**BIOGRAPHICAL SKETCH**

| **NAME** | **POSITION TITLE** |
|---|---|
| Nicoletta Filigheddu | Head, Laboratory of Muscle Biology and Metabolism, Dept. of Translational Medicine, University of Piemonte Orientale (UPO), Novara, Italy |

**EDUCATION/TRAINING**

| **INSTITUTION AND LOCATION** | **DEGREE** | **YEAR** | **FIELD OF STUDY** |
|---|---|---|---|
| UPO, Novara, Italy | Ph.D. in Molecular Medicine | 2005 | Biochemistry, Molecular Biology |
| Faculty of Mathematics, Physics, and Natural Sciences, University of Turin, Italy | Master's Degree in Physics | 1997 | Physics, Physiology |

**Positions**

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| 2020 – | Associate Professor of Applied Medical Technical Sciences; Dept. of Translational Medicine, UPO, Novara, Italy |
| 2020 – | Head of the Laboratory of Muscle Biology and Metabolism, Dept. of Translational Medicine, UPO, Novara, Italy |
| 2006 – 2020 | Assistant Professor, Dept. of Translational Medicine, UPO, Novara, Italy |
| 2005 – 2006 | Post-Doctoral Research Fellow, Laboratory of Gynecology, Dept. of Clinical and Experimental Medicine, UPO; supervisor Prof N. Surico |
| 2004 – 2005 | Post-Doctoral Research Fellow, Laboratory of Biochemistry, Dept. of Clinical and Experimental Medicine, UPO; Supervisor Prof A. Graziani |
| 2000 – 2004 | PhD candidate, Laboratory of Biochemistry, Dept. of Medical Sciences, UPO; Supervisor: Prof A. Graziani. |
| 1999 – 2000 | Trainee, "UNESCO International Training Course on Modern Methods in Biology"; Biological Research Center, Hungarian Academy of Sciences, Szeged, Hungary. |

**Other appointments and Professional Memberships**

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| 2019 – | Faculty of the PhD course in "Food, Health, and Longevity", UPO and University of Turin joint PhD course; commissioner of the curriculum "Aging". |
| 2019 – | Member of the Governance of the Department of Excellence, Translational Medicine, UPO. |
| 2017 – | Member of the Research and Development Committee of the Department of Translational Medicine, UPO. |
| 2016 –2019 | Commissioner of the "Regenerative Medicine and biomaterials" curriculum within the PhD course in Sciences and Medical Biotechnologies, School of Medicine, UPO. |
| 2015 – | Consultant and member of the evaluation committees for various grant programs of the Ministry of University of Research of Italy and international grant agencies. |
| 2013 –2019 | Faculty of the PhD course in Sciences and Medical Biotechnologies, School of Medicine, UPO. |

2021 – Member of the Italian Society of Endocrinology; member of the Commission of Biologists and Biotechnologists in Endocrinological and Laboratory Diagnostics Areas.

2018 – Member of the Associazione di Biologia Cellulare e del Differenziamento

2014 – Member of the Interuniversity Institute of Myology (IIM)

2013 – Member of the Society on Sarcopenia, Cachexia and Wasting Disorders

**Honors and Awards**

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

2011 Scholarship from the Burroughs Wellcome Fund to attend the Frontiers in Reproduction Summer Course.

**Research Support**

2020-2022 Department of Excellence "Molecular determinants of the onset of sarcopenia and osteoporosis and exploration of potential therapeutic strategies" - Role: PI

2019-2021 FAR2019 "Identification of the molecular pathways underlying the activity of vitamin D to prevent skeletal muscle loss" - Role: PI

2016-2019 Cariplo Foundation "Exploring the role of ghrelin peptides in sarcopenia development during aging" - Role: PI

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

**Publications**

1. Salvadori L, Belladonna ML, Castiglioni B, Paiella M, Panfili E, Manenti T, Ercolani C, Cornioli L, Chiappalupi S, Gentili G, Leigheb M, Sorci G, Bosetti M, **Filigheddu N***, Riuzzi F*. KYMASIN UP Natural Product Inhibits Osteoclastogenesis and Improves Osteoblast Activity by Modulating Src and p38 MAPK. Nutrients. 2022 Jul 25;14(15):3053. doi: 10.3390/nu14153053.
2. Cordero-Sanchez C, Pessolano E, Riva B, Vismara M, Trivigno SMG, Clemente N, Aprile S, Ruffinatti FA, Portararo P, **Filigheddu N**, Zaggia I, Bhela IP, Serafini M, Pirali T, Colombo MP, Torti M, Sangaletti S, Bertoni A, Genazzani AA. CIC-39Na reverses the thrombocytopenia that characterizes tubular aggregate myopathy. Blood Adv. 2022 Aug 9;6(15):4471-4484. doi: 10.1182/bloodadvances.2021006378.
3. Raiteri T, Zaggia I, Reano S, Scircoli A, Salvadori L, Prodam F, **Filigheddu N**. The Atrophic Effect of 1,25$(OH)_2$ Vitamin $D_3$ (Calcitriol) on C2C12 Myotubes Depends on Oxidative Stress. Antioxidants (Basel). 2021 Dec 12;10(12):1980. doi: 10.3390/antiox10121980.
4. Ronchi G, Tos P, Angelino E, Muratori L, Reano S, **Filigheddu N**, Graziani A, Geuna S, Raimondo S. Effect of unacylated ghrelin on peripheral nerve regeneration. Eur J Histochem. 2021 Nov 4;65(s1):3287. doi: 10.4081/ejh.2021.3287.
5. Caputo M, Pigni S, Agosti E, Daffara T, Ferrero A, **Filigheddu N**, Prodam F. Regulation of GH and GH Signaling by Nutrients. Cells. 2021 Jun 2;10(6):1376. doi: 10.3390/cells10061376.
6. Klionsky DJ, et al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). Autophagy. 2021 Jan;17(1):1-382. doi: 10.1080/15548627.2020.1797280.
7. Teixeira MA, De Feudis M, Reano S, Raiteri T, Scircoli A, Zaggia I, Ruga S, Salvadori L, Prodam F, Marzullo P, Molinari C, Corà D, **Filigheddu N**. Cholecalciferol (vitamin $D_3$) has a direct protective activity against interleukin 6-induced atrophy in C2C12 myotubes. Aging (Albany NY). 2021 Feb 22;13(4):4895-4910. doi:

10.18632/aging.202669.

8. Caristia S, Vito M, Sarro A, Leone A, Pecere A, Zibetti A, **Filigheddu N**, Zeppegno P, Prodam F, Faggiano F, Marzullo P. Is Caloric Restriction Associated with Better Healthy Aging Outcomes? A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Nutrients. 2020 Jul 30;12(8):2290. doi: 10.3390/nu12082290.

9. Agosti E, De Feudis M, Angelino E, Belli R, Alves Teixeira M, Zaggia I, Tamiso E, Raiteri T, Scircoli A, Ronzoni FL, Muscaritoli M, Graziani A, Prodam F, Sampaolesi M, Costelli P, Ferraro E, Reano S, **Filigheddu N**. Both ghrelin deletion and unacylated ghrelin overexpression preserve muscles in aging mice. Aging (Albany NY). 2020 Jul 26;12(14):13939-13957. doi: 10.18632/aging.103802.

10. Cordero-Sanchez C, Riva B, Reano S, Clemente N, Zaggia I, Ruffinatti FA, Potenzieri A, Pirali T, Raffa S, Sangaletti S, Colombo MP, Bertoni A, Garibaldi M, **Filigheddu N***, Genazzani AA*. A luminal EF-hand mutation in STIM1 in mice causes the clinical hallmarks of tubular aggregate myopathy. Dis Model Mech. 2019 Dec 3;13(2):dmm041111. doi: 10.1242/dmm.041111.

11. Caristia S, **Filigheddu N**, Barone-Adesi F, Sarro A, Testa T, Magnani C, Aimaretti G, Faggiano F, Marzullo P. Vitamin D as a Biomarker of Ill Health among the Over-50s: A Systematic Review of Cohort Studies. Nutrients. 2019 Oct 6;11(10):2384. doi: 10.3390/nu11102384.

12. De Feudis M, Walker GE, Genoni G, Manfredi M, Agosti E, Giordano M, Caputo M, Di Trapani L, Marengo E, Aimaretti G, **Filigheddu N**, Bellone S, Bona G, Prodam F. Identification of Haptoglobin as a Readout of rhGH Therapy in GH Deficiency. J Clin Endocrinol Metab. 2019 Nov 1;104(11):5263-5273. doi: 10.1210/jc.2019-00562.

13. Sustova H, De Feudis M, Reano S, Alves Teixeira M, Valle I, Zaggia I, Agosti E, Prodam F, **Filigheddu N**. Opposing effects of 25-hydroxy- and 1α,25-dihydroxy-vitamin $D_3$ on pro-cachectic cytokine-and cancer conditioned medium-induced atrophy in C2C12 myotubes. Acta Physiol (Oxf). 2019 Jul;226(3):e13269. doi: 10.1111/apha.13269.

14. Angelino E, Reano S, Bollo A, Ferrara M, De Feudis M, Sustova H, Agosti E, Clerici S, Prodam F, Tomasetto CL, Graziani A, **Filigheddu N**. Ghrelin knockout mice display defective skeletal muscle regeneration and impaired satellite cell self-renewal. Endocrine. 2018 Oct;62(1):129-135. doi: 10.1007/s12020-018-1606-4.

15. Wyart E, Reano S, Hsu MY, Longo DL, Li M, Hirsch E, **Filigheddu N**, Ghigo A, Riganti C, Porporato PE. Metabolic Alterations in a Slow-Paced Model of Pancreatic Cancer-Induced Wasting. Oxid Med Cell Longev. 2018 Feb 26;2018:6419805. doi: 10.1155/2018/6419805.

16. Angelino E, Reano S, Ferrara M, Agosti E, Sustova H, Malacarne V, Clerici S, Graziani A, **Filigheddu N**. Mouse Satellite Cell Isolation and Transplantation. Bio Protoc. 2018 Jan 20;8(2):e2696. doi: 10.21769/BioProtoc.2696.

17. Porporato PE*, **Filigheddu N***, Pedro JMB, Kroemer G, Galluzzi L. Mitochondrial metabolism and cancer. Cell Res. 2018 Mar;28(3):265-280. doi: 10.1038/cr.2017.155.

18. Penna F, Camperi A, Muscaritoli M, **Filigheddu N**, Costelli P. The role of vitamin D in cancer cachexia. Curr Opin Support Palliat Care. 2017 Dec;11(4):287-292. doi: 10.1097/SPC.0000000000000302.

19. Reano S, Angelino E, Ferrara M, Malacarne V, Sustova H, Sabry O, Agosti E, Clerici S, Ruozi G, Zentilin L, Prodam F, Geuna S, Giacca M, Graziani A, **Filigheddu N**. Unacylated Ghrelin Enhances Satellite Cell Function and Relieves the Dystrophic Phenotype in Duchenne Muscular Dystrophy mdx Model. Stem Cells. 2017 Jul;35(7):1733-1746. doi: 10.1002/stem.2632.

20. Gortan Cappellari G, Zanetti M, Semolic A, Vinci P, Ruozi G, Falcione A, **Filigheddu N**, Guarnieri G, Graziani A, Giacca M, Barazzoni R. Unacylated Ghrelin Reduces Skeletal Muscle Reactive Oxygen Species Generation and Inflammation and Prevents High-Fat Diet-Induced Hyperglycemia and Whole-Body Insulin Resistance in Rodents. Diabetes. 2016 Apr;65(4):874-86. doi: 10.2337/db15-1019.

21. 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. Correction: Human Cardiac Progenitor Spheroids Exhibit Enhanced Engraftment Potential. PLoS One. 2015 Oct 23;10(10):e0141632. doi:

10.1371/journal.pone.0141632. Erratum for: PLoS One. 2015;10(9):e0137999.

22. 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.

23. 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.

24. 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/β1 integrin pathway in SDF-1α mammary carcinoma invasiveness. PLoS One. 2014 Jun 2;9(6):e97144. doi: 10.1371/journal.pone.0097144.

25. Prodam F, **Filigheddu N**. Ghrelin gene products in acute and chronic inflammation. Arch Immunol Ther Exp (Warsz). 2014 Oct;62(5):369-84. doi: 10.1007/s00005-014-0287-9.

26. Reano S, Graziani A, **Filigheddu N**. Acylated and unacylated ghrelin administration to blunt muscle wasting. Curr Opin Clin Nutr Metab Care. 2014 May;17(3):236-40. doi: 10.1097/MCO.0000000000000049.

27. 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. doi: 10.1016/B978-0-12-410499-0.00008-3.

28. Porporato PE*, **Filigheddu N***, Reano S, Ferrara M, Angelino E, Gnocchi VF, Prodam 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 Feb;123(2):611-22. doi: 10.1172/JCI39920.

29. Baldanzi G, Pighini A, Bettio V, Rainero E, Traini S, Chianale F, Porporato PE, **Filigheddu N**, Mesturini R, Song S, Schweighoffer T, Patrussi L, Baldari CT, Zhong XP, van Blitterswijk WJ, Sinigaglia F, Nichols KE, Rubio I, Parolini O, Graziani A. SAP-mediated inhibition of diacylglycerol kinase α regulates TCR-induced diacylglycerol signaling. J Immunol. 2011 Dec 1;187(11):5941-51. doi:10.4049/jimmunol.1002476.

30. **Filigheddu N**, Sampietro S, Chianale F, Porporato PE, Gaggianesi M, Gregnanin I, Rainero E, Ferrara M, 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 through the G protein-coupled estrogen receptor GPR30. Cell Signal. 2011 Dec;23(12):1988-96. doi: 10.1016/j.cellsig.2011.07.009.

31. Baldanzi G, Pietronave S, Locarno D, Merlin S, Porporato P, Chianale F, **Filigheddu N**, Cantelmo AR, Albini A, Graziani A, Prat M. Diacylglycerol kinases are essential for hepatocyte growth factor-dependent proliferation and motility of Kaposi's sarcoma cells. Cancer Sci. 2011 Jul;102(7):1329-36. doi: 10.1111/j.1349-7006.2011.01953.x.

32. **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. doi: 10.1155/2010/369549.

33. 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. doi: 10.1073/pnas.0908326107.

34. 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. doi: 10.1016/j.jneumeth.2009.09.021.

35. 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. doi: 10.1016/j.ceca.2009.07.003.

36. 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. doi: 10.1091/mbc.e07-02-0177.

37. 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. doi: 10.1038/sj.onc.1210717.

38. **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.

39. **Filigheddu N**, Gnocchi VF, Coscia M, Cappelli M, Porporato PE, Taulli R, Traini S, Baldanzi G, Chianale F, Cutrupi S, Arnoletti E, Ghè 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. doi: 10.1091/mbc.e06-05-0402.

40. 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. doi: 10.1002/ijc.21766.

41. 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. doi: 10.1053/j.gastro.2004.06.018.

42. 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. doi: 10.1038/sj.onc.1207633.

43. Baldanzi G, **Filigheddu N**, Cutrupi S, Catapano F, Bonissoni 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. doi: 10.1083/jcb.200207165.

44. **Filigheddu N**, Fubini A, Baldanzi G, Cutrupi S, Ghè 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. doi: 10.1385/ENDO:14:1:113.