

SUMMER SCHOOL DIRECTOR

Grazia Paola Nicchia, Ph.D. (*Date of birth April 19th 1972*)



Full Professor of Physiology at the Department of Bioscience, Biotechnology and Biopharmaceutics (University of Bari “Aldo Moro”) and Faculty Member (Visiting Professor) at the Dominick P. Purpura Neuroscience Department, A. Einstein College of Medicine, New York (USA). She obtained a Ph.D. in Physiology in 2000 at the University of Naples “Federico II” and was awarded the “SIF Award 2005” for best young Italian scientist in Physiology by the Italian Society of Physiology.

Her research activity is focused on the cellular and molecular physiology and biophysics of water channel proteins called Aquaporins (AQPs). The main interest is the Central Nervous System (CNS) Aquaporin-4 (AQP4) but she is also fascinated by the endothelial Aquaporin-1 (AQP1), both sharing many common features in assisting blood vessel formation in the CNS (AQP4) and outside the CNS (AQP1). She is interested in the molecular mechanisms by which AQPs are able to promote cell volume regulation, changes in cell morphology and calcium signalling, working in concert with TRP and Connexin ion channels. Studies are performed on 1) cell cultures for biophysical analysis, 2) CNS tissue (mammalian brain and retina) to analyse the role for AQP4 at the gliovascular interface and 3) tumours (melanoma mouse model) to analyse the role for AQP1 in tumour angiogenesis. At the molecular level, she is also interested in understanding how AQP4 tetramers are able to spontaneously aggregate into well-ordered structures called Orthogonal Arrays of Particles (OAPs). In particular, she has discovered that OAPs are the target of autoantibodies in Neuromyelitis Optica, a severe form of Multiple Sclerosis, and she is interested in elucidating the molecular mechanisms at the root of the interaction between OAPs and autoantibodies. Since this main goal is strictly related to the knowledge of AQP4 spontaneous aggregation into OAPs, in 2016 she generated the first OAP-null mouse model, using the CRISPR/Cas9 technology. She is currently involved in characterizing this model.

She can rely on a well-equipped laboratory, which has developed biophysics expertise using Total Internal Reflection Microscopy and Stopped Flow Light Scattering for measurements of water transport in cells. The microscopy equipment has been greatly augmented with the PALM (PhotoActivated Localization Microscopy) advanced systems for high-resolution microscopy and gSTED (Stimulated Emission Depletion) for OAP analysis.

She has authored/co-authored 63 full papers and published 3 book chapters with H-index = 30.

COMPLETE LIST OF PUBLICATIONS (March 6th 2018)

H-index (Scopus): 30;

Total Citations (Scopus): 2325

- 1) Frigeri and **G.P. Nicchia**. Response to “The evolving mystery of why skeletal muscle is spared in seropositive neuromyelitisoptica”. *J Cell Mol Med.* (2018) doi: 10.1111/jcmm.13513.
- 2) S. Rosito, **G.P. Nicchia**, C. Palazzo, A. Lia, C. Buccoliero, F. Pisani, M. Svelto, M. Trojano, A. Frigeri. “Supramolecular aggregation of aquaporin-4 is different in muscle and brain: correlation with tissue susceptibility in neuromyelitisoptica”. *J Cell Mol Med.* (2018) 22:1236-1246.
- 3) L. Simone, C.D. Gargano, F. Pisani, A. Cibelli, M.G. Mola, A. Frigeri, M. Svelto, **G.P. Nicchia**. “Aquaporin-1 inhibition reduces metastatic formation in a mouse model of melanoma”. *J Cell Mol Med.* (2018) 22: 904-912.
- 4) F. Pisani, M. Cammalleri, M. Dal Monte, F. Locri, M.G. Mola, **G.P. Nicchia**, A. Frigeri, P. Bagnoli, M. Svelto. “Potential role of the methylation of VEGF gene promoter in response to hypoxia in oxygen-induced retinopathy: beneficial effect of the absence of AQP4”. *J Cell Mol Med.* (2018) 22: 613-627.
- 5) A.M. D'Erchia, A. Gallo, C. Manzari, S. Raho, D.S. Horner, M. Chiara, A. Valletti, I. Aiello, F. Mastropasqua, L. Ciaccia, F. Locatelli, F. Pisani, **G.P. Nicchia**, M. Svelto, G. Pesole, E. Picardi. “Massive transcriptome sequencing of human spinal cord tissues provides new insights into motor neuron degeneration in ALS”. *Sci Rep.* (2017) 7):10046. doi: 10.1038/s41598-017-10488-7.
- 6) M. De Bellis, F. Pisani, M.G. Mola, S. Rosito, L. Simone, C. Buccoliero, M. Trojano, **G.P. Nicchia**, M. Svelto, A. Frigeri. "Translational readthrough generates new astrocyte AQP4 isoforms that modulate supramolecular clustering, glial endfeet localization, and water transport". *Glia.* 65 (2017) 790–803.
- 7) F. Pisani, L. Simone, C.D. Gargano, M. De Bellis, A. Cibelli, M.G. Mola, G. Catacchio, A. Frigeri, M. Svelto, **G.P. Nicchia**. "Role of the H-bond between L53 and T56 for Aquaporin-4 epitope in Neuromyelitis Optica". *Biochim. Biophys. Acta.* 1859 (2017) 368–376.
- 8) M.G. Mola, A. Sparaneo, C.D. Gargano, D.C. Spray, M. Svelto, A. Frigeri, E. Scemes, **G.P. Nicchia**. "The speed of swelling kinetics modulates cell volume regulation and calcium signaling in astrocytes: A different point of view on the role of aquaporins". *Glia.* 64 (2016) 139–54.
- 9) **G.P. Nicchia**, F. Pisani, L. Simone, A. Cibelli, M.G. Mola, M. Dal Monte, A. Frigeri, P. Bagnoli, M. Svelto. "Glio-vascular modifications caused by Aquaporin-4 deletion in the mouse retina". *Exp. Eye Res.* 146 (2016) 259–68.
- 10) T. Posati, A. Pistone, E. Saracino, F. Formaggio, M.G. Mola, E. Troni, A. Sagnella, M. Nocchetti, M. Barbalinardo, F. Valle, S. Bonetti, M. Caprini, **G.P. Nicchia**, R. Zamboni, M. Muccini, V. Benfenati. "A Nanoscale Interface Promoting Molecular and Functional Differentiation of Neural Cells". *Sci. Rep.* 6 (2016) 31226.
- 11) F. Pisani, P. Settanni, S. Rosito, M.G. Mola, R. Iorio, C. Tortorella, M. Ruggieri, M. Trojano, M. Svelto, A. Frigeri, **G.P. Nicchia**. "Development of an Aquaporin-4 Orthogonal Array of Particle-Based ELISA for Neuromyelitis Optica Autoantibodies Detection". *PLoS One.* 10 (2015) e0143679.
- 12) D. Alberga, O. Nicolotti, G. Lattanzi, **G.P. Nicchia**, A. Frigeri, F. Pisani, V. Benfenati, G.F. Mangiatordi. "A new gating site in human aquaporin-4: Insights from molecular dynamics simulations". *Biochim. Biophys. Acta - Biomembr.* 1838 (2014) 3052–3060.
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- 14) M. De Bellis, F. Pisani, M.G. Mola, D. Basco, F. Catalano, **G.P. Nicchia**, M. Svelto, A. Frigeri. "A novel human aquaporin-4 splice variant exhibits a dominant-negative activity: a new mechanism to regulate water permeability". *Mol. Biol. Cell.* 25 (2014) 470–80.
 - 15) F. Pisani, M.G. Mola, L. Simone, S. Rosito, D. Alberga, G.F. Mangiatordi, G. Lattanzi, O. Nicolotti, A. Frigeri, M. Svelto, **G.P. Nicchia**. "Identification of a Point Mutation Impairing the Binding between Aquaporin-4 and Neuromyelitis Optica Autoantibodies". *J. Biol. Chem.* 289 (2014) 30578–30589.
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 - 18) **G.P. Nicchia**, C. Stigliano, A. Sparaneo, A. Rossi, A. Frigeri, M. Svelto. "Inhibition of aquaporin-1 dependent angiogenesis impairs tumour growth in a mouse model of melanoma". *J. Mol. Med. (Berl).* 91 (2013) 613–23.
 - 19) C. Stigliano, S. Aryal, M.D. de Tullio, **G.P. Nicchia**, G. Pascazio, M. Svelto, P. Decuzzi. "siRNA-Chitosan Complexes in Poly(lactic- co -glycolic acid) Nanoparticles for the Silencing of Aquaporin-1 in Cancer Cells". *Mol. Pharm.* 10 (2013) 3186–3194.
 - 20) M. Dal Monte, G. Casini, L. Filippi, **G.P. Nicchia**, M. Svelto, P. Bagnoli. "Functional involvement of β 3-adrenergic receptors in melanoma growth and vascularization". *J. Mol. Med.* 91 (2013) 1407–1419.
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 - 23) F. Pisani, M. Mastrototaro, A. Rossi, **G.P. Nicchia**, C. Tortorella, M. Ruggieri, M. Trojano, A. Frigeri, M. Svelto. "Identification of two major conformational aquaporin-4 epitopes for neuromyelitis optica autoantibody binding". *J. Biol. Chem.* 286 (2011) 9216–24.
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 - 25) F. Pisani, A. Rossi, **G.P. Nicchia**, M. Svelto, A. Frigeri. "Translational regulation mechanisms of aquaporin-4 supramolecular organization in astrocytes". *Glia.* 59 (2011) 1923–32.

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- 37) A. De Luca, B. Nico, J.-F. Rolland, A. Cozzoli, R. Burdi, D. Mangieri, V. Giannuzzi, A. Liantonio, V. Cippone, M. De Bellis, **G.P. Nicchia**, G.M. Camerino, A. Frigeri, M. Svelto, D.C. Camerino. "Gentamicin treatment in exercised mdx mice: Identification of dystrophin-sensitive pathways and evaluation of efficacy in work-loaded dystrophic muscle". *Neurobiol. Dis.* 32 (2008) 243–53.
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Book Chapters:

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 - a. Biomarkers of Astrocyte Microdomains - Focus on Gap Junctions, Purinergic Receptors, and Aquaporins. In: Scemes E and Spray DC. Astrocytes wiring the brain. p. 25-62, Boca Raton: CRC Press, Taylor & Francis Group, ISBN: 978-1-4398-2584-6
- 2) **NICCHIA GP**, NICO B, CAMASSA, L, RIBATTI M, MOLA MG, SPRAY D, SVELTO M, FRIGERI A (2006).
 - a. Responsive astrocytic endfeet: the role of AQP4 in the BBB development and functioning. In: DERMIETZEL R, SPRAY DC, NEDERGAARD M.. Blood-Brain Barriers: from Ontogeny to artificial barriers. Wiley-VCH. vol. 1, p. 209-236, ISBN: 3-527-31088-6
- 3) PIERNO S, DESAPHY JF, DE LUCA A, LIANTONIO A, DE BELLIS M, FRAYSSE B, LEOTY C, FRIGERI A, **NICCHIA GP**, SVELTO M AND CONTE CAMERINO D (2001).
 - a. Modifications of ion channel activity and expression in soleus muscle fibers account for hypogravity-induced functional alterations. In: R. MONTI AND C. BONIFAZI. Microgravity and Space Station Utilization.