

Curriculum Vitae

ENRICA CATERINA PIETRONIGRO, PhD

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PERSONAL INFORMATION

Date and place of birth: November 7 1985, Bussolengo, Verona, Italy

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EDUCATION

2010 - 2013 PhD in Molecular and Cellular Biology and Pathology

Faculty of Medicine, Department of Pathology, University of Verona, Italy.

Oct 2010 Single-cycle Master's degree in Pharmaceutical Chemistry and Technology

Faculty of Pharmacy, University of Padua, Italy

WORK EXPERIENCE

Current position

Jan 2022 – To date

Research Assistant

Section of General Pathology, Department of Medicine, University of Verona, Italy.

Previous positions

August 2020 – Dec 2021

Laboratory Technician position (contract: Categoria D, Pos. Ec. D1)

Section of General Pathology, Department of Medicine, University of Verona, Italy.

Jan 2020 - July 2020

Postdoctoral fellow (7 months) for the project entitled: "Studio del ruolo dei leucociti nei pazienti con malattia di Alzheimer ", Laboratory of Neuroimmunology, Department of Medicine, Section of General Pathology, University of Verona, Italy.

Jan 2017 - Dec 2019

Assegnista di Ricerca (3 years) for the project entitled: “Il ruolo delle cellule del sistema immunitario nella malattia di Alzheimer, finanziato nell’ambito del Progetto Europeo ERC advanced N.695714 ‘The role of immune cells in Alzheimer’s disease, IMMUNOALZHEIMER” Laboratory of Neuroimmunology, Department of Medicine, Section of General Pathology, University of Verona, Italy.

Jan 2014 - Dec 2016

Assegnista di Ricerca (3 years) for the project entitled: “Meccanismi molecolari che controllano il traffico leucocitario in corso di processi infiammatori” finanziato dalla Fondazione Cariverona nell’ambito del progetto “VERONA NANOMEDICINE” (WP4). Department of Pathology, University of Verona, Italy.

2010 – 2013

PhD student,

Department of Pathology, University of Verona, Italy.

The project focused on the role of neutrophils in the pathogenesis of Alzheimer’s disease. The study led to a publication in 2015 on Nature Medicine, in which dr. Pietronigro is the co-first author (Zenaro, Pietronigro et al. “Neutrophils promote Alzheimer’s disease- like pathology and cognitive decline via a mechanism dependent on LFA-1 integrin”, 2015, Nat. Med.)

Supervisor: Prof. G. Constantin.

SUPERVISION OF GRADUATE STUDENTS AND POSTDOCTORAL FELLOWS

Experienced in supervising and coaching Master/Bachelor degree and PhD students: generate ideas and find creative ways to solve problems in pioneering and innovating solutions. Dr. Pietronigro has a good ability to establish effective and constructive interpersonal relationships.

MEMBERSHIPS OF SCIENTIFIC SOCIETIES

Member of the Italian Society of Neuroimmunology (AINI).

PARTICIPATION TO FUNDED INTERNATIONAL AND NATIONAL PROJECTS

- 2016-2022, ERC advanced grant, acronym IMMUNOALZHEIMER, grant agreement nr. 695714, LS6 sector, to study cellular and molecular immune mechanisms leading to neuroinflammation, neurodegeneration and cognitive decline. Project title: The role of immune cells in Alzheimer’s disease. Amount: 2.500.000 €; Project duration: 6 years. Role in the project: key personnel.
- 2016-2017, Grant from the Alzheimer Drug Discovery Foundation (ADDF), USA, in collaboration with Prof. Paul Thompson from the University of Massachusetts Medical School,

USA. Project title: “Inhibiting Neutrophil Extracellular Trap (NET) formation as a novel therapeutic approach to Alzheimer’s disease”. Project code: 20151206. Project duration: 12 months. Amount: 150.000\$ USA (85.000\$ for University of Verona and 65.000\$ for Prof. Thompson’s lab). Role in the project: key personnel.

- 2010-2014 Fondazione Cariverona. Titolo progetto: VERONA NANOMEDICINE INITIATIVE: Therapeutic effect of nanovectors in murine models of atherosclerosis”. Project duration: 4 years. PI: Prof. Luciano Cominacini. Role in the project: key personnel.
- 2010-2011, Fondazione Italiana Sclerosi Multipla (FISM), Genoa, Italy. Project title: Role of T-cell immunoglobulin and mucin domain (TIM)-1 in lymphocyte trafficking in the inflamed central nervous system. Project code: 2010/R/13. Project duration: 12 months. Amount: 50.000 €. Role in the project: key personnel.

SCIENTIFIC ACTIVITY

Dr. Pietronigro graduated in Pharmaceutical Chemistry and Technology (Single-cycle Master’s degree, Faculty of Pharmacy, University of Padua) in October 2010 carrying out a research project in the laboratory of Prof. Gabriela Constantin at the University of Verona. The project was aimed to study the role of vascular inflammation and leukocyte trafficking in experimental animal models of Alzheimer’s disease.

In 2013, Dr. Pietronigro obtained a PhD in Molecular and Cellular Pathology at the University of Verona. During her PhD research program, Dr. Pietronigro worked in the laboratory of Prof. Gabriela Constantin, studying the role of neutrophils in the pathogenesis and cognitive impairments in mouse models of Alzheimer’s disease. The study led to a publication in 2015 on *Nature Medicine*, in which she is the co-first author (Zenaro, Pietronigro et al. “Neutrophils promote Alzheimer’s disease- like pathology and cognitive decline via a mechanism dependent on LFA-1 integrin”, 2015, *Nat. Med.*)

During her stay in the laboratory of Neuroimmunology led by Prof. Gabriela Constantin, Dr. Pietronigro acquired a wide background in neuroimmunology and neuroinflammation studying leukocyte trafficking mechanisms in the central nervous system, she also acquired broad skills in animal behavioral tests and intravital microscopy techniques. Also, Dr. Pietronigro contributed to set up and directs a new facility to perform cognitive tests (Y maze, Open field, Novel object recognition, Contextual Fear Conditioning, Morris Water Maze) necessary to study the role of immune mechanisms in AD-like disease.

In addition, Dr. Pietronigro contributed to studies of leukocyte activation and trafficking during autoimmune disorders and chronic inflammatory diseases. She was key personnel in a project funded by Fondazione Italiana Sclerosi Multipla (FISM, Project title: Role of T- cell immunoglobulin and mucin domain (TIM)-1 in lymphocyte trafficking in the inflamed central nervous system). Moreover, Dr. Pietronigro contributed to the identification of new mechanisms controlling integrin-dependent adhesion in inflamed brain microcirculation and T cell motility inside the spinal cord during experimental autoimmune encephalomyelitis (EAE), which led to publications in 2011, 2014 and 2019 (Rossi B. et al. *Neuroimmunol.* 2011; Angiari S. et al. *Immunity* 2014; Dusi S. et al. *Front Immunol.* 2019).

Dr. Pietronigro contributed to the development of an intravital microscopy setting using two-photon

microscopy to elucidate the role of leukocyte trafficking mechanisms in blood vessels and inside the parenchyma of both AD-like murine models. These efforts led to a published review entitled “Imaging of leukocyte trafficking in Alzheimer’s disease” (Frontiers Immunology, 2016). More recently, Dr. Pietronigro acquired expertise in advanced microscopy and contributed to the setting of high resolution wide-field microscopy platforms to analyze neuropathological changes in human and mouse tissues and for in vitro 3D co-culture systems in the lab (Zeiss AxioImager Z2, AxioExaminer, AxioObserver 7 platforms equipped with Colibri, Apotome and deconvolution, AI sample finder, and softwares Imaris, Zen, ImageJ, and Arivis 4D for image analysis, 3D-rendering, cell tracking, etc).

Dr. Pietronigro also studied the role of neutrophil-dependent damage in the CNS. The discovery of neutrophil-extracellular traps (NETs) inside the AD brain (Zenaro et al. 2015), led to a later review entitled “NETosis in Alzheimer’s disease” by Frontiers Immunology in 2017, and a *manuscript in preparation* collaboration with Prof. Paul Thompson from the University of Massachusetts Medical School, USA. The funded project focused on the inhibition of Neutrophil Extracellular Trap (NETs) formation as a novel therapeutic approach to Alzheimer’s disease.

In the context of an ERC advanced grant entitled “The role of immune cells in Alzheimer’s disease” (Acronym Immunoalzheimer), Dr. Pietronigro (key personnel) contributed to the investigation of the role of $\gamma\delta$ T cells in the induction of neuroinflammation and cognitive decline in animal models of AD.

Dr. Pietronigro also collaborated to the study on the role of Peli-1 in microglial cells in post-mortem brain of patients with Alzheimer’s disease in collaboration with Prof. Xiao from the Chinese Academy of Sciences (Shanghai, China). The study led to a publication in PlosBiology (Xu J. et al. PLoS Biol, 2020). Dr. Pietronigro also collaborated with Prof. Cappelletti from University of Milan, to investigate neutrophil and lymphocyte infiltration in post-mortem brains of patients affected by Parkinson’s disease. In addition, Dr. Pietronigro shared her experience in neuropathological studies with Prof. DeFranceschi (Associate Professor, Dept. Medicine, University of Verona) working on Chorea-Acanthocytosis (ChAc), another neurodegenerative disorder (this collaboration led to a publication by Peikert K. et al. Acta Neuropathol Commun 2021).

Recently, Dr. Pietronigro is collaborating with Prof. Bicego (Associate Professor, Dept. Computer Science, University of Verona) to investigate Alzheimer’s disease progression in AD-like mice through a novel approach comprehensive of systems biology and machine learning. In particular, the project focuses on a new computational approach to study interactions between microglial cells and amyloid-beta deposits.

In conclusion, Dr. Pietronigro is a mature scientist with strong interest in characterizing the molecular mechanisms controlling leukocyte trafficking in the central nervous system and leukocyte-mediated neurotoxic mechanisms during neurodegenerative diseases.

At this career stage, Dr. Pietronigro is an investigator with:

- Good record of publications for her career stage
- Strong history of successful collaboration with members of her own research group and other national and international laboratories.

- Managerial experience via responsibility for mouse behavior and two-photon microscopy facilities.
- Experience mentoring master degree and PhD students.

PUBLICATIONS AND BIBLIOMETRY

- International peer-reviewed publications: 9 (4 as first author)
- Number of citations: 427 (tracked by Scopus Oct 30th 2021)
- Scopus h-index (2011-2021): 6

PUBLICATIONS IN INTERNATIONAL JOURNALS

1. [Therapeutic targeting of Lyn kinase to treat chorea-acanthocytosis](#). Kevin Peikert, Enrica Federti, Alessandro Matte, Gabriela Constantin, [Enrica Caterina Pietronigro](#), Paolo Francesco Fabene, Paola Defilippi, Emilia Turco, Federico Del Gallo, Pietro Pucci, Angela Amoresano, Anna Illiano, Flora Cozzolino, Maria Monti, Francesca Garello, Enzo Terreno, Seth Leo Alper, Hannes Glab, Lisann Pelzl, Katja Akgün, Tjalf Ziemssen, Rainer Ordemann, Florian Lang, Anna Maria Brunati, Elena Tibaldi, Immacolata Andolfo, Achille Iolascon, Giuseppe Bertini, Mario Buffelli, Carlo Zancanaro, Erika Lorenzetto, Angela Siciliano, Massimiliano Bonifacio, Adrian Danek, Ruth Helen Walker, Andreas Hermann & Lucia De Franceschi. *Acta Neuropathol Commun* 9, 81 (2021) <https://doi.org/10.1186/s40478-021-01181-y>. PMID: 33941276
2. [Peli1 impairs microglial A \$\beta\$ phagocytosis through promoting C/EBP \$\beta\$ degradation](#). Xu J, Yu T, Pietronigro EC, Yuan J, Arioli J, Pei Y, et al. (2020) *PLoS Biol* 18(10): e3000837. <https://doi.org/10.1371/journal.pbio.3000837>. PMID: 33017390
3. [LFA-1 Controls Th1 and Th17 Motility Behavior in the Inflamed Central Nervous System](#). Dusi S., Angiari S., [Pietronigro E.C.](#), Lopez N., Angelini G., Zenaro E., DellaBianca V., Tosadori G., Paris F., Amoruso A., Carlucci T., Constantin G., Rossi B. *Front Immunol*. 2019 Oct 18;10:2436. doi:10.3389/fimmu.2019.02436.eCollection2019. PMID: 31681316.
4. [Blockade of \$\alpha\$ 4 integrins reduces leukocyte-endothelial interactions in cerebral vessels and improves memory in a mouse model of Alzheimer's disease](#). [Pietronigro E.](#), Zenaro E., Della Bianca V., Dusi S., Terrabuio E., Iannoto G., Slanzi A., Ghasemi S., Nagarajan R., Piacentino G., Tosadori G., Rossi B., Constantin G. *Sci Rep*. 2019 Aug 19;9(1):12055. doi: 10.1038/s41598-019-48538-x. PMID: 31427644.
5. [NETosis in Alzheimer's Disease](#). [Pietronigro E](#), Della Bianca V, Zenaro E, Constantin G. *Front Immunol*. 2017 Mar 2;8:211. doi: 10.3389/fimmu.2017.00211. eCollection 2017. PMID: 28303140.
6. [Imaging of Leukocyte Trafficking in Alzheimer's Disease](#). [Pietronigro E](#), Zenaro E, Constantin G. *Front Immunol*. 2016 Feb 15;7:33. doi: 10.3389/fimmu.2016.00033. Review. PMID: 26913031.

7. [Neutrophils promote Alzheimer's disease-like pathology and cognitive decline via LFA-1 integrin.](#) Zenaro E, **Pietronigro E***, Della Bianca V, Piacentino G, Marongiu L, Budui S, Turano E, Rossi B, Angiari S, Dusi S, Montresor A, Carlucci T, Nani S, Tosadori G, Calciano L, Catalucci D, Berton G, Bonetti B, Constantin G. *Nat Med.* 2015 Aug;21(8):880-6. doi: 10.1038/nm.3913. PMID: 26214837. (*Contribution as co-first author)
8. [TIM-1 glycoprotein binds the adhesion receptor P-selectin and mediates T cell trafficking during inflammation and autoimmunity.](#) Angiari S, Donnarumma T, Rossi B, Dusi S, **Pietronigro E**, Zenaro E, Della Bianca V, Toffali L, Piacentino G, Budui S, Rennert P, Xiao S, Laudanna C, Casasnovas JM, Kuchroo VK, Constantin G. *Immunity.* 2014 Apr 17;40(4):542-53. doi: 10.1016/j.immuni.2014.03.004. PMID: 24703780.
9. [Inverse agonism of cannabinoid CB1 receptor blocks the adhesion of encephalitogenic T cells in inflamed brain venules by a protein kinase A-dependent mechanism.](#) Rossi B, Zenaro E, Angiari S, Ottoboni L, Bach S, Piccio L, **Pietronigro EC**, Scarpini E, Fusco M, Leon A, Constantin G. *J Neuroimmunol.* 2011 Apr;233(1-2):97-105. doi: 10.1016/j.jneuroim.2010.12.005. Epub 2011 Jan 7. PMID: 21216016.