

CASCIO Paolo, D.V.M., Ph.D. – Group Leader

Address and contacts

Department of Veterinary Sciences

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Education and training

D.V.M. – 1994 University of Turin, Italy

Ph.D. – 2000 University of Turin, Italy

1998-2000 Ph.D. Student in the lab of Prof. Alfred Goldberg, Department of Cell Biology, Harvard Medical School, Boston (MA), USA

2000-2001 Postdoc in the lab of Prof. Alfred Goldberg, Department of Cell Biology, Harvard Medical School, Boston (MA), USA

Academic position

2002-2015 Researcher and Assistant Professor of Biochemistry and Molecular Biology, School of Veterinary Medicine, University of Turin, Italy

2006-2015 Assistant Professor of Cell Biology, School of Medicine, University Vita e Salute San Raffaele, Milano, Italy

2015-2023 Associate Professor of Biochemistry, Department of Veterinary Sciences, University of Turin, Italy

2023-present Full Professor of Biochemistry, Department of Veterinary Sciences, University of Turin, Italy

Educational Activities

(a) Main courses taught:

2002-2014 Molecular biology for D.V.M. and B.A. students, Department of Veterinary Sciences, University of Turin

2015-present General and applied biochemistry for D.V.M. and B.A. students, Department of Veterinary Sciences, University of Turin

2008-present Member and Tutor of the Ph.D. school in Veterinary Sciences, University of Turin

(b) Research students:

Post Docs

Mary Raule 2015

Simone Belmondo 2016-2017

PhD students

Mary Raule 2011-2014

Thesis students

Giulio Partemio 2013-2014

Scholarship holders

Mary Raule 2010

Elisa Chiavassa 2011

Luca Paglietti 2016-2018

Beatrice Alessandria 2017-2018

Jean Yves Alejandro Frayssinhes 2019-2021

Membership in scientific societies and international networks

Since 2002 member of the Italian Society of Biochemistry and Molecular Biology (S.I.B.)

Since 2018 member of the Interdepartmental Centre for Studies on Asbestos and Other Toxic Particulates (Turin University)

Since 2021 member of the ProteoCure COST Action CA20113 - A sound proteome for a sound body: targeting proteolysis for proteome remodelling

Participation in Editorial Board of Scientific Journals

Molecules

Editorial Board Member

(<https://www.mdpi.com/journal/molecules>)

Frontiers in Molecular Biosciences

Review Editor

(<https://www.frontiersin.org/journals/molecular-biosciences#>)

Invited lectures

PA28 γ and PA28 $\alpha\beta$: The Enigmatic Magic Rings of the Proteasome? Department of Cell Biology, Harvard Medical School, Boston, USA, February 7th 2022.

Proteasomal stress is an Achilles heel that can be exploited to fight Malignant Pleural Mesothelioma Interdepartmental Centre for Studies on Asbestos and Other Toxic Particulates (Turin University), July 23th 2020.

PA28 $\alpha\beta$: the enigmatic magic ring of the proteasome? Department of Plant Molecular Biology, Faculty of Biology and Medicine, University of Lausanne, Lausanne, Switzerland. March 29th 2018.

New insights into immunoproteasomes biochemical properties and functions. Division of Genetics and Cell Biology, San Raffaele Scientific Institute, Milan, Italy. June 10th 2014.

Proteostasis: cancer's Achilles heel? Department of Cell Biology, Harvard Medical School, Boston, USA. September 17th 2012.

Proteasome inhibitors as anti-cancer agents: a lesson from Multiple Myeloma. CRS4, Parco Scientifico e Tecnologico della Sardegna, Pula (CA), Italy. July 9th 2012.

Collapse of proteostasis during B cells differentiation can teach us something important about aging? Istituto di Ricerca Genetica e Biomedica (IRGB-CNR), Cittadella Universitaria di Cagliari, Monserrato (CA), Italy. July 6th 2012.

The Load vs. Capacity model: a quantitative approach to understand the exquisite sensitivity of plasma cells to proteasome inhibitors. Department of Cell Biology, Harvard Medical School, Boston, USA. June 23rd 2010.

Imbalance between synthetic load and proteasomal capacity sensitizes normal and malignant plasma cells to proteasome inhibitors. Tyrolean Cancer Research Institute, Innsbruck, Austria. February 4th 2009.

Imbalance between synthetic load and proteasomal capacity sensitizes normal and malignant plasma cells to proteasome inhibitors. Centre de Recherche de Biochimie Macromoléculaire (CRBM-CNRS), Montpellier, France. December 10th 2008.

Role of proteasomes in MHC class-I presentation and in antibodies production. Mario Negri Institute for Pharmacological Research, Milan, Italy. December 15th 2004.

Role of proteasomes in MHC class-I presentation. Department of Experimental Biochemical Sciences, Padova University. January 24th 2000.

Bibliographic indexes October 2023 (from Scopus, <http://www.scopus.com/home.url>)

h index	23
Peer-reviewed publications	42
Total citations	2534

Peer-reviewed publications

1. Cerruti F., Borrelli A., Degiovanni A., Mengozzi G., Borella F., Cascio P. Detection and biochemical characterization of circulating proteasomes in dog plasma. *Research in Veterinary Science*, 2023, 162, 104950 (I.F. 2022 2.4)
2. Tundo G.R., Cascio P., Milardi D., Santoro A.M., Graziani G., Lacal P.M., Bocedi A., Oddone F., Parravano M., Coletta A., Coletta M., Sbardella D. Targeting immunoproteasome in neurodegeneration: A glance to the future. *Pharmacology & Therapeutics*, 2023, 241, 108329 (I.F. 2022 13.5)
3. Sbardella D., Tundo G.R., Mecchia A., Palumbo C., Atzori M.G., Levati L., Boccaccini A., Caccuri A.M., Cascio P., Lacal P.M., Graziani G., Varano M., Coletta M., Parravano M. A novel and atypical NF- κ B pro-inflammatory program regulated by a CamKII-proteasome axis is involved in the early activation of Muller glia by high glucose. *Cell & Bioscience*, 2022, 12:108 (I.F. 7.5)
4. Cantiello M., Carletti M., Giantin M., Gardini G., Capolongo F., Cascio P., Pauletto M., Girolami F., Dacasto M., Nebbia C. Induction by Phenobarbital of Phase I and II Xenobiotic-Metabolizing Enzymes in Bovine Liver: An Overall Catalytic and Immunochemical Characterization. *International Journal of Molecular Sciences*, 2022, 23, 3564 (I.F. 5.6)
5. Cascio P. and Dittmar G. Regulating Proteasome Activity. *Biomolecules*, 2022, 12, 343 (I.F. 5.5)
6. Tundo G.R., Sbardella D., Oddone F., Grasso G., Marini S., Atzori M.G., Santoro A.M., Milardi D., Bellia F., Macari G., Graziani G., Polticelli F., Cascio P., Parravano M., Coletta M. Insulin-Degrading Enzyme Is a Non Proteasomal Target of Carfilzomib and Affects the 20S Proteasome Inhibition by the Drug. *Biomolecules*, 2022, 12, 315 (I.F. 5.5)
7. Frayssinhes J-Y.A., Cerruti F., Laulin J., Cattaneo A., Bachi A., Apcher S., Coux O., Cascio P. PA28 γ -20S proteasome is a proteolytic complex committed to degrade unfolded proteins. *Cellular and Molecular Life Sciences*, Published online 2021 Dec 16;79(1):45 (I.F. 9.2)
8. Cascio P. PA28 γ : new insights on an ancient proteasome activator. *Biomolecules*, 2021, 11, 228 (I.F. 6.1)
9. Boulpicante M., Darrigrand R., Pierson A., Salgues V., Rouillon M., Gaudineau B., Khaled M., Cattaneo A., Bachi A., Cascio P., Apcher S. Tumors escape immunosurveillance by overexpressing the proteasome activator PSME3. *OncoImmunology*, 2020, 9(1): 1-16, 1761205. (I.F. 8.1)
10. Bordini J., Morisi F., Cerruti F., Cascio P., Camaschella C., Ghia P., Campanella A. Iron causes lipid oxidation and inhibits proteasome function in multiple myeloma plasma cells: a proof of concept for novel combination therapies. *Cancers*, 2020, 12(4): 970. (I.F. 6.6)
11. Cerruti, F., Jocollè, G., Salio, C., Oliva, L., Paglietti, L., Alessandria, B., Mioletti, S., Donati, G., Numico, G., Cenci, S., Cascio, P. Proteasome stress sensitizes malignant pleural mesothelioma cells to bortezomib-induced apoptosis. *Scientific Reports*, 2017, 7: 17626. (I.F. 4.1)
12. Oliva L., Orfanelli U., Resnati M., Raimondi A., Orsi A., Milan E., Palladini G., Milani P., Cerruti F., Cascio P., Casarini S., Rognoni P., Touvier T., Marcatti M., Ciceri F., Mangiacavalli S., Corso A., Merlini G., Cenci S. The amyloidogenic light chain is a stressor that sensitizes plasma cells to proteasome inhibitor toxicity. *Blood*, 2017, 129(15): 2132-42. (I.F. 15.1)
13. Crespo H., Bertolotti L., Proffitti M., Cascio P., Cerruti F., Acutis P.L., de Andrés D., Reina R., Rosati S. Low proviral small ruminant lentivirus load as biomarker of natural restriction in goats. *Vet. Microbiology*, 2016, 192: 152-62. (I.F. 2,6)
14. Milan E., Perini T., Resnati M., Orfanelli U., Oliva L., Raimondi A., Cascio P., Bachi A., Marcatti M., Ciceri F., Cenci S. A plastic SQSTM1/p62-dependent autophagic reserve

maintains proteostasis and determines proteasome inhibitor susceptibility in multiple myeloma cells. *Autophagy*, 2015, 11(7): 1161-78. (I.F. 9,1)

15. Raule M., Cerruti F., Cascio P. Comparative study of the biochemical properties of proteasomes in domestic animals. *Veterinary Immunology and Immunopathology*, 2015, 166(1-2): 43-9. (I.F. 1,7)
16. Cascio P., Cerruti F., Marshall R.S., Raule M., Remelli W., Roberts L.M., Ceriotti A. A Quantitative Method to Monitor the Efficacy of Inhibitors Against the Chymotrypsin-Like Activity of the Proteasome in Tobacco Leaf Protoplasts. *Plant Molecular Biology Reporter*, 2015, 33(4): 829-840 (I.F. 2,3)
17. Cascio P. PA28 $\alpha\beta$: The Enigmatic Magic Ring of the Proteasome? *Biomolecules*, 2014, 4: 566-584. (I.F. N.A.)
18. Raule M., Cerruti F., Cascio P. Enhanced rate of degradation of basic proteins by 26S immunoproteasomes. *Biochimica et Biophysica Acta - Molecular Cell Research*, 2014, 1843: 1942-47. (I.F. 5,0)
19. Raule M., Cerruti F., Benaroudj N., Migotti R., Kikuchi J., Bachi A., Navon A., Dittmar G., Cascio P. PA28 $\alpha\beta$ Reduces Size and Increases Hydrophilicity of 20S Immunoproteasome Peptide Products. *Chemistry & Biology*, 2014, 21: 470-480. (I.F. 6,6)
20. Berko D., Tabachnick-Cherny S., Shental-Bechor D., Cascio P., Mioletti S., Levy Y., Admon A., Ziv T., Tirosh B., Goldberg A.L., Navon A. The direction of protein entry into the proteasome determines the variety of products and depends on the force needed to unfold its two termini. *Molecular Cell*, 2012, 48: 1-11. (I.F. 14,2)
21. Cenci S., Oliva L., Cerruti F., Milan E., Bianchi G., Raule M., Mezghrani A., Pasqualetto E., Sitia R., Cascio P. Pivotal Advance: Protein synthesis modulates responsiveness of differentiating and malignant plasma cells to proteasome inhibitors. *Journal of Leukocyte Biology*, 2012, 92: 921-931. (I.F. 5)
22. Favole A., Cascio P., Cerruti F., Sereno A., Tursi M., Tomatis A., Cristina Della Beffa C., Ferrone S., Bollo E. MHC Class I-related antigen-processing machinery component defects in feline mammary carcinoma. *Translational Oncology*, 2012, 5: 48-55. (I.F. 3,4)
23. Reina R., Juganaru M.M., Profiti M., Cascio P., Cerruti F., Bertolotti L., De Meneghi D., Amorena B., Rosati S. Immunological parameters in goats experimentally infected with SRLV genotype E, strain Roccaverano. *Veterinary Immunology and Immunopathology*, 2011, 139: 237-244. (I.F. 2,2)
24. Urru S., Veglianese P., De Luigi A., Fumagalli E., Erba E., Gonella Diaza R., Davoli E., Borsello T., Forloni G., Pengo N., Monzani E., Cascio P., Cenci S., Sitia R., Salmona M. A new fluorogenic peptide determines proteasome activity in single cells. *Journal of Medicinal Chemistry*, 2010, 53: 7452-7460. (I.F. 5,2)
25. Cerruti F., Martano M., Morello E., Buracco P., Cascio P. Proteasomes are not a target for doxorubicin in feline injection-site sarcoma. *Journal of Comparative Pathology*, 2010, 143: 164-172. (I.F. 1,5)
26. Bianchi G., Oliva L., Cascio P., Pengo N., Fontana F., Cerruti F., Orsi A., Pasqualetto E., Mezghrani A., Calbi V., Palladini G., Giuliani N., Anderson K. C., Sitia R., Cenci S. The proteasome load vs. capacity balance determines apoptotic sensitivity of multiple myeloma cells to proteasome inhibition. *Blood*, 2009, 113: 3040-49. (I.F. 10,6)
27. Santoni de Sio F.R., Gritti A., Cascio P., Neri M., Sampaolesi M., Galli C., Luban J. and Naldini L. Lentiviral Vector Gene Transfer is Limited by the Proteasome at Post-Entry Steps in Various Types of Stem Cells. *Stem Cells*, 2008, 26: 2142-2152. (I.F. 7,7)
28. Cascio P., Oliva L., Cerruti F., Mariani E., Pasqualetto E., Cenci S. and Sitia R. Dampening Ab responses using proteasome inhibitors following in vivo B cell activation. *European Journal of Immunology*, 2008, 38: 658-667. (I.F. 4,9)

29. Cerruti F., Martano M., Petterino C., Bollo E., Morello E., Bruno R., Buracco P. and Cascio P. Enhanced expression of γ -interferon induced antigen processing machinery components in a spontaneously occurring cancer. *Neoplasia*, 2007, vol. 9, n.11: 960-969. (I.F. 5,7)
30. Cenci S.*, Mezghrani A.*, Cascio P.*, Bianchi G., Cerruti F., Fra A., Lelouard H., Masciarelli S., Mattioli L., Oliva L., Orsi A., Pasqualetto E., Pierre P., Ruffato E., Tagliavacca L. and Sitia R. Progressively impaired proteasomal capacity during terminal plasma cell differentiation. *The EMBO Journal*, 2006, 25: 1104-13. (I.F. 10,1) (*Joint first authors)
31. Santoni de Sio F.R., Cascio P., Zingale A., Gasparini M. and Naldini L. Proteasome activity restricts lentiviral gene transfer into hematopoietic stem cells and is down-regulated by cytokines that enhance transduction. *Blood*, 2006, 107: 4257-65. (I.F. 10,4)
32. Petterino C., Martano M., Cascio P., Cerruti F., Martini M., Morello E., Bruno R., Castagnaro M., Buracco P. Immunohistochemical Study of STAT3 Expression in Feline Injection-site Fibrosarcomas. *J. Comp. Pathology*, 2006, 134: 91-100. (I.F. 0,9)
33. Cascio P. and Goldberg A.L. Preparation of hybrid (19S-20S-PA28) proteasome complexes and analysis of peptides generated during protein degradation. *Methods in Enzymology*, 2005, 398: 336-352. (I.F. 1,7)
34. Cheroni C., Peviani M., Cascio P., De Biasi S., Monti C. and Bendotti C. Accumulation of human SOD1 and ubiquitinated deposits in the spinal cord of SOD1G93A mice during motor neuron disease progression correlates with a decrease of proteasome. *Neurobiology of Disease*, 2005, 18: 509-22. (I.F. 4)
35. Martano M., Morello E., Ughetto M., Iussich S., Petterino C., Cascio P., Buracco P. Surgery alone *versus* surgery and doxorubicin for the treatment of feline injection-site sarcomas: a report on 69 cases. *The Veterinary Journal*, 2005, 170: 84-90. (I.F. 1,7)
36. Goldberg A.L, Cascio P., Saric T., Rock K. The importance of the proteasome and subsequent proteolytic steps in the generation of antigenic peptides. *Mol. Immunol.*, 2002, 39: 147-164. (I.F. 2,4)
37. Cascio P., Call M., Petre B.M., Walz T., Goldberg A.L. Properties of the hybrid form of the 26S proteasome containing both 19S and PA28 complexes. *The EMBO Journal*, 2002, 21: 2636-45. (I.F. 10,7)
38. Cascio P., Hilton C., Kisselev A., Rock K., Goldberg A.L. 26S proteasomes and immunoproteasomes produce mainly N-extended versions of an antigenic peptide. *The EMBO Journal*, 2001, 20: 2357-2366. (I.F. 12,5)
39. Kohler A., Cascio P., Leggette D.S., Woo K.M., Goldberg A.L., Finley D. The Axial Channel of the Proteasome Core Particle Is Gated by Rpt2 ATPase and Controls Both Substrate Entry and Product Release. *Molecular Cell*, 2001, 7: 1143-1152. (I.F. 16,6)
40. Benaroudj N., Tarcsa E., Cascio P., Goldberg A.L. The unfolding of substrates and ubiquitin-independent protein degradation by proteasomes. *Biochimie*, 2001, 83: 311-318. (I.F. 2,7)
41. Mo X.Y., Cascio P., Lemerise K., Goldberg A.L., Rock K. Distinct Proteolytic Processes Generate the C and N Termini of MHC Class I-binding Peptides. *The Journal of Immunology*, 1999, 163: 5851-5859. (I.F. 7,1)
42. Piccinini M., Merighi A., Bruno R., Cascio P., Curto M., Mioletti S., Ceruti C., Rinaudo M.T. Affinity purification and characterization of protein gene product 9.5 (PGP9.5) from retina. *Biochemical Journal*, 1996, 318: 711-6. (I.F. 3,6)

Book chapters

1. Cascio P., De Maria R. I tumori spontanei negli animali come modelli di studio per l'oncologia comparata. In "I MODELLI ANIMALI SPONTANEI PER LO STUDIO DELLA FISIOLOGIA E PATOLOGIA DELL'UOMO", 2017, 479-479, Fond. Iniz. Zooprofilattiche e Zootecniche.