## BIOGRAPHICAL SKETCH

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| NAME | POSITION TITLE |
|---|---|
| Marco Onorati, Ph.D. | Associate Professor |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | MM/YY | FIELD OF STUDY |
|---|---|---|---|
| University of Pisa, Italy | M.S. | 10/2003 | Biological Sciences |
| Scuola Normale Superiore of Pisa, Italy | Ph.D. | 10/2007 | Neurobiology |
| University of Milan, Italy | Post Doc | 0/2008 | Stem Cell Neurobiology |
| Yale School of Medicine | Ass. Research Scientist | 07/2013 | Cortical development |

### A. Personal Statement

My research focuses on understanding the cellular and molecular events orchestrating neural stem cell differentiation to generate distinct types of neurons in the central nervous system. An important element of this research is the integration of complementary approaches that combines: 1) human pluripotent and neural stem cell models to investigate the mechanisms of neurodevelopment and disease; 2) comparative genomic and cellular analyses to identify human-specific features of brain development and evolution; and 3) genetic and molecular analyses of human neurodevelopmental and neurodegenerative disorders.

I have a solid background in stem cell biology and neuroscience as attested by the last 12 years of work. During my Postdoctoral experience in Prof. Elena Cattaneo's laboratory at the University of Milan, my work was focused on the elucidation of the developmental processes surrounding the generation of medium-spiny neurons (MSNs). MSNs are the most vulnerable neurons in Huntington's disease, a devastating neurodegenerative disorder that causes progressive motor, psychiatric, and cognitive dysfunctions (Onorati et al., 2014 Nature Neuroscience; Delli Carri, Onorati et al., 2013 Development; HD Consortium, 2013 Cell Stem Cell). Then, at the Yale School of Medicine, with the mentorship of Prof. Nenad Sestan, I have set an advanced system of human neuroepithelial stem (NES) cells to model early human neurodevelopment, Zika virus-induced microcephaly and to validate a potential treatment with a drug already approved by the FDA and EMA (Onorati et al., 2016 Cell Reports). I have also investigated the elective integration of human NES cells into a spinal cord injury model (Dell'Anno et al., 2018, Nature Communications). On-going projects in my lab are on ZIKV virus and TORCH-pathogens effects on neural stem cells, *WDR62* mutation in primary microcephaly, Schizophrenia modelling on iPSC-derived neurons, and axonal regeneration in spinal cord injury.

### B. Positions and Honors

- **Positions and Employment**

Nov 2019- Associate Professor, Department of Biology, University of Pisa
Jul 2017- National Scientific Habilitation as Associate Professor in Cytology and Comparative Anatomy
2013-16 Associate Research Scientist Department of Neuroscience, Yale School of Medicine, New Haven (CT), USA (Advisor: Prof. Nenad Sestan)
2008-13 Postdoctoral Associate Department of Biosciences, University of Milan, Italy (Advisor: Prof. Elena Cattaneo)

- **Other Experience and Professional Memberships**

**Institutional responsibilities**
Dec. 2016 – Member of the Committee of the Ph.D. Program in Biology, University of Pisa
Nov. 2016 – Faculty member at Department of Biology, University of Pisa

**Scientific society membership**
Member of Italian Society of Developmental and Cell Biology (GEI-SIBSC) and member of the Research Committee, since 2016
Member of International Society for Stem Cell Research (ISSCR) 2013
Member of the Scientific Committee of NeuroSpine Society since 2019

**Editorial activity**
Reviewer for peer review international journals: “Cell Reports”, “Neuroscience”, “Infection, Genetics and Evolution”, “BMC Neuroscience”, "Frontiers Cellular Neuroscience", “Scientific Reports”, etc.
Guest Editor for Cells https://www.mdpi.com/journal/cells/special_issues/Neural_Stem
Review Editor for Frontiers in Neuroanatomy https://loop.frontiersin.org/people/863867/overview

**Teaching/education**
Since 2016, at the University of Pisa, Frontal Lessons in:
Stem Cell and Neural Stem Cells, Cell Biology, Advanced Cell Biology, Cell Biotechnology

- **Honors**

2003 *Summa cum laude* and honor of "Abbraccio accademico" (top 1% of students in this course), University of Pisa
2007 *Summa cum laude* for Ph.D. dissertation, Scuola Normale Superiore of Pisa
2008 *Best Ph.D. thesis* in 2007 (Prize XIII SIBS)
2012 *FIRB 2010* - Futuro in Ricerca grant (Italian Ministry of University and Research)
2016-2018 *Visiting Research Scientist*, Department of Neuroscience, Yale School of Medicine
2017 *NARSAD young investigator Grant,* Brain & Behavior Research Foundation

## C. Selected Peer-reviewed Publications *(15 best peer-reviewed publications)*

**Researcher unique identifier**: ORCID: 0000-0001-8517-930X

1. Morelli E, Speranza EA, Pellegrino E, Beznoussenko GV, Carminati F, Garré M, Mironov AA, **Onorati M**, Vaccari T. Activity of the SNARE Protein SNAP29 at the Endoplasmic Reticulum and Golgi Apparatus. **Front Cell Dev Biol**. 2021 Feb 18;9:637565.
2. Baggiani M, Maria Teresa Dell'Anno MT, Pistello M, Conti L, **Onorati M**. Human Neural Stem Cell Systems to Explore Pathogen-Related Neurodevelopmental and Neurodegenerative Disorders. **Cells.** 2020 Aug 12;9(8):1893.
3. Castiglioni V*, Faedo A*, **Onorati M***, Bocchi VD*, Li Z, Iennaco R, Vuono R, Bulfamante GP, Muzio L, Martino G, Sestan N, Barker RA, Cattaneo E. Dynamic and Cell-Specific DACH1 Expression in Human Neocortical and Striatal Development. **Cereb Cortex**. 2019 May 1;29(5):2115-2124. *co-first authors
4. Li M, Santpere G, Imamura Kawasawa Y, Evgrafov OV, Gulden FO, Pochareddy S, Sunkin SM, Li Z, Shin Y, Zhu Y, Sousa AMM, Werling DM, Kitchen RR, Kang HJ, Pletikos M, Choi J, Muchnik S, Xu X, Wang D, Lorente-Galdos B, Liu S, Giusti-Rodríguez P, Won H, de Leeuw CA, Pardiñas AF; BrainSpan Consortium; PsychENCODE Consortium; PsychENCODE Developmental Subgroup (**Onorati M** et al.), Hu M, Jin F, Li Y, Owen MJ, O'Donovan MC, Walters JTR, Posthuma D, Reimers MA, Levitt P, Weinberger DR, Hyde TM, Kleinman JE, Geschwind DH, Hawrylycz MJ, State MW, Sanders SJ, Sullivan PF, Gerstein MB, Lein ES, Knowles JA, Sestan N. Integrative functional

genomic analysis of human brain development and neuropsychiatric risks. **Science**. 2018 Dec 14;362(6420).

5. Dell'Anno MT*, Wang X*, **Onorati M***, Li M, Talpo F, Sekine Y, Ma S, Liu F, Cafferty WBJ, Sestan N, Strittmatter SM. Human neuroepithelial stem cell regional specificity enables spinal cord repair through a relay circuit. **Nat Commun.** 2018 Aug 24;9(1):3419 *co-first authors
6. Sousa AMM, Zhu Y, Raghanti MA, Kitchen RR, **Onorati M**, Tebbenkamp ATN, Stutz B, Meyer KA, Li M, Kawasawa YI, Liu F, Perez RG, Mele M, Carvalho T, Skarica M, Gulden FO, Pletikos M, Shibata A, Stephenson AR, Edler MK, Ely JJ, Elsworth JD, Horvath TL, Hof PR, Hyde TM, Kleinman JE, Weinberger DR, Reimers M, Lifton RP, Mane SM, Noonan JP, State MW, Lein ES, Knowles JA, Marques-Bonet T, Sherwood CC, Gerstein MB, Sestan N. Molecular and cellular reorganization of neural circuits in the human lineage. **Science.** 2017 Nov 24;358(6366):1027-1032.
7. **Onorati M**, Li Z, Liu F, Sousa AM, Nakagawa N, Li M, Dell'Anno MT, Gulden FO, Pochareddy S, Tebbenkamp ATN, Han W, Pletikos M, Gao T, Zhu Y, Bichsel C, Varela L, Szigeti-Buck K, Lisgo S, Zhang Y, Testen A, Gao XB, Mlakar J, Popovic M, Flamand M, Strittmatter SM, Kaczmarek LK, Anton ES, Horvath TL, Lindenbach BD, Sestan N. Zika Virus Disrupts Phospho-TBK1 Localization and Mitosis in Human Neuroepithelial Stem Cells and Radial Glia. **Cell Reports**. 2016 16, 2576–2592
8. **Onorati M**, Castiglioni V, Biasci D, Cesana E, Menon R, Vuono R, Talpo F, Goya RL, Lyons PA, Bulfamante GP, Muzio L, Martino G, Toselli M, Farina C, Barker RA, Biella G, Cattaneo E. Molecular and Functional Definition of the Developing Human Striatum. **Nat Neurosci**. 2014 Nov 10.
9. Laterza C, Merlini A, De Feo D, Ruffini F, Menon R, **Onorati M**, Fredrickx E, Muzio L, Lombardo A, Comi G, Quattrini A, Taveggia C, Farina C, Cattaneo E, Martino G. iPSC-derived neural precursors exert a neuroprotective role in immune-mediated demyelination via the secretion of LIF. **Nat Commun.** 2013 Oct 29;4:2597.
10. Delli Carri A*, **Onorati M***, Castiglioni V, Faedo A, Camnasio S, Toselli M, Biella G, Cattaneo E. Human pluripotent stem cell differentiation into authentic striatal projection neurons. **Stem Cell Rev.** 2013 Aug;9(4):461-74. *co-first authors
11. Delli Carri A*, **Onorati M*,** Lelos MJ, Castiglioni V, Faedo A, Menon R, Camnasio S, Vuono R, Spaiardi P, Talpo F, Toselli M, Martino G, Barker RA, Dunnett SB, Biella G, Cattaneo E. Developmentally coordinated extrinsic signals drive human pluripotent stem cell differentiation towards fully functional DARPP-32+ medium-sized spiny neurons. **Development.** 2013 Jan 15;140(2):301-12. *co-first authors
12. The HD iPSC Consortium: Mattis VB, Ebert A, Svendsen SP, Svendsen CN, King A, Casale M, Winokur ST, Batugedara G, Vawter M, Donovan PJ, Lock LF, Thompson LM, Zhu Y, Fossale E, Singh R, Gillis T, Mysore J, Li J, Seong I, Shen Y, Chen X, Wheeler V, MacDonald ME, Gusella JF, Akimov S, Arbez N, Juoppen T, Ratoviski T, Chiang JH, Kim WR, Chighladze E, Watkin E, Zhong C, Makri G, Cole RN, Margolis RL, Song H, Ming G, Ross CA, Kaye JA, Daub A, Sharma P, Mason AR, Finkbeiner S, Yu J, Thomson JA, Rushton D, Brazier SP, Battersby AA, Redfern A, Tseng H, Harrison AW, Kemp PJ, Allen ND, **Onorati M**, Castiglioni V, Cattaneo E, Arjomand J, Svendsen C. Induced Pluripotent Stem Cells from Patients with Huntington's Disease Show CAG Repeat-Expansion-Associated Phenotypes. **Cell Stem Cell.** 2012 Aug 3;11(2):264-78.
13. Castiglioni V, **Onorati M**, Rochon C, Cattaneo E. Induced pluripotent stem cell lines from Huntington's disease mice undergo neuronal differentiation while showing alterations in the lysosomal pathway. **Neurobiol Dis.** 2012 Apr;46(1):30-40.
14. **Onorati M**, Binetti M, Conti L, Camnasio S, Calabrese G, Albieri I, Di Febo F, Toselli M, Biella G, Martynoga B, Guillemot F, Consalez GG, Cattaneo E. Preservation of positional identity in fetus-derived neural stem (NS) cells from different mouse central nervous system compartments. **Cell Mol Life Sci.** 2011 May;68(10):1769-83.
15. **Onorati M**, Camnasio S, Binetti M, Jung CB, Moretti A, Cattaneo E. Neuropotent selfrenewing neural stem (NS) cells derived from mouse induced pluripotent stem (iPS) cells. **Mol Cell Neurosci**. 2010 Mar;43(3):287-95.

**Complete List of Published Work in MyBibliography**:

https://www.ncbi.nlm.nih.gov/myncbi/1J1BYp-Kb6q95u/bibliography/public/

## D. Research Support

- **Ongoing Research Support**

BANDO RICERCA FINALIZZATA 2018 (GR-2018-12367290, Minister of Health)
Title: Neuronal reprogramming in Schizophrenia: a translational approach to unravel sleep endophenotypes
Role: PI (Pisa Unit)

POR FESR 2014-2020 (European Fund for Regional Development - Regione Toscana)
Title: Leather Upgrade
Role: PI (Department of Biology Unit)

Wings for Life – Spinal Cord Research Foundation Project Grant 2021
Title: Stretch-growth and cell therapy: a novel combinatorial approach for treating spinal cord Injuries
Role: Team Leader

- **Completed Research Support**

University of Pisa, PRA 2018
Title: CRISPR/Cas9: gene editing to study gene function in physiological and pathological condition
Role: co-PI

NARSAD Young investigator grant 2017
Brain & Behavior Research Foundation
Title: Understanding TORCH syndrome-associated congenital microcephaly
Role: PI

Fondazione Pisana Per La Scienza, FPS 2017
Title: Dissection of Aß oligomer synaptotoxic signaling in human neocortical neurons
Role: unit PI

FFABR 2017
MIUR (Italian Minister of Education, University and Research)
Funding for Basic Activities Related to Research
Role: PI

Connecticut Regenerative Medicine Research Fund 2015
Title: Human neuroepithelial stem cells in spinal cord injury
Role: co-investigator

Simons Foundation, SFARI 2014
Title: Sexually Dimorphic Gene-Expression and Regulation to Evaluate ASD Sex Bias
Role: PI (subcontract)

Italian Ministry of University and Research Futuro in Ricerca 2010 - FIRB 2010
Title: Target generation of cerebellar and striatal neurons as preventive strategy for CNS disorders
Role: PI

Pisa, 14/06/2021