

# Ilaria Maria Morella, Curriculum Vitae

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## PERSONAL STATEMENT

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My research primarily aims at investigating the molecular basis of cognitive impairments in neuropsychiatric and neurodegenerative disorders, with the goal to identify druggable targets.

My academic training and research experience provided me with relevant expertise in behavioural neuropharmacology in preclinical models and cell biology, that I applied in the field of translational neuroscience.

Since my undergraduate training, I have been working on signal transduction, with a particular interest in the pathophysiology of basal ganglia.

As a post-doctoral fellow in Prof. Brambilla's laboratory, I have tested and validated innovative pharmacological approaches based on drug repositioning and newly designed cell permeable peptides. These compounds proved to be effective in mouse models of cocaine addiction, intellectual disability/autism spectrum disorder and neurodegenerative disorders, by modulating protein-protein interactions. As a complementary approach, I also used viral vector technologies to manipulate gene expression *in vivo*.

During the last years at Cardiff University, I took part in a multidisciplinary project aimed to develop new diagnostic and therapeutic tools for 16p11.2 deletion and duplication syndromes, associated with neurodevelopmental disorders, intellectual disability and autism. To this end, I carried out phenotypic analysis on both mouse models and human induced-pluripotent stem cells as well as biomarkers studies in patients.

## EDUCATION

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### 2022 **Second Level Specialising Master's degree in Dietetics and Clinical Nutrition**

Università di Pavia

Thesis: "Nutrition and exercise as modulators of the "gut-muscle-brain axis": implication for cognitive aging"

Supervisor: Dr. Massimo Negro

Grade: **100/100 cum laude**

### 2013 **PhD in Molecular and Cellular Biology**

Università degli studi di Milano

Thesis: "Development of an ex-vivo system of adult brain slices to investigate the role of ERK pathway in the striatal signalling"

Supervisor: Prof. Renata Zippel, co-supervisor: Prof. Riccardo Brambilla

Grade: **Excellent**

### 2008 **Master's Degree in Molecular Biology**

Università degli studi di Milano

Thesis: "Studying the functional role of the interaction between Ras-GRF1 and Hrs"

Supervisor: Prof. Renata Zippel, co-supervisor: Dr. Graziano Colombo

Grade: **109/110**

### 2006 **Bachelor's Degree in Biological Sciences**

Università degli studi di Milano

Thesis: "Role of the N-terminal region of Ras-GRF1 in stress granules formation"

Supervisor: Prof. Renata Zippel, co-supervisor: Dr. Simona Baldassa

Grade: **110/110**

## RESEARCH POSITIONS

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March 2024-ongoing	<b>Honorary Research Fellow</b> at Cardiff University, School of Medicine, Division of Psychological Medicine and Clinical Neuroscience, Cardiff, UK
1/11/2019-31/12/2023	<b>Post-doctoral researcher</b> at Cardiff University, School of Biosciences, Neuroscience and Mental Health Innovation Institute, Cardiff, UK
1/12/2017-31/10/2019	<b>Early Career Research fellow</b> at Cardiff University, School of Medicine, Neuroscience and Mental Health Innovation Institute, Cardiff, UK
1/12/2018-31/01/2019	<b>Visiting scientist</b> at the Central Institute for Mental Health, Institute of Psychopharmacology, Mannheim, Germany
18/04/2015-30/11/2017	<b>Post-doctoral researcher</b> at Cardiff University, School of Biosciences, Neuroscience and Mental Health Innovation Institute, Cardiff, UK
31/01/2013-17/04/2015	<b>Post-doctoral researcher</b> at Cardiff University, School of Biosciences, Neuroscience and Mental Health Innovation Institute, Cardiff, UK, in collaboration with San Raffaele Research Institute, Milano

## TEACHING

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10/2023-ongoing	<b>Contract professor</b> on “Molecular and Cellular Pharmacology” (24 hours, 3 CFU) for the Bachelor’s Degree in Biotechnology, Università di Pavia
10/2022-ongoing	<b>Contract professor</b> on “Comparative Neurodevelopment and Neural Stem Cells (24 hours, 3 CFU) for the Master’s Degree in Neurobiology, Università di Pavia
05/2023	<b>Instructor</b> on the “Integrated Laboratory of Pharmaceutical Biotechnologies, Pharmacology module” (3 hours) for the Bachelor’s Degree in Biotechnology (curriculum Chem-Pharma-Tech), Università di Pavia
05/2022	Delivered <b>seminars</b> (2 hours) for the Neuropharmacology class, Master’s Degree in Neurobiology, Università di Pavia
2019-2020	<b>Instructor</b> on the “Quantitative analysis practical” for the Fundamental Neuroscience module, Bachelor’s Degree in Neuroscience, Cardiff University, UK
2016-ongoing	<b>Dissertation co-supervisor</b> for 2 Master’s Degree students. Provided supervision to 18 students during laboratory activities

## EDITORIAL AND PEER-REVIEW ACTIVITY

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2024	<b>Grant Reviewer</b> for UK Research and Innovation-BBSRC
01/2023-05/2024	<b>Guest Associate Editor</b> , invited by Frontiers in Cellular Neuroscience to manage the article collection: “Cellular and Molecular Mechanisms in Social and Repetitive Behaviour: A focus on Cortico-Striatal circuitry”
2023-ongoing	<b>Reviewer</b> for: Frontiers in Neuroscience, Neuropharmacology

## CERTIFICATIONS

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2023

**Certificate in Non-Clinical Psychopharmacology**, issued by the British Association of Psychopharmacology after a residential course in Cambridge, UK (March 13-16, 2023)

## FELLOWSHIPS

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- 1/12/2018-31/10-2019 Recipient of an **Early Career Research Fellowship**, awarded by the Wellcome Trust (30867 GBP), to work on the project: “Dissecting the role of Ras-ERK signalling in 16p11.2 deletion and duplication mouse models”
- 1/12/2017-30/11/2018 Recipient of an **Early Career Research Fellowship**, awarded by The Waterloo Foundation (35098 GBP), to work on the project: “Dissecting the role of Ras-ERK signalling in neurodevelopmental disorders”
- 1/11/2018-31/1/2019 Recipient of the **short-term fellowship** “Research stays for University Academics and Scientists”, awarded by the Deutscher Akademischer Austauschdienst (DAAD) (6200 EUR).  
This fellowship funded a 3 months-research visit at the Central Institute for Mental Health, Institute of Psychopharmacology (Prof. Rainer Spanagel’s lab), Mannheim, to work on the project: “Evaluation of the pro-rewarding and anti-depressant properties of a novel cell permeable peptide”

## OTHER AWARDS

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- 10/2023 Recipient of a **travel grant** awarded by The Guarantors of Brain to attend SfN conference 2023, in Washington DC (1000 GBP)
- 04/2018 Recipient of 3 **travel grants** awarded by the British Neuroscience Association (400 GBP), FENS (600 EUR) and The Guarantors of Brain (600 GBP) to attend FENS meeting 2018, in Berlin
- 09/2019 Recipient of a **travel grant** (600 EUR), awarded by the European COST Association (eCOST), to attend the training school/hand-on workshop “Convergence Neuroscience. Phenotyping animal models of neurodevelopmental disorders” at the Italian Institute of Technology, Genova (October 8-12, 2018)

## PATENTS

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- A. Papale, **I. Morella**, S. Fasano and R. Brambilla. Therapeutic for treating neuropsychiatric disorders or conditions (GB1606811.6, 19th Apr 2016)

## SCIENTIFIC SOCIETIES MEMBERSHIPS

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Member of FENS, Society for Neuroscience, Società Italiana di Neuroscienze, Società Italiana di Farmacologia, British Neuroscience Association, British Association for Psychopharmacology

## ATTENDANCE TO SCIENTIFIC MEETINGS

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- September 14-17, 2023, 20th National Congress of the Italian Society for Neuroscience, Turin. Morella et al “Cell signalling modulation of cortical and subcortical development in human and mouse models of 16p11.2 copy number variants”. **Speaker.**

- May 18-20, 2023, Workshop of the European Molecular and Cellular Cognition society, Nora. “ERK signalling in the neurodevelopmental disorders associated with 16p11.2 copy number variations”. **Speaker.**
- November 16-19, 2022, 41th SIF National Congress, Rome. Morella et al “Importin $\alpha$ 1/KPNA2-mediated nuclear ERK1/2 signaling potentiation prevents neurodegeneration and facilitates cognitive enhancement”. **Speaker.**
- July 11-15, 2020, FENS Virtual Forum. Morella et al “Pharmacogenetic potentiation of ERK signalling enhances cognition in mouse models of Huntington’s disease”. **Poster presenter.**
- July 7-11, 2018, FENS Forum, Berlin. Morella et al “Validation in rodent models of a novel approach to treat mood disorders based on ERK stimulation”. **Poster presenter.**
- July 6th, 2018, 8th meeting of the European Molecular and Cellular Cognition Society, Berlin. Morella et al “Validation in rodent models of a novel approach to treat mood disorders based on ERK stimulation”. **Poster presenter.**
- May 24th, 2018, Waterloo Foundation Annual Conference, Cardiff. Morella et al: “Pharmacological inhibition of ERK signalling rescues pathophysiology and behavioural phenotype associated with 16p11.2 chromosomal deletion in mice”. **Poster presenter**
- November 29-30, 2017, 4th Annual Drug Discovery Congress, Life Science Research Network Wales, Cardiff. Morella et al “Validation in rodent models of a novel approach to treat mood disorders based on ERK stimulation”. **Speaker.**
- April 10-13, 2017, BNA2017 Festival of Neuroscience, Birmingham. Morella et al “Impairment of cocaine-mediated behavioural responses by clinically relevant Ras-ERK inhibitors”. **Poster presenter.**
- July 5-9, 2014, FENS Forum, Milan. Morella et al “Validating two novel cell penetrating peptides for the treatment of dopamine-dependent disorders of the basal ganglia”. **Poster presenter.**
- July 3-4, 2014, 6th meeting of the European Molecular and Cellular Cognition Society, Milan. Morella et al “Validating two novel cell penetrating peptides for the treatment of dopamine-dependent disorders of the basal ganglia”. **Poster presenter.**
- July 14-18, 2011, 8th IBRO World Congress of Neuroscience, Florence. Morella et al “Studying the Ras-ERK pathway through single cell analysis in acute brain slices”. **Poster presenter.**
- October 29-31, 2009, EMBL International PhD symposium “Puzzles in biology. Putting the pieces together”, Heidelberg. Morella et al “Ras-GRF1 interacts with Hrs and modulates Hrs-mediated signalling”. **Poster presenter.**

## PUBLICATIONS

### Key bibliometric figures

(14<sup>th</sup> May 2024, Scopus)

Peer-reviewed publications: 17

Pre-prints: 2

Years: 2011-2024

Total number of citations: 315

H index: 10

Kretz PF, Wagner C, Mikhaleva A, Montillot C, Hugel S, **Morella I**, Kannan M, Fischer MC, Milhau M, Yalcin I, Brambilla R, Selloum M, Herault Y, Reymond A, Collins SC, Yalcin B. “Dissecting the autism-associated 16p11.2 locus identifies multiple drivers in neuroanatomical phenotypes and unveils a male-specific role for the major vault protein”. *Genome Biol.* 2023 Nov 15;24(1):261. doi: 10.1186/s13059-023-03092-8.

**Morella I\***, Negro M\*, Dossena M, Brambilla R, D’Antona G. “Gut-muscle-brain axis: molecular mechanisms in neurodegenerative disorders and potential therapeutic efficacy of probiotic supplementation coupled with exercise”. *Neuropharmacology.* 2023 Dec 1;240:109718. doi: 10.1016/j.neuropharm.2023.109718. Epub 2023 Sep 27. \***co-first authors.**

Indrigo M\*, **Morella I\***, Orellana D, d’Isa R, Papale A, Parra R, Gurgone A, Lecca D, Cavaccini A, Tigaret CM, Cagnotto A, Jones K, Brooks S, Ratto GM, Allen ND, Lelos MJ, Middei S, Giustetto M, Carta AR, Tonini

R, Salmons M, Hall J, Thomas K, Brambilla R and Fasano S. “Nuclear ERK1/2 signalling potentiation enhances neuroprotection and cognition via importin $\alpha$ /KPNA2”. *EMBO Molecular Medicine*. 2023 Nov 8;15(11):e15984. doi: 10.15252/emmm.202215984. Epub 2023 Oct 4. **\*co-first authors**.

Pisanò CA, Mercatelli D, Mazzocchi M, Brugnoli A, **Morella I**, Fasano S, Zaveri NT, Brambilla R, O’Keeffe GW, Neubig RR, Morari M. “Regulator of G-Protein Signalling 4 (RGS4) negatively modulates nociceptin/orphanin FQ opioid receptor signalling: Implication for l-Dopa-induced dyskinesia”. *British Journal of Pharmacology*. 2023 Apr. doi: 10.1111/bph.15730.

**Morella IM**, Brambilla R, Morè L. “Emerging roles of brain metabolism in cognitive impairment and neuropsychiatric disorders”. *Neuroscience and Biobehavioral Reviews*. 2022 Nov; 142:104892. doi: 10.1016/j.neubiorev.2022.104892.

**Morella I**, Pohořalá V, Calpe-López C, Brambilla R, Spanagel R, Bernardi RE. “Nicotine self-administration and ERK signaling are altered in RasGRF2 knockout mice”. *Frontiers in Pharmacology*. 2022 Sep 2; 13:986566. doi: 10.3389/fphar.2022.986566.

**Morella I**, Hallum H, Brambilla R. “Dopamine D1 and Glutamate Receptors Co-operate With Brain-Derived Neurotrophic Factor (BDNF) and TrkB to Modulate ERK Signaling in Adult Striatal Slices”. *Frontiers in Cellular Neuroscience*. 2020 Nov 16;14:564106. doi: 10.3389/fncel.2020.564106.

Bernardi RE\*, Olevska A\*, **Morella I\***, Fasano S, Santos E, Brambilla R, Spanagel R. “The Inhibition of RasGRF2, But Not RasGRF1, Alters Cocaine Reward in Mice”. *Journal of Neuroscience*. 2019 Aug 7;39(32):6325-6338. doi: 10.1523/JNEUROSCI.1120-18.2019. Epub 2019 Jun 10. **\* co-first authors**.

Pucilowska J, Vithayathil J, Pagani J, Kelly C, Karlo JC, Robol C, **Morella I**, Gozzi A, Brambilla R, and Landreth GE. Pharmacological “Inhibition of ERK Signaling Rescues Pathophysiology and Behavioral Phenotype Associated with 16p11.2 Chromosomal Deletion in Mice” *Journal of Neuroscience* 2018 Jun 22. doi: 10.1523/JNEUROSCI.0515-17.2018.

Arcuri L, Novello S, Frassinetti M, Mercatelli D, Pisanò C, **Morella I**, Fasano S, Journigan B, Meyer M, Polgar W, Brambilla R, Zaveri N, Morari M. “Antiparkinsonian and antidyskinetic profiles of two novel potent and selective nociceptin/orphanin FQ receptor agonists” *British Journal of Pharmacology*. 2018 Mar;175(5):782-796. doi: 10.1111/bph.14123.

Papale A.\*, **Morella I\***, Indrigo M, Bernardi RE, Marrone L, Marchisella F, Brancale A, Spanagel R, Brambilla R, Fasano S. “Impairment of cocaine-mediated behaviours in mice by clinically relevant Ras-ERK inhibitors” *eLife* 2016, Aug 24. **\*co-first authors**.

Trusel M, Cavaccini A, Gritti M, Greco B, Saintot PP, Nazzaro C, Cerovic M, **Morella I**, Brambilla R, Tonini R. “Coordinated Regulation of Synaptic Plasticity at Striatopallidal and Striatonigral Neurons Orchestrates Motor Control” *Cell Reports*. 2015 Nov 4. pii: S2211-1247(15)01163-8. doi: 10.1016/j.celrep.2015.10.009.

Moncini S, Bonati MT, **Morella I**, Ferrari L, Brambilla R, Riva P. “Differential allelic expression of *SOS1* and hyperexpression of the activating *SOS1* c.775C variant in a Noonan syndrome family” *European Journal of Human Genetics*. 2015 Feb 25. doi: 10.1038/ejhg.2015.20.

Cerovic M, Bagetta V, Pendolino V, Ghiglieri V, Fasano S, **Morella I**, Hardingham N, Heuer A, Papale A, Marchisella F, Giampà C, Calabresi P, Picconi B, Brambilla R. “Derangement of Ras-guanine nucleotide-releasing factor 1 (Ras-GRF1) and extracellular signal-regulated kinase (ERK) dependent striatal plasticity in L-DOPA-induced dyskinesia” *Biological Psychiatry*. 2015 Jan 15; 77(2):106-15. doi: 10.1016/j.biopsych.2014.04.002.

Marti M, Rodi D, Li Q, Guerrini R, Fasano S, **Morella I**, Tozzi A, Brambilla R, Calabresi P, Simonato M, Bezard E, Morari M. “Nociceptin/orphanin FQ receptor agonists attenuate L-DOPA-induced dyskinesias” *Journal of Neuroscience*. 2012 Nov 14;32(46):16106-19. doi: 10.1523/JNEUROSCI.6408-11.2012.

Longoni M, Moncini S, Cisternino M, **Morella IM**, Ferraiuolo S, Russo S, Mannarino S, Brazzelli V, Coi P, Zippel R, Venturin M, Riva P. “*Noonan syndrome associated with both a new Jnk-activating familial SOS1 and a de-novo RAF1 mutations*” American Journal of Medical Genetics A. 2010 Sep;152A(9):2176-84. doi: 10.1002/ajmg.a.33564.

**Book chapter**

Orellana D, **Morella I**, Indrigo M, Papale A, Brambilla R “*The extracellular signal-regulated kinase (ERK) cascade in neuronal cell signalling*” (book chapter) Hideyuki Mukai (ed.), Protein Kinase Technologies, Neuromethods, vol. 68, doi 10.1007/978-1-61779-824-5\_8.