

Curriculum vitae et studiorum

Dr. Francesca R. Fusco

Name: Francesca Romana Fusco

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Date of Birth: January 8th, 1969

Italian Medical council: n° 54356 since January 1994

Specialist Register- Neurology since October 27, 1997

Marital status: married, James H. Lynch, Jr. Two daughters : Stella Fabiola Lynch and Lavinia Weeks Lynch

Graduation from Medical School: July 27, 1993 from the University of Rome Tor Vergata,
Magna cum summa laude

Dissertation: Huntington's Chorea: Morphological and functional changes in the thalamus

Graduation from School of Specialty: University of Tor Vergata Department of Neurology
(October 27th, 1997) under the mentorship of Professor G. Sancesario- Chairman Professor G.
Bernardi *Magna cum summa laude*

Postdoctoral fellowships:

- Summer Rotation in the Neuropathology Department, Mass General Hospital, 1992, with Dr T. Hedley-White
- Virtanen Institute, Kuopio, Finland under the mentorship of Prof. Jari Koistinaho . 1996
- Department of Anatomy and Neurobiology, University of Tennessee, Memphis, Tn, under the mentorship of Prof. Anton Reiner. 1996-1999

Special Interest (clinical): Movement disorders

Special Interest (research): Basal ganglia, Huntington's disease

Training and experiences

-During the last year of Neurology residency, Dr Fusco worked in the Electroencephalography laboratory of the Neurology Department of University of Rome Tor Vergata- Sant'Eugenio Hospital. In the laboratory, she learned the basic histological and immunohistochemical techniques and a surgical model of ischemia in gerbils.

-In 1996 Dr Fusco spent three months at Virtanen Institute where she learned several models of experimental ischemia in rats, such as middle cerebral artery occlusion and four vessels occlusion.

-After graduation from the School of Specialty, Dr Fusco spent two years in the laboratory of Dr. Anton J Reiner at UT Memphis, dealing primarily with experimental neuroscience to acquire the knowledge necessary to set up and maintain a research laboratory, writing grants and scientific articles.

Languages:

Italian mother language

English: excellent, written and spoken

French: excellent, written and spoken

Present employment:

1999-present

- Head of the Day Hospital of Rehabilitation Department “F”, and
- Principal Investigator of the Neuroanatomy laboratory
- Professor of Neuroanatomy at the School of Physical Therapy of the University of Rome Tor Vergata

Santa Lucia Foundation Hospital for Neurological Rehabilitation and Research

Dr. Fusco’s job at the Santa Lucia Foundation is partly dedicated to patients care, partly to the neuroscience research, and partly to teaching.

The neuroscience work takes place in the Neuroscience center of the Hospital Santa Lucia, which has expanded into the new European Brain Research Institute (EBRI) of Rome. In the neuroscience center, Dr. Fusco is the principal investigator of the Neuroanatomy laboratory, which focuses on the molecular mechanisms of cell death in Huntington’s disease, using rodent models and highly specialized microscopy techniques such as the triple laser confocal microscopy. Preclinical studies on the effects of pharmacological compounds of models of HD take place in the Neuroanatomy lab. The clinical work takes place in the day hospital rehabilitation department F, which is specialized in the care of patients with stroke.

The department has an outstanding record of clinical research studies on post-stroke patients. Dr Fusco has participated in several clinical trials that took place in the neurorehabilitation department, both interventional and observational, where her role was to clinically monitor the enrolled patients.

In particular, she took part in the DESTRO observational study for post-stroke depression, which was a multicenter observational study that took place in 53 center with a total of 1064 patients for 9 months after stroke. Her role was the clinical assessment of the patients.

Currently, she is taking part in a European multicenter interventional study (18 centers) on piracetam in post-stroke patients – no sponsoring company- and her role is clinical assessment.

The outpatient clinical practice, which is also held at the Hospital Santa Lucia, deals with general neurology, with a particular interest in the movement disorders such as Parkinson's disease and Huntington's disease.

Moreover, four hours per week of Dr Fusco's schedule are dedicated to teaching Neuroanatomy at the school of Physiotherapy of the University of Rome Tor Vergata. Lessons also take place at the hospital Santa Lucia.

Recent achievements:

- Dr. Fusco has been appointed (November 15, 2013) as a Major of the Italian Army where she serves as a health functional specialist
- Dr. Fusco has been appointed (January 8, 2014) as Associate Professor of Pathology (Professore di seconda fascia in Anatomia Patologica) by the Italian Department of Research and University (Ministero dell'Istruzione, Università e Ricerca)

Scientific Societies:

1996- present: Society for Neuroscience

2000- present: Società Italiana di Neurologia (Italian Society of Neurology)

2009- present: Società Italiana di Neuropatologia e Neurobiologia Clinica (Italian Society of Neuropathology)- *council member* since 2010

History of Funding:

Extramural:

Since 1999 has been successful in being awarded yearly grants from the Italian Department of Health, which have been supporting her research. The grants have been for the amount of 75000 to 120000 Euros every year. The current grant is called Ricerca Finalizzata 2014

Dr Fusco's lab has been funded by a major pharmaceutical company for a project involving pharmacological properties of a phosphodiesterase inhibitor on a mouse model of Huntington's disease. (After the promising results of the study, the compound is currently in phase 3 clinical trial.). Currently, Dr. Fusco's lab is collaborating with another major pharmaceutical company for studies on solid tumors on mice.

Intramural:

Additional support for research comes from Santa Lucia Foundation for an amount of 75000 a year

Journal articles

Aside from the scientific publications in the area of basic research, Dr Fusco has participated in several clinical trials mainly focusing on post-stroke patients, and, to a lesser extent, on multiple sclerosis.

1. Sancesario,G., Morello,M., Massa, R., Fusco, F. & Bernardi, G. (1993) NADPH diaphorase activity is inhibited by EDTA in neurons but not in choroid plexus epithelium. *Neurosci.Lett.*, 158, 101-104.
2. Sancesario,G., Morello,M., Massa, R., Fusco, F.R., D'Angelo,V. & Bernardi, G. (1996) NADPH-diaphorase neurons contacting the cerebrospinal fluid in the ventricles of rat brain. *J.Cereb.Blood Flow Metab*, 16, 517-522.
3. Miettinen, S., Fusco, F.R., Yrjanheikki, J., Keinanen, R., Hirvonen, T., Roivainen, R., Narhi,M., Hokfelt, T. & Koistinaho, J. (1997) Spreading depression and focal brain ischemia induce cyclooxygenase-2 in cortical neurons through N-methyl-D-aspartic acid-receptors and phospholipase A2. *Proc.Natl.Acad.Sci.U.S.A*, 94, 6500-6505.
4. Sancesario G, Pietroiusti A, Cestaro B, Fusco FR, Magrini A, Patacchioli FR, Franceschelli L, Galante A. (1997) *Funct Neurol*. Sep-Oct;12(5):283-91.
5. Sancesario,G., Massa, R., Fabrizi, E., Fusco,F.R., Morello,M., Martorana, A., Porcu, G.S. & Bernardi,G. (1998) Zinc distribution in various tissues, (brain, eye, skin, muscle and blood) of rat during hindlimb suspension. *J.Gravit.Physiol*, 5, 149-150.
6. Fusco, F.R., Chen,Q., Lamoreaux, W.J., Figueredo-Cardenas,G., Jiao,Y., Coffman,J.A., Surmeier, D.J., Honig, M.G., Carlock,L.R. & Reiner,A. (1999) Cellular localization of huntingtin in striatal and cortical neurons in rats: lack of correlation with neuronal vulnerability in Huntington's disease. *J.Neurosci.*, 19, 1189-1202.

7. Jiao, Y., Sun, Z., Lee, T., Fusco, F.R., Kimble, T.D., Meade, C.A., Cuthbertson, S. & Reiner, A. (1999) A simple and sensitive antigen retrieval method for free-floating and slide-mounted tissue sections. *J. Neurosci. Methods*, 93, 149-162.
8. Guatteo, E., Fusco, F.R., Giacomini, P., Bernardi, G. & Mercuri, N.B. (2000) The weaver mutation reverses the function of dopamine and GABA in mouse dopaminergic neurons. *J. Neurosci.*, 20, 6013-6020.
9. Meade, C.A., Figueredo-Cardenas, G., Fusco, F., Nowak, T.S., Jr., Pulsinelli, W.A. & Reiner, A. (2000) Transient global ischemia in rats yields striatal projection neuron and interneuron loss resembling that in Huntington's disease. *Exp. Neurol.*, 166, 307-323.
10. Fusco, F.R., Viscomi, M.T., Bernardi, G. & Molinari, M. (2001) Localization of ataxin-2 within the cerebellar cortex of the rat. *Brain Res. Bull.*, 56, 343-347.
11. Martorana, A., Fusco, F.R., Picconi, B., Massa, R., Bernardi, G. & Sancesario, G. (2001) Dopamine denervation induces neurotensin immunoreactivity in GABA-parvalbumin striatal neurons. *Synapse*, 41, 360-362.
12. Meade, C.A., Deng, Y.P., Fusco, F.R., Del Mar, N., Hersch, S., Goldowitz, D. & Reiner, A. (2002) Cellular localization and development of neuronal intranuclear inclusions in striatal and cortical neurons in R6/2 transgenic mice. *J. Comp. Neurol.*, 449, 241-269.
13. Cavaliere, F., Florenzano, F., Amadio, S., Fusco, F.R., Viscomi, M.T., D'Ambrosi, N., Vacca, F., Sancesario, G., Bernardi, G., Molinari, M. & Volonte, C. (2003) Up-regulation of P2X2, P2X4 receptor and ischemic cell death: prevention by P2 antagonists. *Neuroscience*, 120, 85-98.
14. Fusco, F.R., Zuccato, C., Tartari, M., Martorana, A., De March, Z., Giampa, C., Cattaneo, E. & Bernardi, G. (2003) Co-localization of brain-derived neurotrophic factor (BDNF) and wild-type huntingtin in normal and quinolinic acid-lesioned rat brain. *Eur. J. Neurosci.*, 18, 1093-1102.
15. Fusco, F.R., Martorana, A., De March, Z., Viscomi, M.T., Sancesario, G. & Bernardi, G. (2003) Huntingtin distribution among striatal output neurons of normal rat brain. *Neurosci. Lett.*, 339, 53-56.
16. Martorana, A., Fusco, F.R., D'Angelo, V., Sancesario, G. & Bernardi, G. (2003) Enkephalin, neurotensin, and substance P immunoreactive neurones of the rat GP following 6-hydroxydopamine lesion of the substantia nigra. *Exp. Neurol.*, 183, 311-319.
17. Paolucci, S., Antonucci, G., Grasso, M.G., Bragioni, M., Coiro, P., De Angelis, D., Fusco, F.R., Morelli, D., Venturiero, V., Troisi, E. & Pratesi, L. (2003) Functional Outcome of Ischemic and Hemorrhagic Stroke Patients After Inpatient Rehabilitation. A Matched Comparison. *Stroke*. in press
18. Pisani, A., Bonsi, P., Centonze, D., Martorana, A., Fusco, F., Sancesario, G., De Persis, C., Bernardi, G. & Calabresi, P. (2003) Activation of beta1-adrenoceptors excites striatal cholinergic interneurons through a cAMP-dependent, protein kinase-independent pathway. *J. Neurosci.*, 23, 5272-5282.
19. Tozzi, A., Bengtson, C.P., Longone, P., Cargnani, C., Fusco, F.R., Bernardi, G., Mercuri, N.B. (2003) Involvement of transient receptor potential-like channels in responses to m-GLUR-1 activation in midbrain dopamine neurons. *European J. Neurosci* 18, 2133-2145
20. F. R. Fusco, A. Martorana, C. Giampà, Z. De March, D. Farini, V. D'Angelo, G. Sancesario and G. Bernardi (2004) Immunolocalization of CB1 receptor in rat striatal neurons: a confocal microscopy study. *Synapse*, 53, 159-167

35. Z. De March, C.Giampà, S. Patassini, G. Bernardi, F. R. Fusco (2008) Beneficial effects of Rolipram in the R6/2 mouse model of Huntington's disease. *Neurobiol Dis.* [Epub ahead of print]
36. S. Patassini, C. Giampà, A. Martorana, G. Bernardi, F.R. Fusco (2008) Effects of simvastatin on neuroprotection and modulation of Bcl-2 and BAX in the rat quinolinic acid model of Huntington's disease. *Neurosci Lett.* 2008 Dec 19;448(1):166-9. Epub 2008 Oct
37. Giampà C, Middei S, Patassini S, Borreca A, Marullo F, Laurenti D, Bernardi G, Ammassari-Teule M, Fusco FR. (2009) Phosphodiesterase type IV inhibition prevents sequestration of CREB binding protein, protects striatal parvalbumin interneurons and rescues motor deficits in the R6/2 mouse model of Huntington's disease. *Eur J Neurosci.* 2009 Mar;29(5):902-10
38. Giampà C, Patassini S, Borreca A, Laurenti D, Marullo F, Bernardi G, Menniti FS, Fusco FR. (2009) Phosphodiesterase 10 inhibition reduces striatal excitotoxicity in the quinolinic acid model of Huntington's disease. *Neurobiol Dis.* 2009 Jun;34(3):450-6
39. Massa R, Panico MB, Caldarola S, Fusco FR, Sabatelli P, Terracciano C, Botta A, Novelli G, Bernardi G, Loreni F. *Neuropathol Appl Neurobiol.* 2010 Jun;36(4):275-84. Epub 2009 Nov 20. The myotonic dystrophy type 2 (DM2) gene product zinc finger protein 9 (ZNF9) is associated with sarcomeres and normally localized in DM2 patients' muscles.
40. Fusco FR, Pompa A, Laurenti D, Giampà C, Morello M., Bernardini S, Paolucci S (2010) A Case of PANDAS treated with tetrabenazine and tonsillectomy. *J Child Neurology, J Child Neurol.* May;25(5):614-5
41. Ghiglieri V, Sgobio C, Patassini S, Bagetta V, Fejtová A, Giampà C, Marinucci S, Heyden A, Gundelfinger ED, Fusco FR, Calabresi P, Picconi B. (2010) TrkB/BDNF-dependent striatal plasticity and behavior in a genetic model of epilepsy: modulation by valproic acid. *Neuropsychopharmacology.* Jun;35(7):1531-40
42. Vincent Paille, Barbara Picconi, Vincenza Bagetta, Veronica Ghiglieri, Carmelo Sgobio, Massimiliano Di Filippo, Maria Teresa Viscomi, Carmela Giampa', Francesca Fusco, Fabrizio Gardoni, Giorgio Bernardi, Paul Greengard, Monica Di Luca, and Paolo Calabresi(2010) Distinct levels of dopamine denervation differentially alter striatal synaptic plasticity and NMDA receptor subunit composition *J Neurosci.* Oct 20;30(42):14182-93.
43. Carmela Giampà, Daunia Laurenti, Serenella Anzilotti, Giorgio Bernardi, Frank S. Menniti and Francesca R. Fusco. *PLoS One.* 2010 Oct 15;5(10):e13417 Inhibition of the Striatal Specific Phosphodiesterase PDE10A Ameliorates Striatal and Cortical Pathology in R6/2 Mouse Model of Huntington's Disease.
44. Tozzi A, de Iure A, Di Filippo M, Tantucci M, Costa C, Borsini F, Ghiglieri V, Giampà C, Fusco FR, Picconi B, Calabresi P. The distinct role of medium spiny neurons and cholinergic interneurons in the D2/A2A receptor interaction in the striatum: implications for Parkinson's disease. *J Neurosci.* 2011 Feb 2;31(5):1850-62. Picconi B, Bagetta V, Ghiglieri V, Paillé V, Di Filippo M, Pendolino V, Tozzi A, Giampà C, Fusco FR, Sgobio C, Calabresi P.(2011) Inhibition of phosphodiesterases rescues striatal long-term depression and reduces levodopa-induced dyskinesia. *Brain.* 2011 Feb;134(Pt 2):375-87

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46. Picconi B, Bagetta V, Ghiglieri V, Paillé V, Di Filippo M, Pendolino V, Tozzi A, Giampà C, Fusco FR, Sgobio C, Calabresi P. Inhibition of phosphodiesterases rescues striatal long-term depression and reduces levodopa-induced dyskinesia. *Brain*. 2011 Feb;134(Pt 2):375-87. Epub 2010 Dec 22.
47. Bagetta V, Picconi B, Marinucci S, Sgobio C, Pendolino V, Ghiglieri V, Fusco FR, Giampà C, Calabresi P. (2011) Dopamine-dependent long-term depression is expressed in striatal spiny neurons of both direct and indirect pathways: implications for Parkinson's disease *J Neurosci*. Aug 31;31(35):12513-22
48. Anzilotti S, Giampà C, Laurenti D, Perrone L, Bernardi G, Melone MA, Fusco FR. Immunohistochemical localization of receptor for advanced glycation end (RAGE) products in the R6/2 mouse model of Huntington's disease. *Brain Res Bull*. 2011 Jan 2
49. Fusco FR, Anzilotti S, Giampà C, Dato C, Leuti A, D'Amato LC, Perrone L, Bernardi G, Melone MA. Changes in the expression of extracellular regulated kinase (ERK 1/2) in the R6/2 mouse model of Huntington's disease after phosphodiesterase IV inhibition. *Neurobiol Dis*. 2012 Jan 28. [Epub ahead of print]
- 50 Di Filippo M, Chiasserini D, Gardoni F, Viviani B, Tozzi A, Giampà C, Costa C, Tantucci M, Zianni E, Boraso M, Siliquini S, de Iure A, Ghiglieri V, Colcelli E, Baker D, Sarchielli P, Fusco FR, Di Luca M, Calabresi P. Effects of central and peripheral inflammation on hippocampal synaptic plasticity. *Neurobiol Dis*. 2013 Apr;52:229-36. doi: 10.1016/j.nbd.2012.12.009. Epub 2013 Jan 4. PMID: 23295855 [PubMed - in process]
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52. Arcangeli S, Tozzi A, Tantucci M, Spaccatini C, de Iure A, Costa C, Di Filippo M, Picconi B, Giampà C, Fusco FR, Amoroso S, Calabresi P. Ischemic-LTP in striatal spiny neurons of both direct and indirect pathway requires the activation of D1-like receptors and NO/soluble guanylate cyclase/cGMP transmission. *J Cereb Blood Flow Metab*. 2013 Feb;33(2):278-86. doi: 10.1038/jcbfm.2012.167. Epub 2012 Nov 14.
53. Giampa C., Montagna E., Melone MAB, Dato C. Bernardi G., Fusco FR. Systemic delivery of recombinant Brain Derived Neurotrophic Factor (BDNF) in the R6/2 mouse model of Huntington's disease. *PLOS One* 2013, in press
54. Cardinale A, Paldino E, Giampà C, Bernardi G, Fusco FR. PLoS One. PARP-1 Inhibition Is Neuroprotective in the R6/2 Mouse Model of Huntington's Disease. 2015 Aug 7;10(8):e0134482.
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