Main roles and responsibilities	Research and student tutoring activities for dissertations

EDUCATION AND TRAINING

• Date of achievement	**22/06/2022**
• Qualification obtained	PhD
• Description	PhD in Biochemistry and Molecular Biology BIBIM 2.0. – XXXIV cycle
• Thesis title	A metabolic change towards fermentation drives cancer cachexia in myotubes
• Institution name and address	University of SIENA - Department of Biotechnology, Chemistry and Pharmacy - 53100 SIENA Department of Experimental and Clinical Biochemical Sciences "Mario Serio," Viale Morgagni 50 Florence

• Date of achievement	**21/12/2017**
• Qualification obtained	Master Degree
• Description	Master Degree in Biology LM-6 (Biosanitary Curriculum)
• Mark	110/110 cum laude
• Thesis title	Effetti metabolici e molecolari su cellule muscolari indotti da terreni condizionati di cellule tumorali cachettiche e non cachettiche
• Institution name and address	University of Florence – P.zza S. Marco,4 – FIRENZE Department of Experimental and Clinical Biochemical Sciences "Mario Serio" Viale Morgagni 50 Florence

• Date of achievement	**27/02/2014**
• Qualification obtained	Bachelor Degree
• Description	Bachelor Degree in Biological Sciences L-13
• Mark	106/110
• Thesis title	Attività antibatterica di nanoparticelle d'argento ottenute mediante ablazione laser
• Institution name and address	University of Florence – P.zza S. Marco,4 – FIRENZE Department of Biology, Via Madonna del Piano 6, Sesto Fiorentino – Florence

• Date of achievement	**2010**
• Qualification obtained	High School Diploma
• Description	Scientific High School Diploma
• Mark	65/100
•Institution name	Liceo Scientifico Federigo Enriques – Castelfiorentino (Florence)

TEACHING ASSIGNMENTS

TEACHING ACTIVITIES AT THE UNIVERSITY LEVEL IN ITALY OR ABROAD;

• Date	**ACADEMIC YEAR 2018-2019**
• Degree program	BIOLOGICAL SCIENCES (L-13)
• Teaching	CELLULAR BIOLOGY; Tutoring activities to teaching laboratories
• Disciplinary scientific area	BIO/11
• Hours	18
• School	Mathematical Physical and Natural Sciences
• Institution name and address	Department of Biology, University of Florence – Via Madonna del Piano 6, Sesto Fiorentino – Florence

• Degree program	BIOLOGICAL SCIENCES (L-13)
• Teaching	MOLECULAR BIOLOGY; Tutoring activities to teaching laboratories
• Disciplinary scientific area	BIO/11
• Hours	36
• School	Mathematical Physical and Natural Sciences
• Institution name and address	Department of Biology, University of Florence -Via Madonna del Piano 6, Sesto Fiorentino-Florence

Tutoring activities for students

The candidate has continuously tutored students in the preparation of experimental dissertations.

Correlator of the following dissertations:

1. Bachelor Degree in Biological Sciences (19/04/2023)
Candidate: Elena Nencioni
Supervisor: Prof. Tania Fiaschi
Correlator: Dott. Michele Mannelli
Thesis title: Il lattato promuove la cachessia nei miotubi

2. Bachelor Degree in Biological Sciences (23/02/2022)
Candidate: Marta Montagni
Supervisor: Prof. Tania Fiaschi
Correlator: Dott. Michele Mannelli

Theis title: AdipoRon previene l'insorgenza della cachessia tumorale nei miotubi

2. Bachelor Degree in Biological Sciences (23/02/2022)
Candidate: Chiara Vasta
Supervisor: Prof. Tania Fiaschi
Correlator: Dott. Michele Mannelli
Thesis title: Analisi della cachessia tumorale in muscoli di ratti affetti da tumore al colon e di pazienti con carcinoma ovarico

3. Bachelor Degree in Biological Sciences (21/12/2021)
Candidate: Federica Polverini
Supervisor: Prof. Tania Fiaschi
Correlator: Dott. Michele Mannelli
Thesis title: L'inibizione del trasportatore mitocondriale del piruvato promuove la formazione di miotubi cachettici

4. Master degree thesis in medical and pharmaceutical biotechnology (26/10/2021)
Candidate: Andrea Geri
Supervisor: Prof. Tania Fiaschi
Correlator: Dott. Michele Mannelli
Thesis title: Il trattamento con sodio piruvato o con l'agonista del recettore dell'adiponectina, AdipoRon, blocca la formazione del fenotipo cachettico nei miotubi

PERSONAL SKILLS AND COMPETENCIES

ACQUIRED THROUGHOUT LIFE AND CAREER BUT NOT NECESSARILY RECOGNIZED BY OFFICIAL CERTIFICATES AND DIPLOMAS.

NATIVE SPEAKER: **ITALIAN**

OTHER LANGUAGE

ENGLISH

- Reading skills: Good
- Writing skills: Good
- Oral skills: Good

INTERPERSONAL SKILLS AND COMPETENCIES

ATTENDANCE AND SCIENTIFIC, NATIONAL AND INTERNATIONAL CONGRESSES AND CONFERENCES.

Speaker at scientific, national and international congresses and conferences

1. **Mannelli M.** "A metabolic shift drives cancer cachexia in myotubes". Interuniversity Institute of Myology (IIM) meeting. Assisi (Perugia, Italy), October 2019.

2**. Mannelli M.** "Metabolic changes induced by Aurothiomalate in A2780 ovarian cancer cells"**.** Autumn meeting for young Chemists in Biomedical Sciences AMYC-BIOMED 16th-18th October 2023. Florence (Italy)

TECHNICAL SKILLS AND COMPETENCIES

WITH COMPUTERS, SPECIFIC EQUIPMENT, MACHINERY, ETC.

Consolidated skills in metabolomics, biochemistry techniques, molecular and cellular biology. Detailed description follows.

1. Metabolomics. Analysis of intracellular and extracellular metabolites using a gas chromatograph coupled to a mass spectrometer (Intuvo 9000 GC System-5977B MSD, Agilent Biotechnologies). Qualitative and quantitative metabolomic profiling analysis of muscle and tumour cells.

2. Analysis of cellular energy metabolism. Evaluation of the rate of cellular respiration using the Hansatech oxygraph (Clark-type oxygen electrode manufactured by Hansatech Instruments Ltd) and fermentation using specific assays. Enzymatic assays of the activity of key enzymes in

cellular energy metabolism (mitochondrial and cytoplasmic).

3. Analysis of mitochondrial function. Analysis of mitochondria structure and number, mitochondrial membrane potential using specific fluorescent probes combined with fluorescence and confocal microscopy. Evaluation of the expression of mitochondrial electron transport chain complexes by western blot technique.

4. Biochemistry and molecular biology techniques: SDS-PAGE, western blot. enzyme assays, good skills in enzyme kinetics; PCR, RT-PCR.

5. Cell cultures: Culture of human and murine cells; cell differentiation (muscle cells and adipocytes); cytotoxicity assays (MTT).

6. Analysis and interpretation of Flow Cytometry data.

– The candidate has also acquired the following computer skills and competencies:

1. Excellent knowledge of the Microsoft Office package (Word, Excel, PowerPoint), Photoshop, GraphPad Prism 6.

2. Excellent knowledge of UV Probe 2.61(Shimadzu Corporation) software for analysis of data obtained with UV-1800 spectrometer (Shimadzu Corporation).

3. Good knowledge of Amersham Imager 600 instrument (GE Healthcare) for chemiluminescence detection of western blots and Imager 600 software for quantitative analysis of the images obtained (GE Healthcare)

SPECIFIC PROFESSIONAL EXPERIENCE CHARACTERIZED BY RESEARCH ACTIVITIES.

Scientific activity in detail

2018-2022 The candidate was mainly focused to the development of his PhD. project, regarding the possible role of a metabolic shift toward lactic fermentation underlying the induction of muscle cancer cachexia. *In vitro* studies have shown that conditioned media (CM) obtained from murine and human carcinoma cell lines (known to be able to trigger cachexia *in vivo*), result in the induction of cachexia in differentiated muscle cells (myotubes). Underlying cancer cachexia activation in myotubes was a metabolic shift towards lactic fermentation, characterized by decreased oxygen consumption and OXPHOS expression levels and increased lactate production. Inflammatory stimuli and STAT3 signalling pathway play pivotal roles in the induction of cancer cachexia and related metabolic alterations observed *in vitro*. Metabolomic analysis by GC-MS, taking advantage of the instrumentation made available by the metabolomics facility of the Department of Experimental and Clinical Biomedical Sciences "Mario Serio", subsequently confirmed the induction of metabolic shift toward lactic fermentation (increased levels of intracellular lactate and decreased levels of pyruvate) in cachectic myotubes. Furthermore, cachectic myotubes show a markedly altered intracellular metabolic profile, especially at the level of Krebs cycle intermediates [Mannelli M. *et a*l. Biomedicines (2021) 20;9(6):698; Mannelli M. *et al*. Faseb Journal (2022);36(11): e22598.]. *

In addition to skeletal muscle, the candidate has extended the study of cancer cachexia to adipose tissue. [Mannelli M, Gamberi T, Magherini F, Fiaschi T. The Adipokines in Cancer Cachexia. Int J Mol Sci. (2020);21(14):4860]. * Obtained results highlight that adipose cancer cachexia induction *in vitro* and related metabolic alterations are mediated by LDH up-regulation and Adiponectin down-regulation in which STAT3 pathway activation play pivotal roles [Mannelli et al. 2023 STAT3 Signalling Drives LDH Up-Regulation and Adiponectin Down-Regulation in Cachectic Adipocytes. Int J Mol Sci] *.

In 2019, the candidate started a collaboration with a new project inherent to the use of polymeric biomaterials (Liquid Crystalline Networks, LCNs) as support for the growth and differentiation of undifferentiated muscle cells (myoblasts). The results demonstrate how the stiffness and alignment of the polymers constituting the biomaterials are the nodal points for proper differentiation of muscle cells. [Martella D. et al. iScience (2021) 2;24(9)103077; Rojas-Rodríguez M, Fiaschi T, Mannelli M, et al. ACS Appl Mater Interfaces. (2023);15(11):14122-14130]. *

2022-now The candidate will focus on the characterization of metabolic changes induced by gold complexes in ovarian cancer cell lines. The research activity firstly focused on the determination of the 72-hour IC50s of the gold compounds aurothiomalate, carbene 1 and carbene 2 (gold with oxidation state I) and the compounds Aubipyc and AuL12 (gold with oxidation state III) on the ovarian carcinoma cell model A2780. In order to study the metabolic alterations induced by these compounds, sample preparation for the study of endometaboloma and exometaboloma was conducted using the 72-hour IC50 of the compounds. The metabolic alterations have been analysed after 24 hours of treatment and thus at a timeframe prior to the onset of cell death. Results have shown that treatment with gold compounds with oxidation state I results in increased lactate production and increased glutathione in A2780 ovarian carcinoma cells, reflecting a metabolic shift and redox imbalance induced by the compounds in the cell model used. These data are consistent with previously published findings on the effects of

auranofin use. Regarding the compound aurothiomalate, the metabolomics study also showed a significant intracellular accumulation of succinate, identifying mitochondria as a possible target and suggesting a possible alteration in Krebs cycle. [Cirri. D et al. Molecules. 2023 Jan 20;28(3); Ghini et al RSC Adv. 2023;13(31):21629-21632; Casottini et al 2024 Angewandte Chemie (International ed. in English), 63(40)]*

The candidate is also carrying on with the project regarding cancer cachexia and related metabolic alterations that have been the topic of study since the beginning of his career in oncology research.

* The brackets indicate the main publications related to the described research period.

ADDITIONAL INFORMATION

Overall list of scientific publications

1. Ester Giorgi, Francesca Binacchi, **Michele Mannelli,** Damiano Cirri**,** Andrea Cesari**,** Matteo Boldrini, Carlo Marotta, Claudia Ghelarducci, Diletta Corvaglia, Fabio Bellina, Tania Gamberi, Alessandro Pratesi, Chiara Gabbiani (2025). Trans-Pd(II) complexes: A different approach for the development of promising anticancer drugs. Inorganica Chimica Acta https://doi.org/10.1016/j.ica.2025.122645

2. Veronica Ghini, Ana Isabel Tristán, Giorgio Di Paco, Lara Massai, **Michele Mannelli**, Tania Gamberi, Ignacio Fernández, Antonio Rosato, Paola Turano, and Luigi Messori (2025). Novel NMR-Based Approach to Reveal the 'Metabolic Fingerprint' of Cytotoxic Gold Drugs in Cancer Cells. Journal of Proteome Research. https://doi.org/10.1021/acs.jproteome.4c00904

3.Cosottini, L., Geri, A., Ghini, V., **Mannelli, M**., Zineddu, S., Di Paco, G., Giachetti, A., Massai, L., Severi, M., Gamberi, T., Rosato, A., Turano, P., & Messori, L. (2024). Unlocking the Power of Human Ferritin: Enhanced Drug Delivery of Aurothiomalate in A2780 Ovarian Cancer Cells. Angewandte Chemie (International ed. in English), 63(40), e202410791.

4. Ceccherini, V., Giorgi, E., **Mannelli, M**., Cirri, D., Gamberi, T., Gabbiani, C., & Pratesi, A. (2024). Synthesis, Chemical Characterization, and Biological Evaluation of Hydrophilic Gold(I) and Silver(I) N-Heterocyclic Carbenes as Potential Anticancer Agents. Inorganic chemistry, 63(37), 16949–16963.

5. Bartoloni B, **Mannelli M**, Gamberi T, Fiaschi T. The Multiple Roles of Lactate in the Skeletal Muscle. *Cells*. 2024;13(14):1177. Published 2024 Jul 10. doi:10.3390/cells13141177

6. Giorgi E, **Mannelli M**, Gamberi T, et al. Cytotoxic auranofin analogues bearing phosphine, arsine and stibine ligands: A study on the possible role of the ligand on the biological activity. *J Inorg Biochem*. 2024;251:112452.

7. **Mannelli M**, Bartoloni B, Cantini G, Nencioni E, Magherini F, Luconi M, Modesti A, Gamberi T, Fiaschi T. STAT3 Signalling Drives LDH Up-Regulation and Adiponectin Down-Regulation in Cachectic Adipocytes. Int J Mol Sci. 2023 Nov 15;24(22):16343.

8.Casottini L, Massai L, Ghini V, Zineddu S, Geri A, **Mannelli M**, Ciambellotti S, Severi M, Gamberi T, Messori L, Turano P. Bioconjugation of the gold drug auranofin to human ferritin yields a potent cytotoxin. Journal of Drug Delivery Science and Technology 2023.

9. Ghini V, **Mannelli M**, Massai L, et al. The effects of two cytotoxic gold(i) carbene compounds on the metabolism of A2780 ovarian cancer cells: mechanistic inferences through NMR analysis. RSC Adv. 2023;13(31):21629-21632. Published 2023 Jul 19.

10. Chiaverini L, Baglini E, **Mannelli M**, Poggetti V, Da Settimo F, Taliani S, Gamberi T, Barresi E, La Mendola D, Marzo T. A complex bearing TSPO PIGA ligand coordinated to the [Au(PEt3)]+ pharmacophore is highly cytotoxic against ovarian cancer cells. Biometals. 2023 Mar 4. (IF: 3.4)

11. Rojas-Rodríguez M, Fiaschi T, **Mannelli M**, Mortati L, Celegato F, Wiersma DS, Parmeggiani C, Martella D. Cellular Contact Guidance on Liquid Crystalline Networks with Anisotropic Roughness. ACS Appl Mater Interfaces. 2023 Feb 15;15(11):14122–30. (IF: 10.4)

12. Cirri D, Geri A, Massai L, **Mannelli M**, Gamberi T, Magherini F, Becatti M, Gabbiani C, Pratesi A, Messori L. Chemical Modification of Auranofin Yields a New Family of Anticancer Drug Candidates: The Gold(I) Phosphite Analogues. Molecules. 2023 Jan 20;28(3). (IF: 4.9)

13. **Mannelli M**, Gamberi T, Garella R, Magherini F, Squecco R, Fiaschi T. Pyruvate prevents the onset of the cachectic features and metabolic alterations in myotubes downregulating STAT3 signaling. FASEB J. 2022 Nov;36(11). (IF: 5.4)

14. Bernacchioni C, Squecco R, Gamberi T, Ghini V, Schumacher F, **Mannelli M**, Garella R, Idrizaj E, Cencetti F, Puliti E, Bruni P, Turano P, Fiaschi T, Donati C. S1P Signalling Axis is

necessary for Adiponectin-directed regulation of Electrophysiological properties and oxidative metabolism in C2C12 myotubes. Cells. 2022 Feb 17; 11,713. (IF: 6.6)

15. Martella D, **Mannelli M**, Squecco R, Garella R, Idrizaj E, Antonioli D, Laus M, Gamberi T, Paoli P, Parmeggiani C, Fiaschi T. Cell instructive Liquid Crystalline Networks for myotubes formation. iScience. 2021 Sept 2;24(9)103077. (IF: 5)

16. **Mannelli M**, Gamberi T, Magherini F, Fiaschi T. A metabolic change towards fermentation drives cancer cachexia in myotubes. Biomedicines. 2021 Jun 20;9(6):698. (IF: 6.1)

17. **Mannelli M**, Gamberi T, Magherini F, Fiaschi T. The adipokines in cancer cachexia. Int J of Molecular Sciences. 2020 Jul;21(14):4860. (IF: 5.92)

18. Lorito N, Bacci M, Smiriglia A, **Mannelli M**, Parri M, Comito G, Ippolito L, Giannoni E, Bonechi M, Benelli M, Migliaccio I, Malorni L, Chiarugi P, Morandi A. Glucose metabolic reprogramming of ER+ breast cancer in acquired resistance to the CDK4/6 inhibitor palbociclib. Cells 2020 Mar;9(3):668. (IF: 6.6)

19. Magherini F, Fiaschi T, Marzocchini R, **Mannelli M**, Gamberi T, Modesti P, Modesti A. Oxidative stress in exercise training: the involvement of inflammation and peripheral signals. Free Radical Research. 2019 Dec;53(11-12):1155-1165. 103:103-20. (IF: 3.61)

20. Gamberi T, Magherini F, **Mannelli M**, Chrisam M, Cescon M, Castagnaro S, Modesti A, Braghetta P, Fiaschi T. Role of adiponectin in the metabolism of skeletal muscles in collagen VI-related myopthaties. Journal Of Molecular Medicine. 2019 Jun;97(6):793-801. (IF: 4.59)

21. Gorini G, Gamberi T, Fiaschi T, **Mannelli M**, Modesti A, Magherini F. Irreversible plasma and muscle protein oxidation and physical exercise. Free Radical Research. 2019 Feb;53(2):126-138. (IF: 3.61)

PERSONAL DATA PROCESSING, INFORMATION AND CONSENT

The undersigned is aware that:
- is subject to the penalties provided for by the Criminal Code and the special laws on the subject if he/she issues false statements, forms or makes use of false documents or exhibits documents containing data no longer corresponding to the truth (art. 76 Presidential Decree no. 445 of December 28, 2000);
- forfeits any benefits resulting from the measure issued on the basis of the untrue statement if the check carried out by the Administration reveals the untruthfulness of the contents of the statement (Articles 71 and 75 Presidential Decree no. 445 of December 28, 2000).

In addition, the undersigned authorizes the processing of personal data, in accordance with the provisions of Legislative Decree 196/03

Date and place

30/04/2025 Florence, Italy

Signature