BIOGRAPHICAL SKETCH

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NAME: Pietro De Camilli

POSITION TITLE: Professor and Investigator

eRA COMMONS USER NAME (credential, e.g., agency login): PIETRO

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Lyceum Manzoni, Milan, Italy	Maturita' Classica	1966	Liceo Classico
University of Milano School of Medicine, Italy	M.D.	1972	
University of Pavia School of Medicine, Italy	Post Grad	1975	Medical Endocrinology

A. Personal Statement

The goal of my laboratory is to understand the dynamics of cell membranes, with a special emphasis on the contribution of these mechanisms to the function of the nervous system and of synapses. Within this broad theme, I am particularly interested in how proteins remodel the bilayer during membrane transport and in how these changes, in turn, are regulated by the chemistry and metabolic changes of bilayer lipids. Presynaptic nerve terminals are highly specialized for the generation and recycling of synaptic vesicles and, as such, are a powerful model system that I have used to elucidate fundamental mechanisms underpinning membrane dynamics. Conversely, I have built upon basic information concerning membrane biology obtained from other systems to advance knowledge of neuronal function. Given my training as an MD, I have a special interest in understanding the relationships between the disruption of these mechanisms and disease.

In the early stages of my scientific career I helped pioneer the molecular characterization of synaptic vesicles. Subsequently, I focused on the mechanisms underlying the biogenesis of synaptic vesicles and their endocytic recycling at synapses. My studies of synaptic vesicle membranes and of their dynamics have contributed to the general fields of exocytosis and endocytosis, and had an impact in the field of lipid signaling, phosphoinositide-dependent signaling in particular. Building on this work, I have recently become interested in the role of membrane contact sites in the control of the homeostasis of bilayer lipids. This is a new and rapidly expanding area of research.

My research has also contributed to the elucidation of pathogenetic mechanisms in human diseases such as neurological and psychiatric diseases, including neuroimmunological diseases (PMID:2135382), epilepsy, diabetes (PMID:1697648) and several genetic conditions. In more recent work, I have become interested in the role of dysfunction of membrane traffic, primarily membrane traffic along the endocytic pathway, in neurodegenerative disease including ALS, Alzheimer (PMID:26124111) and Parkinson (PMID:23804563; PMID:25471590)

B. Positions and Honors

Positions and employment

1972-1978 Assistant Professor, Department of Medical Pharmacology and CNR Center of Cytopharmacology, University of Milano, Italy
1978-1979 Postdoctoral Fellow, Department of Pharmacology (laboratory of Paul Greengard), Yale University School of Medicine
1979-1981 Assistant Professor, Section of Cell Biology, Yale University School of Medicine
1981-1987 Associate Professor, Department of Medical Pharmacology and CNR Center of Cytopharmacology, University of Milano, Italy

1987-1988	Visiting Associate Professor, Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University, New York
1988-1992	Associate Professor with tenure, Department of Cell Biology, Yale University
1992-	Professor, Department of Cell Biology; Investigator, Howard Hughes Medical Institute, Yale University School of Medicine
1997-2000	Chairman, Department of Cell Biology
2004-	Member, Kavli Institute for Neuroscience at Yale University
2005-	Professor, (secondary appointment) Department of Neurobiology, Yale University School of Medicine
2005-	Founding Director, Yale Program in Cellular Neuroscience, Neurodegeneration and Repair
2015-	Chairman, Department of Neuroscience, Yale University School of Medicine
2015-	Director, Kavli Institute for Neuroscience at Yale University

Honors

+ Elected memberships: 1987, European Molecular Biology Organization (EMBO); 2001, American Academy of Arts and Sciences; 2001, National Academy of Sciences, USA (5/2009 Chair of Section 24) (USA); 2005, National Academy of Medicine (formerly the Institute of Medicine); 2012, Fellow of the American Association for the Advancement of Science (AAAS); 2013, Elected, Accademia Nazionale dei Lincei.

+ Other: 1978-81, Fulbright-Hays Visiting Scholar in Pharmacology (Yale University); 1978-79, Fellowship from the Muscular Dystrophy Association of America; 1989, Klingenstein Neuroscience Award; 1990, Max-Planck Research Prize (shared with Dr. R. Jahn, Münich); 1991, McKnight Research Project Award; 1995, DATTA Lecturer and Medal Recipient, Federation of European Biochemical Societies (FEBS)); 1997, Keith Porter Lecture, American Society for Cell Biology Meeting (Washington, DC); 2003, Eugene Higgins Professor of Cell Biology, Yale University; 2004, Harvey Lectures Series, The Harvey Society, (New York, NY); 2005, Honorary Member, Italian Society for Neuroscience; 2009, NARSAD Distinguished Investigator Award; 2010, Javitz Neuroscience Investigator Award; 2012, Sir Bernard Katz Award by the Endocytosis and Exocytosis Subgroup of the Biophysical Society; 2013, Honorary Doctorate, Okayama University (Okayama, Japan): 2014, John Klingenstein Professor of Neuroscience, Yale University; 2015, Julius Axelrod Prize, Society for Neuroscience.

+ Selected Scientific Advisory Boards (SABs), Review Panels, Societies: 1994-1997, SAB of the Max-Planck Institute for Medical Research, Heidelberg, (Germany); 1997-2003, National Advisory Board, Pew Scholars Program for Biochemical Science; 2001-2005, NIH Study Section SYN, formerly MCDN1 (2005-2006 Chair); 2002-2011, SAB of the Max-Planck Institute for Molecular Cell Biology and Genetics, Dresden, (Germany); 2004-2006, Council of the American Society for Cell Biology; 2004-2008, Latin American Fellows Program, Pew Scholars Program in Biological Sciences; 2003-2009, McKnight Endowment Fund for Neuroscience; 2005-2011 SAB of Telethon (Italy); 2006-2009 and 2013- Scientific Review Committee, Armenise Foundation, Rome (Italy); 2013-2016 SAB of Jane Coffin Childs fund; 2017 President-elect of the American Society for Cell Biology.

+Selected keynote or named lectureships (last 5 years): 2011: John Cebra Lecture (Woods Hole, MA); 2012: Keynote Lecture, EuroMEMBRANE International, “Membrane Dynamics in Physiology and Disease” (Basel, Switzerland); 2012: Keynote Lecture, Joint Meeting of the French Societies of Cell Biology and Developmental Biology (Montepellier, France); 2012: Fouad A. and Val Imm Bashour Distinguished Lectureship in Physiology, University of Texas Southwestern Medical Center (Dallas, TX); 2012: Keynote lecture, “Inositide Signaling in Health and Disease”, Coorg, India; 2013: Keynote Lecture, ABCD (Italian Society of Cell Biology and Differentiation) meeting (Ravenna, Italy); 2014: Dennis Shields lecture, 9th EMBO/Annaberg Meeting: Protein and Lipid Function in Secretion and Endocytosis (Goldegg, Austria); 2014: C. Warren Olanow Lecture, Friedman Brain Institute, Mount Sinai Medical School (New York, NY); 2014: Hille Lecture, Department of Physiology, University of Washington (Seattle, WA); 2014: Herbert Lecture, Vollum Institute, (Portland, OR); 2014: Walter Massey Family Lecture (Woods Hole, MA); 2014: 21st Severo Ochoa Memorial Lecture, Centro de Biologia Molecular Severo Ochoa, University of Madrid (Madrid, Spain); 2015: Keynote Lecture, Toxins 2015, Lisbon (Portugal); 2015: Keynote Lecture, Membrane Dynamics and Protein Sorting meeting, Israeli Society for Cell Biology (Weizmann Institute, Israel); 2015: Keynote Lecture, Membrane Biology Gordon Conference, Andover, NH; 2015, EMBO Keynote Lecture, Signalling 2015: Cellular Functions of Phosphoinositides and Inositol Phosphates, (Biochemical Society, Cambridge, UK); 2015, Keynote lecture, Organelle Crosstalk in Membrane Dynamics and Cell Signaling (Biochemical Society, Edinburgh, UK); 2016: Keynote Lecture, Sphingonet International Colloquium (Amsterdam); 2016: Keynote Lecture, Cell Biology of

the Neuron Gordon Conference (Waterville Valley, NH); Keynote lecture, FASEB meeting "Phospholipid Signaling in Cancer, Neurodegeneration and Cardiovascular Disease" (Steamboat Springs, CO).

C. Contribution to Science (selected papers since the mid-1990')

1. Molecular mechanisms in endocytosis

I have made numerous contributions to the elucidation of sequence of events and regulatory mechanisms involved in endocytosis at the neuronal synapse and in other systems. I have also identified and functionally characterized general and synapse-specific factors implicated in endocytosis.

McPherson PS, Garcia EP, Slepnev V, David C, Zhang X, Grabs D, Sossin WS, Bauerfeind R, Nemoto Y, and De Camilli P. 1996. A presynaptic inositol-5-phosphatase. *Nature*. 379: 353-357.

Takei K, Haucke V, Slepnev V, Farsad K, Salazar M, Chen H, and De Camilli P. 1998. Generation of coated intermediates of clathrin-mediated endocytosis on protein-free liposomes. *Cell.* 94: 131-141.

Milosevic I, Giovedi S, Lou X, Raimondi A, Collesi C, Paradise S, Shen H, O'Toole E, Ferguson S, Cremona O, and De Camilli P. 2011. Recruitment of endophilin to clathrin coated pit necks is required for uncoating but is dispensable for fission. *Neuron.* 72: 587-601. PMCID: PMC3258500.

Messa M, Fernanez-Busnadiego R, Sun EW, Chen H, Czapla H, Wrasman K, Wu Y, Ko G, Ross T, Wendland B, and De Camilli P. 2014. Epsin deficiency impairs endocytosis by stalling the actin-dependent invagination of endocytic clathrin coated pits. *Elife.* 3: e03311. PMCID: PMC4161027.

2. The fission reaction of endocytosis

I provided key insight into the mechanism of action of the GTPase dynamin in the fission reaction of endocytosis, including endocytosis at neuronal synapses.

Takei K, McPherson P, Schmid SL, and De Camilli P. 1995. Tubular membrane invaginations coated in dynamin rings are induced by GTP-gs in nerve terminals. *Nature.* 374: 186-190.

Roux A, Uyhazi K, Frost A, and De Camilli P. 2006. GTP-dependent twisting of dynamin implicates both constriction and tension in membrane fission. *Nature.* 441: 528-531.

Ferguson SM, Brasnjo G, Hayashi M, Wölfel M, Collesi C, Giovedi S, Raimondi A, Gong LW, Paradise S, O'Toole E, Flavell R, Cremona O, Miesenböck, Ryan TA, and De Camilli P. 2007. A selective activity-dependent requirement for dynamin 1 in synaptic vesicle endocytosis. *Science.* 316: 570-574.

Ferguson S, Raimondi A, Paradise S, Shen H, Mesaki K, Destaing O, Ko G, Cremona O, O'Toole E, and De Camilli P. 2009. Coordinated actions of actin and BAR proteins upstream of dynamin at endocytic clathrin-coated pits. *Dev. Cell.* 17: 811-822. PMCID: PMC2861561.

3. Bilayer deforming proteins and membrane shape

As part of my studies of endocytosis at the neuronal synapse, I established that some endocytic proteins bind directly to membrane bilayers and also deform them, thus helping coordinate the assembly of endocytic factors with membrane deformation. This work, which demonstrated for the first time the membrane shaping properties of BAR domain containing proteins, had a seminal impact in cell biology and started a completely new field of research.

Takei K, Slepnev VI, Haucke V, and De Camilli P. 1999. Functional partnership between amphiphysin and dynamin in clathrin-mediated endocytosis. *Nat. Cell Biol.* 1: 33-39.

Farsad K, Ringstad N, Takei K, Floyd SR, and De Camilli P. Generation of high curvature membranes mediated by direct endophilin-bilayer interactions. 2001. *J. Cell Biol.* 155: 193-200.

Itoh T, Erdmann KS, Roux A, Habermann B, Werner H, and De Camilli P. 2005. Dynamin and the actin cytoskeleton cooperatively regulate plasma membrane invagination by BAR and F-BAR proteins. *Dev. Cell.* 6: 791-804.

Frost A, Roux A, Perera R, Spasov K, Destaing O, Egelman EH, De Camilli P, and Unger VM. 2008. Structural basis of membrane invagination by F-Bar domains. *Cell.* 132: 807-817. PMCID: PMC2384079.

4. Phosphoinositide metabolism in membrane traffic

I discovered the role of phosphoinositide metabolism in synaptic vesicle recycling at synapses. Building on this finding, I made several additional key contributions to the field of phosphoinositide signaling (basic mechanisms, role in disease, methodology to study phosphoinositide metabolism, including optogenetic

approaches).

Cremona O, Di Paolo G, Wenk M, Luthi A, Kim WT, Takei K, Daniell L, Nemoto Y, Flavell RA, McCormick DA and De Camilli P. 1999. Essential role of phosphoinositide metabolism in synaptic vesicle recycling. *Cell*. 99: 179-188.

Di Paolo G, and De Camilli P. 2006. Phosphoinositides in cell regulation and membrane dynamics. *Nature*. 443: 651-657 (cited more than 1500 times).

Zoncu R, Perera R, Balkin DM, Toomre D, and De Camilli P. 2009. A phosphoinositide switch controls the maturation and signaling properties of APPL endosomes. *Cell*. 136: 1110-1121. PMCID: PMC2705806.

Baskin JM, Wu X, Christiano R, Oh M, Schauder CM, Gazzerro E, Messa M, Baldassari S, Assereto S, Biancheri R, Zara F, Minetti C, Raimondi A, Simons M, Walther TC, Reinisch KM, and De Camilli P. 2015. The leukodystrophy protein FAM126A/Hyccin regulates PI4P synthesis at the plasma membrane. *Nat. Cell Biol.* 18: 132-138. PMCID: PMC4689616

5. Lipid dynamics at membrane contact sites

I revealed new mechanisms in the cross-talk between the ER and other membranes mediated by direct contact sites. I also provided evidence for a role of these contacts in lipid transfer.

Giordano F, Saheki Y, Idevall-Hagren O, Colombo S, Pirruccello M, Milosevic I, Gracheva E, Bagriantsev SN, Borgese N and De Camilli P. 2013. PI(4,5)P2-dependent and Ca2+-regulated ER-PM interactions mediated by the extended-synaptotagmins. *Cell*. 153: 1494-1509. PMCID: PMC3716012.

Schauder CM, Wu X, Saheki Y, Narayanaswamy P, Torta F, Wenk MR, De Camilli P*, and Reinisch KM*. 2014. Structure of a lipid-bound Extended-Synaptotagmin indicates a role in lipid transfer. *Nature*. 510: 552-555. PMCID: PMC4135724

Chung J, Torta F, Masai K, Lucast L, Czapla H, Tanner LB, Narayanaswamy P, Wenk MR, Nakatsu F, and De Camilli P. 2015. PI4P/phosphatidylserine countertransport at ORP5 and ORP8-mediated ER-plasma membrane contacts. *Science.* 349: 428-432. (News and Views in Nature: Menon and Levine, Nature 525, 191-192, 2015). PMCID: PMC4638224

Dong R, Saheki Y, Swarup S, Lucast L, Harper JW, De Camilli P. 2016. Endosome-ER contacts control actin nucleation and retromer function through VAP-dependent regulation of PI4P. *Cell.* 166: 408-423. PMCID: PMC4963242

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=De+Camilli+P