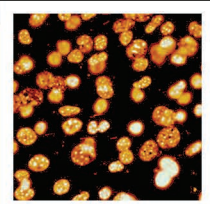
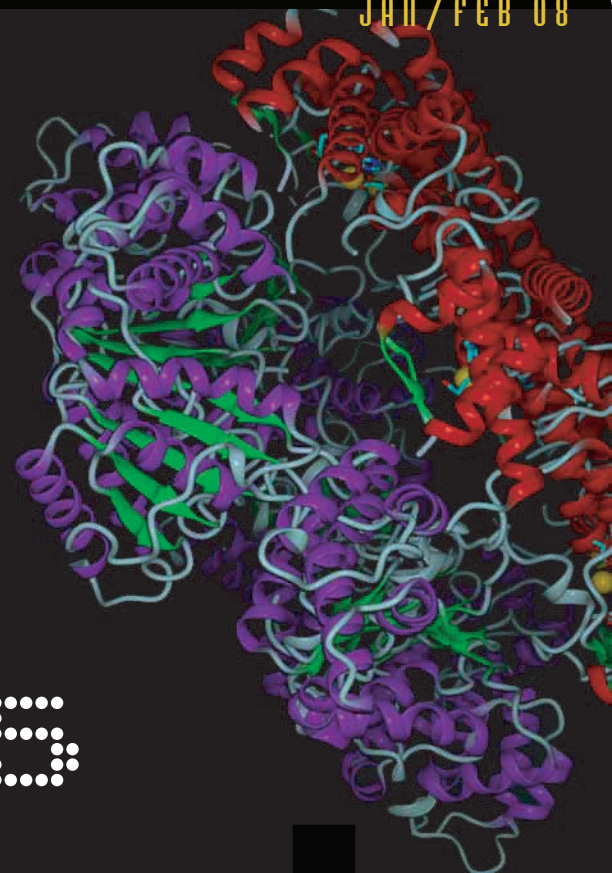


IN THIS ISSUE:

- PMAP - A Web-Based Protease Resource
- Meeting Reports
- Photos from IPS 5th General Meeting Petras, Greece
- Important Protease Papers
- Job Listings
- New Product Offerings

INTERNATIONAL PROTEOLYSIS SOCIETY

QUICK CUTS



YOUR PREMIERE RESOURCE
FOR ALL OF YOUR IMPORTANT PROTEASE QUESTIONS

A Message From the President:

2007 has come to a close and I hope that you all have had a productive year both scientifically and personally. This year has brought significant changes to the IPS. We have established a new format for our QuickCuts newsletter and we have re-designed our website and membership dues payment system. We have also launched a new protease blog site where members can discuss important protease related topics. We just recently held our 5th General Meeting of the society in Petras Greece. This meeting was highly successful and was attended by the largest number of delegates of any meeting of the society. Our membership numbers continue to grow and with over 500 protease research scientists in attendance at our meeting it is clear that the IPS has matured into a very significant society that can make many important contributions in broad areas of biology, chemistry and biomedical sciences.

In this issue of QuickCuts we have assembled a compilation of interesting articles that I hope you will enjoy. In particular this issue contains a highlight on a new web-based protease research tool and several updates from the satellite meetings associated with the main general meeting this past October. While we would have liked to include a complete meeting report for the general meeting itself, we are currently working to generate such a report for publication in a prominent journal.

As always this issue of QuickCuts has an extensive list of important protease papers that have been published since our last issue in April along with job listings and new product offerings. I am happy to report that I am receiving a large number of responses to my queries for content for the newsletter and we therefore have an impressive list of papers highlighted in this issue.

I would like to close by thanking Georgia Sotiropoulou for all her hard work making the IPS2007 meeting a great success. These meetings are a key part of our society and I hope that you all will continue to use them as a forum to contribute your best protease research to the community. Thanks also to all our IPS members and best wishes for a productive 2008!

Mathew Bogyo - IPS President - mbogyo@stanford.edu

COUNCIL OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

Matthew Bogyo - President of the Council
Klaudia Brix - Vice President of the Council
Hiroshi Kido - Secretary
Christian Sommerhoff - Treasurer
Rob Pike - ex officio - Former IPS President

COUNCILLORS - EUROPE/AFRICA

Klaudia Brix	Christian Sommerhoff
Carlos Lopez-Otin	Ed Sturrock

COUNCILLORS - ASIA/AUSTRALIA

Kohei Oda	Phil Bird
Kenji Yamamoto	Hiroshi Kido

COUNCILLORS - Americas

Chris Overall	Maria-Luiza Oliva
Johanna Joyce	Matthew Bogyo

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

Changes in the IPS

Matthew Bogyo, IPS President

One of the main tasks for our members at the general meetings is to elect new council members. At IPS2007 this was accomplished and I am pleased to report that the following new council members were elected:

The Americas

Johanna Joyce
Maria-Luiza Oliva

Europe/Africa

Carlos Lopez-Otin
Christian Sommerhoff

Australia/Asia

Hiroshi Kido
Phil Bird

The council elected Matthew Bogyo as the new President, Klaudia Brix as Vice President, Hiroshi Kido as Secretary and Christian Sommerhoff as treasurer. We look forward to working with the new council as we move into 2008.

In addition to the election of new council members the site of the next IPS meeting was announced at the final general session of the meeting. IPS2009 will take place in Surfer's Paradise in the Gold Coast of Australia. This should be a great site for the next meeting and we hope that you all can already start to make plans to attend. We plan to announce more details in the next issue of QuickCuts.

Finally, we added a new sponsor member of the IPS.



We hope to see an increasing number of corporate sponsors of the IPS especially as we head into 2009 so that we can offer a significant number of travel awards for the meeting in Australia.

As we gain in momentum from the highly successful meeting in October I hope we can continue to increase the amount of communication among members and also continue to build our member numbers. Your input and suggestions are always welcome and are key to helping to continue to improve the society. Please do your part to make people aware of the IPS and to encourage protease researchers you know to join the society.

Post-doctoral fellowships in 2008

Alzheimer's disease and related disorders

The Center for Dementia Research of the Nathan Kline Institute, an affiliate of New York University School of Medicine, invites applications from highly motivated individuals with a strong background in molecular biology or neuroscience to investigate disease mechanisms in transgenic mouse models of Alzheimer's disease and related disorders. Unique research and training opportunities are available to combine molecular, genetic, morphologic, and in vivo imaging approaches in a multidisciplinary setting. Research involves development and characterization of new transgenic and knockout mice modeling disease-related abnormalities of protease and vesicular trafficking leading to altered protein processing and neuronal cell death. These studies use a broad range of molecular, cell biological, and morphological techniques. NKI is located 12 miles north of the GW Bridge on the 150-acre campus of Rockland Psychiatric Center. Send resume, statement of research interests, and a list of 3 references to Ralph A. Nixon, Ph.D., M.D., Center for Dementia Research, Nathan Kline Institute, 140 Old Orangeburg Rd., Orangeburg, NY 10962; Fax: 845-398-5422; e-mail: cdrinfo@nki.rfmh.org

CONTACT: by email to: Ralph Nixon cdrinfo@nki.rfmh.org

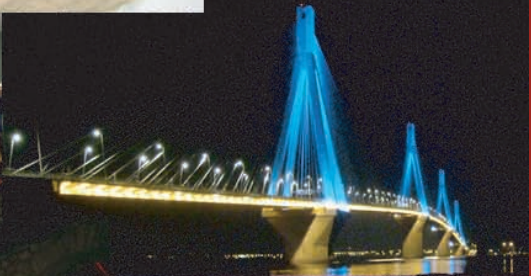
Pathogenesis of inflammatory bowel diseases

Department of Rheumatology and Clinical Immunology, Inselspital, University of Bern, Switzerland The candidate will work in the framework of the EU-funded collaborative research project "IBDase" (<http://www.rheumabern.ch/5509.html>). The IBDase consortium involves nine European research groups from different disciplines, including genetics, biochemistry, molecular biology, mucosal immunology, microbiology, and translational medicine, to address the pathogenesis of inflammatory bowel diseases in patients and animal models with a focus on proteases and protease inhibitors. The interdisciplinary research effort is coordinated by the University of Bern, Switzerland. Earliest start date 1st of March 2008.

Tasks will include: Meta-analysis of published literature and online databases, in particular genetic association studies, to define protease and protease inhibitor candidate genes in inflammatory bowel disease. Analysis of expression regulation and biochemical properties of polymorphic variants of protease / protease inhibitor genes in cell culture and organ culture models and in human intestinal tissue specimens. Defining the role of miRNAs in the expression regulation of protease and protease inhibitor genes. Contribution to the development of novel IBD mouse models, in collaboration with other research groups.

Please send your CV and cover letter by email to: daniel.lottaz@insel.ch Dr. Daniel Lottaz, MD / PhD, IBDase coordinator Department of Rheumatology and Clinical Immunology Inselspital, University of Bern.

Images of IPS 2007 - Oct 20-24 Petras, Greece



Meeting Reports:

IPS 2007 - Postgraduate Courses - Student Reports

As satellite events of the IPS2007 meeting three Postgraduate Courses on 'Bioinformatics - Computational Methods in Biological Data Mining', 'Proteomics - Methodologies and Applications', and 'Enzyme Mechanisms and Kinetics' were organized. Comprising both theoretical seminars and hands-on practical sessions these courses were hosted at the Campus of the University of Patras. Around 60 participants from around the world participated in these sessions that gave younger scientists not only a chance to freshen up skills and to engage specialists in the field, but also to meet colleagues and make new friends before the meeting.

Bioinformatics – Computational Methods in Data Mining

Mitchell Lawrence
Queensland University of Technology, Australia

The bioinformatics postgraduate course organised by Georgia Sotiropoulou (University of Patras, Greece), Georgios Spyroulias (University of Patras, Greece) and Sophia Kossida (Academy of Athens Foundation for Biomedical Research, Greece) and hosted by the University of Patras covered the gamut of ways that information technology can help generate and validate hypotheses in biological research. The interesting list of speakers explained the benefits of their favourite programs in the context of their own research before giving us some tips and tricks for using them.

The course began with Artemis Hatzigeorgiou (University of Pennsylvania, USA), who described the growing field of miRNA research, particularly the development of search engines for matching miRNA with their potential targets. Then, later in the day, Artemis ran a tutorial so we could try these programs out for ourselves and learn how to apply them to our own projects. Next James Whisstock (Monash University, Australia) explained how to identify novel, evolutionarily-related proteins using Position Specific Iterated BLAST (PSIBLAST) to mine for patterns of amino acid conservation amongst overall low sequence similarity.

After gathering for lunch, Sophia Kossida gave us a crash course in molecular phylogenetics and helped demystify the workings of the sequence comparison programs that many of us had treated as black boxes in the past. Erik Bongcam-Rudloff (Uppsala University, Sweden) then talked about current initiatives to integrate bioinformatics into the laboratory and customise workflows and outputs to make them more intuitive for scientists. Finally, Georgios Spyroulias, explained the management and use of the RCSB Protein Data Bank before showing us how to upload and appraise the quality of structures ourselves.

In the end, the bioinformatics postgraduate course was a great mix of speakers and sessions that whetted our appetite before the broader society meeting.

Enzyme Mechanisms and Kinetics

Pedro Castanheira and Isaura Simões
Biocant - Cantanhede, Portugal

One of the exciting things about IPS2007 was the possibility to attend postgraduate courses in different areas of research. Since protein chemistry is our field of work, Enzyme Mechanisms and Kinetics was the right course for us. Although we had tried to do kinetics before we felt that most of the relevant information did not come from textbooks and this would therefore be a great opportunity to ask all the questions about how to correctly do protease kinetics. In other words, our expectations were high!

After a long trip from Portugal to Patras (Greece) with a night of no sleep we finally were there. The next morning we found Georgia Sotiropoulou (Chair of IPS2007) with a big smile welcoming us and taking us to the lab at the Department of Pharmacy School of Health Sciences at Patras University. There we found Christian Sommerhoff and Dorit Nägler (both LMU, Munich) struggling to get all the equipment running and working properly... We started with a welcome session where we introduced ourselves, and then Christian gave us a very nice introduction to protease kinetics – from the basic theory to the technical details of protease inhibition kinetics. After a short lunch, we were divided into two groups and before we moved to the lab, we had an introduction to Steady-State Kinetics (Christian group) and Pre-Steady State Kinetics (Dorit group). The steady-state experiments consisted of the inhibition of Trypsin and Tryptase by a Kazal-type inhibitor where we were asked to determine what conditions we should use to titrate the inhibitor and to determine the K_i . The pre-steady state experiments consisted of determining the type of inhibition of two different inhibitors, and the determination of constants of inhibition.

The next day the groups were swapped, so everybody did both steady-state and pre-steady state kinetics. At the end of the course we were quite pleased; the course really fulfilled our initial expectations. We could now understand what we were doing correctly as well as a areas in which we had made mistakes in our own experiments. Above all we became aware of the many details one needs to take into account when doing protease inhibition kinetics.

Besides the scientific relevance of this postgraduate course we really have to also emphasize its social part. In fact, one of the best things about these postgraduate courses is the opportunity to meet and exchange experiences with other people. The group attending this course was really nice and very heterogeneous and we had a good time together not only during the course but also throughout the entire meeting. Last, but – definitely - not least, we have to thank Dorit and Christian for their patience, kindness and for being so committed to making everything work. We attended the 5th General Meeting of the International Proteolysis Society, which was a great meeting with outstanding presentations, showing us the latest developments in the field of proteolysis. We ended up returning to Portugal with many new ideas to implement in our own projects.

ISK2007- 2nd International Kallikrein and Kallikrein-Related Peptidases Symposium

Santorini Island, Greece Oct 16-18, 2007

Litsa Talieri, ISK2007 President

The 2nd Kallikrein and Kallikrein-Related Peptidases Symposium (ISK2007), held under the auspices of the Hellenic Anticancer Institute, took place on the beautiful Greek Island of Santorini from 16 -18th of October and was associated with the 5th International Proteolysis Meeting held in Patras from 20-24th of October. ISK2007 president, Litsa Talieri and the scientific advisory board chair, Judith Clements, with advice and generous help of Eleftherios Diamandis, organized a very successful conference as reflected by the multidisciplinary program and organized social events. From the 1st Kallikrein Symposium, organized by David Deperthes in Lausanne 2005, to the 2nd ISK the number of participants doubled, showing that the Kallikreins are becoming more attractive targets for scientists engaged in many areas of both academic and applied research. One hundred and thirty five participants coming from 19 different countries contributed 18 lectures, 18 short oral presentations and 53 posters. The topics covered aspects of biochemistry, molecular biology, cell biology, physiology, pathophysiology, pathobiochemistry as well as medicine. All participants had the opportunity to present and discuss their results with scientists in the contemporary venue "Nomikos Conference Center" which had a magnificent view over the Caldera and the Volcano of Santorini. The excellent weather and friendly atmosphere created by the organizers, the unique natural beauty of Santorini Island and its rich history created an environment for lively discussions and new co-operations.

The congress started with the structure, function and activation of kallikreins with Peter Goettig presenting the structural determinants of the zinc inhibition of KLKs and Michael Blaber outlining the activation profiles and regulatory cascades of the human KLKs. It continued with the functional roles of the newer KLKs, with Torbjorn Engelrud presenting the functional roles of KLKs in the physiology and pathology of the skin and James Simmer explaining KLK4 function during dental enamel formation. One of the meeting highlights was the award of the Frey-Werle Commemorative Gold Metal to Judith Clements by Hans Fritz and the first day's program closed with her keynote address summarizing the discoveries concerning the KLK family from mice to man during the last two decades. Following the first session, participants visited the Pre-history Museum of Santorini Island in Fira and were guided by the Curator of Antiquities for the Cyclades Islands Dr. Mariza Marthari. Finally the day ended with a welcome cocktail party and dinner at the Restaurant Zafora in Fira.

The second day of the Symposium brought a session dedicated to the classical sites of KLK action such as heart, kidney and prostate, with Francois Alhenc-Gelas explaining the role of tissue kallikreins and angiotensin 1-converting enzyme (ACE) in cardiovascular and renal regulation. Carsten Tschöpe presented new perspectives on the tissue kallikrein-

kinin system in cardiac failure, followed by Matthew Bogoy who presented on the application of small molecule activity based probes to study protease function. Chris Overall presented an array of new proteomic methods to search for KLK substrates, including the CLIP-TAILS technique. The afternoon session focused on cell signaling and protease function and had as representative speakers Morley Hollenberg and John Hooper discussing the role of proteinase-activated receptors (PARs) and Bonnie Sloane presenting the identification and functional



View of Santorini from the meeting site

imaging of proteases in breast cancer. At the following business meeting participants decided that the next Kallikrein Society Meeting will take place in Munich in 2009 and Manfred Schmitt will be the organizer. The day continued with a visit to the winery Sato at the village of Pyrgos for Santorinian wine tasting and sunset viewing and ended with the Gala dinner at the Tavern Pyrgos, where the participants had the opportunity to taste local specialties and enjoy traditional Greek music and dance under the sounds of a traditional Santorinian band. The night ended with

music provided by Eleftherios Diamandis and played by the DJ and Ph. D. student, Andreas Andröulakakis.

The last day of the Symposium was dedicated to the therapeutic targets and inhibitor design with representative speakers David Deperthes and Hannu Koisten and closed with a session on the role of kallikreins as cancer biomarkers by Jeremy Squire, Manfred Schmitt and an update given by Eleftherios Diamandis. At the closing ceremony, president Litsa Talieri presented three travel awards to young participants. Two of them, sponsored by the Hellenic Anticancer Institute, were given to Nathalie Heuze-Vourc'h (France) for her oral presentation on the "Novel role of kallikrein related peptidase-6 in lung cancer development" and to Washington Sanchez (Australia) for his poster entitled "Sex hormone-binding globulin is a substrate for kallikrein-related protease-4 (KLK4) and possesses binding-affinity to pro-KLK4". The third award was sponsored by Prof. Sofia Kakari and was awarded to Nathalie Beaufort (Germany) for her oral presentation on human kallikrein-related peptidase activators. Finally, the organizing committee decided to give a 4th travel award to Katerina Oikonomopoulou (Canada) for her poster on the role of "Kallikreins as inflammatory modulators in cancer".

In addition to the outstanding talks, there were a diverse range of excellent posters presented throughout the meeting. During the meeting the participants had the opportunity to admire the permanent exhibition of special copies of the spectacular frescoes from the excavations of the pre-historic city of Akrotiri on Santorini island, depicting the civilization and the culture of the island 4000 years ago (for more information about Santorini go to <http://wikitravel.org/en/Santorini>). Finally, a number of ISK participants, on their return to Athens, were guided to the Asclepieion, at the foothill of the Acropolis by the Archaeologist Dr. Vanda Papaeuthimiou, who explained to them the use and purpose of Asclepieia in ancient Greece. Overall, a highly successful meeting that will pass the momentum to Munich in 2009!



The Proteolysis Map (PMAP)

A REASONING ENVIRONMENT FOR THE STUDY OF PROTEOLYTIC PATHWAYS

Introduction to the PMAP Website

Part of the Center on Proteolytic Pathways

PMAP, a Web-based resource to explore proteolysis in biological context

PMAP (Proteolysis Map) is an integrated Web-based bioinformatics resource developed at the Center on Proteolytic Pathways (CPP). This Center, hosted at Burnham Institute for Medical Research in La Jolla, CA, and is supported by an NIH Roadmap grant to Dr. Jeffrey W. Smith. The ultimate objective of the PMAP project is to develop a reasoning environment supporting in silico analysis, modeling, generation, and testing of hypotheses in the field of proteolysis and associated cellular pathways. Currently, PMAP has the following major components:

- **CutDB** – proteolytic events database (distributed community annotation platform) -CutDB is one of the first systematic efforts to build an easily accessible collection of proteolytic events documented for natural proteins in vivo or in vitro. The current CutDB stores 4,024 records, which includes 1,192 unique substrates. A user may query the database using multiple search criteria, such as organism, protease or substrate name, and/or known cleavage site.
- **ProfileDB** – PMAP protease specificity profiling database (data integration and analysis). ProfileDB was developed as a repository of regular and high-throughput data on protease specificity (such as phage display or peptide library analysis). This is a community resource for data integration and comparative analysis in which the user can search and submit specificity profiling data, create protease specificity models (position weight matrix, PWM) and predict substrate cleavage sites using PMAP specificity models.
- **Molecule Pages** – A collection of automated annotations that contains all proteases and inhibitors included in the latest release of Merops, as well as all protein substrates captured in the current version of CutDB. In addition to a set of basic fields (sequence, homologs, links to other resources), Molecule Pages provide access to the visualization of known 3D structures and homology-based 3D models.
- **Protease Toolbox** – an expanding collection of tools specifically designed to support proteolysis-oriented research, including: Consensus Disorder Prediction (CDP); Active Site Recognition in Proteases; Protease Mining Utility; Geometrical and Energy Consequences of Proteolytic Events (CutProt)

PMAP has more than 45,000 molecule pages for proteases and inhibitors (based on the Merops database), 1,500 molecule pages for known substrates, 4,000 proteolytic events with a major focus on regulatory proteolysis in mammalian cells, 14,000 associated 3D structures, and 38,000 structural models. PMAP is a community database providing unrestricted access to all types of integrated data and supporting community-wide annotation and curation of proteolytic events (CutDB), as well as supporting submission and analysis of protease specificity profiling data (ProfileDB). For more information visit <http://pmap.burnham.org> or e-mail: pmap_info@burnham.org.

CutDB

CutDB, the database of proteolytic events provided by PMAP. A. Searchable interface with optional authentication for data input and curation. B. Summary of proteolytic events returned for a chosen search pattern (e.g. a selected protease, MT1-MMP). C. Network of primary proteolytic events automatically generated for a selected protease. D. Details of an individual proteolytic event, a curation environment. E. The structural context of a selected proteolytic event (cut-site outlined by color).

<http://pmap.burnham.org>

ProfileDB

Welcome to ProfileDB: the PMAP protease specificity database

Search ProfileDB

- Search ProfileDB for specificity data
- View all records

Create Specificity Models and Predict Substrates

Create a PoPS model from specificity data in ProfileDB:

- Phage data
- Peptide library data

Search the PMAP proteome with specificity data from ProfileDB:

- Phage data
- Peptide library data

Predict substrate cleavage using an existing PoPS model or specificity motif(s):

- Single substrate
- Fasta file of substrates
- The PMAP proteome

Submit data to ProfileDB

Upload specificity data to ProfileDB. Data should be submitted using the appropriate form for the specificity data source (e.g. phage, peptide library, etc.). Note that you need to be a registered user to submit data.

Phage data:

- Submission form
- Documentation

Peptide library data:

- Submission form
- Documentation

Table B: Proteome-wide prediction of MMPs substrates

Substrate	Description	PoPS score
hs_09744	lysine anchor protein 1 precursor [Homo sapiens]	72.8
hs_21453	arabidopsis thaliana chitinase-like protein 11 [Arabidopsis thaliana]	72.44
hs_09694	arabidopsis thaliana chitinase-like protein 12 [Arabidopsis thaliana]	72.44
hs_14204	plasmogenic adiponectin gene-like 1 isoform 2 [Homo sapiens]	72.32
hs_01045	PSE-1-123 hypofunctional protein [Homo sapiens]	71.95
hs_01418	PSE-1-123 hypofunctional protein [Homo sapiens]	71.71
hs_09498	heat shock protein, alpha A class member 2 [Homo sapiens]	71.69
hs_13889	hypofunctional protein [Homo sapiens]	71.59
hs_09351	collipin 4 type 1 receptor protein [Homo sapiens]	71.29
hs_02410	ricin homolog protein [Homo sapiens]	71.14
hs_04446	PSE-1-123 hypofunctional protein [Homo sapiens]	71.1
hs_04843	PSE-1-123 hypofunctional protein [Homo sapiens]	71.1
hs_03027	PSE-1-123 hypofunctional protein [Homo sapiens]	71.1
hs_02147	PSE-1-123 hypofunctional protein [Homo sapiens]	71.1
hs_02222	parvovirus minute virus acid (PMAV) receptor, beta type	71.09
hs_17441	collipin-like 24 isoform 2 [Homo sapiens]	70.98
hs_04948	collipin 4 type 2 precursor [Homo sapiens]	70.98
hs_03006	collipin 4 type 2 precursor [Homo sapiens]	70.98
hs_17438	collipin-like 24 isoform 1 [Homo sapiens]	70.98
hs_16480	collipin 4 type 1 receptor [Homo sapiens]	70.98
hs_04117	collipin 4 type 1 receptor protein [Homo sapiens]	70.98
hs_06848	ricin [Homo sapiens]	70.88
hs_03603	PSE-1-123 hypofunctional protein [Homo sapiens]	70.88
hs_04844	ricin [Homo sapiens]	70.88
hs_04846	ricin [Homo sapiens]	70.88
hs_24322	Elis van Crelt [Homo sapiens]	70.88
hs_17001	collipin [Homo sapiens]	70.88
hs_02551	hnv and dengue virus glycoprotein [Homo sapiens]	70.88
hs_14043	PSE-1-123 hypofunctional protein [Homo sapiens]	70.88
hs_04942	collipin, type 2 [Homo sapiens]	70.88
hs_14160	Nirx1711-202 [Homo sapiens]	70.88
hs_16529	PSE-1-123 hypofunctional protein [Homo sapiens]	70.88

Table C: Results for search of PMAP proteome protein hs_12874 by PoPS model 'sd_high_3_fm.pops'

- Only sites in predicted disordered regions were retained
- Sites predicted to be in beta sheet or alpha helix were excluded
- Search protein localized to Extracellular. Please note: various confidence of prediction = 0

Table D: Presentation of predicted cut-sites on the sequence

```

1 11 21 31 41 51 61 71
SUBSTRATE: HGLFPLFFLALPMGLLGMVFFRFRGKGVSRDEQVAGAGVLAADFAIREFLFDVDFVDFRST
DISSORDER: -----
SECONDARY: -----

81 91 101 111 121 131 141 151
SUBSTRATE: ELVTYELFAEFPALQTHFFCRSESSILFPTTMRRLPOTSRDQSTLEALATGQAKRIFLELDFRDFRSE
DISSORDER: -----
SECONDARY: -----

161 171 181 191 201 211 221 231
SUBSTRATE: SAEVKQDQFFSFRVRFVQVYVFAKRSSEARITGAEQTDGVLGSRVLEALLSRVLELENKSLFSLA
DISSORDER: -----
SECONDARY: -----

241 251 261 271 281 291 301 311
SUBSTRATE: GEEDGRRSSSQVYGVQEEVVAEKLRFATIESARTELAQGDGAFAPVADAKAQDQVTEGKQHEKDRIDRERES
DISSORDER: -----
SECONDARY: -----
    
```

ProfileDB, proteome-wide substrate search in a few clicks: A. ProfileDB interface; B. proteome-wide prediction of MMPs substrates; C. result for individual protein; D. presentation of predicted cut-sites on the sequence.

Molecule Pages

Protease Toolbox

External Data

- PDB PROTEIN DATA BANK
- PubMed
- MEROPS The Peptidase Database
- Human Protein Reference Database
- GenCards
- OMIM Online Mendelian Inheritance in Man
- Ensembl Human GeneView

NAME: gi2493285|sp|P55957|BID_HUMAN BH3 interacting domain death agonist (BID)

LENGTH: 195

CONSENSUS: NDCEVNRGSSLRdecelnlvfglqgednefrreldalghelplvlgpewydeqtdDNRRSHRLRTEADSESG

COLLS: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

REH46S: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

HOTLOOPS: NDCEVNRGSSLRdecelnlvfglqgednefrreldalghelplvlgpewydeqtdDNRRSHRLRTEADSESG

DISSORDER: NDCEVNRGSSLRdecelnlvfglqgednefrreldalghelplvlgpewydeqtdDNRRSHRLRTEADSESG

GLOBPIPE: mdceVNRGSSLRdecelnlvfglqgednefrreldalghelplvlgpewydeqtdDNRRSHRLRTEADSESG

CONSENSUS: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

COLLS: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

REH46S: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

HOTLOOPS: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

DISSORDER: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

GLOBPIPE: diltmrarhrlagvqsdmrsippglvnglaqlrNTSRSESRrdtatelellqyppdwekvmlvllakv

Active site residues: CYS25 HIS159

Active site residues: [Diagram showing active site residues]

Pockets predicted by PASS algorithm: [Diagram showing predicted pockets]

Molecule pages were created for ~47,000 proteases, protease inhibitors, and substrates. A. Protease classification; B. an entry molecule page for Thrombin; C. external data and links used in the PMAP; D. interactive molecule graphics for PDB structures and models.

Results of Tools application in PMAP: A. consensus disorder prediction for BID, BH3 interacting domain death antagonist; B. BID structure; C. protease active site recognition in whole PDB or single protein (pocket prediction by PASS algorithm—see the right side of the screen shoot—is added to ensure that active site residues are in a cavity)

The next update for PMAP is scheduled for Spring 2008. We plan to implement a new interface, advanced search capabilities, molecule pages for the entire human proteome, a pathways exploration tool, an update for all component databases, and customized news feeds. The two key aspects of the future development are: (i) visualization and analysis of proteolytic pathways and networks; and (ii) tight integration of all PMAP components and databases within a single portal. Content by: Alexey Eroshkin, Andrei Osterman, Burnham Institute for Medical Research

The PMAP development team (past and current) includes Yoshinobu Igarashi, Piotr Cieplak, Ying Zhang, Emily Heureux, Kutbuddin Doctor, Kosi Gramatikoff, Alexey Eroshkin, Andrei Osterman, Adam Godzik, Jeffrey Smith (all from Burnham Institute for Medical Research) and Sarah Boyd (Monash University, Australia).

IMPORTANT PROTEASE PAPERS I

Research Publications

Dean RA, Butler GS, Hamma-Kourbali Y, Delbé J, Brigstock DR, Courty J and Overall CM.

Identification of Candidate Angiogenic Factors Processed by MMP-2 in Cell Based Proteomic Screens: Disruption of VEGF / HARP (Pleiotrophin) and VEGF / CTGF Angiogenic Inhibitory Complexes by MMP-2 Proteolysis.

Molecular Cellular Biology 2007 27, 8454-8465

Büth H, Buttigieg PL, Ostafe R, Rehders M, Dannemann SR, Schaschke N, Stark HJ, Boukamp P and Brix K.

Cathepsin B is essential for regeneration of scratch-wounded normal human epidermal keratinocytes.

Eur. J. Cell Biol. 2007 86, 747-761.

Ong PC, McGowan S, Pearce MC, Irving JA, Kan WT, Grigoryev SA, Turk B, Silverman GA, Brix K, Bottomley SP, Whisstock JC and Pike PN.

DNA accelerates the inhibition of human cathepsin V by serpins.

J. Biol. Chem. 2007 282, 36980-36986.

Reisener A, Eickelberg O, Wille A, Heimburg A, Reinhold A, Sloane BF, Welte T, Bühling F.

Increased carcinogenic potential of myeloid tumor cells induced by aberrant TGF-beta1-signaling and upregulation of cathepsin B.

Biol Chem. 2007 388, 639-50.

Hayama M, Okumura Y, Takahashi E, Shimabukuro A, Tamura M, Takeda N, Kubo T, Kido H.

Identification and analysis of the promoter region of the type II transmembrane serine protease polyserase-1 and its transcript variants.

Biol Chem. 2007 388, 853-8.

Decock J, Long JR, Laxton RC, Shu XO, Hodgkinson C, Hendrickx W, Pearce EG, Gao YT, Pereira AC, Paridaens R, Zheng W, Ye S.

Association of matrix metalloproteinase-8 gene variation with breast cancer prognosis.

Cancer Res. 2007 67, 10214-21.

Hook G, Hook VY and Kindy M.

Cysteine protease inhibitors reduce brain beta-amyloid and beta-secretase activity in vivo and are potential Alzheimer's disease therapeutics.

Biol Chem. 2007 388, 979-83.

Shin M, Kadowaki T, Iwata J, Kawakubo T, Yamaguchi N, Takii R, Tsukuba T and Yamamoto K.

Association of cathepsin E with tumor growth arrest through angiogenesis inhibition and enhanced immune responses.

Biol Chem. 2007 388, 1173-81.

Chee J, Singh J, Naran A, Misso NL, Thompson PJ and Bhoola KD.

Novel expression of kallikreins, kallikrein-related peptidases and kinin receptors in human pleural mesothelioma.

Biol Chem 2007 388, 1235-1242.

Saska I, Gillon A, Hatsugai N, Dietzgen R, Hara-Nishimura I, Anderson M, and Craik DJ.

An Asparaginyl Endopeptidase Mediates in Vivo Protein Backbone Cyclization.

J. Biol. Chem. 2007 282, 29721 – 29728

Erdmann S, Ricken A, Merkwitz C, Struman I, Castino R, Hummitzsch K, Gaunitz F, Isidoro C, Martial J, Spänzel-Borowski K.

The expression of prolactin and its cathepsin D-mediated cleavage in the bovine corpus luteum vary with the estrous cycle.

Am J Physiol Endocrinol Metab. 2007 293, E1365-77.

Follo C, Castino R, Nicotra G, Trincheri NF, Isidoro C.

Folding, activity and targeting of mutated human cathepsin D that cannot be processed into the double-chain form.

Int J Biochem Cell Biol. 2007 39, 638-49.

Cosgrove S, Rogers L, Hewage CM, and Malthouse JPG.

An NMR study of the inhibition of pepsin by glyoxal inhibitors: Mechanism of tetrahedral intermediate stabilization by the aspartyl proteases.

Biochemistry 2007 46, 11205-15.

Spink E, Hewage CM and Malthouse JPG.

Determination of the structure of tetrahedral transition state analogues bound at the active site of chymotrypsin using 18O and 2H isotope shifts in the 13C-NMR spectra of glyoxal inhibitors.

Biochemistry, 2007 46, 12868-12874.

Barrett AJ and Rawlings ND.

'Species' of peptidases.

Biol. Chem. 2007 388:1151-1157.

Rawlings ND, Morton FR, Kok CY, Kong J and Barrett AJ.

MEROPS: the peptidase database.

Nucleic Acids Research 2007 Epub November 8.

IMPORTANT PROTEASE PAPERS II

Rawlings ND and Morton FR.

The MEROPS batch BLAST: A tool to detect peptidases and their non-peptidase homologues in a genome.

Biochimie 2007 Epub 29 September.

Sato T, Diehl TS, Narayanan S, Funamoto S, Ihara Y, De Strooper B, Steiner H, Haass C, Wolfe MS.

Active γ -secretase complexes contain only one of each component.

J. Biol. Chem. 2007 282. 33985-33993.

Kotsyfakis M, Karim S, Andersen JF, Mather TN, Ribeiro JM.

Selective cysteine protease inhibition contributes to blood-feeding success of the tick *Ixodes scapularis*.

J Biol Chem. 2007 282, 29256-63.

Lazic A, Goetz DH, Nomura AM, Marnett AB, Craik CS.

Substrate modulation of enzyme activity in the herpesvirus protease family.

J Mol Biol. 2007 373, 913-23.

Darragh MR, Bhatt AS, Craik CS.

MT-SP1 proteolysis and regulation of cell-microenvironment interactions.

Front Biosci. 2008 13, 528-39.

Hostetter DR, Loeb CR, Chu F, Craik CS.

Hip is a pro-survival substrate of granzyme B.

J Biol Chem. 2007 282, 27865-74.

Goetz DH, Choe Y, Hansell E, Chen YT, McDowell M, Jonsson CB, Roush WR, McKerrow J, Craik CS.

Substrate specificity profiling and identification of a new class of inhibitor for the major protease of the SARS coronavirus.

Biochemistry. 2007 46, 8744-52.

Ljunggren A, Redzynia I, Alvarez-Fernandez M, Abrahamson M, Mort JS, Krupa JC, Jaskolski M, Bujacz G.

Crystal structure of the parasite protease inhibitor chagasin in complex with a host target cysteine protease.

J Mol Biol 2007 371, 137-53.

Hawinkels LJ, Van Rossenberg SM, Jonge-Muller ES, Mole-naar TJ, Appeldoorn CC, Van Berkel TJ, Sier CF and Biessen EA.

Efficient degradation-aided selection of protease inhibitors by phage display.

Biochem.Biophys.Res.Commun. 2007 364, 549-555.

Bylander JE, Bertenshaw GP, Matters GL, Hubbard SJ, Bond JS.

Human and mouse homo-oligomeric meprin A metalloendopeptidase: Substrate and inhibitor specificities.

Biol Chem 2007 388, 1163-1172.

Hawinkels LJ, Verspaget HW, van den BM, Hanemaaijer R and Sier CF.

Determination of matrilysin activity in gastrointestinal neoplasia.

Eur.J Clin Invest 2007 37, 598-599.

Kubben FJ, Sier CF, Schram MT, Witte AM, Veenendaal RA, Van Duijn W, Verheijen JH, Hanemaaijer R, Lamers CB and Verspaget HW.

Eradication of *Helicobacter pylori* infection favourably affects altered gastric mucosal MMP-9 levels.

Helicobacter 2007 12, 498-504.

Kubben FJ, Sier CF, Hawinkels LJ, Tschesche H, Van Duijn W, Zuidwijk K, Van der Reijden JJ, Hanemaaijer R, Griffioen G, Lamers CB and Verspaget HW.

Clinical evidence for a protective role of lipocalin-2 against MMP-9 autodegradation and the impact for gastric cancer.

Eur. J Cancer 2007 43, 1869-1876.

Meijer MJ, Mieremet-Ooms MA, van der Zon AM, Van Duijn W, Van Hogeand RA, Sier CF, Hommes DW, Lamers CB, and Verspaget HW.

Increased mucosal matrix metalloproteinase-1, -2, -3 and -9 activity in patients with inflammatory bowel disease and the relation with Crohn's disease phenotype.

Dig. Liver Dis. 2007 39: 733-739.

Sier CF, Hawinkels LJ, Zijlmans HJ, Zuidwijk K, Jonge-Muller ES, Ferreira V, Hanemaaijer R, Mulder-Stapel AA, Kenter GG, Verspaget HW and Gorter A.

Endothelium specific matrilysin (MMP-7) expression in human cancers.

Matrix Biol. 2007[Epubahead of print].

CONTINUED NEXT PAGE ►

IMPORTANT PROTEASE PAPERS III

Research Publications

Iju W, Valencia CA, Pang H, Ke Y, Gao W, Dong B, Liu R.

Proteome-wide identification of family member-specific natural substrate repertoire of caspases.

Proc Natl Acad Sci U S A. 2007 104, 14294-9.

Blum G, von Degenfeld G, Merchant MJ, Blau HM, Bogoy M.

Noninvasive optical imaging of cysteine protease activity using fluorescently quenched activity-based probes.

Nat Chem Biol. 2007 3, 668-77.

Drag M, Mikolajczyk J, Krishnakumar IM, Huang Z, Salvesen GS.

Activity profiling of human deSUMOylating enzymes (SENPs) with synthetic substrates suggests an unexpected specificity of two newly characterized members of the family.

Biochem J. 2008 409, 461-9.

Timmer JC, Enoksson M, Wildfang E, Zhu W, Igarashi Y, Denault JB, Ma Y, Dummitt B, Chang YH, Mast AE, Eroshkin A, Smith JW, Tao WA, Salvesen GS.

Profiling constitutive proteolytic events in vivo.

Biochem J. 2007 407, 41-8.

Kakehashi H, Nishioku T, Tsukuba T, Kadowaki T and Yamamoto K.

Differential regulation of the nature and functions of dendritic cells and macrophages by cathepsin E.

J. Immunol. 2007 179, 5728-5737.

Shin M, Kadowaki T, Iwata J, Kawakubo T, Yamaguchi N, Takii R, Tsukuba T and Yamamoto K.

Association of cathepsin E with tumor growth arrest through angiogenesis inhibition and enhanced immune responses.

Biol. Chem. 2007 388, 1173-1181.

Kawakubo T, Okamoto K, Iwata J, Shin M, Okamoto Y, Yasukochi A, Nakayama KI, Kadowaki T, Tsukuba T and Yamamoto K.

Cathepsin E prevents tumor growth and metastasis by catalyzing the proteolytic release of soluble TRAIL from tumor cell surface.

Cancer Res. 2007 67, 10869-10878.

Goulet B, Sansregret L, Leduy L, Bogoy M, Weber E, Chauhan SS, Nepveu A.

Increased expression and activity of nuclear cathepsin L in cancer cells suggests a novel mechanism of cell transformation.

Mol Cancer Res. 2007 5, 899-907.

REVIEWS

Overall CM and Butler GS.

Protease Yoga: Extreme Flexibility of a Matrix Metalloproteinase.

Structure 2007 15, 1159-1161.

Selkoe DJ and Wolfe MS.

Presenilin: running with scissors in the membrane.

Cell 2007 131, 215-221.

Borissenko L and Groll M.

Diversity of proteasomal missions: fine tuning of the immune response.

Biol Chem. 2007 388, 947-55.

Victor BC and Sloane BF.

Cysteine cathepsin non-inhibitory binding partners: modulating intracellular trafficking and function.

Biol Chem. 2007 388, 1131-40.

Zavasnik-Bergant T and Turk B.

Cysteine proteases: destruction ability versus immunomodulation capacity in immune cells.

Biol Chem. 2007 388, 1141-9.

Keller UA, Doucet A and Overall CM.

Protease research in the era of systems biology.

Biol Chem. 2007 388, 1159-62.

Pampalakis G, Sotiropoulou G.

Tissue kallikrein proteolytic cascade pathways in normal physiology and cancer.

Biochim Biophys Acta 2007 1776, 22-31.

Kadowaki T, Takii R, Yamatake K, Kawakubo T, Tsukuba T and Yamamoto K.

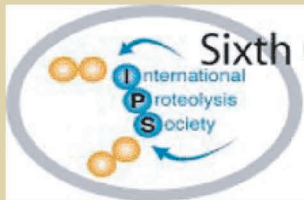
A role for gingipains in cellular responses and bacterial survival in Porphyromonas gingivalis-infected cells.

Frontiers in Biosci. 2007 12, 4800-4809.

Ponder EL, Bogoy M.

Ubiquitin-like modifiers and their deconjugating enzymes in medically important parasitic protozoa.

Eukaryot Cell. 2007 6, 1943-52.



Sixth General Meeting of the International Proteolysis Society

Surfers Paradise Marriott Resort & Spa

26th - 30th October 2009



Visit

www.ips2009.org

for all details and to register interest

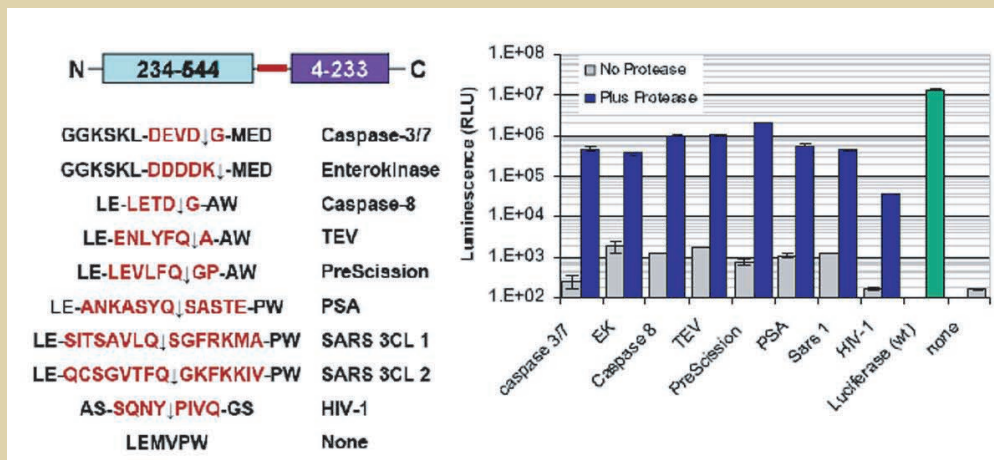


New Product Offerings



New GloSensor Protease Substrates for Luminescence Assays

The GloSensor Protease Assay is a novel system to detect protease activity using bioluminescence. The result of the system protocol is a circularly permuted form of firefly luciferase with a peptide containing a cloned protease site of interest expressed in a cell-free lysate. The cognate protease is used to interrogate the cloned sequence; cleavage of the active recognition sequence leads to the generation of an active luciferase fusion protein that emits light correlated to activity of the protease. Mutant luciferases are easily generated by in vitro transcription/translation and used directly in the protease assay.



Examples of GloSensor Substrates. Substrates are available for multiple proteases that make use of different specific cleavage sequences in the circularly permuted firefly luciferase. Results with these substrates are shown.

For additional information on this new technology, please contact:

Neal Cosby, PhD, Strategic Marketing Manager neal.cosby@promega.com

INTERNATIONAL PROTEOLYSIS SOCIETY

QUICKCUTS

THANKS AGAIN TO OUR CORPORATE SPONSORS

Primary Sponsors



Full Sponsors



Sponsors

