

## **Dott. Alberto Martire CURRICULUM VITAE ET STUDIORUM.**

### STUDI UNIVERSITARI

Dicembre 2001: Laurea in Scienze Biologiche presso l'Università "La Sapienza" di Roma.

Dicembre 2009: Dottorato di ricerca in Farmacologia, presso l'Università "La Sapienza" di Roma.

### ESPERIENZE PROFESSIONALI

Marzo 2000 - Luglio 2001: tesista presso il Servizio Qualità e Sicurezza della Sperimentazione Animale dell'Istituto Superiore di Sanità sotto la supervisione del Dott. Corrado Spadafora.

Giugno 2002: conseguimento del titolo professionale di biologo mediante relativo esame di stato presso l'Università degli Studi di Viterbo.

Ottobre 2002 - Ottobre 2013: in servizio presso il Laboratorio di Farmacologia (poi Dipartimento del Farmaco) dell'Istituto Superiore di Sanità in qualità di Collaboratore Tecnico Enti di Ricerca, VI livello professionale.

Agosto 2006: ricercatore ospite presso il National Institute on Drug Abuse (National Institutes of Health, Department of Health and Human Services, Baltimore, Maryland, USA), sotto la supervisione del Dr. Sergi Ferré.

Settembre 2009: ricercatore ospite presso il Bordeaux PENS (Programme of European Neuroscience Schools) Training Center nell'ambito della Summer School "Synaptic Mechanisms and Synaptopathies".

Ottobre 2013 - Febbraio 2024: in servizio come Ricercatore di ruolo presso il reparto di Farmacologia del Sistema Nervoso Centrale del Dipartimento del Farmaco, da gennaio 2017 Centro nazionale per la ricerca e la valutazione preclinica e clinica dei farmaci (Istituto Superiore di Sanità, Roma).

Aprile 2018: ricercatore ospite presso il laboratorio di "Neurofisiologia delle malattie neurodegenerative", diretto dal Prof. Filippo Tempia (Istituto di Neuroscienze della Fondazione Cavalieri-Ottolenghi, Torino).

Da gennaio 2023: in servizio come Esperto Nazionale Distaccato (Seconded National Expert) presso la European Medicines Agency di Amsterdam.

Da marzo 2024 a oggi: in servizio come Primo ricercatore di ruolo presso il reparto di Farmacologia del Sistema Nervoso Centrale del Centro nazionale per la ricerca e la valutazione preclinica e clinica dei farmaci (Istituto Superiore di Sanità, Roma).

## POSIZIONE ATTUALE

Primo ricercatore, Reparto di Farmacologia del Sistema Nervoso Centrale, Centro nazionale per la ricerca e la valutazione preclinica e clinica dei farmaci (Istituto Superiore di Sanità, Roma).

Dal 16/01/2023 - in corso, in distacco presso European Medicines Agency (Domenico Scarlattilaan 6, 1083 HS Amsterdam, Paesi Bassi) come Esperto Nazionale Distaccato.

## LINGUE

Inglese (avanzato), Olandese (elementare), Francese (pre-intermedio).

## DESCRIZIONE DELL'ATTIVITÀ PROFESSIONALE

La carriera professionale presso l'Istituto Superiore di Sanità è stata sempre caratterizzata dalla coesistenza di ricerca sperimentale (di base, preclinica, traslazionale) e di attività istituzionale nel settore regolatorio del farmaco e nell'ambito delle scienze del benessere animale. L'attività di ricerca ha riguardato prevalentemente lo studio del potenziale terapeutico dei ligandi dei recettori A2A dell'adenosina nelle patologie del sistema nervoso centrale, con approfondimenti sulla corea di Huntington, la malattia di Niemann-Pick di tipo C e più di recente sulla sindrome dell'X Fragile.

Tale attività ha portato a un buon numero di pubblicazioni scientifiche e presentazioni a convegni, ma soprattutto alla partecipazione (come responsabile scientifico o collaboratore) a progetti di ricerca nazionali ed internazionali e allo sviluppo di numerose collaborazioni scientifiche, testimoniate anche da periodi di formazione professionale trascorsi in altre istituzioni di ricerca italiane ed estere. L'attività istituzionale ha riguardato inizialmente la formulazione di pareri sulla parte non clinica dei dossier relativi alla sperimentazione clinica di Fase I e sulla valutazione tecnico-scientifica delle richieste di autorizzazione alla sperimentazione animale. Lo sviluppo professionale è culminato con l'incarico di Esperto Nazionale Distaccato\* (Seconded National Expert) presso la European Medicines Agency di Amsterdam per lo svolgimento dei seguenti compiti: consulenza in questioni pertinenti alle neuroscienze e lo sviluppo non clinico dei farmaci; consulenza scientifica nelle procedure centralizzate di autorizzazione all'immissione in commercio relative a farmaci per malattie neurologiche e psichiatriche; coordinamento scientifico e supporto in progetti riguardanti i suddetti ambiti; partecipazione a commissioni e tavoli istituzionali a livello sovranazionale. Nel corso di tale esperienza, grazie anche ad un processo di formazione continua proposto dall'EMA, il campo di interesse e il livello di qualificazione si sono allargati a tutti gli aspetti della sperimentazione clinica, della legislazione farmaceutica europea, del *project management*, dell'applicazione dell'intelligenza artificiale in ambito regolatorio e dell'*Horizon scanning* nella ricerca.

\*Relativamente all'esperienza maturata (dal 16 gennaio 2023 – in corso, documentazione aggiuntiva disponibile su richiesta) come Esperto Nazionale Distaccato (Seconded National Expert) presso la European Medicines Agency di Amsterdam, si fa presente che la suddetta esperienza costituisce titolo di merito preferenziale ai sensi del seguente articolo di legge:

**Decreto legislativo del 30/03/2001 n. 165**

**Norme generali sull'ordinamento del lavoro alle dipendenze delle amministrazioni pubbliche.**

**Articolo 32 - Scambio di funzionari appartenenti a Paesi diversi e temporaneo servizio all'estero.**  
(Art. 33-bis del D.Lgs. n. 29 del 1993, aggiunto dall'art. 11 del D.Lgs. n. 387 del 1998)

**In vigore dal 17/08/2023**

**Modificato da: Decreto-legge del 22/06/2023 n. 75 Articolo 28 ter**

COMMA 4:

Il personale che presta servizio temporaneo all'estero resta a tutti gli effetti dipendente dell'amministrazione di appartenenza. **L'esperienza maturata all'estero costituisce titolo preferenziale** per l'accesso a posizioni economiche superiori o a progressioni orizzontali e verticali di carriera all'interno dell'amministrazione pubblica ed è adeguatamente valorizzata, se di durata almeno biennale, nei bandi di concorso per l'accesso alla dirigenza, nonché nelle procedure di conferimento di incarichi dirigenziali qualora attinenti all'esperienza stessa.

#### CAT. 1) PUBBLICAZIONI SCIENTIFICHE

Autore di 51 pubblicazioni scientifiche *peer-reviewed*

H index (Scopus): 26

Citazioni totali (Scopus): 1795

1. Mollinari C, Cardinale A, Lupacchini L, **Martire A**, Chiodi V, Martinelli A, Rinaldi AM, Fini M, Pazzaglia S, Domenici MR, Garaci E, Merlo D. The DNA repair protein DNA-PKcs modulates synaptic plasticity via PSD-95 phosphorylation and stability. EMBO Rep. 2024 Aug;25(8):3707-3737. doi: 10.1038/s44319-024-00198-3. Epub 2024 Jul 31. PMID: 39085642; PMCID: PMC11315936.
2. Di Rocco M, Galosi S, Follo FC, Lanza E, Folli V, **Martire A**, Leuzzi V, Martinelli S. Phenotypic Assessment of Pathogenic Variants in GNAO1 and Response to Caffeine in C. elegans Models of the Disease. Genes (Basel). 2023 Jan 26;14(2):319. doi: 10.3390/genes14020319. PMID: 36833246; PMCID: PMC9957173.
3. Borreca A, De Luca M, Ferrante A, Boussadia Z, Pignataro A, **Martire A**, Ammassari-Teule M. Fmr1-KO mice failure to detect object novelty associates with a post-test decrease of structural and synaptic plasticity upstream of the hippocampus. Sci Rep. 2023 Jan 14;13(1):755. doi: 10.1038/s41598-023-27991-9. PMID: 36641518; PMCID: PMC9840621.
4. Boussadia Z, Chiodi V, Pazienti A, **Martire A**. A major role for adenosine A2A receptor in the interaction between astrocytes and myelinated neurons: possible implications for the therapy of neurodegenerative disorders. Purinergic Signal. 2022 Jan 23. doi: 10.1007/s11302-021-09835-1. Epub ahead of print. PMID: 35066787.
5. Pisa E, **Martire A**, Chiodi V, Traversa A, Caputo V, Hauser J, Macrì S. Exposure to 3'Sialyllactose-Poor Milk during Lactation Impairs Cognitive Capabilities in Adulthood. Nutrients. 2021 Nov 23;13(12):4191. doi: 10.3390/nu13124191. PMID: 34959743; PMCID: PMC8707534.
6. Di Rocco M, Galosi S, Lanza E, Tosato F, Caprini D, Folli V, Friedman J, Bocchinfuso G, **Martire A**, Di Schiavi E, Leuzzi V, Martinelli S. Caenorhabditis elegans provides an

- efficient drug screening platform for GNAO1-related disorders and highlights the potential role of caffeine in controlling dyskinesia. *Hum Mol Genet.* 2021 Oct 8;ddab296. doi: 10.1093/hmg/ddab296. Epub ahead of print. PMID: 34622282.
7. Bernardo A, De Nuccio C, Visentin S, **Martire A**, Minghetti L, Popoli P, Ferrante A. Myelin Defects in Niemann-Pick Type C Disease: Mechanisms and Possible Therapeutic Perspectives. *Int J Mol Sci.* 2021 Aug 17;22(16):8858. doi: 10.3390/ijms22168858. PMID: 34445564; PMCID: PMC8396228.
  8. Hauser J, Pisa E, Arias Vásquez A, Tomasi F, Traversa A, Chiodi V, Martin FP, Sprenger N, Lukjancenko O, Zollinger A, Metairon S, Schneider N, Steiner P, **Martire A**, Caputo V, Macrì S. Sialylated human milk oligosaccharides program cognitive development through a non-genomic transmission mode. *Mol Psychiatry.* 2021 Mar 4. doi: 10.1038/s41380-021-01054-9. PMID: 33664475.
  9. **Martire A**, Pepponi R, Liguori F, Volonté C, Popoli P. P2X7 Receptor Agonist 2'(3')-O-(4-Benzoylbenzoyl)ATP Differently Modulates Cell Viability and Corticostriatal Synaptic Transmission in Experimental Models of Huntington's Disease. *Front Pharmacol.* 2021 Feb 19; 11:633861. doi: 10.3389/fphar.2020.633861. PMID: 33679392; PMCID: PMC7933594.
  10. Ferrante A, Boussadia Z, Borreca A, Mallozzi C, Pedini G, Pacini L, Pezzola A, Armida M, Vincenzi F, Varani K, Bagni C, Popoli P, **Martire A**. Adenosine A2A receptor inhibition reduces synaptic and cognitive hippocampal alterations in Fmr1 KO mice. *Transl Psychiatry.* 2021 Feb 5;11(1):112. doi: 10.1038/s41398-021-01238-5. PMID: 33547274; PMCID: PMC7864914.
  11. Ferrante A, Visentin S, De Nuccio C, **Martire A**, Popoli P. Adenosine and Adenosine A2A Receptors as Targets for the Treatment of Niemann Pick Type C Disease. *Journal of Caffeine and Adenosine Research.* Sep 2019. 98-103. <http://doi.org/10.1089/caff.2019.0014>.
  12. De Nuccio C, Bernardo A, Ferrante A, Pepponi R, **Martire A**, Falchi M, Visentin S, Popoli P, Minghetti L. Adenosine A2A receptor stimulation restores cell functions and differentiation in Niemann-Pick type C-like oligodendrocytes. *Sci Rep.* 2019 Jul 5;9(1):9782. doi: 10.1038/s41598-019-46268-8. PMID: 31278313; PMCID: PMC6611770.
  13. Domenici MR, Ferrante A, **Martire A**, Chiodi V, Pepponi R, Tebano MT, Popoli P. Adenosine A2A receptor as potential therapeutic target in neuropsychiatric disorders. *Pharmacol Res.* 2019 Sep; 147:104338. doi: 10.1016/j.phrs.2019.104338. Epub 2019 Jul 2. PMID: 31276772.
  14. **Martire A**, Lambertucci C, Pepponi R, Ferrante A, Benati N, Buccioni M, Dal Ben D, Marucci G, Klotz KN, Volpini R, Popoli P. Neuroprotective potential of adenosine A1 receptor partial agonists in experimental models of cerebral ischemia. *J Neurochem.* 2019 Apr;149(2):211-230. doi: 10.1111/jnc.14660. Epub 2019 Feb 11. PMID: 30614535.
  15. Ferrante A, Pezzola A, Matteucci A, Di Biase A, Attorri L, Armida M, **Martire A**, Chern Y, Popoli P. The adenosine A2A receptor agonist T1-11 ameliorates neurovisceral symptoms and extends the lifespan of a mouse model of Niemann-Pick type C disease. *Neurobiol Dis.* 2018 Feb; 110:1-11. doi: 10.1016/j.nbd.2017.10.013. Epub 2017 Oct 25. PMID: 29079454.
  16. Ferrante A, Tebano MT, **Martire A**, Domenici MR, Popoli P. Book Chapter: Neuronal vs Glial Cell Contribution to Adenosine A2A Receptor-Induced Neurodegeneration. In

- David Blum and Luísa V.Lopes, editors: Blum - Adenosine Receptors in Neurodegenerative Diseases, Oxford: Academic Press , 2017 , pp. 131 - 150.
17. Cilli P, Ventura I, Minoprio A, Meccia E, **Martire A**, Wilson SH, Bignami M, Mazzei F. Oxidized dNTPs and the OGG1 and MUTYH DNA glycosylases combine to induce CAG/CTG repeat instability. *Nucleic Acids Res.* 2016 Jun 20;44(11):5190-203. doi: 10.1093/nar/gkw170. Epub 2016 Mar 14. PMID: 26980281; PMCID: PMC4914090.
  18. Ferrante A, De Nuccio C, Pepponi R, Visentin S, **Martire A**, Bernardo A, Minghetti L, Popoli P. Stimulation of adenosine A2A receptors reduces intracellular cholesterol accumulation and rescues mitochondrial abnormalities in human neural cell models of Niemann-Pick C1. *Neuropharmacology.* 2016 Apr; 103:155-62. doi: 10.1016/j.neuropharm.2015.11.022. Epub 2015 Nov 26. PMID: 26631535.
  19. Popoli P, Domenici MR, **Martire A**, Tebano MT. Book Chapter: Functional Interactions of Adenosine Receptors and their Possible Implications in Central Nervous System Diseases. Chapter 13, pp. 265-294, in "Adenosine Signaling Mechanisms: Pharmacology, Functions and Therapeutic Aspects". 2015. Vickram Ramkumar and Roberto Paes de Carvalho Eds. Nova Science Publishers.
  20. De Felice A, Confaloni A, Crestini A, De Simone R, Malchiodi-Albedi F, **Martire A**, Matteucci A, Minghetti L, Popoli P, Venerosi A, Calamandrei G. Book Chapter: Branched Chain Amino Acids in Experimental Models of Amyotrophic Lateral Sclerosis, in "Branched Chain Amino Acids in Clinical Nutrition". 2015. Springer New York.
  21. Ferrante A, **Martire A**, Pepponi R, Varani K, Vincenzi F, Ferraro L, Beggiato S, Tebano MT, Popoli P. Expression, pharmacology and functional activity of adenosine A1 receptors in genetic models of Huntington's disease. *Neurobiol Dis.* 2014 Nov; 71:193-204. doi: 10.1016/j.nbd.2014.08.013. Epub 2014 Aug 15. PMID: 25132555.
  22. De Luca G, Ventura I, Sanghez V, Russo MT, Ajmone-Cat MA, Cacci E, **Martire A**, Popoli P, Falcone G, Michelini F, Crescenzi M, Degan P, Minghetti L, Bignami M, Calamandrei G. Prolonged lifespan with enhanced exploratory behavior in mice overexpressing the oxidized nucleoside triphosphatase hMTH1. *Aging Cell.* 2013 Aug;12(4):695-705. doi: 10.1111/accel.12094. Epub 2013 May 30. PMID: 23648059.
  23. **Martire A**, Pepponi R, Domenici MR, Ferrante A, Chiodi V, Popoli P. BDNF prevents NMDA-induced toxicity in models of Huntington's disease: the effects are genotype specific and adenosine A2A receptor is involved. *J Neurochem.* 2013 Apr;125(2):225-35. doi: 10.1111/jnc.12177. Epub 2013 Feb 27. PMID: 23363456.
  24. Blum D, **Martire A**, Burnouf S, Sablonnière B, Krystkowiak P, Ledent C, Lopes LV, Popoli P. Book Chapter: Adenosine receptors in Huntington's disease. Chapter 20 in "Adenosine: a Key Link between Metabolism and CNS Activity". 2013. Masino & Boison Eds. Springer.
  25. Scattoni ML, **Martire A**, Cartocci G, Ferrante A, Ricceri L. Reduced social interaction, behavioural flexibility and BDNF signalling in the BTBR T+ tf/J strain, a mouse model of autism. *Behav Brain Res.* 2013 Aug 15; 251:35-40. doi: 10.1016/j.bbr.2012.12.028. Epub 2012 Dec 25. PMID: 23270976.
  26. Burnouf S, **Martire A**, Derisbourg M, Laurent C, Belarbi K, Leboucher A, Fernandez-Gomez FJ, Troquier L, Eddarkaoui S, Grosjean ME, Demeyer D, Muhr-Tailleux A, Buisson A, Sergeant N, Hamdane M, Humez S, Popoli P, Buée L, Blum D. NMDA receptor dysfunction contributes to impaired brain-derived neurotrophic factor-induced facilitation of hippocampal synaptic transmission in a Tau transgenic model.

- Aging Cell. 2013 Feb;12(1):11-23. doi: 10.1111/accel.12018. Epub 2012 Nov 23. PMID: 23082852.
27. Tebano MT, **Martire A**, Popoli P. Adenosine A(2A)-cannabinoid CB(1) receptor interaction: an integrative mechanism in striatal glutamatergic neurotransmission. *Brain Res.* 2012 Oct 2;1476:108-18. doi: 10.1016/j.brainres.2012.04.051. Epub 2012 May 4. PMID: 22565012.
  28. Chiodi V, Uchigashima M, Beggiato S, Ferrante A, Armida M, **Martire A**, Potenza RL, Ferraro L, Tanganelli S, Watanabe M, Domenici MR, Popoli P. Unbalance of CB1 receptors expressed in GABAergic and glutamatergic neurons in a transgenic mouse model of Huntington's disease. *Neurobiol Dis.* 2012 Mar;45(3):983-91. doi: 10.1016/j.nbd.2011.12.017. Epub 2011 Dec 23. PMID: 22207189.
  29. Venerosi A, **Martire A**, Rungi A, Pieri M, Ferrante A, Zona C, Popoli P, Calamandrei G. Complex behavioral and synaptic effects of dietary branched chain amino acids in a mouse model of amyotrophic lateral sclerosis. *Mol Nutr Food Res.* 2011 Apr; 55(4):541-52. doi: 10.1002/mnfr.201000296. Epub 2011 Jan 5. PMID: 21462321.
  30. **Martire A**, Tebano MT, Chiodi V, Ferreira SG, Cunha RA, Köfalvi A, Popoli P. Pre-synaptic adenosine A2A receptors control cannabinoid CB1 receptor-mediated inhibition of striatal glutamatergic neurotransmission. *J Neurochem.* 2011 Jan; 116(2):273-80. doi: 10.1111/j.1471-4159.2010.07101.x. Epub 2010 Dec 2. PMID: 21062287.
  31. Tebano MT, **Martire A**, Chiodi V, Ferrante A, Popoli P. Role of adenosine A(2A) receptors in modulating synaptic functions and brain levels of BDNF: a possible key mechanism in the pathophysiology of Huntington's disease. *ScientificWorldJournal.* 2010 Sep 1; 10:1768-82. doi: 10.1100/tsw.2010.164. PMID: 20842321; PMCID: PMC5763899.
  32. Ferrante A, **Martire A**, Armida M, Chiodi V, Pézzola A, Potenza RL, Domenici MR, Popoli P. Influence of CGS 21680, a selective adenosine A(2A) receptor agonist, on NMDA receptor function and expression in the brain of Huntington's disease mice. *Brain Res.* 2010 Apr 6; 1323:184-91. doi: 10.1016/j.brainres.2010.01.080. Epub 2010 Feb 4. PMID: 20138162.
  33. **Martire A**, Ferrante A, Potenza RL, Armida M, Ferretti R, Pézzola A, Domenici MR, Popoli P. Remodeling of striatal NMDA receptors by chronic A(2A) receptor blockade in Huntington's disease mice. *Neurobiol Dis.* 2010 Jan;37(1):99-105. doi: 10.1016/j.nbd.2009.09.012. Epub 2009 Oct 3. PMID: 19804830.
  34. Tebano MT, **Martire A**, Chiodi V, Pepponi R, Ferrante A, Domenici MR, Frank C, Chen JF, Ledent C, Popoli P. Adenosine A2A receptors enable the synaptic effects of cannabinoid CB1 receptors in the rodent striatum. *J Neurochem.* 2009 Sep; 110(6):1921-30. doi: 10.1111/j.1471-4159.2009.06282.x. Epub 2009 Jul 17. PMID: 19627447.
  35. Pepponi R, Ferrante A, Ferretti R, **Martire A**, Popoli P. Region-specific neuroprotective effect of ZM 241385 towards glutamate uptake inhibition in cultured neurons. *Eur J Pharmacol.* 2009 Sep 1;617(1-3):28-32. doi: 10.1016/j.ejphar.2009.07.016. Epub 2009 Jul 18. PMID: 19619523.
  36. Tebano MT, **Martire A**, Pepponi R, Domenici MR, Popoli P. Is the functional interaction between adenosine A(2A) receptors and metabotropic glutamate 5 receptors a general mechanism in the brain? Differences and similarities between the striatum and the hippocampus. *Purinergic Signal.* 2006 Nov; 2(4):619-25. doi:

- 10.1007/s11302-006-9026-y. Epub 2006 Sep 28. PMID: 18404464; PMCID: PMC2096652.
37. Potenza RL, Tebano MT, **Martire A**, Domenici MR, Pepponi R, Armida M, Pèzzola A, Minghetti L, Popoli P. Adenosine A(2A) receptors modulate BDNF both in normal conditions and in experimental models of Huntington's disease. *Purinergic Signal*. 2007 Sep; 3(4):333-8. doi: 10.1007/s11302-007-9066-y. Epub 2007 Sep 15. PMID: 18404446; PMCID: PMC2072926.
  38. Tebano MT, **Martire A**, Potenza RL, Grò C, Pepponi R, Armida M, Domenici MR, Schwarzschild MA, Chen JF, Popoli P. Adenosine A(2A) receptors are required for normal BDNF levels and BDNF-induced potentiation of synaptic transmission in the mouse hippocampus. *J Neurochem*. 2008 Jan; 104(1):279-86. doi: 10.1111/j.1471-4159.2007.05046.x. Epub 2007 Nov 14. PMID: 18005343.
  39. Popoli P, Pepponi R, **Martire A**, Armida M, Pèzzola A, Galluzzo M, Domenici MR, Potenza RL, Tebano MT, Mollinari C, Merlo D, Garaci E. Neuroprotective effects of thymosin beta4 in experimental models of excitotoxicity. *Ann N Y Acad Sci*. 2007 Sep; 1112:219-24. doi: 10.1196/annals.1415.033. PMID: 17947590.
  40. Domenici MR, Scattoni ML, **Martire A**, Lastoria G, Potenza RL, Borioni A, Venerosi A, Calamandrei G, Popoli P. Behavioral and electrophysiological effects of the adenosine A2A receptor antagonist SCH 58261 in R6/2 Huntington's disease mice. *Neurobiol Dis*. 2007 Nov;28(2):197-205. doi: 10.1016/j.nbd.2007.07.009. Epub 2007 Jul 24. PMID: 17720507.
  41. Bisogno T, **Martire A**, Petrosino S, Popoli P, Di Marzo V. Symptom-related changes of endocannabinoid and palmitoylethanolamide levels in brain areas of R6/2 mice, a transgenic model of Huntington's disease. *Neurochem Int*. 2008 Jan;52(1-2):307-13. doi: 10.1016/j.neuint.2007.06.031. Epub 2007 Jul 4. PMID: 17664017.
  42. **Martire A**, Calamandrei G, Felici F, Scattoni ML, Lastoria G, Domenici MR, Tebano MT, Popoli P. Opposite effects of the A2A receptor agonist CGS21680 in the striatum of Huntington's disease versus wild-type mice. *Neurosci Lett*. 2007 Apr 24;417(1):78-83. doi: 10.1016/j.neulet.2007.02.034. Epub 2007 Feb 14. PMID: 17331645.
  43. Popoli P, Blum D, **Martire A**, Ledent C, Ceruti S, Abbracchio MP. Functions, dysfunctions and possible therapeutic relevance of adenosine A2A receptors in Huntington's disease. *Prog Neurobiol*. 2007 Apr;81(5-6):331-48. doi: 10.1016/j.pneurobio.2006.12.005. Epub 2007 Jan 9. PMID: 17303312.
  44. Mallozzi C, **Martire A**, Domenici MR, Metere A, Popoli P, Di Stasi AM. L-NAME reverses quinolinic acid-induced toxicity in rat corticostriatal slices: Involvement of src family kinases. *J Neurosci Res*. 2007 Sep;85(12):2770-7. doi: 10.1002/jnr.21178. PMID: 17265464.
  45. Pintor A, Tebano MT, **Martire A**, Grieco R, Galluzzo M, Scattoni ML, Pèzzola A, Coccurello R, Felici F, Cuomo V, Piomelli D, Calamandrei G, Popoli P. The cannabinoid receptor agonist WIN 55,212-2 attenuates the effects induced by quinolinic acid in the rat striatum. *Neuropharmacology*. 2006 Oct;51(5):1004-12. doi: 10.1016/j.neuropharm.2006.06.013. Epub 2006 Aug 8. PMID: 16895732.
  46. Tebano MT, **Martire A**, Rebola N, Pepponi R, Domenici MR, Grò MC, Schwarzschild MA, Chen JF, Cunha RA, Popoli P. Adenosine A2A receptors and metabotropic glutamate 5 receptors are co-localized and functionally interact in the hippocampus: a possible key mechanism in the modulation of N-methyl-D-aspartate effects. *J Neurochem*. 2005 Nov;95(4):1188-200. doi: 10.1111/j.1471-4159.2005.03455.x. PMID: 16271052.

47. Domenici MR, Potenza RL, **Martire A**, Coccurello R, Pèzzola A, Reggio R, Tebano MT, Popoli P. Chronic treatment with the mGlu5R antagonist MPEP reduces the functional effects of the mGlu5R agonist CHPG in the striatum of 6-hydroxydopamine-lesioned rats: possible relevance to the effects of mGlu5R blockade in Parkinson's disease. *J Neurosci Res*. 2005 Jun 1;80(5):646-54. doi: 10.1002/jnr.20489. PMID: 15880742.
48. Domenici MR, Pepponi R, **Martire A**, Tebano MT, Potenza RL, Popoli P. Permissive role of adenosine A2A receptors on metabotropic glutamate receptor 5 (mGluR5)-mediated effects in the striatum. *J Neurochem*. 2004 Sep;90(5):1276-9. doi: 10.1111/j.1471-4159.2004.02607.x. PMID: 15312183.
49. Tebano MT, Pintor A, Frank C, Domenici MR, **Martire A**, Pepponi R, Potenza RL, Grieco R, Popoli P. Adenosine A2A receptor blockade differentially influences excitotoxic mechanisms at pre- and postsynaptic sites in the rat striatum. *J Neurosci Res*. 2004 Jul 1;77(1):100-7. doi: 10.1002/jnr.20138. PMID: 15197743.
50. Popoli P, Pintor A, Tebano MT, Frank C, Pepponi R, Nazzicone V, Grieco R, Pèzzola A, Reggio R, Minghetti L, De Berardinis MA, **Martire A**, Potenza RL, Domenici MR, Massotti M. Neuroprotective effects of the mGlu5R antagonist MPEP towards quinolinic acid-induced striatal toxicity: involvement of pre- and post-synaptic mechanisms and lack of direct NMDA blocking activity. *J Neurochem*. 2004 Jun;89(6):1479-89. doi: 10.1111/j.1471-4159.2004.02448.x. PMID: 15189351.
51. Sciamanna I, Barberi L, **Martire A**, Pittoggi C, Beraldi R, Giordano R, Magnano AR, Hogdson C, Spadafora C. Sperm endogenous reverse transcriptase as mediator of new genetic information. *Biochem Biophys Res Commun*. 2003 Dec 26;312(4):1039-46. doi: 10.1016/j.bbrc.2003.11.024. PMID: 14651976.

## CAT. 2: ATTIVITA' ISTITUZIONALE

### **Attività istituzionale svolta come ricercatore/primo ricercatore presso l'Istituto Superiore di Sanità.**

Formulazione di pareri su:

sezione non clinica dei dossier relativi alla sperimentazione clinica di Fase I (ai sensi del DPR 439/2001, del D.lvo 211/2003, del D.lvo 200/2007 e della legge 8.11.2012 n.189 e DM 27.04.2015), n= 43 tra marzo 2017 e novembre 2022;

sezione non clinica dei dossier relativi a procedure centralizzate EMA (n=1);

valutazione tecnico-scientifica delle richieste di autorizzazione alla sperimentazione animale (n=61 tra febbraio 2014 e agosto 2021).

### **Nomine come ricercatore/primo ricercatore presso l'Istituto Superiore di Sanità.**

Nomina AIFA come esperto europeo che fornisce competenza scientifica alle attività dell'EMA:

[https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-experts?f%5B0%5D=ema\\_expert\\_full\\_name%3Aalberto%20martire](https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-experts?f%5B0%5D=ema_expert_full_name%3Aalberto%20martire)

Nomina come esperto scientifico di area tematica (Farmacologia) dell'Organismo Preposto per il Benessere Animale (OPBA) dell'Istituto Superiore di Sanità.

**Attività istituzionale svolta come Esperto Nazionale Distaccato (Seconded National Expert) presso la European Medicines Agency di Amsterdam (dal 16 gennaio 2023 – in corso).**

Gestione e valutazione come *Product Lead/Procedure Manager* di procedure centralizzate EMA relative a farmaci (chimici, biologici, biotecnologici, ATMP) con indicazione nell'ambito delle malattie neurologiche e psichiatriche e con partecipazione attiva alle sedute periodiche dei comitati scientifici EMA (CHMP, PRAC, COMP, CAT):

Type II variation n. 15

PSUSA n. 10

Line extension n. 2

Renewal n. 2

PAM n. 1

Initial Marketing Authorisation n. 10

**Ruoli di responsabilità ricoperti presso EMA:**

Scientific coordinator dell'Opioids Task Force (TF): questo progetto consiste nel supportare/potenziare una TF sugli oppioidi in grado a sua volta di a) coordinare la rete di regolamentazione dell'UE in materia, b) collaborare con gli altri organismi dell'UE coinvolti in iniziative pertinenti al tema e c) supportare i comitati EMA sugli argomenti riguardanti l'uso, l'abuso, l'overdose e la dipendenza da oppioidi.

Non clinical assessor per PRIME priority medicines: PRIME è un programma gestito dall'EMA per migliorare il supporto allo sviluppo di medicinali che mirano a risolvere un bisogno medico insoddisfatto. Questo programma volontario si basa su un dialogo tempestivo con gli sviluppatori di medicinali promettenti, al fine di ottimizzare i piani di sviluppo e accelerare la valutazione in modo che questi medicinali possano raggiungere il prima possibile i pazienti.

Non clinical assessor per ITF briefing meetings: le riunioni informative dell'Innovation Task Force (ITF) offrono agli sviluppatori di medicinali innovativi un forum per un dialogo precoce con l'EMA. Gli esperti assistono gli sviluppatori nella decisione sui passaggi successivi nei loro programmi di sviluppo. Le riunioni informative dell'ITF riguardano consultazioni normative, tecniche e scientifiche riguardanti medicinali, tecnologie e metodologie innovative in una fase precoce del loro sviluppo; consentono lo scambio informale di informazioni e indicazioni nel processo di sviluppo, integrando le procedure formali EMA già esistenti; sono rivolte a tutti i tipi di sviluppatori, inclusi ricercatori accademici, micro, piccole e medie imprese (PMI) e grandi aziende farmaceutiche.

Scientific coordinator del Neuroscience EMA/FDA cluster: lo scopo del progetto è stato l'istituzione di una collaborazione permanente EMA-FDA nell'ambito delle neuroscienze e delle terapie per disturbi neurologici e psichiatrici. L'obiettivo principale di questo cluster è quello di rafforzare la

collaborazione già in atto tra l'ufficio H-TA-NEU presso l'EMA e la Divisione di psichiatria/Ufficio di neuroscienze nel Centro per la valutazione e la ricerca sui farmaci della FDA.

**Nomine come Esperto Nazionale Distaccato (Seconded National Expert) presso la European Medicines Agency di Amsterdam (dal 16 gennaio 2023 – in corso).**

Membro, come Esperto Nazionale Distaccato presso l'European Medicines Agency, dell'European Rare Diseases Research Alliance (ERDERA) Regulatory Support Group (RSG), come esperto di non clinica.

Membro, come Esperto Nazionale Distaccato presso l'European Medicines Agency, dell'EMA Pharmacogenomics Community: gli scopi di questo gruppo di lavoro sono i seguenti, 1) coordinare le competenze nel campo della farmacogenomica, 2) promuovere un forum per la condivisione delle conoscenze in materia di farmacogenomica a supporto del personale dell'EMA, 3) mantenere, condividere e sviluppare le conoscenze relative alla farmacogenomica traslazionale e clinica all'interno dell'Agenzia, 4) attività di supporto alla stesura di linee guida nel seguente ambito: non clinical/clinical genomic biomarkers qualification (inclusi biomarker epigenetici, ad esempio basi del DNA modificate/epigenetic marks come 5-metilcitosina).

Membro, come Esperto Nazionale Distaccato presso l'European Medicines Agency, (esperto di non clinica) del gruppo interno EMA per la classificazione/certificazione degli advanced therapies medicinal products (ATMP): il Comitato per le terapie avanzate (CAT) dell'EMA offre una procedura di certificazione per i medicinali per terapie avanzate (ATMP) in fase di sviluppo da parte di micro, piccole e medie imprese (PMI). La procedura di certificazione prevede la valutazione scientifica dei dati di qualità e, quando disponibili, dei dati non clinici che le PMI hanno generato in qualsiasi fase del processo di sviluppo dell'ATMP.

**Le responsabilità scientifiche di progetto sono elencate e descritte nella categoria 4.**

**CAT. 3) ESPERIENZA MANAGERIALE**

L'esperienza manageriale è maturata nell'ambito delle responsabilità scientifiche dei progetti (bandi competitivi, nazionali ed internazionali; si veda l'apposita categoria 4 di seguito nel presente documento) finanziati da committenti italiani ed esteri. Le attività sono state svolte in autonomia di gestione e con la diretta responsabilità delle risorse umane, tecniche o finanziarie (stipula di contratti per il personale, gestione acquisti apparecchiature e materiale consumabile) e della relativa rendicontazione (documentazione disponibile su richiesta). I risultati conseguiti sono rappresentati dalle pubblicazioni scientifiche relative alle tematiche oggetto di finanziamento (Niemann-Pick type C disease e Sindrome dell'X Fragile), dall'intensificazione delle collaborazioni scientifiche nazionali ed estere, testimoniate dalle numerose *authorship* presenti nei lavori non riconducibili all'ente di appartenenza, e dalla conseguente promozione della dimensione internazionale delle attività di ricerca. La capacità di acquisire fondi è supportata dai finanziamenti ottenuti come ricercatore esclusivamente tramite bandi competitivi *peer reviewed*, soprattutto internazionali, nell'arco temporale 2013-2023 (per i dettagli documentazione disponibile su richiesta).

L'aver svolto contemporaneamente attività istituzionale come ricercatore/primo ricercatore presso l'Istituto Superiore di Sanità (si veda categoria 2) mi ha consentito di acquisire le competenze relative alla legislazione farmaceutica nazionale ed europea; la conoscenza di tali aspetti normativi è indispensabile per dirigere le attività regolatorie del CNRVF e fondamentale per poter orientare le attività sperimentali del Centro verso approcci più applicativi di ricerca preclinica e traslazionale. Ho potuto constatare che proprio l'expertise misto (scientifico/regolatorio) che il CNRVF fornisce al suo personale è estremamente apprezzato nei consessi internazionali come l'EMA e le altre agenzie europee (ad esempio l'EUDA, European Union Drugs Agency).

Le capacità manageriali richieste dal presente bando sono state ulteriormente sviluppate nel corso della mia esperienza professionale internazionale presso l'EMA come Esperto Nazionale Distaccato (dal 16 gennaio 2023, in corso) grazie alle attività di coordinamento scientifico di gruppi di lavoro, *task force*, *cluster* (riportate nella categoria 2). Inoltre, la formazione continua all'EMA ha previsto anche lo svolgimento di *training* appositi per il *project management*, in particolare del corso *P3i (people, process, and product) Project governance*:

Obiettivo del corso: questo modulo fornisce una visione completa di come gestire programmi e progetti, coprendo i seguenti argomenti:

- Principi di *governance* dei progetti
- Ambiente P3i
- Conformità alla legislazione
- Disposizioni di *governance*
- *Reporting ed escalation*

La formazione continua ha riguardato inoltre argomenti la cui conoscenza è di primaria importanza per la gestione di strutture complesse di ricerca e attività istituzionale come quelle dell'ISS. Per fare alcuni esempi: protezione dei dati, cybersecurity, gestione della divulgazione involontaria di informazioni confidenziali e dati personali, gestione delle richieste di accesso agli atti, gestione del conflitto di interessi, codice di condotta del personale, salute e sicurezza del personale, *real world evidence*, statistica dei trial clinici, tossicologia (documentazione disponibile su richiesta). Infine, l'esperienza presso l'EMA mi ha consentito di sviluppare un network di interazioni professionali, sia con staff interno che delle *National Competent Authorities* regolatorie, potenzialmente utile per promuovere la dimensione internazionale delle attività di ricerca e istituzionali del Centro.

#### CAT. 4) TITOLI FORMATIVI E PROFESSIONALI, QUALI DOTTORATI DI RICERCA, SPECIALIZZAZIONI, INCARICHI DI RESPONSABILITÀ NELLA GESTIONE DI STRUTTURE, INCARICHI DI RESPONSABILITÀ DI PROGETTI, INCARICHI UNIVERSITARI, DOCENZE IN CORSI ISTITUZIONALI

##### **Dottorato**

Dottorato di ricerca in Farmacologia (XXI ciclo), conseguito il 17 dicembre 2009 presso l'Università "La Sapienza" di Roma; Relatori: Prof.ssa Daniela Melchiorri, Prof. Ferdinando Nicoletti. Titolo della

tesi: "Effetti dell'antagonista dei recettori A2A dell'adenosina SCH58261 sulle subunità dei recettori NMDA striatali in un modello animale di Corea di Huntington".

### **Riconoscimenti in ambito nazionale ed internazionale**

Aprile 2017: "*invited researcher*" all' evento FENS "The Brain Conference, Learning, Memory and Synaptic Plasticity", Rungsted Kyst - North Copenhagen, Denmark.

Ottobre 2017: "*invited researcher*" all'edizione 2017 di "TWIST Training at Lisbon Addictions 2017", Lisbona, Portogallo.

Da gennaio 2023: Esperto Nazionale Distaccato (Seconded National Expert) presso la European Medicines Agency di Amsterdam (ruoli di responsabilità ricoperti: Scientific coordinator dell'Opioids Task Force (TF), Nonclinical assessor per PRIME priority medicines, Nonclinical assessor per ITF briefing meetings, Scientific coordinator del Neuroscience EMA/FDA cluster).

### **Responsabilità scientifiche di progetto**

Dal gennaio 2014: responsabile scientifico del seguente progetto: GR-2011-02348150 "Adenosine A2A receptors as a possible therapeutic target in Niemann-Pick type C disease" (Finanziamento Giovani Ricercatori di Euro 342.000,00 dal Ministero della Salute per gli anni 2014-2015-2016).

Dall'ottobre 2018: responsabile scientifico del seguente progetto: "Characterization of Adenosine Receptors in a Mouse Model of Fragile X Syndrome" (contributo di 90.000,00 USD dalla FRAXA Research Foundation per il 2018-2019). <https://www.fraxa.org/coffee-tea-and-chocolate-adenosine-receptors-in-fragile-x/>

Dall'ottobre 2021: collaboratore nel seguente progetto: "Characterization of microglia transcriptional profile in fmr1ko mice model"; FRAXA Research Foundation; 2021-2023.

Da luglio 2021: responsabile scientifico del seguente progetto: "Exosomes as a source of Therapeutical Biomarkers in Experimental Models of Fragile X Syndrome"; finanziamento intramurale ISS; 2020-2022.

Dall'ottobre 2022: responsabile scientifico del seguente progetto: "Exosomes as a source of Therapeutical Biomarkers in Experimental Models of Fragile X Syndrome " (contributo di 100.000,00 USD dalla FRAXA Research Foundation per il 2023-2024). <https://www.fraxa.org/using-exosomes-to-discover-fragile-x-biomarkers/>

Responsabilità scientifica di protocolli per la sperimentazione animale come da funzioni di cui all'ARTICOLO 1, COMMA 1, LETT. A), C) E D) DEL D.M. 5 AGOSTO 2021.

### **Responsabilità di accordi di collaborazione**

Responsabile scientifico del seguente accordo di collaborazione ISS - Associazione Italiana X Fragile (AIXF): "Studio del potenziale terapeutico degli antagonisti del recettore A2A dell'adenosina nella sindrome dell'X Fragile".

Responsabile scientifico del seguente accordo di collaborazione ISS - Istituto di Neuroscienze del Consiglio Nazionale delle Ricerche: "Characterization of microglia transcriptional profile in fmr 1 ko mice model".

Responsabile scientifico del seguente accordo di collaborazione ISS - Dipartimento di Scienze della Vita e dell'Ambiente (DISVA) dell'UNIVPM per attività di ricerca congiunta: "Characterization of a novel CYFIP1-derived peptidomimetic restoring the dysregulated mRNAs translation: toward an innovative therapeutic strategy for FXS".

Responsabile scientifico del seguente accordo di collaborazione ISS - Dipartimento di Scienze della Vita e dell'Ambiente (DISVA) dell'UNIVPM per svolgimento di dottorato di ricerca presso ISS: "Characterization of a novel CYFIP1-derived peptidomimetic restoring the dysregulated mRNAs translation: toward an innovative therapeutic strategy for FXS" e "Exosomes as a source of therapeutic biomarkers in experimental models of Fragile Syndrome".

### **Curatore di tesi**

Titolo della tesi: "Il potenziale neuroprotettivo di agonisti parziali del recettore A1 dell'adenosina in modelli sperimentali di ischemia cerebrale". Relatore interno: Prof. Luca Ferraro. Relatore esterno: Dott. Alberto Martire. Data discussione: 07 marzo 2016. Durata tirocinio tesi: Gennaio 2015 – Febbraio 2016. Committente: UNIVERSITA' DEGLI STUDI DI FERRARA.

### **Abilitazione professionale**

Conseguimento, nel giugno 2002 e mediante esame di stato, del titolo professionale di biologo, presso l'Università degli Studi di Viterbo.

### **Referee per la valutazione di progetti**

Referaggio del progetto "The role of Nrf2 in endogenous neuroprotection of ischemia-resistant region of hippocampus", proposto all'agenzia governativa polacca National Science Centre (Narodowe Centrum Nauki - NCN; <http://www.ncn.gov.pl>).

### **Relatore in convegni e workshop**

Relatore all'8° International Symposium on Adenosine and Adenine Nucleotides, tenutosi a Ferrara dal 24 al 28 maggio 2006. Titolo: "Opposite effects of the A2A receptor agonist CGS21680 in the striatum of Huntington's disease (HD) versus wild-type mice".

Relatore al 34 Congresso Nazionale Società Italiana Farmacologia tenutosi a Rimini dal 14 al 17 ottobre 2009. Titolo: "Remodelling of striatal NMDA receptors by chronic A2a receptor activation or blockade in Huntington's disease mice".

Relatore al Congresso "5th Joint Italian-German Purine Club Meeting - Fostering translational research on Purines by Italian-German joint efforts" tenutosi a Rimini dal 19 al 20 settembre 2013. Titolo: "Potential therapeutic targets for Huntington's Disease: focus on adenosine A1 receptors".

Relatore alla “Riunione annuale del Purine Club Italiano”, Roma, Istituto Superiore di Sanità, 15 gennaio 2016. Titolo: “Neuroprotective potential of adenosine A1R partial agonists in ex vivo and in vitro experimental models of ischemia”.

Relatore all’Assemblea annuale dei soci della Associazione Italiana Sindrome X Fragile, Roma, 13 aprile 2019, Università Cattolica del Sacro Cuore. Presentazione dei dati relativi al progetto finanziato da FRAXA Research Foundation e dall’Associazione Italiana Sindrome X Fragile (Characterization of Adenosine Receptors in a Mouse Model of Fragile X Syndrome);

Relatore al “19th International Workshop on Fragile X and other Neurodevelopmental Disorders”, Sorrento (NA), 18-21 Settembre 2019. Titolo: “Adenosine A2A receptor inhibition reverses synaptic and behavioral abnormalities in Fmr1 KO mice.”

Relatore al “XVIII Congresso Nazionale SINS”, Perugia, 28 settembre 2019. Titolo “Potential therapeutic role of adenosine A2A receptors in Central Nervous System disorders”.

Relatore al “39° Congresso Nazionale della Società Italiana di Farmacologia”, Firenze, 20-23 Novembre 2019. Titolo “Potential therapeutic role of adenosine A2A receptors in a mouse model of Fragile X Syndrome”.

Presentazione alla riunione della CNS Community dell’EMA, 8 dicembre 2023. Titolo: “Huntington disease: state of the art of the research on molecular pathogenesis and experimental models”.

Presentazione allo Scientific Coordination Board (SciCoBo) dell’EMA, 6 maggio 2024. Titolo: “Opioid Task Force: mandate and workplan”.

Presentazione alla seduta plenaria del CMDh (Coordination Group for Mutual Recognition and Decentralised Procedures – Human) dell’EMA, 28 maggio 2024. Titolo: “Opioid Task Force: mandate and workplan”.

### **Referee per la valutazione di pubblicazioni scientifiche**

*Referee per:*

*European Journal of Pharmacology*

*Neuroscience and Biobehavioral Reviews*

*Neuroscience*

*Brain Research Bulletin*

*British Journal of Pharmacology*

*Journal of Neuroscience Research*

*Molecular Neurobiology*

*Journal of Neurochemistry*

*Neurobiology of disease*

Roma,

firma  
Alberto Martire

**Autorizzo il trattamento dei miei dati personali presenti nel cv e nell'elenco dei titoli ai sensi dell'art. 13 del Decreto Legislativo 30 giugno 2003, n. 196 "Codice in materia di protezione dei dati personali" e dell'art. 13 del GDPR (Regolamento UE 2016/679).**

Roma,

firma  
Alberto Martire

**Dr. Alberto Martire CURRICULUM VITAE ET STUDIORUM.**

**EDUCATION**

December 2001: Degree in Biological Sciences at the University “La Sapienza” of Rome.

December 2009: PhD in Pharmacology, at the University “La Sapienza” of Rome.

**WORK EXPERIENCE AND TRAINING**

March 2000 - July 2001: thesis training at the Quality and Safety Service for Animal Experimentation of the Istituto Superiore di Sanità under the supervision of Dr. Corrado Spadafora.

June 2002: achievement of the professional title of biologist through the relevant exam at the University of Viterbo.

October 2002 - October 2013: in service at the Laboratory of Pharmacology of the Istituto Superiore di Sanità as a Technical Collaborator for Research Institutions, VI professional level.

August 2006: guest researcher at the National Institute on Drug Abuse (National Institutes of Health, Department of Health and Human Services, Baltimore, Maryland, USA), under the supervision of Dr. Sergi Ferré.

September 2009: visiting researcher at the Bordeaux PENS (Programme of European Neuroscience Schools) Training Center as part of the Summer School “Synaptic Mechanisms and Synaptopathies”.

October 2013 - February 2024: in service as a Researcher at the Central Nervous System Pharmacology Section of the National Centre for Drug Research and Evaluation (Istituto Superiore di Sanità, Rome).

April 2018: visiting researcher at the Laboratory of “Neurophysiology of Neurodegenerative Diseases”, directed by Prof. Filippo Tempia (Institute of Neuroscience of the Cavalieri-Ottolenghi Foundation, Turin).

January 2023 - onwards: in service as a Seconded National Expert at the European Medicines Agency in Amsterdam.

March 2024 - onwards: in service as Senior Researcher at the Central Nervous System Pharmacology Section of the National Centre for Drug Research and Evaluation (Istituto Superiore di Sanità, Rome).

## CURRENT POSITION

Senior Researcher at the Central Nervous System Pharmacology Section of the National Centre for Drug Research and Evaluation (Istituto Superiore di Sanità, Rome).

From 16/01/2023 - ongoing, on secondment to the European Medicines Agency (Domenico Scarlattilaan 6, 1083 HS Amsterdam, The Netherlands) as Seconded National Expert.

## LINGUISTIC SKILLS

English (advanced), Dutch (elementary), French (pre-intermediate).

## PROFESSIONAL DEVELOPMENT

My professional career at the Istituto Superiore di Sanità has always been characterized by the coexistence of experimental research (basic, preclinical, translational) and institutional activity in the drug regulatory sector and in the field of animal welfare sciences. My research activity has mainly concerned the study of the therapeutic potential of adenosine A2A receptor ligands in central nervous system diseases, with in-depth studies on Huntington's disease, Niemann-Pick type C disease and more recently on Fragile X syndrome. This activity has led to a good number of scientific publications and presentations at meetings, but above all to participation (as principal investigator or collaborator) in national and international research projects and to the development of several scientific collaborations, also supported by periods of professional training spent in other Italian and foreign research institutions. The institutional activity initially concerned the formulation of opinions on the non-clinical section of the dossiers relating to Phase I clinical trials and on the technical-scientific evaluation of requests for authorization to animal testing. The professional development culminated with the appointment as Seconded National Expert\* at the European Medicines Agency in Amsterdam for the following tasks: consultancy on issues pertaining to neuroscience and non-clinical drug development; scientific consultancy in centralized marketing authorization procedures relating to drugs for neurological and psychiatric diseases; scientific coordination and support in projects relating to the aforementioned areas; participation in institutional committees at European level. During this experience, thanks to a continuous training process proposed by the EMA, the field of interest and the level of qualification have expanded to all the aspects of clinical trials, European pharmaceutical legislation, project management, the application of artificial intelligence in the regulatory field and Horizon scanning in research.

\*Regarding the experience gained (from 16 January 2023 – ongoing, additional documentation available upon request) as Seconded National Expert at the European Medicines Agency in Amsterdam, it should be noted that the experience constitutes a preferential qualification in public competitions pursuant to the following article of law:

**Legislative Decree of 03/30/2001 n. 165**

**General rules on the organization of work for public administration employees.**

**Published in the Official Journal n. 106 of 05/09/2001 - ordinary supplement**

**Article 32 - Exchange of officials belonging to different countries and temporary service abroad. (Article 33-bis of Legislative Decree n. 29 of 1993, added by art. 11 of Legislative Decree n. 387 of 1998)**

**In force from 08/17/2023**

**Amended by: Legislative Decree of 06/22/2023 n. 75 Article 28 ter**

PARAGRAPH 4:

Personnel who provide temporary service abroad remain in all respects employees of the administration to which they belong. Experience gained abroad constitutes a preferential qualification for access to higher economic positions or to horizontal and vertical career progressions within the public administration and is adequately valued, if of at least two years' duration, in competition notices for access to management, as well as in procedures for the assignment of management positions when relevant to the experience itself.

### CAT. 1) PUBLICATIONS

Author of 51 *peer-reviewed* publications

H index (Scopus): 26

Total citations (Scopus): 1795

1. Mollinari C, Cardinale A, Lupacchini L, **Martire A**, Chiodi V, Martinelli A, Rinaldi AM, Fini M, Pazzaglia S, Domenici MR, Garaci E, Merlo D. The DNA repair protein DNA-PKcs modulates synaptic plasticity via PSD-95 phosphorylation and stability. *EMBO Rep.* 2024 Aug;25(8):3707-3737. doi: 10.1038/s44319-024-00198-3. Epub 2024 Jul 31. PMID: 39085642; PMCID: PMC11315936.
2. Di Rocco M, Galosi S, Follo FC, Lanza E, Folli V, **Martire A**, Leuzzi V, Martinelli S. Phenotypic Assessment of Pathogenic Variants in GNAO1 and Response to Caffeine in *C. elegans* Models of the Disease. *Genes (Basel)*. 2023 Jan 26;14(2):319. doi: 10.3390/genes14020319. PMID: 36833246; PMCID: PMC9957173.
3. Borreca A, De Luca M, Ferrante A, Boussadia Z, Pignataro A, **Martire A**, Ammassari-Teule M. Fmr1-KO mice failure to detect object novelty associates with a post-test decrease of structural and synaptic plasticity upstream of the hippocampus. *Sci Rep.* 2023 Jan 14;13(1):755. doi: 10.1038/s41598-023-27991-9. PMID: 36641518; PMCID: PMC9840621.
4. Boussadia Z, Chiodi V, Pazienti A, **Martire A**. A major role for adenosine A2A receptor in the interaction between astrocytes and myelinated neurons: possible implications for the therapy of neurodegenerative disorders. *Purinergic Signal.* 2022 Jan 23. doi: 10.1007/s11302-021-09835-1. Epub ahead of print. PMID: 35066787.
5. Pisa E, **Martire A**, Chiodi V, Traversa A, Caputo V, Hauser J, Macrì S. Exposure to 3'Sialyllactose-Poor Milk during Lactation Impairs Cognitive Capabilities in Adulthood. *Nutrients.* 2021 Nov 23;13(12):4191. doi: 10.3390/nu13124191. PMID: 34959743; PMCID: PMC8707534.
6. Di Rocco M, Galosi S, Lanza E, Tosato F, Caprini D, Folli V, Friedman J, Bocchinfuso G, **Martire A**, Di Schiavi E, Leuzzi V, Martinelli S. Caenorhabditis elegans provides an

- efficient drug screening platform for GNAO1-related disorders and highlights the potential role of caffeine in controlling dyskinesia. *Hum Mol Genet.* 2021 Oct 8;ddab296. doi: 10.1093/hmg/ddab296. Epub ahead of print. PMID: 34622282.
7. Bernardo A, De Nuccio C, Visentin S, **Martire A**, Minghetti L, Popoli P, Ferrante A. Myelin Defects in Niemann-Pick Type C Disease: Mechanisms and Possible Therapeutic Perspectives. *Int J Mol Sci.* 2021 Aug 17;22(16):8858. doi: 10.3390/ijms22168858. PMID: 34445564; PMCID: PMC8396228.
  8. Hauser J, Pisa E, Arias Vásquez A, Tomasi F, Traversa A, Chiodi V, Martin FP, Sprenger N, Lukjancenko O, Zollinger A, Metairon S, Schneider N, Steiner P, **Martire A**, Caputo V, Macrì S. Sialylated human milk oligosaccharides program cognitive development through a non-genomic transmission mode. *Mol Psychiatry.* 2021 Mar 4. doi: 10.1038/s41380-021-01054-9. PMID: 33664475.
  9. **Martire A**, Pepponi R, Liguori F, Volonté C, Popoli P. P2X7 Receptor Agonist 2'(3')-O-(4-Benzoylbenzoyl)ATP Differently Modulates Cell Viability and Corticostriatal Synaptic Transmission in Experimental Models of Huntington's Disease. *Front Pharmacol.* 2021 Feb 19; 11:633861. doi: 10.3389/fphar.2020.633861. PMID: 33679392; PMCID: PMC7933594.
  10. Ferrante A, Boussadia Z, Borreca A, Mallozzi C, Pedini G, Pacini L, Pezzola A, Armida M, Vincenzi F, Varani K, Bagni C, Popoli P, **Martire A**. Adenosine A2A receptor inhibition reduces synaptic and cognitive hippocampal alterations in Fmr1 KO mice. *Transl Psychiatry.* 2021 Feb 5;11(1):112. doi: 10.1038/s41398-021-01238-5. PMID: 33547274; PMCID: PMC7864914.
  11. Ferrante A, Visentin S, De Nuccio C, **Martire A**, Popoli P. Adenosine and Adenosine A2A Receptors as Targets for the Treatment of Niemann Pick Type C Disease. *Journal of Caffeine and Adenosine Research.* Sep 2019. 98-103. <http://doi.org/10.1089/caff.2019.0014>.
  12. De Nuccio C, Bernardo A, Ferrante A, Pepponi R, **Martire A**, Falchi M, Visentin S, Popoli P, Minghetti L. Adenosine A2A receptor stimulation restores cell functions and differentiation in Niemann-Pick type C-like oligodendrocytes. *Sci Rep.* 2019 Jul 5;9(1):9782. doi: 10.1038/s41598-019-46268-8. PMID: 31278313; PMCID: PMC6611770.
  13. Domenici MR, Ferrante A, **Martire A**, Chiodi V, Pepponi R, Tebano MT, Popoli P. Adenosine A2A receptor as potential therapeutic target in neuropsychiatric disorders. *Pharmacol Res.* 2019 Sep; 147:104338. doi: 10.1016/j.phrs.2019.104338. Epub 2019 Jul 2. PMID: 31276772.
  14. **Martire A**, Lambertucci C, Pepponi R, Ferrante A, Benati N, Buccioni M, Dal Ben D, Marucci G, Klotz KN, Volpini R, Popoli P. Neuroprotective potential of adenosine A1 receptor partial agonists in experimental models of cerebral ischemia. *J Neurochem.* 2019 Apr;149(2):211-230. doi: 10.1111/jnc.14660. Epub 2019 Feb 11. PMID: 30614535.
  15. Ferrante A, Pezzola A, Matteucci A, Di Biase A, Attorri L, Armida M, **Martire A**, Chern Y, Popoli P. The adenosine A2A receptor agonist T1-11 ameliorates neurovisceral symptoms and extends the lifespan of a mouse model of Niemann-Pick type C disease. *Neurobiol Dis.* 2018 Feb; 110:1-11. doi: 10.1016/j.nbd.2017.10.013. Epub 2017 Oct 25. PMID: 29079454.
  16. Ferrante A, Tebano MT, **Martire A**, Domenici MR, Popoli P. Book Chapter: Neuronal vs Glial Cell Contribution to Adenosine A2A Receptor-Induced Neurodegeneration. In

- David Blum and Luísa V.Lopes, editors: Blum - Adenosine Receptors in Neurodegenerative Diseases, Oxford: Academic Press , 2017 , pp. 131 - 150.
17. Cilli P, Ventura I, Minoprio A, Meccia E, **Martire A**, Wilson SH, Bignami M, Mazzei F. Oxidized dNTPs and the OGG1 and MUTYH DNA glycosylases combine to induce CAG/CTG repeat instability. *Nucleic Acids Res.* 2016 Jun 20;44(11):5190-203. doi: 10.1093/nar/gkw170. Epub 2016 Mar 14. PMID: 26980281; PMCID: PMC4914090.
  18. Ferrante A, De Nuccio C, Pepponi R, Visentin S, **Martire A**, Bernardo A, Minghetti L, Popoli P. Stimulation of adenosine A2A receptors reduces intracellular cholesterol accumulation and rescues mitochondrial abnormalities in human neural cell models of Niemann-Pick C1. *Neuropharmacology.* 2016 Apr; 103:155-62. doi: 10.1016/j.neuropharm.2015.11.022. Epub 2015 Nov 26. PMID: 26631535.
  19. Popoli P, Domenici MR, **Martire A**, Tebano MT. Book Chapter: Functional Interactions of Adenosine Receptors and their Possible Implications in Central Nervous System Diseases. Chapter 13, pp. 265-294, in "Adenosine Signaling Mechanisms: Pharmacology, Functions and Therapeutic Aspects". 2015. Vickram Ramkumar and Roberto Paes de Carvalho Eds. Nova Science Publishers.
  20. De Felice A, Confaloni A, Crestini A, De Simone R, Malchiodi-Albedi F, **Martire A**, Matteucci A, Minghetti L, Popoli P, Venerosi A, Calamandrei G. Book Chapter: Branched Chain Amino Acids in Experimental Models of Amyotrophic Lateral Sclerosis, in "Branched Chain Amino Acids in Clinical Nutrition". 2015. Springer New York.
  21. Ferrante A, **Martire A**, Pepponi R, Varani K, Vincenzi F, Ferraro L, Beggiato S, Tebano MT, Popoli P. Expression, pharmacology and functional activity of adenosine A1 receptors in genetic models of Huntington's disease. *Neurobiol Dis.* 2014 Nov; 71:193-204. doi: 10.1016/j.nbd.2014.08.013. Epub 2014 Aug 15. PMID: 25132555.
  22. De Luca G, Ventura I, Sanghez V, Russo MT, Ajmone-Cat MA, Cacci E, **Martire A**, Popoli P, Falcone G, Michelini F, Crescenzi M, Degan P, Minghetti L, Bignami M, Calamandrei G. Prolonged lifespan with enhanced exploratory behavior in mice overexpressing the oxidized nucleoside triphosphatase hMTH1. *Aging Cell.* 2013 Aug;12(4):695-705. doi: 10.1111/accel.12094. Epub 2013 May 30. PMID: 23648059.
  23. **Martire A**, Pepponi R, Domenici MR, Ferrante A, Chiodi V, Popoli P. BDNF prevents NMDA-induced toxicity in models of Huntington's disease: the effects are genotype specific and adenosine A2A receptor is involved. *J Neurochem.* 2013 Apr;125(2):225-35. doi: 10.1111/jnc.12177. Epub 2013 Feb 27. PMID: 23363456.
  24. Blum D, **Martire A**, Burnouf S, Sablonnière B, Krystkowiak P, Ledent C, Lopes LV, Popoli P. Book Chapter: Adenosine receptors in Huntington's disease. Chapter 20 in "Adenosine: a Key Link between Metabolism and CNS Activity". 2013. Masino & Boison Eds. Springer.
  25. Scattoni ML, **Martire A**, Cartocci G, Ferrante A, Ricceri L. Reduced social interaction, behavioural flexibility and BDNF signalling in the BTBR T+ tf/J strain, a mouse model of autism. *Behav Brain Res.* 2013 Aug 15; 251:35-40. doi: 10.1016/j.bbr.2012.12.028. Epub 2012 Dec 25. PMID: 23270976.
  26. Burnouf S, **Martire A**, Derisbourg M, Laurent C, Belarbi K, Leboucher A, Fernandez-Gomez FJ, Troquier L, Eddarkaoui S, Grosjean ME, Demeyer D, Muhr-Tailleux A, Buisson A, Sergeant N, Hamdane M, Humez S, Popoli P, Buée L, Blum D. NMDA receptor dysfunction contributes to impaired brain-derived neurotrophic factor-induced facilitation of hippocampal synaptic transmission in a Tau transgenic model.

- Aging Cell. 2013 Feb;12(1):11-23. doi: 10.1111/accel.12018. Epub 2012 Nov 23. PMID: 23082852.
27. Tebano MT, **Martire A**, Popoli P. Adenosine A(2A)-cannabinoid CB(1) receptor interaction: an integrative mechanism in striatal glutamatergic neurotransmission. *Brain Res.* 2012 Oct 2;1476:108-18. doi: 10.1016/j.brainres.2012.04.051. Epub 2012 May 4. PMID: 22565012.
  28. Chiodi V, Uchigashima M, Beggiato S, Ferrante A, Armida M, **Martire A**, Potenza RL, Ferraro L, Tanganelli S, Watanabe M, Domenici MR, Popoli P. Unbalance of CB1 receptors expressed in GABAergic and glutamatergic neurons in a transgenic mouse model of Huntington's disease. *Neurobiol Dis.* 2012 Mar;45(3):983-91. doi: 10.1016/j.nbd.2011.12.017. Epub 2011 Dec 23. PMID: 22207189.
  29. Venerosi A, **Martire A**, Rungi A, Pieri M, Ferrante A, Zona C, Popoli P, Calamandrei G. Complex behavioral and synaptic effects of dietary branched chain amino acids in a mouse model of amyotrophic lateral sclerosis. *Mol Nutr Food Res.* 2011 Apr; 55(4):541-52. doi: 10.1002/mnfr.201000296. Epub 2011 Jan 5. PMID: 21462321.
  30. **Martire A**, Tebano MT, Chiodi V, Ferreira SG, Cunha RA, Köfalvi A, Popoli P. Pre-synaptic adenosine A2A receptors control cannabinoid CB1 receptor-mediated inhibition of striatal glutamatergic neurotransmission. *J Neurochem.* 2011 Jan; 116(2):273-80. doi: 10.1111/j.1471-4159.2010.07101.x. Epub 2010 Dec 2. PMID: 21062287.
  31. Tebano MT, **Martire A**, Chiodi V, Ferrante A, Popoli P. Role of adenosine A(2A) receptors in modulating synaptic functions and brain levels of BDNF: a possible key mechanism in the pathophysiology of Huntington's disease. *ScientificWorldJournal.* 2010 Sep 1; 10:1768-82. doi: 10.1100/tsw.2010.164. PMID: 20842321; PMCID: PMC5763899.
  32. Ferrante A, **Martire A**, Armida M, Chiodi V, Pézzola A, Potenza RL, Domenici MR, Popoli P. Influence of CGS 21680, a selective adenosine A(2A) receptor agonist, on NMDA receptor function and expression in the brain of Huntington's disease mice. *Brain Res.* 2010 Apr 6; 1323:184-91. doi: 10.1016/j.brainres.2010.01.080. Epub 2010 Feb 4. PMID: 20138162.
  33. **Martire A**, Ferrante A, Potenza RL, Armida M, Ferretti R, Pézzola A, Domenici MR, Popoli P. Remodeling of striatal NMDA receptors by chronic A(2A) receptor blockade in Huntington's disease mice. *Neurobiol Dis.* 2010 Jan;37(1):99-105. doi: 10.1016/j.nbd.2009.09.012. Epub 2009 Oct 3. PMID: 19804830.
  34. Tebano MT, **Martire A**, Chiodi V, Pepponi R, Ferrante A, Domenici MR, Frank C, Chen JF, Ledent C, Popoli P. Adenosine A2A receptors enable the synaptic effects of cannabinoid CB1 receptors in the rodent striatum. *J Neurochem.* 2009 Sep; 110(6):1921-30. doi: 10.1111/j.1471-4159.2009.06282.x. Epub 2009 Jul 17. PMID: 19627447.
  35. Pepponi R, Ferrante A, Ferretti R, **Martire A**, Popoli P. Region-specific neuroprotective effect of ZM 241385 towards glutamate uptake inhibition in cultured neurons. *Eur J Pharmacol.* 2009 Sep 1;617(1-3):28-32. doi: 10.1016/j.ejphar.2009.07.016. Epub 2009 Jul 18. PMID: 19619523.
  36. Tebano MT, **Martire A**, Pepponi R, Domenici MR, Popoli P. Is the functional interaction between adenosine A(2A) receptors and metabotropic glutamate 5 receptors a general mechanism in the brain? Differences and similarities between the striatum and the hippocampus. *Purinergic Signal.* 2006 Nov; 2(4):619-25. doi:

- 10.1007/s11302-006-9026-y. Epub 2006 Sep 28. PMID: 18404464; PMCID: PMC2096652.
37. Potenza RL, Tebano MT, **Martire A**, Domenici MR, Pepponi R, Armida M, Pèzzola A, Minghetti L, Popoli P. Adenosine A(2A) receptors modulate BDNF both in normal conditions and in experimental models of Huntington's disease. *Purinergic Signal*. 2007 Sep; 3(4):333-8. doi: 10.1007/s11302-007-9066-y. Epub 2007 Sep 15. PMID: 18404446; PMCID: PMC2072926.
  38. Tebano MT, **Martire A**, Potenza RL, Grò C, Pepponi R, Armida M, Domenici MR, Schwarzschild MA, Chen JF, Popoli P. Adenosine A(2A) receptors are required for normal BDNF levels and BDNF-induced potentiation of synaptic transmission in the mouse hippocampus. *J Neurochem*. 2008 Jan; 104(1):279-86. doi: 10.1111/j.1471-4159.2007.05046.x. Epub 2007 Nov 14. PMID: 18005343.
  39. Popoli P, Pepponi R, **Martire A**, Armida M, Pèzzola A, Galluzzo M, Domenici MR, Potenza RL, Tebano MT, Mollinari C, Merlo D, Garaci E. Neuroprotective effects of thymosin beta4 in experimental models of excitotoxicity. *Ann N Y Acad Sci*. 2007 Sep; 1112:219-24. doi: 10.1196/annals.1415.033. PMID: 17947590.
  40. Domenici MR, Scattoni ML, **Martire A**, Lastoria G, Potenza RL, Borioni A, Venerosi A, Calamandrei G, Popoli P. Behavioral and electrophysiological effects of the adenosine A2A receptor antagonist SCH 58261 in R6/2 Huntington's disease mice. *Neurobiol Dis*. 2007 Nov;28(2):197-205. doi: 10.1016/j.nbd.2007.07.009. Epub 2007 Jul 24. PMID: 17720507.
  41. Bisogno T, **Martire A**, Petrosino S, Popoli P, Di Marzo V. Symptom-related changes of endocannabinoid and palmitoylethanolamide levels in brain areas of R6/2 mice, a transgenic model of Huntington's disease. *Neurochem Int*. 2008 Jan;52(1-2):307-13. doi: 10.1016/j.neuint.2007.06.031. Epub 2007 Jul 4. PMID: 17664017.
  42. **Martire A**, Calamandrei G, Felici F, Scattoni ML, Lastoria G, Domenici MR, Tebano MT, Popoli P. Opposite effects of the A2A receptor agonist CGS21680 in the striatum of Huntington's disease versus wild-type mice. *Neurosci Lett*. 2007 Apr 24;417(1):78-83. doi: 10.1016/j.neulet.2007.02.034. Epub 2007 Feb 14. PMID: 17331645.
  43. Popoli P, Blum D, **Martire A**, Ledent C, Ceruti S, Abbracchio MP. Functions, dysfunctions and possible therapeutic relevance of adenosine A2A receptors in Huntington's disease. *Prog Neurobiol*. 2007 Apr;81(5-6):331-48. doi: 10.1016/j.pneurobio.2006.12.005. Epub 2007 Jan 9. PMID: 17303312.
  44. Mallozzi C, **Martire A**, Domenici MR, Metere A, Popoli P, Di Stasi AM. L-NAME reverses quinolinic acid-induced toxicity in rat corticostriatal slices: Involvement of src family kinases. *J Neurosci Res*. 2007 Sep;85(12):2770-7. doi: 10.1002/jnr.21178. PMID: 17265464.
  45. Pintor A, Tebano MT, **Martire A**, Grieco R, Galluzzo M, Scattoni ML, Pèzzola A, Coccurello R, Felici F, Cuomo V, Piomelli D, Calamandrei G, Popoli P. The cannabinoid receptor agonist WIN 55,212-2 attenuates the effects induced by quinolinic acid in the rat striatum. *Neuropharmacology*. 2006 Oct;51(5):1004-12. doi: 10.1016/j.neuropharm.2006.06.013. Epub 2006 Aug 8. PMID: 16895732.
  46. Tebano MT, **Martire A**, Rebola N, Pepponi R, Domenici MR, Grò MC, Schwarzschild MA, Chen JF, Cunha RA, Popoli P. Adenosine A2A receptors and metabotropic glutamate 5 receptors are co-localized and functionally interact in the hippocampus: a possible key mechanism in the modulation of N-methyl-D-aspartate effects. *J Neurochem*. 2005 Nov;95(4):1188-200. doi: 10.1111/j.1471-4159.2005.03455.x. PMID: 16271052.

47. Domenici MR, Potenza RL, **Martire A**, Coccurello R, Pèzzola A, Reggio R, Tebano MT, Popoli P. Chronic treatment with the mGlu5R antagonist MPEP reduces the functional effects of the mGlu5R agonist CHPG in the striatum of 6-hydroxydopamine-lesioned rats: possible relevance to the effects of mGlu5R blockade in Parkinson's disease. *J Neurosci Res.* 2005 Jun 1;80(5):646-54. doi: 10.1002/jnr.20489. PMID: 15880742.
48. Domenici MR, Pepponi R, **Martire A**, Tebano MT, Potenza RL, Popoli P. Permissive role of adenosine A2A receptors on metabotropic glutamate receptor 5 (mGluR5)-mediated effects in the striatum. *J Neurochem.* 2004 Sep;90(5):1276-9. doi: 10.1111/j.1471-4159.2004.02607.x. PMID: 15312183.
49. Tebano MT, Pintor A, Frank C, Domenici MR, **Martire A**, Pepponi R, Potenza RL, Grieco R, Popoli P. Adenosine A2A receptor blockade differentially influences excitotoxic mechanisms at pre- and postsynaptic sites in the rat striatum. *J Neurosci Res.* 2004 Jul 1;77(1):100-7. doi: 10.1002/jnr.20138. PMID: 15197743.
50. Popoli P, Pintor A, Tebano MT, Frank C, Pepponi R, Nazzicone V, Grieco R, Pèzzola A, Reggio R, Minghetti L, De Berardinis MA, **Martire A**, Potenza RL, Domenici MR, Massotti M. Neuroprotective effects of the mGlu5R antagonist MPEP towards quinolinic acid-induced striatal toxicity: involvement of pre- and post-synaptic mechanisms and lack of direct NMDA blocking activity. *J Neurochem.* 2004 Jun;89(6):1479-89. doi: 10.1111/j.1471-4159.2004.02448.x. PMID: 15189351.
51. Sciamanna I, Barberi L, **Martire A**, Pittoggi C, Beraldi R, Giordano R, Magnano AR, Hogdson C, Spadafora C. Sperm endogenous reverse transcriptase as mediator of new genetic information. *Biochem Biophys Res Commun.* 2003 Dec 26;312(4):1039-46. doi: 10.1016/j.bbrc.2003.11.024. PMID: 14651976.

## CAT. 2: INSTITUTIONAL ACTIVITY

### **Institutional activity carried out as researcher/senior researcher at the Istituto Superiore di Sanità.**

Formulation of assessments on:

non-clinical section of the dossiers relating to Phase I clinical trials (pursuant to Presidential Decree 439/2001, Legislative Decree 211/2003, Legislative Decree 200/2007 and Law 8.11.2012 n.189 and Ministerial Decree 27.04.2015), n= 43 between March 2017 and November 2022;

non-clinical section of the dossiers relating to EMA centralized procedures (n=1);

technical-scientific evaluation of requests for authorization to animal testing (n=61 between February 2014 and August 2021).

### **Assignments carried out as researcher/senior researcher at the Istituto Superiore di Sanità.**

Appointed by AIFA as a European expert who provides scientific expertise to EMA's activities:

[https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-experts?f%5B0%5D=ema\\_expert\\_full\\_name%3Aalberto%20martire](https://www.ema.europa.eu/en/about-us/how-we-work/european-medicines-regulatory-network/european-experts?f%5B0%5D=ema_expert_full_name%3Aalberto%20martire)

Appointed as scientific expert in the thematic area Pharmacology of the Animal Welfare Body (OPBA) of the Italian National Institute of Health.

**Institutional activity carried out as Seconded National Expert at the European Medicines Agency in Amsterdam (from 16 January 2023 – ongoing).**

Management and evaluation as Product Lead/Procedure Manager of centralized EMA procedures relating to drugs (chemicals, biologics, biotechnological, ATMP) with indication in the field of neurological and psychiatric diseases and with active participation in the periodic plenary meetings of the EMA scientific committees (CHMP, PRAC, COMP, CAT):

Type II variation n. 15

PSUSA n. 10

Line extension n. 2

Renewal n. 2

PAM n. 1

Initial Marketing Authorisation n. 10

**Roles of responsibility held at EMA:**

Scientific coordinator of the Opioids Task Force (TF): this project consists of supporting/strengthening a TF on opioids that can in turn a) coordinate the EU regulatory network on opioids, b) collaborate with other EU bodies involved in initiatives relevant to the topic and c) support EMA committees on topics related to opioid use, abuse, overdose and dependence.

Non-clinical assessor for PRIME priority medicines: PRIME is a program managed by EMA to improve support for the development of medicines that aim to address an unmet medical need. This voluntary program is based on early dialogue with developers of promising medicines, to optimise development plans and accelerate assessment so that these medicines can reach patients as quickly as possible.

Non-clinical assessor for ITF briefing meetings: the Innovation Task Force (ITF) briefing meetings provide developers of innovative medicines with a forum for early dialogue with EMA. Experts assist developers in deciding on the next steps in their development programs. ITF briefing meetings cover regulatory, technical and scientific consultations regarding innovative medicines, technologies and methodologies at an early stage of their development; they enable informal exchange of information and guidance in the development process, complementing existing formal EMA procedures; they are aimed at all types of developers, including academic researchers, micro, small and medium-sized enterprises (SMEs) and large pharmaceutical companies.

Scientific coordinator of the Neuroscience EMA/FDA cluster: the aim of the project was to establish a permanent EMA-FDA collaboration in the field of neuroscience and therapies for neurological and psychiatric disorders. The main objective of this cluster is to strengthen the existing collaboration

between the H-TA-NEU Office at EMA and the Division of Psychiatry/Office of Neurosciences in the FDA's Center for Drug Evaluation and Research.

**Assignments carried out as Seconded National Expert at the European Medicines Agency in Amsterdam (from 16 January 2023 – ongoing).**

Member, as a Seconded National Expert at the European Medicines Agency, of the European Rare Diseases Research Alliance (ERDERA) Regulatory Support Group (RSG), as non-clinical expert.

Member, as a Seconded National Expert to the European Medicines Agency, of the EMA Pharmacogenomics Community: the aims of this working group are the following: 1) to coordinate expertise in the field of pharmacogenomics, 2) to promote a forum for sharing knowledge in pharmacogenomics to support EMA staff, 3) to maintain, share and develop knowledge related to translational and clinical pharmacogenomics within the Agency, 4) to support the drafting of guidelines in the following area: non-clinical/clinical genomic biomarkers qualification (including epigenetic biomarkers, e.g. modified DNA bases/epigenetic marks such as 5-methylcytosine).

Member, as a Seconded National Expert to the European Medicines Agency (non-clinical expert) of the EMA internal group for the classification/certification of advanced therapy medicinal products (ATMPs): EMA's Committee for Advanced Therapies (CAT) offers a certification procedure for ATMPs under development by micro, small, and medium-sized enterprises (SMEs). The certification procedure involves the scientific evaluation of quality data and, where available, non-clinical data that SMEs have generated at any stage of the ATMP development process.

**The activities as principal investigator of projects are listed and described in category 4.**

**CAT. 3) MANAGERIAL EXPERIENCE**

The managerial experience was gained in the context of the scientific responsibilities of the projects (national and international competitive grant applications; see the specific category 4 below in this document) financed by Italian and foreign institutions. The activities were carried out in management autonomy and with direct responsibility for human, technical or financial resources (drafting of contracts for personnel, management of equipment and consumable purchases) and related reporting (documentation available upon request). The results achieved are represented by scientific publications relating to the topics subject to funding (Niemann-Pick type C disease and Fragile X Syndrome), by the intensification of national and foreign scientific collaborations, demonstrated by the several Authorships present in the scientific papers, and by the consequent international promotion of the research activities. The ability to acquire funds is supported by the achievements obtained as a researcher exclusively through competitive peer-reviewed calls, mainly international, in the period 2013-2023 (for details, documentation available upon request).

To carry out simultaneously institutional activities as a researcher at the Istituto Superiore di Sanità (see category 2) allowed me to acquire expertise in national and European pharmaceutical legislation; the proper knowledge of these regulatory aspects is essential for managing the CNRVF activities and fundamental for directing the experimental activities toward more applied approaches of preclinical and translational research. I have personally observed that the combined expertise (scientific/regulatory) that CNRVF provides to its staff members is highly valued in international forums such as the EMA and the other European agencies (e.g. EUDA, European Union Drugs Agency).

The managerial skills required by this application have been further developed during the international professional experience at EMA through the direct scientific coordination of working groups, task forces, clusters (reported in category 2). Furthermore, EMA continuous training also included specific courses for project management, in particular the *P3i (people, process, and product) Project governance course*:

Course objective: this module provides a comprehensive overview of how to manage programs and projects, covering the following topics:

- Project governance principles
- P3i environment
- Compliance with legislation
- Governance provisions
- Reporting and escalation

Continuous training also covered topics whose knowledge is of primary importance for the management of complex research structures and institutional activities such as those of the ISS. To give some examples: data protection, cybersecurity, management of unintended disclosure of confidential information and personal data, management of requests for access to documents, management of conflicts of interest, staff code of conduct, staff health and safety, real world evidence, statistics for clinical trials, toxicology (for details, documentation available upon request). Finally, my experience at the EMA allowed me to develop a network of professional interactions, both with internal staff and with the National Competent Regulatory Authorities, potentially useful for promoting CNRVF research and institutional activities at international level.

#### CAT. 4) EDUCATIONAL AND PROFESSIONAL QUALIFICATIONS, SUCH AS PHD, SPECIALIZATIONS, RESPONSIBILITY ASSIGNMENTS IN THE MANAGEMENT OF STRUCTURES, RESPONSIBILITY ASSIGNMENTS FOR PROJECTS, UNIVERSITY ASSIGNMENTS, TEACHING IN INSTITUTIONAL COURSES

##### **PhD**

PhD in Pharmacology (XXI cycle), obtained on December 17, 2009 at the University "La Sapienza" of Rome; Supervisors: Prof. Daniela Melchiorri, Prof. Ferdinando Nicoletti. Thesis title: "Effects of the

adenosine A2A receptor antagonist SCH58261 on striatal NMDA receptor subunits in an animal model of Huntington's disease".

### **National and international awards**

April 2017: invited researcher at the FENS event "The Brain Conference, Learning, Memory and Synaptic Plasticity", Rungsted Kyst - North Copenhagen, Denmark.

October 2017: invited researcher at the 2017 edition of "TWIST Training at Lisbon Addictions 2017", Lisbon, Portugal.

Since January 2023: Seconded National Expert at the European Medicines Agency in Amsterdam (roles of responsibility covered: Scientific coordinator of the Opioids Task Force (TF), Nonclinical assessor for PRIME priority medicines, Nonclinical assessor for ITF briefing meetings, Scientific coordinator of the Neuroscience EMA/FDA cluster).

### **Responsibilities as principal investigator/collaborator of projects**

Since January 2014: principal investigator of the following project: GR-2011-02348150 "Adenosine A2A receptors as a possible therapeutic target in Niemann-Pick type C disease" (Young Researchers Funding of Euro 342,000.00 from the Ministry of Health for the years 2014-2015-2016).

Since October 2018: principal investigator of the following project: "Characterization of Adenosine Receptors in a Mouse Model of Fragile X Syndrome" (contribution of 90,000.00 USD from the FRAXA Research Foundation for 2018-2019). <https://www.fraxa.org/coffee-tea-and-chocolate-adenosine-receptors-in-fragile-x/>

Since October 2021: collaborator in the following project: "Characterization of microglia transcriptional profile in fmr1ko mice model"; FRAXA Research Foundation; 2021-2023.

Since July 2021: principal investigator of the following project: "Exosomes as a source of Therapeutic Biomarkers in Experimental Models of Fragile X Syndrome"; ISS intramural funding; 2020-2022.

Since October 2022: principal investigator of the following project: "Exosomes as a source of Therapeutic Biomarkers in Experimental Models of Fragile X Syndrome" (contribution of 100,000.00 USD from the FRAXA Research Foundation for 2023-2024). <https://www.fraxa.org/using-exosomes-to-discover-fragile-x-biomarkers/>

Scientific responsibility for animal testing protocols as per the functions referred to ARTICLE 1, PARAGRAPH 1, LETTERS A), C) AND D) OF THE MINISTERIAL DECREE 5 AUGUST 2021.

### **Responsibilities for agreements between institutions**

Scientific manager of the following collaboration agreement between ISS and Italian Fragile X Association (AIXF): "Study of the therapeutic potential of adenosine A2A receptor antagonists in Fragile X syndrome".

Scientific manager of the following collaboration agreement between ISS and the Institute of Neuroscience of the National Research Council: “Characterization of microglia transcriptional profile in *fmr 1 ko* mice model”.

Scientific manager of the following collaboration agreement between ISS and the Department of Life and Environmental Sciences (DISVA) of UNIVPM for joint research activities: “Characterization of a novel CYFIP1-derived peptidomimetic restoring the dysregulated mRNAs translation: toward an innovative therapeutic strategy for FXS”.

Scientific manager of the following collaboration agreement between ISS and the Department of Life and Environmental Sciences (DISVA) of UNIVPM for a PhD at ISS: “Characterization of a novel CYFIP1-derived peptidomimetic restoring the dysregulated mRNAs translation: toward an innovative therapeutic strategy for FXS” and “Exosomes as a source of therapeutic biomarkers in experimental models of Fragile Syndrome”.

### **Thesis supervisor**

Thesis title: “The neuroprotective potential of partial agonists of the adenosine A1 receptor in experimental models of cerebral ischemia”. Supervisor: Prof. Luca Ferraro. Additional supervisor: Dr. Alberto Martire. Discussion date: 07 March 2016. Thesis internship duration: January 2015 – February 2016. Client: UNIVERSITY OF FERRARA.

### **Professional qualification**

Achievement, in June 2002 and through proper examination, of the professional title of biologist, at the University of Viterbo.

### **Referee for the evaluation of projects**

Reviewer of the project “The role of Nrf2 in endogenous neuroprotection of ischemia-resistant region of hippocampus”, proposed to the Polish government agency National Science Centre (Narodowe Centrum Nauki - NCN; <http://www.ncn.gov.pl>).

### **Speaker at conferences and workshops**

Speaker at the 8th International Symposium on Adenosine and Adenine Nucleotides, held in Ferrara from 24 to 28 May 2006. Title: “Opposite effects of the A2A receptor agonist CGS21680 in the striatum of Huntington’s disease (HD) versus wild-type mice”.

Speaker at the 34th National Congress of the Italian Society of Pharmacology held in Rimini from 14 to 17 October 2009. Title: “Remodelling of striatal NMDA receptors by chronic A2a receptor activation or blockade in Huntington’s disease mice”.

Speaker at the Congress “5th Joint Italian-German Purine Club Meeting - Fostering translational research on Purines by Italian-German joint efforts” held in Rimini from 19 to 20 September 2013. Title: “Potential therapeutic targets for Huntington’s Disease: focus on adenosine A1 receptors”.

Speaker at the “Annual Meeting of the Italian Purine Club”, Rome, Istituto Superiore di Sanità, 15 January 2016. Title: “Neuroprotective potential of adenosine A1R partial agonists in ex vivo and in vitro experimental models of ischemia”.

Speaker at the Annual Assembly of the members of the Italian Fragile X Syndrome Association, Rome, 13 April 2019, Università Cattolica del Sacro Cuore. Presentation of the data relating to the project funded by FRAXA Research Foundation and the Italian Fragile X Syndrome Association (Characterization of Adenosine Receptors in a Mouse Model of Fragile X Syndrome);

Speaker at the “19th International Workshop on Fragile X and other Neurodevelopmental Disorders”, Sorrento (NA), 18-21 September 2019. Title: “Adenosine A2A receptor inhibition reverses synaptic and behavioral abnormalities in Fmr1 KO mice.”

Speaker at the “XVIII SINS National Congress”, Perugia, 28 September 2019. Title: “Potential therapeutic role of adenosine A2A receptors in Central Nervous System disorders”.

Speaker at the “39th National Congress of the Italian Society of Pharmacology”, Florence, 20-23 November 2019. Title: “Potential therapeutic role of adenosine A2A receptors in a mouse model of Fragile X Syndrome”.

Presentation at the EMA CNS Community meeting, 8 December 2023. Title: “Huntington disease: state of the art of the research on molecular pathogenesis and experimental models”.

Presentation to the EMA Scientific Coordination Board (SciCoBo), 6 May 2024. Title: “Opioid Task Force: mandate and workplan”.

Presentation to the EMA CMDh (Coordination Group for Mutual Recognition and Decentralised Procedures – Human) Plenary, 28 May 2024. Title: “Opioid Task Force: mandate and workplan”.

### **Referee for the evaluation of scientific publications**

Referee for:

*European Journal of Pharmacology*

*Neuroscience and Biobehavioral Reviews*

*Neuroscience*

*Brain Research Bulletin*

*British Journal of Pharmacology*

*Journal of Neuroscience Research*

*Molecular Neurobiology*

*Journal of Neurochemistry*

*Neurobiology of disease*

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**The undersigned Alberto Martire, within the meaning of Art. 13 of the EU General Data Protection Regulation EU/2016/679 (GDPR), declares to have been informed that the personal data contained in this curriculum vitae will be processed, also with IT tools, exclusively in the context of this application and for the formation of any acts related to it, in the ways and limits to pursue these purposes.**

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