

BIOGRAPHICAL SKETCH

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NAME: JESSICA MANDRIOLI

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POSITION TITLE: Full Professor in Neurology, University of Modena and Reggio Emilia

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
University of Modena, Medical School, ITALY	M.D.	09/2000	MEDICINE
University of Modena, ITALY	Post Degree	11/2005	NEUROLOGY
University of Modena, ITALY		2008	Medical statistics

A. Personal Statement

I have the expertise, leadership, training, and motivation necessary to successfully carry out the proposed research project on amyotrophic lateral sclerosis (ALS). My background in motor neuron diseases (MND) is broad, with specific training and experience in epidemiology, clinical research, trial coordination, genetics, biomarker discovery, diagnostic and prognostic tools, and laboratory methods applied to ALS and related disorders.

Since 2007, I have served as Chief of the multidisciplinary MND Centre at the University Hospital of Modena, a regional referral center for ALS diagnosis and care. The center provides comprehensive, patient-centered care to approximately 400 ALS patients annually, following them from diagnosis through advanced disease, both in hospital and at home. Our model ensures continuity of care “across time and space.” The center is actively engaged in clinical and translational research and collaborates with numerous national and international institutions. I have served as Principal Investigator (PI) in 32 clinical trials on ALS, including phase II and III studies.

I am a member of the ITALSGEN Consortium, which contributed to the discovery of several ALS-associated genes, such as VCP, C9ORF72, MATRN3, KIF5A. I also have strong expertise in data analysis, particularly in the clinical and epidemiological domains. Since 2009, I have coordinated the Emilia Romagna ALS Registry, which covers a population of over 4.5 million people.

I have led four multicenter randomized controlled trials on ALS (ERMOSLA, RAP-ALS, Co-ALS, FETR-ALS) and established the Modena Neurobiobank, which I currently direct. My etiological research has investigated environmental risk factors for ALS, in collaboration with Prof. M. Vinceti and Prof. B. Michalke (Munich), and more recently has focused on the gut microbiota. I coordinated the first clinical trial on fecal microbiota transplantation in ALS, which received worldwide attention from the ALS patient community.

My research spans the entire disease spectrum—from basic science to clinical practice and palliative care. As PI or co-investigator, I have established protocols for deep clinical phenotyping and biosample collection in ALS patients, laying the foundation for the proposed research. I have also successfully led

several funded research projects, overseeing staffing, ethics approvals, and budgets, and I have consistently produced peer-reviewed publications from each study.

From 2013 to 2017, I was elected national coordinator of the Italian Study Group on MND, which includes over 140 neurologists with expertise in ALS. To date, I have raised over €6 million in competitive research funding.

Currently, I am working with colleagues at the University of Modena to build an interdisciplinary network of researchers dedicated to ALS, spanning basic science to patient care. I am also leading the development of a new Italian twin cohort with ALS, funded by the National Recovery and Resilience Plan (NRRP), to be studied using a multi-omic approach. This project provides a platform for several future initiatives aimed at understanding disease mechanisms. The current proposal is a natural extension of this body of work..

B. Positions, Scientific Appointments, and Honors

Positions

2006-2007: Consultant neurologist at the Department of Neuroscience, University of Modena, St. Agostino-Estense Hospital, Modena, Italy.

2007-2021: Permanent full-time Neurologist at the Department of Neuroscience, University of Modena, St. Agostino-Estense Hospital, Modena, Italy.

2007-current: Chief of Multidisciplinary Centre for MND in Modena, Italy

2021-2024: Associate Professor in Neurology, University of Modena and Reggio Emilia

2024-current: Full Professor in Neurology, University of Modena and Reggio Emilia

2024-current: Director of the Neurology Unit, University Hospital of Modena

2024-current: Director Residency School in Neurology, University of Modena and Reggio Emilia

2024-current: Director of the Neurobiobank of Modena

Other Experience and Professional Memberships

2013-2017: Coordinator of the Motor Neuron Disease Study Group of the Italian Neurological Society (SIN).

2009-current: Coordinator of the Emilia Romagna Register for Amyotrophic Lateral Sclerosis (4.5 million population).

2002-current: Member of the Società Italiana di Neurologia (SIN)

2008-current: Member of the ITALSGEN Consortium (Italian Consortium for genetic studies on ALS)

Member of ENCALS (European Network for the Care of ALS) and TRICALS

Scientific Committee of the Italian ALS Association (AISLA)

2017-2019: Member of the EAN panel “Palliative Care”

2019-current: Member of the EAN panel “Amyotrophic Lateral Sclerosis and Frontotemporal Dementia”

C. Contribution to Science

1. I contributed to **genetic understanding in ALS**. I directly contributed to the discovery of the role of VCP gene in ALS and I collaborated to many studies on several other ALS-related genes mutations (C9ORF72, MATR3, KIF5A, SPTCL1, in collaboration with ITALSGEN Consortium and Prof. B.J. Traynor (NIH, Bethesda). Relevant articles for this contribution are: .

1. Johnson JO*, **Mandrioli J***, Benatar M, Abramzon Y, Van Deerlin VM, Trojanowski JQ, Gibbs JR, Brunetti M, Gronka S, Wu J, Ding J, McCluskey L, Martinez-Lage M, Falcone D, Hernandez DG, Arepalli S, Chong S, Schymick JC, Rothstein J, Landi F, Wang YD, Calvo A, Mora G, Sabatelli M, Monsurro MR, Battistini S, Salvi F, Spataro R, Sola P, Borghero G; ITALSGEN Consortium, Galassi G, Scholz SW, Taylor JP, Restagno G, Chiò A, Traynor BJ. Exome sequencing reveals VCP mutations as a cause of familial ALS. *Neuron*. 2010 Dec 9;68(5):857-64. doi: 10.1016/j.neuron.2010.11.036.***Contributed equally. FWCI 18.53**

2. Bartolome F, Wu HC, Burchell VS, Preza E, Wray S, Mahoney CJ, Fox NC, Calvo A, Canosa A, Moglia C, **Mandrioli J**, Chiò A, Orrell RW, Houlden H, Hardy J, Abramov AY, Plun-Favreau H. Pathogenic VCP mutations induce mitochondrial uncoupling and reduced ATP levels. *Neuron*. 2013 Apr 10;78(1):57-64. doi: 10.1016/j.neuron.2013.02.028. **FWCI 2.74**
3. Nicolas A, Kenna KP, Renton AE, Ticozzi N, Faghri F, Chia R, Dominov JA, Kenna BJ, Nalls MA, Keagle P, Rivera AM, van Rheenen W, Murphy NA, van Vugt JJFA, Geiger JT, Van der Spek RA, Pliner HA, Shankaracharya, Smith BN, Marangi G, Topp SD, Abramzon Y, Gkazi AS, Eicher JD, Kenna A; ITALSGEN Consortium, Mora G, Calvo A, Mazzini L, Riva N, **Mandrioli J**, Caponnetto C, Battistini S, Volanti P, LaBella V, Conforti FL, Borghero G, Messina S, Simone IL, Trojsi F, Salvi F, Logullo FO, D'Alfonso S, Corrado L, Capasso M, Ferrucci L; ...Silani V, Chiò A, Shaw CE, Traynor BJ, Landers JE. Genome-wide Analyses Identify KIF5A as a Novel ALS Gene. *Neuron*. 2018 Mar 21;97(6):1268-1283.e6. doi: 10.1016/j.neuron.2018.02.027. **FWCI 16.63**

Ongoing grants: 2023-now: Italian Ministry of Health: "GENIALITY" Genetics and Environment iNtersection In the Amyotrophic Lateral Sclerosis - FrontoTemporal Dementia spectrum: an Italian Twins cohort study with a Multi-Omics approach." €990.600

2. **Biomarkers research and disease pathomechanisms.** I have investigated the role of wet biomarkers in ALS and participated in basic and translational studies to better understand disease pathogenesis:

1. Martinelli I, Zucchi E, Simonini C, Gianferrari G, Bedin R, Biral C, Ghezzi A, Fini N, Carra S, **Mandrioli J**. SerpinA1 levels in amyotrophic lateral sclerosis patients: An exploratory study. *Eur J Neurol*. 2024 Jan;31(1):e16054. doi: 10.1111/ene.16054. Epub 2023 Sep 7. **FWCI 4.37**
2. Zucchi E, Banchelli F, Simonini C, De Biasi S, Martinelli I, Gianferrari G, Lo Tartaro D, Cossarizza A, D'Amico R, **Mandrioli J**. Tregs levels and phenotype modifications during Amyotrophic Lateral Sclerosis course. *Front Immunol*. 2025 Jan 8;15:1508974. doi: 10.3389/fimmu.2024.1508974. eCollection 2024. **FWCI NA**
3. Zucchi E, Bonetto V, Sorarù G, Martinelli I, Parchi P, Liguori R, **Mandrioli J**. Neurofilaments in motor neuron disorders: towards promising diagnostic and prognostic biomarkers. *Mol Neurodegener*. 2020 Oct 15;15(1):58. doi: 10.1186/s13024-020-00406-3. **FWCI 1.87**

Ongoing grants (2023-): Italian Ministry of Health: "NEURALSTOP" Neurosteroids against Neuroinflammation: a way to fight Neurodegeneration in Amyotrophic Lateral Sclerosis? €432.000

3. **Treatment research and clinical trials in ALS.** My research group and I have investigated the effects of several treatments in ALS, by participating as local PI in several clinical trials, by leading multicenter clinical trials and by coordinating no-profit studies on repurposing of drugs for ALS. Relevant articles for this contribution are:

1. **Mandrioli J**, D'Amico R, Zucchi E, De Biasi S, Banchelli F, Martinelli I, Simonini C, Lo Tartaro D, Vicini R, Fini N, Gianferrari G, Pinti M, Lunetta C, Gerardi F, Tarlarini C, Mazzini L, De Marchi F, Scognamiglio A, Sorarù G, Fortuna A, Lauria G, Bella ED, Caponnetto C, Meo G, Chio A, Calvo A, Cossarizza A. Randomized, double-blind, placebo-controlled trial of rapamycin in amyotrophic lateral sclerosis. *Nat Commun*. 2023 Aug 17;14(1):4970. doi: 10.1038/s41467-023-40734-8. **FWCI 3.75**
2. Gianferrari G, Cuoghi Costantini R, Crippa V, Carra S, Bonetto V, Pansarasa O, Cereda C, Zucchi E, Martinelli I, Simonini C, Vicini R, Fini N, Trojsi F, Passaniti C, Ticozzi N, Doretti A, Diamanti L, Fiamingo G, Conte A, Dalla Bella E, D'Errico E, Scarian E, Pasetto L, Antoniani F, Galli V, Casarotto E; Co-ALS Investigators Group; D'Amico R, Poletti A, **Mandrioli J**. Colchicine treatment in amyotrophic lateral sclerosis: safety, biological and clinical effects in a randomized clinical trial. *Brain Commun*. 2024 Sep 5;6(5):fcae304. doi: 10.1093/braincomms/fcae304. eCollection 2024. **FWCI 2.25**

4. One of my field of interest is represented by epidemiology of MND. I created the Emilia Romagna Registry of ALS and coordinated several national studies on ALS epidemiology:

1. **Mandrioli J**, Zucchi E, Martinelli I, Van der Most L, Gianferrari G, Moglia C, Manera U, Solero L, Vasta R, Canosa A, Grassano M, Brunetti M, Mazzini L, De Marchi F, Simonini C, Fini N, Tupler R, Vinceti M, Chiò A, Calvo A. Factors predicting disease progression in C9ORF72 ALS patients. *J Neurol*. 2023 Feb;270(2):877-890. doi: 10.1007/s00415-022-11426-y. **FWCI 3.15**
2. Faghri F, Brunn F, Dadu A; PARALS consortium; ERRALS consortium; Zucchi E, Martinelli I, Mazzini L, Vasta R, Canosa A, Moglia C, Calvo A, Nalls MA, Campbell RH, **Mandrioli J***, Traynor BJ*, Chiò A*. Identifying and predicting amyotrophic lateral sclerosis clinical subgroups: a population-based machine-learning study. *Lancet Digit Health*. 2022 May;4(5):e359-e369. doi: 10.1016/S2589-7500(21)00274-0.*Contributed equally. **FWCI 3.46**
3. Calvo A, Moglia C, Lunetta C, Marinou K, Ticozzi N, Ferrante GD, Scialo C, Sorarù G, Trojsi F, Conte A, Falzone YM, Tortelli R, Russo M, Chiò A, Sansone VA, Mora G, Silani V, Volanti P, Caponnetto C, Querin G, Monsurrò MR, Sabatelli M, Riva N, Logroscino G, Messina S, Fini N, **Mandrioli J**. Factors predicting survival in ALS: a multicenter Italian study. *J Neurol*. 2017 Jan;264(1):54-63. doi: 10.1007/s00415-016-8313-y. **FWCI 4.66**

5. Finally, I contributed to the study of environmental risk factors in ALS and more recently on the role of microbiota. I am coordinating studies on the role of gut microbiota and toxins in ALS and the first clinical trial on fecal microbiota transplantation in ALS

1. Vinceti M, **Mandrioli J**, Borella P, Michalke B, Tsatsakis A, Finkelstein Y. Selenium neurotoxicity in humans: bridging laboratory and epidemiologic studies. *Toxicol Lett*. 2014 Oct 15;230(2):295-303. doi: 10.1016/j.toxlet.2013.11.016. **FWCI 4.16**
2. Vinceti M, Urbano T, Filippini T, Bedin R, Simonini C, Sorarù G, Trojsi F, Michalke B, **Mandrioli J**. Changes in Cerebrospinal Fluid Concentrations of Selenium Species Induced by Tofersen Administration in Subjects with Amyotrophic Lateral Sclerosis Carrying SOD1 Gene Mutations. *Biol Trace Elem Res*. 2025 Apr;203(4):2355-2364. doi: 10.1007/s12011-024-04311-4. Epub 2024 Jul 17. **FWCI 11.24**
3. Niccolai E, Di Pilato V, Nannini G, Baldi S, Russo E, Zucchi E, Martinelli I, Menicatti M, Bartolucci G, **Mandrioli J**, Amedei A. The Gut Microbiota-Immunity Axis in ALS: A Role in Deciphering Disease Heterogeneity? *Biomedicines*. 2021 Jun 29;9(7):753. doi: 10.3390/biomedicines9070753. **FWCI 2.63**
4. **Mandrioli J**, Michalke B, Solovyev N, Grill P, Violi F, Lunetta C, Conte A, Sansone VA, Sabatelli M, Vinceti M. Elevated Levels of Selenium Species in Cerebrospinal Fluid of Amyotrophic Lateral Sclerosis Patients with Disease-Associated Gene Mutations. *Neurodegener Dis*. 2017;17(4-5):171-180. doi: 10.1159/000460253. **FWCI 2.87**
5. **Mandrioli J**, Amedei A, Cammarota G, Niccolai E, Zucchi E, D'Amico R, Ricci F, Quaranta G, Spanu T, Masucci L. FETR-ALS Study Protocol: A Randomized Clinical Trial of Fecal Microbiota Transplantation in Amyotrophic Lateral Sclerosis. *Front Neurol*. 2019 Sep 20;10:1021. doi: 10.3389/fneur.2019.01021. **FWCI 2.37**

Ongoing Grants: 2023-now: Italian Ministry of Research “MYSTICALS” Microorganisms, Toxins and Immunity InterSecTion In AmyotrophIc LateraAL Sclerosis -Frontotemporal Dementia: targeting disease heterogeneity”. € 242,999

Author of 191 peer-reviewed papers, H-index: 46, Citations: 7157.

Complete list of Published Work in: <https://www.ncbi.nlm.nih.gov/pubmed/?term=mandrioli+j>