

NICOLETTA FILIGHEDDU, PhD
Curriculum Vitae

Department of Translational Medicine
Università del Piemonte Orientale
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EDUCATION

PhD in Molecular Medicine (Jun 17th, 2005)

University of Piemonte Orientale, Dept. of Medical Sciences, Novara, Italy;
Supervisor: Prof. A. Graziani
Field of study: Biochemistry and Cell Biology

Master Degree in Physics (Nov 22nd, 2007)

University of Turin, Dept. of Animal and Human Biology;
Supervisor: Prof. R. Levi
Field of study: Physiology

APPOINTMENTS

Faculty (December 2006 – present)

Dept. of Translational Medicine, University of Piemonte Orientale, Novara, Italy;

Post-Doctoral Research Fellow (Jan 2006 – Dec 2006)

Laboratory of Gynecology, Dept. of Clinical and Experimental Medicine, University of Piemonte Orientale; supervisor Prof N. Surico;

Post-Doctoral Research Fellow (Nov 2004 – Dec 2005)

Laboratory of Biochemistry, Dept. of Clinical and Experimental Medicine, University of Piemonte Orientale; Supervisor Prof A. Graziani;

PhD candidate (Nov 2000 – Oct 2004)

Laboratory of Biochemistry, Dept. of Medical Sciences, University of Piemonte Orientale;
Supervisor: Prof A. Graziani.

FELLOWSHIPS - HONORS

Research Fellowship (2005-2006). 1-year fellowship awarded by University of Piemonte Orientale to study the role of estrogenic treatment in the control of mammary cancer cells proliferation. Supervisor: Prof N. Surico

Research Fellowship (2002-2004). 2-year fellowship awarded by University of Piemonte Orientale to study the role of ghrelin on cardiac and skeletal myoblasts. Supervisor Prof. A. Graziani.

Research Fellowship (2001-2002). 1-year fellowship awarded by University of Piemonte Orientale to study the regulatory mechanisms of signal transduction of growth and pro-survival factors.

Supervisor Prof. A. Graziani.

Italian Society of Endocrinology Research Fellowship (2000-2001). 1-year fellowship for the study of the cardiovascular activities of synthetic GH-secreting molecules. Supervisor Prof. A. Graziani.

Foundation for the Study of Metabolic-Endocrinological Diseases Research Fellowship (1998-1999). 1-year fellowship from to study the cardiovascular activities of new synthetic and non natural peptides. Supervisor Prof. A. Graziani.

Burroughs Wellcome Fund Scholarship (2011) to attend the *Frontiers in Reproduction* Summer Course.

The Endocrine Society Travel Grant Award (2009) for exceptional research presented at the 91st Annual Meeting of The Endocrine Society Washington, DC June 10-13 2009.

RESEARCH INTERESTS

SKELETAL MUSCLE REGENERATION

CANCER-ASSOCIATED CACHEXIA

SKELETAL MUSCLE DYSTROPHIES

SARCOPENIA

The main scientific interest of Nicoletta Filigheddu concerns the biological activities of acylated and unacylated ghrelin (AG, UnAG), in particular the protective action of these hormones on cardiac and skeletal muscle. The research group Filigheddu was associated with has been the first to demonstrate a biological activity for UnAG, showing that it shares with AG an anti-apoptotic activity on cardiomyocytes and endothelial cells and a pro-differentiative activity on skeletal muscle myoblasts. The research group has also generated a transgenic mouse overexpressing the ghrelin gene under a cardiac promoter and featuring high levels of circulating UnAG. This mouse is a very useful tool to study in vivo the effects of UnAG.

OTHER EXPERIENCES AND PROFESSIONAL MEMBERSHIPS

International Training Course (Oct 1999- Sep 2000)

Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary;
Supervisor: Dr. Maria Szucs

Editorial activities

Ad hoc reviewer for: Acta Biochimica et Biophysica Sinica; Acta Physiologica; BMC Genomics; British Journal of Cancer; Cancer Research; Cell Death & Disease; Current Stem Cell Research & Therapy; Endocrine; European Journal of Obstetrics & Gynecology and Reproductive Biology; Growth Factors; Human Reproduction; Journal of Endocrinological Investigation; Molecular and Cellular Endocrinology; Oncogene; Psychoneuroendocrinology.

Translation of selected chapters for the Italian edition of “Principles of Medical Biochemistry”, 3rd edition, Gerhard Meisenberg & William H. Simmons, Ed. Elsevier Saunders.

Memberships

Italian Society of Biochemistry and Molecular Biology
Interuniversity Institute of Myology

PUBLICATIONS

Bibliometric indicators

H index (Scopus): 13

Citations, excluding self-citations (Scopus): 939

In preparation or submitted:

Filigheddu N, Gregnanin I, D'Agostino C, Francescato R, Brustia A, Baldanzi G, Surico D, Graziani A, Surico N. Role of miR-200c and its target diacylglycerol kinase alpha in endometriosis. *Submitted to Human Reproduction, under revision*

Published:

(*coauthorship, ✉corresponding author)

Gortan Cappellari G, Zanetti M, Semolic A, Vinci P, Ruozi G, De Nardo M, **Filigheddu N**, Guarnieri G, Giacca M, Graziani A, Barazzoni R. Unacylated ghrelin does not alter mitochondrial function, redox state and triglyceride content in rat liver in vivo. *Clinical Nutrition Experimental. In press*

Oltolina F, Zamperone A, Colangelo D, Gregoletto L, Reano S, Pietronave S, Merlin S, Talmon M, Novelli E, Diena M, Nicoletti C, Musarò A, **Filigheddu N**, Follenzi A, Prat M. Human Cardiac Progenitor Spheroids Exhibit Enhanced Engraftment Potential. *PLoS One*. 2015 Sep 16;10(9):e0137999. doi: 10.1371/journal.pone.0137999.

Ruozi G, Bortolotti F, Falcione A, Dal Ferro M, Ukovich L, Macedo A, Zentilin L, **Filigheddu N**, Gortan Cappellari G, Baldini G, Zweyer M, Barazzoni R, Graziani A, Zacchigna S, Giacca M. AAV-mediated in vivo functional selection of tissue-protective factors against ischaemia. *Nat Commun*. 2015 Jun 11;6:7388. doi: 10.1038/ncomms8388.

Angelino E, Reano S, Ferrara M, Agosti E, Graziani A, **Filigheddu N**✉. Antifibrotic activity of acylated and unacylated ghrelin. *Int J Endocrinol*. 2015;2015:385682. doi: 10.1155/2015/385682.

Rainero E, Cianflone C, Porporato PE, Chianale F, Malacarne V, Bettio V, Ruffo E, Ferrara M, Benecchia F, Capello D, Paster W, Locatelli I, Bertoni A, **Filigheddu N**, Sinigaglia F, Norman JC, Baldanzi G, Graziani A. The diacylglycerol kinase α /atypical PKC/ β 1 integrin pathway in SDF-1 α mammary carcinoma invasiveness. *PLoS One*. 2014;9(6):e97144.

Prodám F, **Filigheddu N**✉. Ghrelin gene products in acute and chronic inflammation. *Arch Immunol Ther Exp (Warsz)*. 2014;62(5):369-84. (*Invited review*)

Reano S, Graziani A, **Filigheddu N**✉. Acylated and unacylated ghrelin administration to blunt muscle wasting. *Curr Opin Clin Nutr Metab Care*. 2014;17(3):236-40. (*Invited review*)

Raimondo S, Ronchi G, Geuna S, Pascal D, Reano S, **Filigheddu N**, Graziani A. Ghrelin: A novel neuromuscular recovery promoting factor? *Int Rev Neurobiol*. 2013;108:207-21. (*Invited review*)

Porporato PE*, **Filigheddu N**✉, Reano S, Ferrara M, Angelino E, Gnocchi VF, Prodám F, Ronchi G, Fagoonee S, Fornaro M, Chianale F, Baldanzi G, Surico N, Sinigaglia F, Perroteau I, Smith RG,

Sun Y, Geuna S, Graziani A. Acylated and unacylated ghrelin impair skeletal muscle atrophy in mice. *J Clin Invest.* **2013**;123:611-22.

Baldanzi G, Pighini A, Rainero E, Traini S, Chianale F, Porporato PE, **Filigheddu N**, Mesturini R, Song S, Schweighoffer T, Zhong X-P, van Blitterswijk WJ, Sinigaglia F, Nichols KE, Rubio I, Parolini O, Graziani A. SAP-mediated inhibition of diacylglycerol kinase alpha regulates TCR-induced diacylglycerol signaling. *J Immunol* **2011**;187:5941-51.

Filigheddu N[✉], Sampietro S, Porporato PE, Gaggianesi M, Chianale F, Rainero E, Ferrara M, Gregnanin I, Perego B, Riboni F, Baldanzi G, Graziani A, Surico N. Diacylglycerol kinase α mediates 17- β -estradiol-induced proliferation, motility and anchorage-independent growth of Hec-1A endometrial cancer cell line. *Cell Signal.* **2011**;23:1988-96.

Baldanzi G, Pietronave S, Locarno D, Merlin S, Porporato PE, Chianale F, **Filigheddu N**, Cantelmo AM, Albin A, Graziani A, Prat M. Diacylglycerol kinases are essential for HGF-dependent proliferation and motility of Kaposi's Sarcoma cells. *Cancer Sci.* **2011**;102:1329-36.

Filigheddu N[✉], Gregnanin I, Porporato PE, Surico D, Perego B, Galli L, Patrignani C, Graziani A, Surico N. Differential expression of microRNAs between eutopic and ectopic endometrium in ovarian endometriosis. *J Biomed Biotechnol.* **2010**; 2010:369549.

Chianale F, Rainero E, Cianflone C, Bettio V, Pighini A, Porporato PE, **Filigheddu N**, Serini G, Sinigaglia F, Baldanzi G, Graziani A. Diacylglycerol kinase alpha mediates HGF-induced Rac activation and membrane ruffling by regulating atypical PKC and RhoGDI. *Proc Natl Acad Sci U S A.* **2010** Mar 2;107(9):4182-7.

Audisio C, Raimondo S, Nicolino S, Gambarotta G, Di Scipio F, Macrì L, Montarolo F, Giacobini-Robecchi MG, Porporato P, **Filigheddu N**, Graziani A, Geuna S, Perroteau I. Morphological and biomolecular characterization of the neonatal olfactory bulb ensheathing cell line. *J Neurosci Methods.* **2009** Dec 15;185(1):89-98.

Erriquez J, Bernascone S, Ciarletta M, **Filigheddu N**, Graziani A, Distasi C. Calcium signals activated by ghrelin and D-Lys(3)-GHRP-6 ghrelin antagonist in developing dorsal root ganglion glial cells. *Cell Calcium.* **2009** Sep;46(3):197-208.

Chianale F, Cutrupi S, Rainero E, Baldanzi G, Porporato PE, Traini S, **Filigheddu N**, Gnocchi VF, Santoro MM, Parolini O, van Blitterswijk WJ, Sinigaglia F, Graziani A. Diacylglycerol kinase-alpha mediates hepatocyte growth factor-induced epithelial cell scatter by regulating Rac activation and membrane ruffling. *Mol Biol Cell.* **2007** Dec;18(12):4859-71.

Baldanzi G, Cutrupi S, Chianale F, Gnocchi V, Rainero E, Porporato P, **Filigheddu N**, van Blitterswijk WJ, Parolini O, Bussolino F, Sinigaglia F, Graziani A. Diacylglycerol kinase-alpha phosphorylation by Src on Y335 is required for activation, membrane recruitment and Hgf-induced cell motility. *Oncogene.* **2008** Feb 7;27(7):942-56.

Filigheddu N[✉], Cutrupi S, Porporato PE, Riboni F, Baldanzi G, Chianale F, Fortina E, Piantanida P, De Bortoli M, Vacca G, Graziani A, Surico N. Diacylglycerol kinase is required for HGF-induced invasiveness and anchorage-independent growth of MDA-MB-231 breast cancer cells. *Anticancer Res.* **2007** May-Jun;27(3B):1489-92.

Filigheddu N[✉], Gnocchi VF, Coscia M, Cappelli M, Porporato PE, Taulli R, Traini S, Baldanzi G, Chianale F, Cutrupi S, Arnoletti E, Ghigo C, Fubini A, Surico N, Sinigaglia F, Ponzetto C, Muccioli G, Crepaldi T, Graziani A. Ghrelin and des-acyl ghrelin promote differentiation and fusion of C2C12 skeletal muscle cells. *Mol Biol Cell*. **2007** Mar;18(3):986-94. Epub 2007 Jan 3.

Coltella N, Rasola A, Nano E, Bardella C, Fassetta M, **Filigheddu N**, Graziani A, Comoglio PM, Di Renzo MF. p38 MAPK turns hepatocyte growth factor to a death signal that commits ovarian cancer cells to chemotherapy-induced apoptosis. *Int J Cancer*. **2006** Jun 15;118(12):2981-90.

Carini R, Grazia De Cesaris M, Splendore R, Baldanzi G, Nitti MP, Alchera E, **Filigheddu N**, Domenicotti C, Pronzato MA, Graziani A, Albano E. Role of phosphatidylinositol 3-kinase in the development of hepatocyte preconditioning. *Gastroenterology*. **2004** Sep;127(3):914-23.

Baldanzi G, Mitola S, Cutrupi S, **Filigheddu N**, van Blitterswijk WJ, Sinigaglia F, Bussolino F, Graziani A. Activation of diacylglycerol kinase alpha is required for VEGF-induced angiogenic signaling in vitro. *Oncogene*. **2004** Jun 17;23(28):4828-38.

Baldanzi G, **Filigheddu N**, Cutrupi S, Catapano F, Bonisconi S, Fubini A, Malan D, Baj G, Granata R, Broglio F, Papotti M, Surico N, Bussolino F, Isgaard J, Deghenghi R, Sinigaglia F, Prat M, Muccioli G, Ghigo E, Graziani A. Ghrelin and des-acyl ghrelin inhibit cell death in cardiomyocytes and endothelial cells through ERK1/2 and PI 3-kinase/AKT. *J Cell Biol*. **2002** Dec 23;159(6):1029-37.

Filigheddu N, Fubini A, Baldanzi G, Cutrupi S, Ghigo C, Catapano F, Broglio F, Bosia A, Papotti M, Muccioli G, Ghigo E, Deghenghi R, Graziani A. Hexarelin protects H9c2 cardiomyocytes from doxorubicin-induced cell death. *Endocrine*. **2001** Feb;14(1):113-9.

RESEARCH SUPPORT

Ongoing:

2016-2018 Fondazione Cariplo "Exploring the role of ghrelin peptides in sarcopenia development during aging" € 350,000
Role: PI

2014-2017 Muscular Dystrophy Association "Exploring the therapeutic potential of unacylated ghrelin for muscular dystrophy" \$ 253,800
Role: PI

Past:

2013-2015 University of Piemonte Orientale/Compagnia di San Paolo Foundation "Identification of unacylated ghrelin receptor and its involvement in skeletal muscle wasting" € 50,000
Role: co-PI (PI: Andrea Graziani)