

CURRICULUM VITAE ET STUDIORUM

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EDUCATION

April 2009: **PhD in Cellular Biology and Physiology**, Department of Biology, University of Bologna (Italy).

March 2005: **MSc in Pharmaceutical Biotechnology** (Five Years Academic Degree), Faculty of Mathematics, Physics and Natural Science and Faculty of Pharmacy, University of Bologna.

PROFESSIONAL EXPERIENCE

June 2016 – to date:

Assistant Professor of Molecular Biology, Dept. BIOMETEC, Univ. of Catania.

Scientific interests:

- ✓ Parkinson's disease and molecular mechanisms of CNS protection and repair
- ✓ Cell-to-cell communication via extracellular vesicles, including exosomes
- ✓ Horizontal RNA transfer (coding and non-coding)
- ✓ Immunometabolism
- ✓ Nanotechnologies and Synthetic Biology

December 2011 – May 2016:

Research Fellow, Dept. of Clinical Neurosciences, Univ. of Cambridge (UK).

Description of the Research Activities:

The development of stem cell-based therapies to promote tissue repair in central nervous system (CNS) diseases, represents one of the most challenging areas of investigation in the field of **regenerative medicine**. Recent evidences indicate that adult neural stem/precursor cells (NPCs) efficiently protect the CNS from chronic degeneration induced by **inflammation** both in small rodents and in primates. NPCs show the capacity to engage a complex mechanism of cell-to-cell communication with the host, which finally mediate **neuroprotection** and **immunomodulation**.

Nevertheless, a detailed understanding at the molecular level of the mechanisms behind this stem cells' therapeutic plasticity is still lacking. As such, my first strand of investigation focussed at a novel mechanism of intercellular communication that works through the transfer of extracellular vesicles (EVs), including **exosomes**. With my work I contributed to demonstrate that:

- (i) NPCs secrete EVs mainly comprising of exosomes;
 - (ii) mRNA and protein sorting in EVs/exosomes is regulated by inflammatory cytokines;
 - (iii) IFN- γ /Ifngr1 complex on EVs promotes the intercellular induction of Stat1 signalling;
 - (iv) EVs are metabolically active and alter enzymatically the metabolic environment;
 - (v) Mouse and human NPC-derived EVs are enriched in L-asparaginase activity (via Asrg11).
- Taken together these results revealed a mechanism of **cell-to-cell communication** by which NPCs may signal with the microenvironment via EVs. This is potentially relevant both in physiological conditions (e.g. neurogenesis) and in the context of neurodegenerative diseases.

Supervisor: Stefano Pluchino, MD, PhD.

February 2011 – November 2011:

Postdoc contract (Rapporto di Collaborazione Coordinata e Continuativa a Progetto) with Centro San Raffaele del Monte Tabor Foundation (Milan, Italy).

Research project: Mechanisms and implications of "mobile" ncRNAs in neural stem cells.

Research carried out at the Dept. of Clinical Neurosciences, Univ. of Cambridge (see above).

January 2009 – January 2011:

Postdoc at the Dept. of Biology, Univ. of Bologna.

Subjects of research:

- ✓ MYCN-mediated transcriptional repression in neuroblastoma
- ✓ MYC as a regulator of ABC genes in Chronic Myeloid Leukemia (CML) CD34+ hematopoietic progenitor cells
- ✓ Role of IKAROS in Adult B-Progenitor Acute Lymphoblastic Leukemia
- ✓ Identification of novel miRNAs suppressing BCR-ABL expression in CML.

January 2006 – December 2008:

PhD student at the Dept. of Biology, Univ. of Bologna.

PhD thesis: Complexity of MYCN transcriptional function in childhood neuroblastoma.

April 2004 – December 2005:

Undergraduate/graduate student at the Dept. of Biology, Univ. of Bologna.

MSc thesis: Transcriptional induction of TRKA and p75NTR genes in neuroblastoma by histone deacetylase inhibitor Trichostatin A (TSA).

Supervisor: Professor Giovanni Perini, PhD (from April 2004 to January 2011).

ACHIEVEMENTS

- ✓ **Tenure-Track Position (RTD-B)**, Dept. BIOMETEC, Univ. of Catania - June 2016 (Chiamata Diretta SSD BIO/11)
- ✓ **“Brains2South” grant** (Fondazione con il Sud - Bando Capitale Umano ad Alta Qualificazione 2015): *“Characterization of exosomes as natural messengers of bioactive molecules in the glial-neuronal signaling in Parkinson's disease.”* Principal Investigator, amount granted: € 250,000 for 3 years. Dept. BIOMETEC, Univ. of Catania.
- ✓ **Emerging Research Leaders’ Development Programme (ERLDP) 2014**, organised by the University of Cambridge: selected (after application).
- ✓ **The Evelyn Trust 2013 grant:** *“Cell signalling through secreted extracellular RNAs in neuro-immune interactions.”* Co-applicant, amount granted: £ 244,565 for 2 years. From Dec 2013 to Nov 2015. Dept. of Clinical Neurosciences, Univ. of Cambridge
- ✓ **The FEBS Long-Term Fellowship:** *“Mechanisms of mobile ncRNAs in stem cells.”* From December 2011 to November 2013. Dept. of Clinical Neurosciences, University of Cambridge
- ✓ **“Centro Interdipartimentale di Ricerca sul Cancro Giorgio Prodi” Fellowship:** *“Eradication of acute and chronic leukemic stem cells through interference of the self renewal mediated by the Smo Inhibitors.”* From January 2010 to December 2010, at the Department of Biology - University of Bologna.
- ✓ **NOVARTIS Fellowship:** *“Identification and characterization of microRNAs that block the function of Bcr-Abl in Philadelphia positive leukemias.”* From January 2009 to December 2009, at the Department of Biology - University of Bologna.
- ✓ **Award “Premio di Operosità”:** *“Transcriptional mechanisms mediated by oncoprotein N-Myc in neuroblastoma.”* Granted by NOVARTIS in February 2008, at the Department of Biology - University of Bologna.

EDITORIAL INITIATIVES / MEMBERSHIPS

- ✓ 2016 – to date: Research Topic Editor at **Frontiers in Molecular Biosciences**: *Cell-to-cell communication by extracellular vesicles: from biogenesis and functions to clinical use as novel biomarkers and therapeutic tools*.
- ✓ 2014 – to date: Editorial Board Member of **Frontiers in Molecular Neuroscience**.
- ✓ 2013 – to date: Editorial Board Member of **Neuroimmunology and Neuroinflammation** (Medknow Publications).
- ✓ 2014 – 2015: Member of the **International Society of Neuroimmunology (ISNI)**.
- ✓ 2014 – 2015: Member of the **British Neuroscience Association (BNA, UK)**.
- ✓ 2011 – 2014: Member of the **Biochemical Society (BS, UK)**.
- ✓ 2018 – to date: Member of the **Società Italiana di Biochimica e Biologia Molecolare (SIB, Italy)**

REVIEWER ACTIVITIES

- ✓ Frontiers in Molecular Neuroscience (IF: 5.076).
- ✓ Stem Cell Research & Therapy (IF: 4.211).
- ✓ Frontiers in Pharmacology (IF: 4.400).
- ✓ International Journal of Molecular Sciences (IF: 3.226).
- ✓ European Biophysics Journal (IF: 1.472).
- ✓ Biotechnology and Biological Sciences Research Council (BBSRC, UK).
- ✓ The Research Foundation - Flanders (FWO, Belgium).
- ✓ Judge at the School of Clinical Medicine Research Day, University of Cambridge.

TEACHING AND OTHER ACTIVITIES

Academic year 2017-2018:

Signaling vescicolare intra e inter-cellulare (course code 1015603; SSD BIO/11; 6 CFU)
MSc in Medical Biotechnology, Dept. BIOMETEC, Univ. of Catania.

July 2015 – December 2015:

Divisional Biological Safety Officer (DBSO) – Dept. of Clinical Neurosciences, Univ. of Cambridge.

Academic years 2007-2008 / 2008-2009 / 2009-2010:

Teaching Assistant and Laboratory Instructor. “Laboratory of Genetics”, MSc in Molecular Biology. Dept. of Biology, Univ. of Bologna.

Academic years 2005-2006 / 2006-2007:

Teaching Assistant and Laboratory Instructor. “Molecular Biology laboratory I”, BSc in Biological Science. Dept. of Biology, Univ. of Bologna.

Mentor/Supervisor Activities:

- ✓ Loredana Leggio (2017 - ongoing) – Postdoc, Dept. BIOMETEC, Univ. of Catania
- ✓ Florian Gessler (2014-2016) – PhD in Clinical Neurosciences, Univ. of Cambridge.
- ✓ Julia Schaeffer (2012-2013) – MPhil, Univ. of Cambridge.
- ✓ Matilde Stefanini (2011-2012) – MSc in Cellular and Molecular Medical Biotechnology, Univ. Vita & Salute, Milan.
- ✓ Roberta Napolitano (2010) – BSc in Bio-sanitary Biotechnology, Univ. of Bologna.
- ✓ Francesco Sottile (2009) – BSc in Molecular and Industrial Biotechnology, Univ. of Bologna.
- ✓ Emanuele Valli (2007-2010) – MSc in Molecular and Industrial Biotechnology and PhD in Cellular Biology and Physiology, Univ. of Bologna.

PUBLICATIONS

Scopus ID: **55597087097**

H index: **15**

Total citations: **830**

1. Peruzzotti-Jametti L, Bernstock JD, Vicario N, Costa ASH, Kwok CK, Leonardi T, Booty LM, Bicci I, Balzarotti B, Volpe G, Mallucci G, Manferrari G, Donegà M, **Iraci N**, Braga A, Hallenbeck JM, Murphy MP, Edenhofer F, Frezza C, Pluchino S.
Macrophage-Derived Extracellular Succinate Licenses Neural Stem Cells to Suppress Chronic Neuroinflammation.
Cell Stem Cell. 2018 Mar 1;22(3):355-368.e13. (IF: **22.387**; PMID: 29478844)
2. L'Episcopo F, Caniglia S, Tirolo C, Serapide MF, Testa N, Leggio L, Vivarelli S, **Iraci N**, Pluchino S, Marchetti B.
Microglia Polarization, Gene-Environment Interactions and Wnt/ β -catenin Signalling: Emerging Roles of Glia-Neuron and Glia-Stem/Neuroprogenitor Crosstalk for Dopaminergic Neurorestoration in Aged Parkinsonian Brain.
Front. Aging Neurosci. 2018 Feb 12;10:12. (IF: **4.504**; PMID: 29483868)
3. Leggio L, Vivarelli S, L'Episcopo F, Tirolo C, Caniglia S, Testa N, Marchetti B, **Iraci N**.
microRNAs in Parkinson's Disease: From Pathogenesis to Novel Diagnostic and Therapeutic Approaches.
Int J Mol Sci. 2017 Dec 13;18(12):2698. (IF: **3.226**; PMID: 29236052)
4. **Iraci N***, Gaude E*, Leonardi T, Costa ASH, Cossetti C, Peruzzotti-Jametti L, Bernstock JD, Saini HK, Gelati M, Vescovi AL, Bastos C, Faria N, Occhipinti LG, Enright AJ, Frezza C, Pluchino S.
Extracellular vesicles are independent metabolic units with asparaginase activity.
Nat Chem Biol. 2017 Sep;13(9):951-955. (IF: **15.066**; PMID: 28671681)
* Equal contribution.
5. Pathan M, Keerthikumar S, Chisanga D, Alessandro R, Ang CS, Askenase P, Batagov AO, Benito-Martin A, Camussi G, Clayton A, Collino F, Di Vizio D, Falcon-Perez JM, Fonseca P, Fonseka P, Fontana S, Gho YS, Hendrix A, Hoen EN, **Iraci N**, Kastaniegaard K, Kislinger T, Kowal J, Kurochkin IV, Leonardi T, Liang Y, Llorente A, Lunavat TR, Maji S, Monteleone F, Øverbye A, Panaretakis T, Patel T, Peinado H, Pluchino S, Principe S, Ronquist G, Royo F, Sahoo S, Spinelli C, Stensballe A, Théry C, van Herwijnen MJC, Wauben M, Welton JL, Zhao K, Mathivanan S.
A novel community driven software for functional enrichment analysis of extracellular vesicles data.
J Extracell Vesicles. 2017 May 26;6(1):1321455. (PMID: 28717418)
6. **Iraci N***, Leonardi T*, Gessler F, Vega B and Pluchino S.
Focus on extracellular vesicles: Physiological role and signalling properties of extracellular membrane vesicles.
Int J Mol Sci. 2016 Feb 6;17(2). (IF: **2.862**; PMID: 26861302)
* Equal contribution.
7. Fuster-Matanzo A, Gessler F, Leonardi T, **Iraci N** and Pluchino S.
Acellular approaches for regenerative medicine: on the verge of clinical trials with extracellular membrane vesicles?
Stem Cell Res Ther. 2015 Dec 2;6:227. (IF: **3.368**; PMID: 26631254)
8. Tannahill GM*, **Iraci N***, Gaude E, Frezza C and Pluchino S.
Metabolic reprogramming of mononuclear phagocytes in progressive multiple sclerosis.

- Front Immunol.** 2015 Mar 11;6:106. (PMID: 25814990)
* Equal contribution.
9. C Cossetti*, **N Iraci***, TR Mercer, T Leonardi, E Alpi, D Drago, C Alfaro-Cervello, ME HK Saini, MP Davis, J Schaeffer, B Vega, M Stefanini, CJ Zhao, W Muller, JM Garcia-Verdugo, S Mathivanan, A Bachi, AJ Enright, JS Mattick, S Pluchino
Extracellular vesicles from neural stem cells transfer IFN- γ via Ifngr1 to activate Stat1 signalling in target cells.
Mol Cell. 2014 Oct 23;56(2):193-204. (IF: 14.464; PMID: 25242146)
* Equal contribution.
 10. Smith JA, Leonardi T, Huang B, **Iraci N**, Vega B, Pluchino S.
Extracellular vesicles and their synthetic analogues in aging and age-associated brain diseases.
Biogerontology. 2015 Apr;16(2):147-85. (IF: 3.010; PMID: 24973266)
 11. Drago D, Cossetti C, **Iraci N**, Gaude E, Musco G, Bachi A, Pluchino S.
The stem cell secretome and its role in brain repair.
Biochimie. 2013 Dec;95(12):2271-85. (IF: 3.142; PMID: 23827856)
 12. Iacobucci I*, **Iraci N***, Messina M, Lonetti A, Chiaretti S, Valli E, Ferrari A, Papayannidis C, Paoloni F, Vitale A, Storlazzi CT, Ottaviani E, Guadagnuolo V, Durante S, Vignetti M, Soverini S, Pane F, Foà R, Baccarani M, Mùschen M, Perini G, Martinelli
IKAROS deletions dictate a unique gene expression signature in patients with adult B-cell acute lymphoblastic leukemia.
PLoS One. 2012;7(7):e40934. (IF: 3.730; PMID: 22848414)
* Equal contribution.
 13. Cossetti C, Smith JA, **Iraci N**, Leonardi T, Alfaro-Cervello C, Pluchino S.
Extracellular membrane vesicles and immune regulation in the brain.
Front Physiol. 2012;3:117. (PMID: 22557978)
 14. Henderson MJ, Haber M, Porro A, Munoz MA, **Iraci N**, Xue C, Murray J, Flemming CL, Smith J, Fletcher JI, Gherardi S, Kwek CK, Russell AJ, Valli E, London WB, Buxton AB, Ashton LJ, Sartorelli AC, Cohn SL, Schwab M, Marshall GM, Perini G, Norris MD.
ABCC multidrug transporters in childhood neuroblastoma: clinical and biological effects independent of cytotoxic drug efflux.
J Natl Cancer Inst. 2011 Aug 17;103(16):1236-51. (IF: 14.336; PMID: 21799180)
 15. Marshall GM, Liu PY, Gherardi S, Scarlett CJ, Bedalov A, Xu N, **Iraci N**, Valli E, Ling D, Thomas W, van Bekkum M, Sekyere E, Jankowski K, Trahair T, Mackenzie KL, Haber M, Norris MD, Biankin AV, Perini G, Liu T.
SIRT1 promotes N-Myc oncogenesis through a positive feedback loop involving the effects of MKP3 and ERK on N-Myc protein stability.
PLoS Genet. 2011 Jun;7(6):e1002135. (IF: 8.517; PMID: 21698133)
 16. Porro A*, **Iraci N***, Soverini S, Diolaiti D, Gherardi S, Terragna C, Durante S, Valli E, Kalebic T, Bernardoni R, Perrod C, Haber M, Norris MD, Baccarani M, Martinelli G, Perini G.
c-MYC oncoprotein dictates transcriptional profiles of ATP-binding cassette transporter genes in chronic myelogenous leukemia CD34+ hematopoietic progenitor cells.
Mol Cancer Res. 2011 Aug;9(8):1054-66. (IF: 4.353; PMID: 21693596)
* Equal contribution.

17. **Iraci N***, Diolaiti D*, Papa A, Porro A, Valli E, Gherardi S, Herold S, Eilers M, Bernardoni R, Della Valle G, Perini G.
A SP1/MIZ1/MYCN repression complex recruits HDAC1 at the TRKA and p75NTR promoters and affects neuroblastoma malignancy by inhibiting the cell response to NGF.
Cancer Res. 2011 Jan 15;71(2):404-12. (IF: 8.650; PMID: 21123453)
* Equal contribution.
18. Porro A, Crochemore C, Cambuli F, **Iraci N**, Contestabile A and Perini G.
Nitric oxide control of MYCN expression and multi drug resistance genes in tumors of neural origin.
Curr Pharm Des. 2010;16(4):431-9. (IF: 3.311; PMID: 20236072)
19. Marshall GM, Gherardi S, Xu N, Neiron Z, Trahair T, Scarlett CJ, Chang DK, Liu PY, Jankowski K, **Iraci N**, Haber M, Norris MD, Keating J, Sekyere E, Jonquieres G, Stossi F, Katzenellenbogen BS, Biankin AV, Perini G, Liu T.
Transcriptional upregulation of histone deacetylase 2 promotes Myc-induced oncogenic effects.
Oncogene. 2010 Nov 4;29(44):5957-68. (IF: 7.357; PMID: 20697349)
20. Chen L, **Iraci N**, Gherardi S, Gamgle LD, Wood KM, Perini G, Lunec J, Tweddle DA.
p53 is a Direct Transcriptional Target of MYCN in Neuroblastoma.
Cancer Res. 2010 Feb 15;70(4):1377-88. (IF: 8.650; PMID: 20145147)
21. Porro A, Haber M, Diolaiti D, **Iraci N**, Henderson M, Gherardi S, Valli E, Munoz MA, Xue C, Flemming C, Schwab M, Wong JH, Marshall GM, Della Valle G, Norris MD, Perini G.
Direct and coordinate regulation of ATP-binding cassette transporter genes by Myc factors generates specific transcription signatures that significantly affect the chemoresistance phenotype of cancer cells.
J Biol Chem. 2010 Jun 18;285(25):19532-43. (IF: 4.651; PMID: 20233711)
22. Liu T, Tee A, Porro A, Smith SA, Dwarte T, Liu PY, **Iraci N**, Sekyere E, Haber M, Norris MD, Diolaiti D, Della Valle G, Perini G and Marshall GM.
Activation of tissue transglutaminase transcription by histone deacetylase inhibition as a therapeutic approach for Myc oncogenesis.
Proc Natl Acad Sci USA. 2007 Nov 20; 104(47):18682-87. (IF: 9.737; PMID: 18003922)

Book chapters:

1. **Iraci N***, Tyzack GE, Cossetti C, Alfaro-Cervello C and Pluchino S*.
Viral Manipulation of neural stem/precursor cells.
Viral Vectors Approaches in Neurobiology and Brain Diseases. Neuromethods, Volume 82, 2014, pp 269-288. Humana Press publishers. ISBN: 978-1-62703-609-2.
* Co-corresponding authors.
2. Smith JA, Alfaro-Cervello C, Cossetti C, **Iraci N**, Stefanini M, and Pluchino S (2013).
Extracellular Membrane Vesicles (EMVs) and EMV-Based Therapeutics for Brain Diseases.
RNA Nanotechnology and Therapeutics. July 9, 2013, pp 409-428. P Guo and F. Haque (Eds); CRC Press, Taylor & Francis Group. ISBN: 9781466505667.

MEETING ABSTRACTS (SELECTED)

- **Invited speaker** at the First Brainstorming Research Assembly of Young Neuroscientists (BraYn), 29-30 Jun 2018, Genova, Italy. *Extracellular vesicles as a novel strategy of cell-to-cell communication.*
- **Invited speaker** at the First International GIBB Meeting, 14-16 Jun 2017, Catania, Italy. *Extracellular vesicles are independent metabolic units with asparaginase activity*
- **Invited speaker** at the Joint Meeting of the SIF Workgroups “Neurodegenerative Disease” and “Inflammation”, 9-10 Jun 2016, Catania, Italy. *Controversies in Neurodegeneration.*
- Abstract selected for **oral presentation** and **travel grant** at the UK/Russia joint workshop Extracellular vesicles, 1-5 March 2015, Moscow (Russian Federation). *Extracellular vesicles secreted by neural stem cells as a novel mechanism of cell-to-cell communication.*
- **Invited speaker** at the Cambridge Centre for Brain Repair Away Day, 6 Jan 2015, Girton College, Cambridge, UK.
- **Invited speaker** and **Biochemical Society Travel Grant** at the 4th Optic Nerve Meeting, 3-5 Dec 2014, Obergurgl, Austria. *Extracellular vesicles secreted by neural stem cells as a novel mechanism of cell-to-cell communication.*
- **Poster** and **travel grant** at the FEBS EMBO Conference, 30 Aug-4 Sep 2014, Paris, France. *Mechanisms of mobile ncRNAs in neural stem/precursor cells.*
- Abstract selected for **oral presentation** and **travel grant** at the American Society of Hematology, 51th Annual Meeting and Exposition, 5-8 Dec 2009, New Orleans, LA, USA. *Suppression of Bcr-Abl Expression in CML by A Panel of miRNAs.*
- **Invited speaker** at the AICC Annual Meeting, 26-28 Nov 2008, Bologna, Italy. *Direct and coordinate regulation of ABC transporter genes by the transcription factor Myc.*