CURRICULUM VITAE

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Education

Catholic University of Rome: 1993 Medical Degree summa cum laude
Catholic University of Rome: 1997 **Residency in Neurology summa cum laude**

Training and professional experience

1987-1993	**Catholic University of Rome, Medical School, MD**
1990-1991	**Catholic University of Rome, Internship in Pathology**
1991-1993	**Catholic University of Rome, Internship in Neurology**
1993-1997	**Catholic University of Rome, Resident in Neurology**
1998-2000	**Postdoctoral Research Fellow, Department of Neurology,Columbia University, New York, NY**
2000-2001	**Postdoctoral Research Fellow, TIGEM- Telethon, Department of Human Genetics, Naples, Italy**
2002-2009	**Senior Research Fellow, Department of Neurogenetic, National Institute of Neurology " C. Besta", Milan, Italy**
July 2006	**Working visit, MRC Dunn Human Nutrition Unit, Cambridge, UK**
January 2009-January 2010	**Senior Research Fellow, MRC Mitochondrial Biology Unit, Cambridge, UK**

January 2010-January 2013	Group Leader, Mitochondrial biogenesis, MRC Mitochondrial Biology Unit, Cambridge, UK
January 2013-present	Group leader, Mitochondrial Biogenesis, MRC National Institute for Medical Research

PUBLISHED ARTICLES

1. *Pearce S, Nezich CL, Spinazzola A. Mitochondrial diseases: Translation matters.
Mol Cell Neurosci.2012 Sep 7.doi: 10.1016/j.mcn.2012.08.013. [Epub ahead of print]
A comprehensive review of the new emerging field of mitochondrial translation related disorders.

2.* He J, Cooper HM, Reyes A, Di Re M, Sembongi H, Litwin TR, Gao J, Neuman KC, Fearnley IM, Spinazzola A, Walker JE, Holt IJ. Mitochondrial nucleoid interacting proteins support mitochondrial protein synthesis. Nucleic Acids Res. 2012 Mar;40(13):6109-21.
The report pioneered the concept of coupling of the translation machinery to mitochondrial DNA during its assembly.

3.Spinazzola A. Mitochondrial DNA mutations and depletion in pediatric medicine.
SeminFetal Neonatal Med. 2011 Aug;16(4):190-6.

4. Burgunder JM, Schöls L, Baets J, Andersen P, Gasser T, Szolnoki Z, Fontaine B, Van Broeckhoven C, Di Donato S, De Jonghe P, Lynch T, Mariotti C, Spinazzola A, Tabrizi SJ, Tallaksen C, Zeviani M, Harbo HF, Finsterer J. EFNS guidelines for the molecular diagnosis of neurogenetic disorders: motoneuron, peripheral nerve and muscle disorders Eur J Neurol. 2011 Feb;18(2):207-17.

5. Burgunder JM, Finsterer J, Szolnoki Z, Fontaine B, Baets J, Van Broeckhoven C, Di Donato S, De Jonghe P, Lynch T, Mariotti C, Schöls L, Spinazzola A, Tabrizi SJ, Tallaksen C, Zeviani M, Harbo HF, Gasser T. EFNS guidelines on the molecular diagnosis of channelopathies, epilepsies, migraine, stroke, and dementias. Eur J Neurol. 2010 May;17(5):641-8.

6. Gasser T, Finsterer J,,Baets J, Van Broeckhoven C, Di Donato S, Fontaine B, De Jonghe P, Lossos A, Lynch T, Mariotti C, Schöls L, Spinazzola A, Szolnoki Z, Tabrizi SJ, Tallaksen C, Zeviani M, Burgunder JM, Harbo HF; (2009)EFNS guidelines on the molecular diagnosis of ataxias and spastic paraplegias. Eur J Neurol. 2010 Feb;17(2):179-88.

7. Finsterer J,HarboHF ,Baets J, Van Broeckhoven C, Di Donato S, Fontaine B, De Jonghe P, Lossos A, Lynch T, Mariotti C, Schöls L, Spinazzola A, Szolnoki Z, Tabrizi SJ, Tallaksen C, Zeviani M. , Burgunder JM, Gasser T; EFNS guidelines on the molecular diagnosis of mitochondrial disorders. Eur J Neurol. 2009 Dec;16(12):1255-64.

8. Poulton J, Hirano M, Spinazzola A, Arenas Hernandez M, Jardel C, Lombès A, Czermin B, Horvath R, Taanman JW, Rotig A, Zeviani M, Fratter C. Collated mutations in mitochondrial DNA (mtDNA) depletion syndrome (excluding the mitochondrial gamma polymerase, POLG1). BiochimBiophysActa. 2009 Dec;1792(12):1109-12.

9. Harbo HF, Finsterer J, Baets J, Van Broeckhoven C, Di Donato S, Fontaine B, De Jonghe P, Lossos A, Lynch T, Mariotti C, Schöls L, Spinazzola A, Szolnoki Z, Tabrizi SJ, Tallaksen C, Zeviani M, Burgunder JM, Gasser T; EFNS

guidelines on the molecular diagnosis of neurogenetic disorders: general issues, Huntington's disease, Parkinson's disease and dystonias. Eur J Neurol. 2009,16:777-85.

10. Spinazzola A, Zeviani M. Disorders from perturbations of nuclear-mitochondrial intergenomiccross-talk. J Intern Med. 2009, 26:174-92.

11. Spinazzola A, Invernizzi F, Carrara F, Lamantea E, Donati A, Dirocco M, Giordano I, Meznaric-Petrusa M, Baruffini E, Ferrero I, Zeviani M. Clinical and molecular features of mitochondrial DNA depletion syndromes. J Inherit Metab Dis. 2009,32:143-58.

12. Parini R, Furlan F, Notarangelo L, Spinazzola A, Uziel G, Strisciuglio P, Concolino D, Corbetta C, Nebbia G, Menni F, Rossi G, Maggioni M, Zeviani M. Glucose metabolism and diet-based prevention of liver dysfunction in MPV17 mutant patients. J Hepatol. 2009,50:215-21.

13. Valente M, Piga D, Lamantea E, Carrara F, Uziel G, Cudia P, Farina L, Morandi L, Mora M, Spinazzola A, Zeviani M, Tiranti V. Identification of novel mutations in five patients with mitochondrial encephalomyopathy. BiochimBiophysActa. 2009, 1787:491-501.

14. * Viscomi C, Spinazzola A, Maggioni M, et al. Early-onset liver mtDNA depletion and late-onset proteinuric nephropathy in Mpv17 knockout mice. Hum Mol Genet. 2009, 18:12-26.
The Mpv17 KO mouse recapitulates several features of the human disease and therefore is a useful animal model to study the pathophysiological of MPV17 deficiency.

15. Spinazzola A, Santer R, Akman OH, Tsiakas K, Schaefer H, Ding X, Karadimas CL, Shanske S, Ganesh J, Di Mauro S, Zeviani M. Hepatocerebral form of mitochondrial DNA depletion syndrome: novel MPV17 mutations. Arch Neurol. 2008,65:1108-13.

16.*Spinazzola A, Massa V, Hirano M, Zeviani M. Lack of founder effect for an identical mtDNA depletion syndrome (MDS)-associated MPV17 mutation shared by Navajos and Italians. NeuromusculDisord. 2008,18:315-8.

17. Spinazzola A, Zeviani M. Disorders of Nuclear-Mitochondrial Intergenomic Communication. Biosci Rep. 2007, 27:39-51.

18. Spinazzola A, Viscomi C, Fernandez-Vizarra E, Carrara F, D'Adamo P, Calvo S, Marsano RM, et al MPV17 encodes an inner mitochondrial membrane protein and is mutated in infantile hepatic mitochondrial DNA depletion. Nat Genet. 2006,38:570-5.**
MPV17 is a 19 kDa mitochondrial inner membrane protein of unknown function. The clinical presentation varies from fulminant hepatic failure to cerebellar and sensory ataxia with moderate liver involvement. Similar to humans, Mpv17 knockout mice show severe mtDNA depletion in liver and to a lesser extent muscle.

19. **Calvo S, Jain M, Xie X, Sheth SA, Chang B, Goldberger OA, Spinazzola A, Zeviani M, Carr SA, Mootha VK. Systematic identification of human mitochondrial disease genes through integrative genomics. Nat Genet. 2006, 38:576-82.
The authors describe an integrated genomic approach for the definition of the mitochondrial proteome, which is estimated to be comprise 1500 gene products in humans, and experimental evidence is provided which validates the specificity and sensitivity of the methodology.

20. Spinazzola A, Zeviani M. Disorders of nuclear-mitochondrial intergenomicsignaling. Gene. 2005, 354:162-8.

21. Hirano M, Marti R, Spinazzola A, Nishino I, Nishigaki Y.Thymidine phosphorylase deficiency causes MNGIE: an autosomal recessive mitochondrial disorder. Nucleosides Nucleotides Nucleic Acids. 2004. 23:1217-25.

22. Spinazzola A, Carrara F, Mora M, Zeviani M. Mitochondrial myopathy and ophthalmoplegia in a sporadic patient with the 5698G→A mitochondrial DNA mutation. NeuromusculDisord. 2004,14:815-7.

23. Marti R, Spinazzola A, Tadesse S, Nishino I, Nishigaki Y, Hirano M. Definitive diagnosis of mitochondrial neurogastrointestinalencephalomyopathy by biochemical assays. Clin Chem. 2004,50:120-4.

24. Zeviani M, Spinazzola A, Carelli V. Nuclear genes in mitochondrial disorders. CurrOpin Genet Dev. 2003, 13:262-70.

25. Zeviani M, Spinazzola A. Mitochondrial disorders. CurrNeurolNeurosci Rep. 2003, 3:423-32.

26. Marti R, Spinazzola A, Nishino I, Andreu AL, Naini A, Tadesse S, Oliver JA, Hirano M.Mitochondrial neurogastrointestinalencephalomyopathy and thymidine metabolism: results and hypotheses. Mitochondrion. 2002,2:143-7.

27. Spinazzola A, Marti R, Nishino I, Andreu AL, Naini A, Tadesse S, Pela I, Zammarchi E, Donati MA, Oliver JA, Hirano M. Altered thymidine metabolism due to defects of thymidine phosphorylase. J Biol Chem. 2002, 277:4128-33.**
Patients with this condition display elevated levels of circulating thymidine, leading to the suggestion that uptake of excess thymidine by mitochondria stimulates salvage synthesis of dTTP, which in turn unbalances the other dNTP pools and stimulates mutagenesis.

28. Di Giovanni S, Mirabella M, Spinazzola A, Crociani P, Silvestri G, Broccolini A, Tonali P, Di Mauro S, Servidei S. Coenzyme Q10 reverses pathological phenotype and reduces apoptosis in familial CoQ10 deficiency. Neurology. 2001, 57:515-8.

29. Manfredi G, Spinazzola A, Checcarelli N, Naini A. Assay of mitochondrial ATP synthesis in animal cells. Methods Cell Biol. 2001,65:133-45.

30. Nishino I, Spinazzola A, Hirano M. MNGIE: from nuclear DNA to mitochondrial DNA. NeuromusculDisord. 2001,11:7-10.

31. Nishino I, Spinazzola A, Papadimitriou A, Hammans S, Steiner I, Hahn CD, Connolly AM, Verloes A, Guimaraes J, Maillard I, Hamano H, Donati MA, Semrad CE, Russell JA, Andreu AL, Hadjigeorgiou GM, Vu TH, Tadesse S, Nygaard TG, Nonaka I, Hirano I, Bonilla E, Rowland LP, DiMauro S, Hirano M. Mitochondrial neurogastrointestinalencephalomyopathy: an autosomal recessive disorder due to thymidine phosphorylase mutations. Ann Neurol. 2000,47:792-800.

32. Servidei S, Capon F, Spinazzola A, Mirabella M, Semprini S, de Rosa G, Gennarelli M, Sangiuolo F, Ricci E, Mohrenweiser HW, Dallapiccola B, Tonali P, Novelli G. A distinctive autosomal dominant vacuolarneuromyopathy linked to 19p13. Neurology. 1999, 53:830-7.

33. Manfredi G, Gupta N, Vazquez-Memije ME, Sadlock JE, Spinazzola A, De Vivo DC, Schon EA. Oligomycin induces a decrease in the cellular content of a pathogenic mutation in the human mitochondrial ATPase 6 gene. J Biol Chem. 1999, 274:9386-91.

34. Nishino–I, Spinazzola A, Hirano M. Thymidine phosphorylase gene mutations in MNGIE, a human mitochondrial disorder. Science. 1999,83:689-92.**

The study showed that MNGIE results from a deficiency of thymidine phosphorylase, an enzyme that catalyzes the reversible breakdown of thymidine to thymine plus deoxyribose-1-phosphate. The report underlies the importance of understanding the nature and sources of mitochondrial DNA precursor pools since represent the first discovery of a human disease in which mitochondrial genomic instability or inability to maintain adequate levels of mtDNA were found to be correlated with mutations affecting an enzymes involved in nucleotide metabolism.

35. Silvestri G, Servidei S, Rana M, Ricci E, Spinazzola A, Paris E, Tonali P.A novel mitochondrial DNA point mutation in the tRNA(Ile) gene is associated with progressive external ophthalmoplegia. BiochemBiophys Res Commun. 1999, 220:623-7.

Chapters

Zeviani M, Spinazzola A. Farina L. Simonati A. Malattiemitocondriali "Trattato di Neuropatologia - Vol I" Editors G.L. Mancardi, F Tagliavini, G. Vita – A.I.N.P. AssociazioneItaliana di NeuropatologiaaderenteallaSocietàItaliana di Neurologia S.I.N. – 2006 – pp 835- 883.

SpinazzolaA, Zeviani M.: Disorders of nuclear-mitochondrial intergenomic communication (www.medlink.com)

Contributions to commercial, clinical and public health research outcomes.
Dr Spinazzola developed a biochemical assay to measure thymidine phosphorylase activity to diagnose mitochondrial neurogastrointestinalencephalomyopathy (MNGIE) (Science 1999, JBC 2000, and ClinChem 2004). A modified version of the test is now used in a fee-for-service diagnostic laboratory at Columbia University.

Supervision of students
Dr Spinazzola has supervised the work of 6 graduate students, more than 10 medical students and four technicians in the laboratory.
Dr Spinazzola regularly reviews papers for a broad range of scientific and clinical journals

Dr Spinazzola is a faculty member of European Genetic Foundation (www.eurogene.org)

Dr Spinazzola has been a member of the European Federation of Neurological Societies (EFNS) Task Force of Neurogenetics 2008-2010 and is author of the chapters included in the series of guidelines on molecular diagnosis and treatment of neurogenetic disorders.

HONOURS AND AWARDS

Catholic University of Rome, Postdoctoral Research Fellowship (1997- 1998) Columbia University

Postdoctoral Research Fellowship of the American Muscular Dystrophy Association (MDA) (1998)

Columbia University, Telethon Postdoctoral Research Fellowship (1999- 2000)

CNR, Postdoctoral Research Fellowship (1999- 2000)

National Neurologic Institute "C. Besta", Postdoctoral Research Fellowship 2002-2004

National Neurologic Institute "C. Besta", Senior Research Fellowship 2004-April 2009

MRC Mitochondrial Biology Unit, Cambridge, Senior Research Fellowship May-Dec 2009

Marie Curie Intra-European Fellowships for Career Development (IEF), May 2010- May 2012