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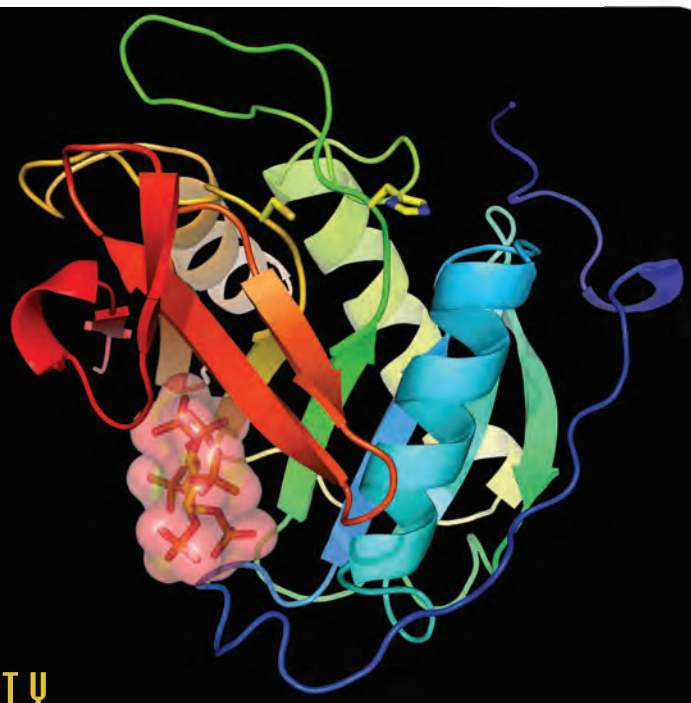
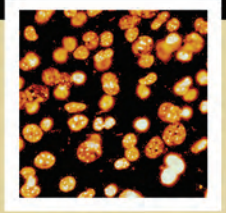


INTERNATIONAL PROTEOLYSIS SOCIETY
QUICKCUTS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Johanna Joyce
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Matthew Bogyo

Email addresses can be found on the IPS website: www.protease.org

A Message From the President:

Overall, the field of proteolysis research continues to gain momentum. This continued increase in the number of scientists working on proteases is reflected in our increased membership and attendance at our general meetings. Our meeting in 2007 in Patras, Greece was a great success and had the largest number of attendees of any of our general meetings to date. I am hopeful that, with this momentum, we be able to have a great meeting in October, 2009 in Surfer's Paradise, Australia. Since this is a difficult economic time throughout the world, we are going to need your help as members to find ways to support our next generation of protease research scientists to attend this meeting. As always, the bulk of the funds that the society raises through membership dues go towards support of travel awards for members-in-training to attend our general meeting. Therefore, I hope you will all make plans to renew your membership if you have not already done so. As a reminder, membership is for 2 years and gives you access to significant discounts in the registration rate for our general meeting, access to our newsletter and the ability to post job listings on our website.

This issue of QuickCuts contains a number of new job listings as well as information about our general meeting. It also has information about how to renew your membership and a few new product listings that should be of interest to the protease community. Finally, this issue has an extensive list of important protease papers that have come out in the past 10 months. I have been really pleased with the response I am getting when asking members for suggestions of papers for this section.

I hope you will find this issue enjoyable to read. Please feel free to send feedback to me about the newsletter by emailing ipssecretary@gmail.com. It is always great to get ideas and suggestions from our members. Please remember that this is your society and the more active you are in helping to shape the direction it goes, the more successful it will be.

Thanks again for your support of the IPS. See you all in 2009……

Mathew Bogyo - IPS President - mbogyo@stanford.edu

Post-doctoral fellowships in 2008/2009

Proteases in inflammatory bowel diseases

For a collaborative EU-research project on the role of proteases in inflammatory bowel diseases (www.ibdase.org), we are looking for a Postdoc (PhD, MD/PhD) with excellent methodological skills and great interest in in bioinformatics and statistics, preferably in the analysis of microarrays. Good communication skills and motivation to collaborate with other research groups are essential. The project addresses the role of mucosal proteases in the pathogenesis of inflammatory bowel diseases in patients and animal models of disease. It represents a collaborative effort of European research groups and iscoordinated by the University of Bern, Switzerland.

The position is limited to 18 months with the option of prolongation dependent on the excellence of the research activity.
Start of position: immediately.

CONTACT: Daniel Lottaz, MD / PhD IBDase cooordinator
Department of Rheumatology, Clinical Immunology and Allergology
Inselspital, University of Bern 3010 Bern Switzerland
Telephone +41 31 632 1278 (office) / 9842 (lab) / 8017 (secretariat)
Fax +41 31 632 0585
Email daniel.lottaz@insel.ch
www.rheumabern.ch www.ibdase.org

Structure and Function of HIV Protease

Ben Dunn at the University of Florida College of Medicine has a Post-doctoral opening for studies on the structure and function of HIV-1 protease variants from non-B subtypes. In addition, studies of polyprotein processing will be pursued. This work is supported by a MERIT award from NIH that has been approved for a second five-year term. Salary will depend on experience and will be at the NIH level. Expertise in site-directed mutagenesis and recombinant protein expression is important. Email to bdunn@ufl.edu and include a CV, list of publications, and names of references.

Please send your CV and cover letter by email to: bdunn@ufl.edu

Functional Studies of Malaria Proteases

A Postdoctoral position is available in the laboratory of Dr. Doron Greenbaum in the Department of Pharmacology, University of Pennsylvania School of Medicine to study malarial proteases in a collaborative project with an industrial partner. Our research focuses on studying protease function in the malaria parasite, P.falciparum, using a range of techniques including: (1) Functional characterization of malarial proteases using chemical, biochemical and genetic tools (2) Development of small molecule Activity-Based Probes for genome-wide protease discovery and characterization (3) Protease substrate discovery through the application of proteomics techniques to uncover proteolytic pathways (4) Recombinant expression, characterization of protease specificity and inhibitor assay development. Candidates must have a Ph.D. and/or M.D., or equivalent degree. Qualifications for the position include strong background in molecular biology and biochemistry, and a record of peer-reviewed publications.

Interested individuals should e-mail a letter of intent, CV and names of three potential referees to dorong@upenn.edu.

Faculty Positions

Faculty Position in Molecular Biology and Genetics

The Department of Biochemistry and Molecular Biology at the Penn State University College of Medicine invites applications for a full-time tenure-track position at any level. Research programs should address fundamental questions in molecular biology and genetics, epigenetics, and/or genomics. For additional information, please visit: http://www.hmc.psu.edu/college/faculty/index.htm. Penn State is committed to affirmative action, equal opportunity and diversity.

Applicants should submit a curriculum vitae, a brief statement of research plans and arrange to have three letters of reference sent to: Judith S. Bond, Ph.D., Professor and Chair, Department of Biochemistry and Molecular Biology H171, The Penn State University College of Medicine, Hershey PA 17033.

Research Position in Cancer Biology

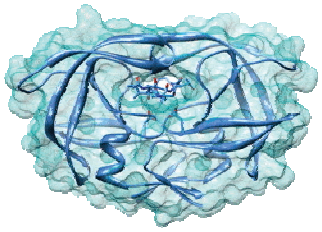
UMC Utrecht

European Research Council

Applications are invited for 1 Postdoctoral position to work on a project investigating the role of Notch cleavage in cancer in the group of Dr. Marc Vooijs in the Department of Pathology. The successful candidate will work as a team in a multidisciplinary approach to isolate, characterize and target proteases involved in regulating Notch receptor cleavage in vivo using genomic, chemical and proteomic approaches and to validate these in mouse models for cancer. This work is funded by the ERC. We are looking for highly motivated individuals with good social skills, a solid background in molecular biology and a strong interest in translating basic research biology into clinical application for diagnosis or treatment in patients. Postdoctoral or PhD applicants with medicinal chemistry background and interest are encouraged to apply. We offer an excellent research environment in a leading academic university in Europe in an internationally oriented group performing basic and applied oncology with strong international collaborations.

Applications (CV, letter of motivation and three references) should be sent as a single pdf by email to:
Marc Vooijs (m.vooijs@umcutrecht.nl)
UMC Utrecht
Department of Pathology (H04.312)
Heidelberglaan 100
3584 CX Utrecht, The Netherlands
Tel: +31-88-7558316
Fax: +31-302544990
http://www.umcutrecht.nl/subsite/pathology/Researchers/HIFNotch+Signaling/
* only applicants that will be invited for an interview will be contacted.

A symposium entitled "HIV Protease and Beyond: The Past, Present, and Future of HIV Structural Biology" will be held on the Frederick campus of the National Cancer Institute on January 30 and 31, 2009. The symposium commemorates the 20th anniversary of the publication of the crystal structure of HIV protease, a turning point in the utilization of structural information for drug design. In addition, the relationship between structural biology and drug design for other HIV targets will be emphasized. The meeting format will consist of oral presentations by the invited speakers, as well as of contributed posters. Speakers and poster presenters will address both the historical aspects of structural studies of HIV proteins as well as their current and planned research.



Invited speakers include: S. Oroszlan (NCI), D. Davies (NIDDK), M. Jaskolski (A. Mickiewicz U., Poznan), P. Fitzgerald (Merck, Retired), A. Wlodawer (NCI), D. Kempf (Abbott), D. Davis (NCI), C. Schiffer (U. Mass.), E. Freire (Johns Hopkins), I. Weber (Georgia State), J. Konvalinka (IOCHB, Prague), S. Le Grice (NCI), S. Hughes (NCI), W. Yang (NIDDK), R. Craigie (NIDDK), Y. Pommier (NCI), D. Hazuda (Merck), M. Clore (NIDDK), R. Wyatt (VRC), E. Freed (NCI), and H.-G. Kräusslich, (U. Heidelberg).

Interested participants should register before January 9 2009. No registration fee is required. More information about the program of the meeting, local arrangements and accommodations, and how to register can be found on the web page http://web.ncifcrf.gov/events/hivprotease. Additional information can be obtained from Julia Lam via phone (301-228-4141) or e-mail (lamjl@mail.nih.gov).

In Memoriam: Dr. Darrel Goll

by Hans Fritz, David Hartshorne and Joy Winzerling

It is with great sadness that we noted the passing of our colleague and friend, Darrel Goll, Professor in the Departments of Nutritional Sciences and of Biochemistry and Molecular Biophysics of the University of Arizona in Tuscon USA, on July 21st this year.

The major objective criterium for the success of a scientist is his publication productivity, especially regarding peer-reviewed full-length research papers. After his first report on a Ca2+-activated protease in 1976, Darrel Goll published continuously an increasing number of papers on the calpain-calpastatin system until today. Originally his work was devoted to cellular components such as α-actinin, myosin and tropomyosin, potential substrates of the calpains as turned out later. From 1985 onwards Darrel Goll focussed his research primarily on the properties of the "Ca2+-dependent proteinase" and a newly discovered tissue inhibitor of this enzyme. A very fruitful period began with work on the regulation and function of the Ca2+-dependent proteinases, the calpains, and their specific inhibitor, the calpastatin. Darrel Goll clarified the molecular mechanisms of (i) calpain activation (including autolysis and Ca2+-influence), (ii) the calpain-calpastatin interaction, and (iii) interactions of calpains with cellular substrates and membrane constituents. He showed the localization of calpains and calpastatin in platelets as well as in skeletal muscle dystrophy and inflammatory myopathies. Further studies were devoted to the role of the calpain-calpastatin system in muscle turnover and growth, its behaviour during post-mortem tenderization and its influence on the formation of integrin clusters. He identified the calpastatin gene promoter and several calpastatin isoforms, and developed convenient assays for the detection of calpains (and other proteinases) e.g. in tissue extracts as well as methods for rapid immunoaffinity purification of these difficult to handle enzymes.

More then 135 original research papers are complemented by numerous abstracts (contributions at meetings mainly) and 30 review articles in which the current knowledge of biochemistry, cell biology and functional aspects of the calpain-calpastatin system and its role in skeletal muscle growth, integrity and metabolism as well as in post-mortem tenderization is described extensively.

The published work of Darrel Goll is outstanding in many respects. Using adequate and modern techniques, he was able to contribute significantly to the elucidation of sophisticated molecular mechanisms regulating a multiple component cellular system to achieve biological or patho/physiological effects. The scientific community owes Darrel Goll major contributions leading to new insights in the calpain-calpastatin field and in associated systems. Darrel Goll´s scientific work can be classified as unique in view of the broad experience and profound knowledge gained and applied by him in this particular field.

As a consequence of this extensive expertise may be regarded the world-wide engagement of Darrel Goll in numerous professional activities (>100 listed in his C.V.), e.g. as (i) editorial board member of scientific journals, (ii) member of scientific program review and advisory committees as well as of peer-review committees for national research initiatives, (iii) lecturer at NIH workshops, (iv) lecturer and session chair at several Gordon Research Conferences and ULCA Symposia, (v) lecturer and session chair as well as plenary and keynote speaker at several international meetings (e.g. Symposia on Proteolysis and on Protease Inhibitors and Biological Control, Winter Schools on Proteases Recent Developments, Conferences on Cysteine Proteina¬ses and Their Inhibitors, Symposium on Calpains), (vi) opening lecturer and session chair at two FASEB Summer Research Conferences on "Calpains in Agriculture, Health and Disease", and (vii) chair and organizer of the FASEB Summer Research Conference on "The Calpain System in Health and Disease" and (viii) co-chair of the FASEB Summer Conference on "The Calpain Gene Family in Health and Disease."

This impressive listing of Darrel Goll´s professional scientific activities shows unequivocally his outstanding national and international reputation as leading scientist in the field of biochemistry, cell biology and molecular biology of the calpain system and its target substrates, in particular regarding the role of the calpain-calpastatin system in skeletal muscle development, growth, degeneration and post-mortem tenderization. The detailed knowledge of the molecular mechanisms underlying this system in health and disease will be the basis for the development of new strategies in animal agriculture as well as in veterinary and human medicine.

The high reputation of Darrel Goll´s scientific work and its personal integrity is also convincingly acknowledged by the substantial number of awards and fellowships he obtained from professional societies and universities.

In Darrel' s passing the academic community lost a highly respected University Professor, a very successful scientist and an estimated teacher. His colleagues, particularly also in the proteolysis field, will miss his keen intellectual assessments and wisdom and, on a more personal level, his friends will miss his optimism, sense of humor and warmth. Darrel will live on in our memories and hearts.

INTERNATIONAL PROTEOLYSIS SOCIETY PRESENTS

6th General Meeting – Queensland, Australia **26th – 30th October 2009**

The 6th General Meeting of the International Proteolysis Society will be held from October 26th – 30th at the Surfers Paradise Marriott Resort & Spa, Gold Coast, Queensland, Australia. This meeting represents the main event of the IPS and is expected to be attended by several hundred protease scientists.

Preliminary Session Themes

1) Cancer and Metastasis
2) Degradomics
3) From Bench to Bedside
4) Immunity
5) Infectious Disease
6) Proteases in Cardiovascular Disease
7) Proteases in Developmental Biology
8) Proteases in Metabolism
9) Proteases in Neurobiology and Neurodegenerative Disease
10) Proteases in Protein Homeostasis

Speakers

Ben Cravatt, The Scripps Research Institute, USA ◦ **Ana Maria Cuervo,** Albert Einstein College of Medicine, USA ◦ **Matthew Freeman,** University of Cambridge, UK ◦ **Martin Gebbink,** University Medical Center Utrecht, The Netherlands ◦ **James Huntington,** University of Cambridge, UK ◦ **Sharad Kumar,** Hanson Institute, Australia ◦ **Carlos Lopez-Otin,** Universidad de Oviedo, Spain ◦ **Alex Loukas,** Queensland Institute for Medical Research, Australia ◦ **Motoharu Seiki,** University of Tokyo, Japan ◦ **Nancy Thornberry,** Merck Research Laboratories, USA ◦ **Joe Trapani,** Peter Macullum Cancer Centre, Australia ◦ **Sinisa Urban,** Johns Hopkins University, USA ◦ **Petra Van Damme,** Ghent University, Belgium ◦ **James Wells,** University of California, USA ◦ **Michael Wolfe,** Harvard University, USA

Local Organising Committee

James Whisstock, (Chair), Monash University, Victoria
Hiroshi Kido, (Co-Chair), University of Tokushima, Japan

For further information please visit www.ips2009.org




IMPORTANT **PROTEASE** PAPERS I

Research Publications

Schreiner P., Chen X., Husnjak K., Randles L., Zhang N., Elsasser S., Finley D., Dikic I., Walters K. and Groll M.

Ubiquitin docking at the proteasome via a novel PH domain interaction.

Nature 2008 453 (7194), 548-552.

Nordström H, Gossas T, Hämäläinen M, Källblad P, Nyström, S, Wallberg H, Danielson UH

Identification of MMP-12 Inhibitors by Using Biosensor-Based Screening of a Fragment Library.

J Med Chem. 2008 51(12), 3449-3459.

Cheng T, van Vlijmen-Willems IM, Hitomi K, Pash MC, van Erp PE, Schalkwijk J, and Zeeuwen PL

Colocalization of cystatin M/E and its target proteases suggests a role in terminal differentiation of the human hair follicle and nail.

J.Invest.Dermatol. 2008, doi: 10.1038/jid.2008.353.

Van Damme P, Maurer-Stroh S, Plasman K, Van Durme J, Colaert N, Timmerman E,Debock PJ, Goethals M, Rousseau F, Schymkowitz J, Vandekerckhove J, Gevaert K.

Analysis of protein processing by N-terminal proteomics reveals novelspecies-specific substrate determinants of granzyme B orthologs.

Mol Cell Proteomics. 2008 Oct 3. [Epub ahead of print]

Lamkanfi M, Kanneganti TD, Van Damme P, Vanden Berghe T, Vanoverberghe I, Vandekerckhove J, Vandenabeele P, Gevaert K, Núñez G.

Targeted peptide-centric proteomics reveals caspase-7 as a substrate of the caspase-1 inflammasomes.

Mol Cell Proteomics. 2008 Jul 30. [Epub ahead of print]

Sanglas L, Valnickova Z, Arolas JL, Pallarés I, Guevara T, Solà M, Kristensen T, Enghild JJ, Avilés FX, Gomis-Rüth FX.

Structure of activated thrombin-activatable fibrinolysis inhibitor, a molecular link between coagulation and fibrinolysis.

Mol Cell 2008 31, 598-606.

Lupardus PJ, Shen A, Bogyo M, Garcia KC.

Small molecule-induced allosteric activation of the Vibrio cholerae RTX cysteine protease domain.

Science. 208 322, 265-8.

Mallorquí-Fernández N, Manandhar SP, Mallorquí-Fernández G, Usón I, Wawrzonek K, Kantyka T, Solà M, Thøgersen IB, Enghild JJ, Potempa J, Gomis-Rüth FX.

A new autocatalytic activation mechanism for cysteine proteases revealed by Prevotella intermedia interpain A.

J Biol Chem 2008 283, 2871-2882.

Pagano M, Clodic G, Bolbach G, Michiel M, Haddag S, Reboud-Ravaux M.

Liberation of an N-terminal proline-rich peptide from the cryptic proteinase of fibronectin by auto-proteolysis.

Arch Biochem Biophys. 2008 479,158-62.

Formicola L, Maréchal X, Basse N, Bouvier-Durand M, Bonnet-Delpon D, Milcent T, Reboud-Ravaux M, Ongeri S.

Novel fluorinated pseudopeptides as proteasome inhibitors.

Bioorg. Med. Chem. Lett. 2008, doi:10.1016/j.bmcl.2008.11;012.

Groll M., Balskus E.P., Jacobsen E.N

Structural analysis of spiro beta-lactone proteasome inhibitors.

J Am Chem Soc 2008 130, 14981-3.

Hines J., Groll M., Fahnestock M. and Crews CM

Proteasome Inhibition by Fellutamide B Induces Nerve Growth Factor Synthesis.

Chem & Biol 2008 15, 501-512.

Groll M., Schellenberg B., Bachmann AS., Archer CR., Huber R., Powell TK., Lindow S., Kaiser M. and Dudler R.

A plant pathogen virulence factor inhibits the eukaryotic proteasome by a novel mechanism.

Nature 2008 452, 755-8.

Huguenin M, Müller EJ, Trachsel-Rösmann S, Oneda B, Ambort D, Sterchi EE, Lottaz D

The metalloprotease meprinbeta processes E-cadherin and weakens intercellular adhesion.

PLoS ONE. 2008 May 14;3(5):e2153.

Ambort D, Stalder D, Lottaz D, Huguenin M, Oneda B, Heller M, Sterchi EE.

A novel 2D-based approach to the discovery of candidate substrates for the metalloendopeptidase meprin.

FEBS J. 2008 275, 4490-509.

Hinman, JD, Oh, S-Y, Chen, C-D, Hollander, W and Abraham, CR.

Age-dependent accumulation of ubiquitinated CNP in myelin lipid rafts.

Glia. 2008 56, 118-33.

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IMPORTANT **PROTEASE** PAPERS II

Kastrup, C.J., Boedicker, J.Q., Pomerantsev, A.P., Moayeri, M., Bian, Y. Pompano, R.R., Kline, T.R., Sylvestre, P., Shen, F., Leppla, S.L., Tang, W.J., Ismagilov, R.F.

Spatial localization of bacteria controls coagulation of human blood by "quorum acting".

Nature Chem Bio 2008 4, 742-750.

Malito, E., Ralat, L.A. Manolopoulou, M., Tsay, J.L., Wadlington, N.L. and Tang, W.-J.

Molecular Bases for the recognition of short peptide substrates and cysteine-directed modifications of human insulin-degrading enzyme.

Biochemistry 2008 47, 12822-12834.

Schneck JL, Villa JP, McDevitt P, McQueney MS, Thrall SH, Meek TD.

Chemical mechanism of a cysteine protease, cathepsin c, as revealed by integration of both steady-state and pre-steady-state solvent kinetic isotope effects.

Biochemistry. 2008 47, 8697-710.

Abboud-Jarrous G, Atzmon R, Peretz T, Palermo C, Gadea B, Joyce JA and Vlodavsky I.

Cathepsin L is responsible for processing and activation of proheparanase through multiple cleavages of a linker segment.

J Biol Chem. 2008 283, 18167-18176.

Trivedi NN, Raymond WW, Caughey GH.

Chimerism, point mutation and truncation dramatically transformed mast cell delta tryptases during primate evolution.

J Allergy Clin Immunol 2008 121, 1262-8.

Caughey GH, Beauchamp J, Schlatter D, Raymond WW, Trivedi NN, Banner D, Mauser H, Fingerle J

Guinea pig chymase is leucine-specific: a novel example of functional plasticity in the chymase/granzyme family of serine peptidases.

J Biol Chem 2008 283, 13943-51.

Arastu-Kapur S., Ponder E.L., Fonovic U., Yeoh S., Yuan F., Fonovic, M., Grainger M., Phillips C.I., Powers J.C., and Bogyo M.

A small molecule screen identifies proteases that regulate erythrocyte rupture by the human malaria parasite Plasmodium falciparum.

Nature Chemical Biology, 2008 4, 203-213.

Wisniewska M, Goettig P, Maskos K, Belouski E, Winters D, Hecht R, Black R, Bode W.

Structural Determinants of the ADAM Inhibition by TIMP-3: Crystal Structure of the TACE-N-TIMP-3 Complex.

J Mol Biol. 2008 381, 1307-1319.

Salameh MA, Soares AS, Hockla A, Radisky E.

Structural basis for accelerated cleavage of bovine pancreatic trypsin inhibitor (BPTI) by human mesotrypsin.

J Biol Chem. 2008 283, 4115-23.

Clemente JC Robbins A, Graña P, Paleo MR, Correa JF, Villaverde MC, Sardina FJ, Govindasamy L, Agbandje-McKenna M, McKenna R, Dunn BM, and Sussman S.

Design, Synthesis, Evaluation, and Crystallographic-Based Structural Studies of HIV-1 Protease Inhibitors with Reduced Response to the V82A Mutation.

J Med Chem 2008, 51, 852-60.

Coman RM, Robbins AH, Goodenow MM, Dunn BM, McKenna R.

High-resolution structure of unbound human immunodeficiency virus 1 subtype C protease: implications of flap dynamics and drug resistance,

Acta Crystallographica Section D Biological Crystallography, 2008 64,754-63.

Janka L, Clemente JC, Vaiana N, Sparatore A, Romeo S, and Dunn BM.

Targeting the plasmepsin 4 orthologs of Plasmodium sp. With "Double-Drug" inhibitors.

Protein and Peptide Letters, 2008 15, 868-73.

Farady, C.T., Egea, P.F., Schneider, E.L., Darragh, M.R., Craik, C.S.

Structure of an Fab-Protease Complex Reveals a Highly Specific Non-canonical Mechanism of Inhibition.

J Mol Biol 2008 380, 351-60.

Igarashi Y, Heureux E, Doctor KS, Talwar P, Gramatikova S, Gramatikoff K, Zhang Y, Blinov M, Ibragimova SS, Boyd S, Ratnikov B, Cieplak P, Godzik A, Smith JW, Osterman AL, Eroshkin AM.

PMAP: databases for analyzing proteolytic events and pathways.

Nucleic Acids Res. 2008 Oct 8. [Epub ahead of print] PMID: 18842634.

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IMPORTANT **PROTEASE** PAPERS III

Research Publications

Raorane DA, Lim MD, Chen FF, Craik CS, Majumdar A.

Quantitative and Label-Free Technique for Measuring Protease Activity and Inhibition using a Microfluidic Cantilever Array.

Nano Lett. 2008 10, 8, 2968-2974.

Urban S and RP Baker.

In vivo analysis reveals substrate-gating mutants of a rhomboid intramembrane protease display increased activity in living cells.

Biological Chemistry 2008 389, 1107-1115.

Baxt L, Baker RP, Singh U and S Urban.

An Entamoeba histolytica rhomboid protease with atypical specificity cleaves a surface lectin involved in phagocytosis and immune evasion.

Genes & Development 2008 22, 1636-46.

Kurschus FC, Fellows E, Stegmann E, Jenne DE.

Granzyme B delivery via perforin is restricted by size, but not by heparan sulfate-dependent endocytosis.

Proc Natl Acad Sci U S A. 2008 105, 13799-804.

Buzza MS, Dyson JM, Choi H, Gardiner EE, Andrews RK, Kaiserman D, Mitchell CA, Berndt MC, Dong JF, Bird PI.

Antihemostatic activity of human granzyme B mediated by cleavage of von Willebrand factor.

J Biol Chem. 2008 283, 22498-504.

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Reduced tumour cell proliferation and delayed development of high-grade mammary carcinomas in cathepsin B-deficient mice.

Oncogene. 2008 27, 4191-9.

Halle A, Hornung V, Petzold GC, Stewart CR, Monks BG, Reinheckel T, Fitzgerald KA, Latz E, Moore KJ, Golenbock DT.

The NALP3 inflammasome is involved in the innate immune response to amyloid-beta.

Nat Immunol. 2008 9(8), 857-65.

Conus S, Perozzo R, Reinheckel T, Peters C, Scapozza L, Yousefi S, Simon HU.

Caspase-8 is activated by cathepsin D initiating neutrophil apoptosis during the resolution of inflammation.

J Exp Med. 2008 205, 685-98.

Fan F, Binkowski BF, Butler BL, Stecha PF, Lewis MK, Wood KV.

Novel genetically encoded biosensors using firefly luciferase.

ACS Chem. Biol. 2008 3, 346-351.

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Displacement of the occluding loop by the parasite protein, chagasin, results in efficient inhibition of human cathepsin B.

J Biol Chem 2008 283 22815-25.

Vincents B, Vindebro R, Abrahamson M, von Pawel-Rammingen U.

The human protease inhibitor cystatin C is an activating cofactor for the streptococcal cysteine protease IdeS.

Chem Biol 2008 15 960-8.

Gutiérrez-Fernández A, Fueyo A, Folgueras AR, López-Otín C.

Matrix metalloproteinase-8 functions as a metastasis suppressor through modulation of tumor cell adhesion and invasion.

Cancer Res 2008 68, 2755-63.

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Combined treatment with statins and aminobisphosphonates extends longevity in a mouse model of human premature aging.

Nature Med. 2008 14, 767-72.

Funkelstein L, Toneff T, Hwang SR, Reinheckel T, Peters C, and Hook V.

Major role of cathepsin L for producing ACTH, beta-endorphin, and alpha-MSH peptide hormones derived from POMC, illustrated by gene knockout and expression.

J Biol Chem 2008 Oct 10. [Epub ahead of print].

REVIEWS

Palermo C and Joyce JA.

Cysteine cathepsin proteases as pharmacological targets in cancer.

Trends in Pharmacological Sciences. 2008 29, 22-28.

López-Otín C, Bond JS.

Proteases: multifunctional enzymes in life and disease.

J Biol Chem 2008 283, 30433-7.

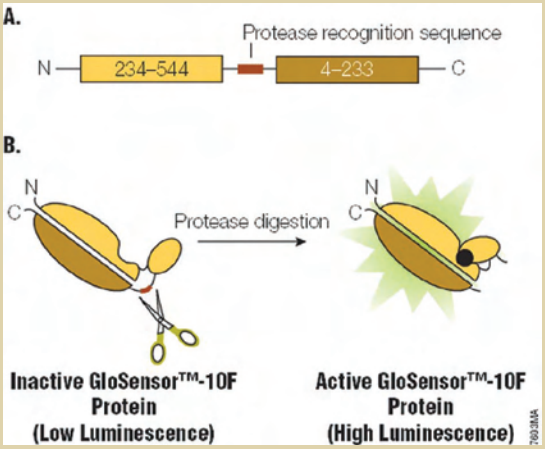
Van Damme P, Vandekerckhove J, Gevaert K.

Disentanglement of protease substrate repertoires.

Biol Chem. 2008 389, 371-81.

Interrogate Your Protease of Interest

The Protease-Glo™ Assay* (Cat.# G9451) is a novel method to detect and measure protease activities using a genetically engineered firefly (Photinus pyralis) luciferase and represents one example of the GloSensor™ platform technology (1). The assay uses a circularly permuted firefly luciferase, the GloSensor™-10F protein, with a protease recognition site as the protease substrate. This assay system allows rapid generation of protease substrates through molecular cloning and coupled transcription/translation cell-free expression, thus enabling the facile evaluation of protease function. Oligonucleotides encoding a protease recognition sequence are designed and cloned into the GloSensor™-10F gene located on a linearized vector. The GloSensor™ protein containing the protease site of interest is then synthesized in a cell-free protein expression system and subsequently used as a protease substrate. Cleavage of the protease recognition sequence leads to activation of the GloSensor™ protein and light emission. The level of luminescence correlates to protease activity (2). The Protease-Glo™ Assay has the advantage of a bioluminescent readout, which provides easy quantitation, high sensitivity and wide dynamic range (1–3).



Visit the web application, Protease-Glo™ Assay Oligonucleotide Designer at: **www.promega.com/techserv/tools/proteaseglo/** to see how to generate your protease recognition site of interest in the pGloSensor™-10F Linear Vector and express the protein using cell-free translation.

For ordering information and more, please see: **http://www.promega.com/applications/cellularanalysis/protease.htm**

Features

- Flexible: Use with P' requiring proteases.
- Avoid Fluorescent Background Problems: Physical and chemical features of luminescence overcome problems due to fluorescence interference.
- Greater Sensitivity: Ease and dynamic range of luminescence.
- Open Platform System: Create your own recognition substrates.
- Interrogate Sequences: Excellent tool to determine optimal protease recognition sequences or effects of amino acid substitutions.
- Web Application: Makes proper oligo design fast and easy; simply enter your amino acid sequence of interest. See: www.promega.com/techserv/tools/proteaseglo/.

Applications

- Measure specificity of proteases or protease recognition sequences.
- Compare related proteases against the same substrate (e.g., viral strains).
- Determine protease substrate specificity (length of essential sequence, what specific amino acids are essential).
- Screen for protease inhibitors, and determine inhibitor potencies (IC50).

References

1. **Fan, F. et al. (2008) Novel genetically encoded biosensors using firefly luciferase. ACS Chem. Biol. 3, 346–51.**
2. **Wigdal, S. et al. (2008) A novel bioluminescent protease assay using engineered firefly luciferase. Curr. Chem. Genomics 1, 94–106.**
3. **Fan, F. and Wood, K.V. (2007) Bioluminescent assays for high-throughput screening. Assay Drug. Dev. Technol. 5, 127–136.**

For additional information on this new technology, please contact:
Neal Cosby, PhD, Strategic Marketing Manager **neal.cosby@promega.com**

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