

BIOGRAPHICAL SKETCH

NAME: Andrea , Cortese

POSITION TITLE: Academic Neurologist

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Pavia, Italy	MD	09/2007	Medical School - 110/110 with honors
University of Pavia, Italy	Residency	03/2013	Neurology - 50/50 with honors
University of Pavia, Italy	Ph.D.	10/2016	Biomedical Sciences – Neuroscience
University College London, UK	Post-doctoral training	09/2019	Post-doctoral Fellowship in Neurogenetics

A. Personal Statement

I am a neurologist and clinical scientist. Stemming from a broader interest in neuromuscular disorders, over the last years I have been fully committed towards the discovery, modelling and treatment of novel causes of inherited neuropathies, with particular interest in repeat expansion disorders and conditions caused by variations in non-coding DNA. With the progressive implementation of short and long read whole-genome sequencing in the diagnostic work-up of genetic diseases, the fraction of cases caused by changes in non-coding regions of the DNA is likely to rise consistently. I am committed to precision medicine and to provide patients affected by Charcot-Marie-Tooth disease (CMT) with effective and innovative treatments. It is rewarding to notice that only two years after the identification of SORD neuropathy as the most common cause of recessive CMT, a phase 3 trial is actively recruiting patients and hold promise to represent the first treatment for CMT.

B. Positions and Honors**Positions and Employment**

08/2025-	Associate professor at University of Milan and Consultant Neurologist at Fondazione IRCCS C. Besta National Neurological Institute
11/2024-	Associate Professor (principal research fellow) at UCL Institute of Neurology, Dept of Neuromuscular Diseases
11/2019-	Independent Clinician Scientist (PI) and Consultant Neurologist at UCL Institute of Neurology, Dept of Neuromuscular Diseases, MRC Centre for Neuromuscular Diseases, London, UK a
2019-2024	Ricercatore a tempo definito at University of Pavia - Department of Brain and Behaviour Sciences University of Pavia, Italy.
2016-2019	Senior clinical fellow at UCL Institute of Neurology, Dept of Neuromuscular Diseases, MRC Centre for Neuromuscular Diseases, London, UK. Supervisors M.Reilly and H.Houlden
2018-2018	Visiting Scholar at Hussmann Institute of Human Genomic - University of Miami – Miller school of Medicine, Miami, Fl, USA. Supervisor S.Zuchner
2013-2016	Consultant Neurologist at IRCCS C Mondino National Neurological Institute, Pavia Italy and Amyloid Research and Treatment Centre, Pavia, Italy

Other Experience and Professional Memberships

2015-	Reviewer for international peer reviewed journals including Nature Genetics, Brain, Neurology, JNNP and for National and International Funders
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2018-	Editorial Board, Journal of Peripheral Nervous System
2020-	Board Member of the Charcot-Marie-Tooth and related diseases
2022-	Board Member of Associazione Italiana Sistema Nervoso Periferico
2024-	PNS Education committee Board member

Honors

2013	Best poster prize awarded by Societa' Italiana di Neurologia
2016	Best Paper prize awarded by Istituto Neurologico Nazionale "C.Mondino"
2019	Prize ACMT Rete / Associazione Italiana Sistema Nervoso Periferico
2019	PK Thomas Prize for best paper in inherited neuropathies Peripheral Nerve Society
2019	Investigator Award 5th Congress of the European Academy of Neurology
2023	CMTA-STAR 40 under 40 (https://www.cmtausa.org/cmtas-40-under-40/)

C. Contribution to Science

i. My early work stemmed from clinical observations during my residency training. I was given the opportunity to spend one year of my residency training at the UCL Institute of Neurology where I started developing my translational interest in progressive neurodegenerative conditions. My work focused on investigating RNA metabolism in inclusion body myopathy, a progressive degenerative condition affecting the muscle with striking pathological similarities to other degenerative CNS diseases. I gathered experience in analysis and interpretation of RNAseq data, splicing analysis, qRT-PCR, immunohistochemistry.

1. Cortese A., Tavazzi E., Del Bue S et al. A case of polyradiculoneuritis during VZV reactivation in normal immune setting, *Neurology*. 2009;73(16):1334-5.
2. Piccolo G, Cortese A, Tavazzi E et al. Late onset oculopharyngeal muscular dystrophy with prominent neurogenic features and short GCG trinucleotide expansion. *Muscle Nerve*. 2011;43(1):141-2
3. Cortese A, Tucci A, Piccolo G et al. Novel CLN3 mutation causing autophagic vacuolar myopathy. *Neurology*. 2014;82(23):2072-6 .
4. Cortese A, Machado P, Morrow J et al. Longitudinal observational study of sporadic Inclusion Body Myositis: implications for clinical trials. *Neuromuscular Disorders*. 2013. 23(5):404-12
5. Cortese A, Plagnol V, Brady S et al. Widespread RNA metabolism impairment in sporadic inclusion body myositis TDP43-proteinopathy. *Neurobiol Aging*. 2014;35(6):1491-8

ii. During my PhD my research focused on neuromuscular diseases, exploring both inherited causes, with focus on ATTR amyloid neuropathy, and inflammatory causes, with focus on the novel autoantibodies in chronic inflammatory demyelinating neuropathy

1. Berk JL, Suhr OB, Obici L et al. Repurposing diflunisal for familial amyloid polyneuropathy: a randomized clinical trial. *JAMA*. 2013;310(24):2658-67
2. Cortese A, Vita G, Luigetti M et al. Monitoring safety and effectiveness of Tafamidis in transthyretin amyloidosis in Italy. *J Neurol*. 2016 May;263(5):916-24
3. Cortese A, Devaux JJ, Zardini E et al. Neurofascin-155 as a putative antigen in combined central and peripheral demyelination. *Neurol Neuroimmunol Neuroinflamm*. 2016;3(4):e238.
4. Cortese A, Vegezzi E, Lozza A et al. Diagnostic challenges in transthyretin amyloidosis: avoiding misdiagnosis of a treatable hereditary neuropathy. *J Neurol Neurosurg Psychiatry*. 2017.jnnp-2016-315262.
5. Cortese A, et al. Antibodies to neurofascin, contactin-1, and contactin-associated protein 1 in CIDP: Clinical relevance of IgG isotype. *Neurol Neuroimmunol Neuroinflamm*. 2019 Nov 21;7(1)

iii. During my postdoc at UCL and University of Miami I have been fully committed towards the discovery and modelling of novel causes of inherited rare neurological disorders, with particular interest in repeat expansion disorders and conditions caused by variations in non-coding regions of the DNA. As part of my work I have identified a novel repeat expansion in RFC1 as the most common cause of late-onset ataxia and biallelic mutation in SORD as one of the most common causes of progressive motor neuropathy

1. Cortese A, Simone R, Sullivan R et al. Biallelic expansion of an intronic AAGGG repeat in RFC1 is a common cause of late-onset ataxia. *Nat Genet.* 2019 Apr;51(4):649-658.
2. Cortese A, Laura M, Casali C et al. Altered TDP-43 dependent splicing in HSPB8-related distal hereditary motor neuropathy and myofibrillar myopathy. *Eur J Neurol.* 2018 Jan;25(1):154-163.
3. Cortese A, Wilcox JE, Polke JM et al. Targeted next-generation sequencing panels in the diagnosis of Charcot-Marie-Tooth disease. *Neurology.* 2020 Jan 7;94(1):e51-e61.
4. Cortese A., Tozza S, Yau W, Cerebellar Ataxia, Neuropathy, Vestibular Areflexia Syndrome Due To RFC1 Repeat Expansion. *Brain.* 2020 Feb 1;143(2):480-490.
5. Cortese A et al. Biallelic mutations in *SORD* cause a common and potentially treatable hereditary neuropathy. *Nat Genetics, Nat Genet.* 2020 May;52(5):473-481.

iv. During the last five years, thanks to the support of a prestigious MRC clinician scientist fellowship and more recently, ERC StG, I transitioned to independence and now lead my own lab which focuses on three main line of research 1. Genetic discovery in genetically unsolved neurogenetic conditions 2. functional modelling RFC1 repeat expansion disease and other conditions caused by variations in non-coding DNA 3. Genetic modifier studies with focus ATTR amyloidosis

1. Cortese A. [...] Ravenscroft G (2024) A CCG expansion in ABCD3 causes oculopharyngodistal myopathy in individuals of European ancestry. *Nature Communications.* 15(1):6327. doi: 10.1038/s41467-024-49950-2.
2. Vegezzi E, [...] Cortese A. Normal and pathogenic variation of RFC1 repeat expansions: implications for clinical diagnosis. *Lancet Neurol.* ;23(7):725-739. doi: 10.1016/S1474-4422(24)00167-4.
3. Cortese, A., Vegezzi, E., & Houlden, H. (2024). Contraction or sequence variant of an intergenic repeat-Alu element leads to inherited thyroid disease. *Nature Genetics.* doi:10.1038/s41588-024-01723-9
4. Curro', R., Dominik, N., Facchini, S., Vegezzi, E., Sullivan, R., Galassi Deforie, V., . . . Cortese, A. (2024). Role of the repeat expansion size in predicting age of onset and severity in RFC1 disease. *Brain.* doi:10.1093/brain/awad436
5. Dominik, N., Magri, S., Curro, R., Abati, E., Facchini, S., Corbetta, M., . . . Cortese, A. (2024). Normal and pathogenic variation of RFC1 repeat expansions: implications for clinical diagnosis (vol 146, pg 5060, 2023). *Brain*, 147(2), e23. doi:10.1093/brain/awad386

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing/Awarded Research Support

ERC starting grant, 1.5 M euro, 1,5M euro (GEMREX) 04/2025-03/2031
 Genomic observation and perturbation: genetic modifiers to untangle disease mechanisms of RFC1 repeat expansion
 Aim of this study is to further elucidate the disease-causing mechanisms of RFC1 expansion and identify potentially druggable genetic modifiers
 Role: PI

National Ataxia Foundation, 810,000 USD 04/2024-03/2027
 Developing Precision Therapies For CANVAS/ RFC1 Repeat Expansions
 Aim of this study is to collect clinical longitudinal data on patients carrying RFC1 expansion and develop disease relevant models including iPSC neurons and murine model
 Role: PI

AFM Telethon Amount awarded 200,000 euro 11/2024-10/2026
 Long-read Sequencing In Undiagnosed Neuromuscular Diseases
 Aim of this project is to perform LRS in patients with unsolved neuromuscular conditions and in particular sensory ganglionopathy (RFC1 negative), oculopharyngodistal myopathy (ABCD3 negative) and non-5q SMA.
 Role:PI

Muscular dystrophy-UK, Amount awarded £160,000 11/2024-10/2026
 Pairing Mice With Patients To Understand And Treat SORD Neuropathy
 Aim of this study is to characterize a mouse model of SORD neuropathy and compare metabolic profile and axonal degeneration biomarkers in the murine model and patients diagnosed with SORD-CMT

Role: Co-PI with Dr James Sleigh

Charcot-Marie-Tooth Association, awarded 230,000 USD

Long read sequencing in undiagnosed axonal CMT patients

Aim of this project is to perform LRS in patients with unsolved axonal CMT cases

Role: PI

Completed Research Support

MRC Clinician Scientist Fellowship(MR/T001712/1) amount awarded £1.3M 01/11/2019-31/10//2023

The AAGGG repeat expansion in RFC1 associated with late-onset ataxia and sensory neuropathy: from genetic cause to defining the functional mechanism

The main objective of this project is to investigate the molecular mechanisms underlying neurodegeneration in the presence of biallelic AAGGG expansions in RFC1 in iPSC sensory neurons and fly model

Role: PI

UCL Capital Equipment Fund (CEF) 4 call for the Faculties of Life and Medical Sciences £87,662 2023

Purchase of Bionano Optical Genome Mapping Saphyr

Role: PI

CARIPLO Biomedical Research amount awarded euro 235,000 01/01/2020-31/12/2023

Genetic spectrum and functional mechanisms of the intronic AAGGG repeat expansion in RFC1 causing CANVAS and late-onset ataxia

The goal of this study is to fully characterize the full clinical spectrum of the RFC1 repeat expansion and investigate the molecular mechanism in cellular and zebrafish model with focus on the DNA damage response

Role: PI

Fondazione Regionale Ricerca Biomedica

Cortese (PI) amount awarded euro 450,000 01/06/2021-31/05/2024

Genetic modifiers of hereditary and acquired ATTR amyloidosis

Objective of this study is to investigate the presence of genetic modifiers in ATTR amyloidosis using a combination of unbiased genome-wide association (GWA) analysis followed by long read sequencing of TTR gene and GWAS significant loci.

Role: PI

Transthyretin Amyloid Polyneuropathy (ATTR-PN) Research Competitive Grant - Program for Junior Investigators (Grant Reference: 60787987) Amount awarded USD 150'000 01/01/20201 – 31/12/2023

Genetic Modifiers of onset and progression of ATTR amyloidosis.

Objective of the study is to identify genetic modifiers of onset, phenotype and severity of hereditary and wild-type TTR amyloidosis at genome-wide level (GWAS)

Role: PI

NIH Inherited Neuropathy Consortium Pilot Award amount awarded 50,000 USD 01/01/20201 – 31/12/2021

Untangling the genomics of axonal Charcot-Marie-Tooth disease

The study aims at investigating the missing heritability in axonal neuropathy taking advantage of long-read WGS technology

Role: PI

204841/Z/16/Z

Wellcome ISSF Flexible Support Awards – Post doctoral fellowship awarded £35,000 01/06/2018 – 31/05/2019

Aim of this fellowship was to support my research in genetic discovery of inherited neurodegenerative diseases

Role: Post-doctoral Fellow

NIH Rare Diseases Clinical Research Network (RDCRN) - INC Fellowship

01/06/2016 –31/05/2018

Goal of my fellowship was to discover novel genetic cases on inherited neuropathy

Role: Post doctoral fellow