

IN THIS ISSUE:

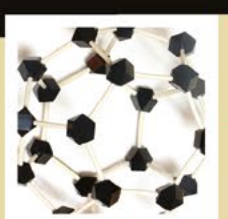
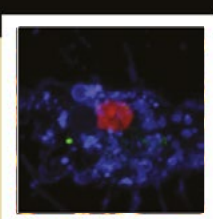
- Membership Renewal Reminder
- 9th General Meeting of the IPS
- Protease Papers
- Meeting Reports
- Meeting Announcements

JUNE 2015



INTERNATIONAL PROTEOLYSIS SOCIETY QUICKCUTS

Editors:
Sheena McGowan (Monash University)
Aimee Shen (University of Vermont)



THE PREMIER RESOURCE
FOR ALL YOUR IMPORTANT PROTEASE QUESTIONS

A Message From the President

Our biennial meeting for the IPS (www.ips2015.org) is approaching quickly! This promises to be another excellent meeting covering a diverse array of protease research. The 9th General Meeting of the IPS will be October 4-8 in the Australasia part of the world as we travel to Penang, Malaysia. Judith Clements and her team are organizing the meeting and have put together a fantastic group of international speakers! Earlybird registration ends June 26, so act soon!

The International Advisory Committee will be recommending additional speakers from submitted abstracts – please take time to submit your abstracts before the June 26 deadline. There will also be special training workshops as part of the special early career forum for young scientists on October 3-4. These are run by experts in the field and cover 4 areas: a) practical protease kinetics b) imaging and advanced imaging techniques c) degradomics and mass spectrometry and d) genetically modified mice. We will be inducting a new Honorary Lifetime Member as well as selecting new officers and choosing our next meeting site, which moves to the Americas.

I want to thank all of you who have renewed your membership or joined so far – for all others, please take a moment to join/renew now - remember that your dues are tax deductible and support our mission - they primarily go to support travel grants to students. www.protease.org/membership

Please send suggestions or feedback to any of the IPS officers or councilors about the society or the newsletter by contacting us. We want to hear from you! This is your society - the more active you are - the more successful it will be!

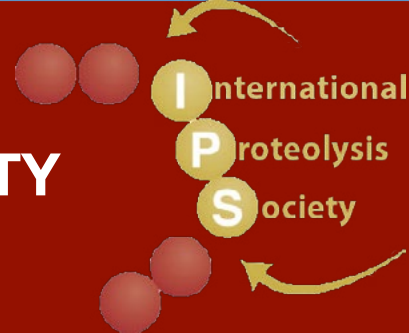
Many thanks for your support of the IPS!

Bob Lazarus, IPS President

Email: lazarus.bob@gene.com

THE 9TH GENERAL MEETING OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

4 – 8 October, 2015

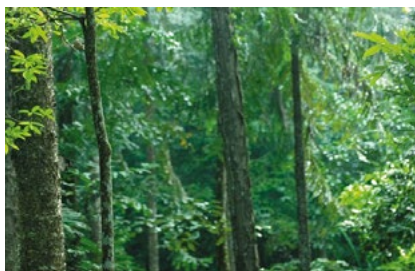


WHAT A VENUE!

What better place to hold the 'oceania' IPS meeting than smack bang in the middle of Oceania? The 9th General Meeting of the IPS will therefore be held in **Penang, Malaysia**.



The conference will be held at the Golden Sands Conference Centre at Batu Feringgi Beach in Penang. The conference centre has daily activities that include beach & water volleyball, an Eco centre and turtle care project, pitch & putt, guided jungle walks, recreational gym, tennis, golf and, of course, pools!



Locally (walking distance), Batu Feringgi offers beach-side bars, para-sailing, night markets and food bazaars. For those of you looking for something a bit more up-market for dinner, the Spice Market restaurant is just next door.

Further afield (20 mins by car) is George Town, a UNESCO World Heritage Site. Transport is easy with taxi's or drivers readily available from the conference centre.

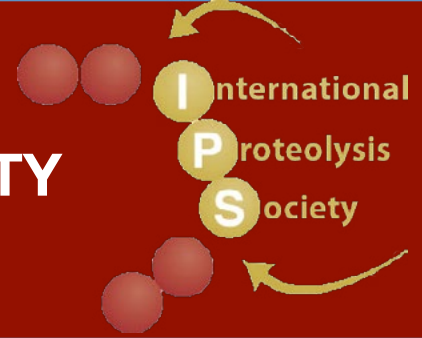


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THE 9TH GENERAL MEETING OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

4 – 8 October, 2015



“Systems Biology of Proteolytic Networks”

PROGRAM THEMES

Proteolytic networks outside the cell
Proteolytic networks inside the cell
Degradomics & proteomics
Proteolysis and cell signalling
Developmental mechanisms & proteolytic processing
Proteases in disease & in pathogens
Drug design & therapeutic approaches

PROGRAM HIGHLIGHTS

- 13 scientific sessions inc
- Invited speakers
- Abstract selected orals
- 3 poster sessions
- Free afternoons
- Conference dinner
- Early Career Forum

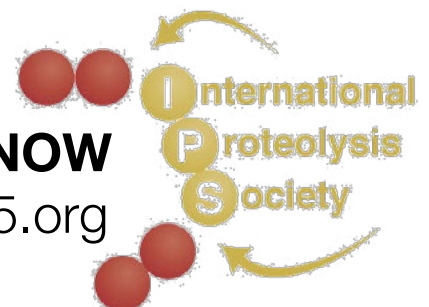
EARLY CAREER FORUM 3-4 October

IPS 2015 will hold a dedicated meeting for our members in training and early career protease biologists. This will feature the IPS training workshops, rapid fire oral presentations and professional development talks.

See Pg 6-8 of QuickCuts for more details
or www.ips2015.org/ecr-forum/

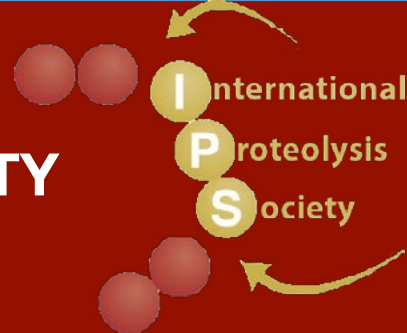
**EARLY BIRD
REGISTRATION
CLOSES**
26 JUNE, 2015

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THE 9TH GENERAL MEETING OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

4 – 8 October, 2015



INVITED SPEAKERS (to date)



Chris Overall
University of
British Columbia
Canada



Matthew Bogyo
Stanford University
USA



Joanne Lemieux
University of Alberta
Canada



Jennie Lill
Genentech
USA



John Hooper
Mater Medical
Research Institute
Australia



Charles Craik
UCSF
USA



Grant Blouse
Novo Nordisk
Denmark



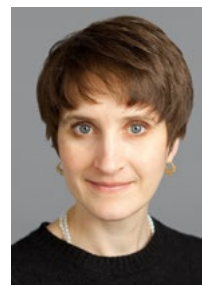
Bonnie Sloane
Wayne State University
USA



Karin List
Wayne State
University
USA



R Manjunatha Kini
National University
Singapore
Singapore



Ingrid Wertz
Genentech
USA



David Granville
UBC James Hogg
Research Centre
Canada



Irit Sagi
Weizmann Institute
Israel



Taisuke Tomita
University of Tokyo
Japan



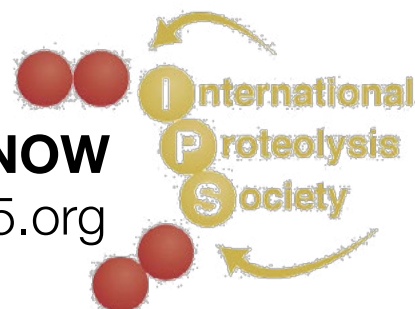
Charaf Benarafa
University of Bern
Switzerland



Christoph Becker-Pauly
University of Kiel
Germany

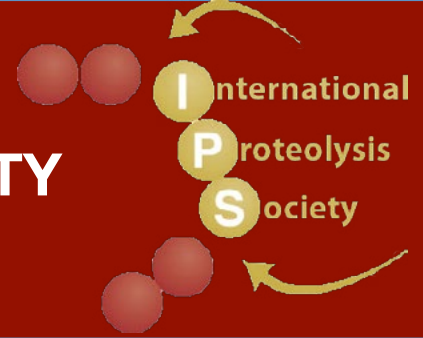
**ABSTRACTS
CLOSE
26 JUNE, 2015**

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THE 9TH GENERAL MEETING OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

4 – 8 October, 2015



IPS 2015 Organising Committee

Judith Clements (Chair), Australia
Sheena McGowan, Australia
Rob Pike, Australia
James Whisstock, Australia

International Advisory Committee

Phil Bird, Australia
Galia Blum, Israel
Matt Bogyo, USA
Klaudia Brix, Germany
Charles Craik, USA
Marcin Drag, Poland
Matthew Freeman, UK
Hans Fritz, Germany
Mark Gorrell, Australia
Jim Huntington, UK
Johanna Joyce, USA
Bob Lazarus, USA
Agnes Noel, Belgium
Christoph Peters, Germany
Jan Potempa, Poland
Thomas Reinheckel, Germany
Guy Salvesson, USA
Nabil G Seidah, Canada
Aimee Shen, USA
Bonnie Sloane, USA
Christian Sommerhoff, Germany
Hiroyuki Sorimachi, Japan
Henning Stennicke, Denmark
Ed Sturrock, South Africa
Boris Turk, Slovenia
Sin Urban, UK
Maria Luiza Vilela Olivia, Brazil

BRINGING THE FAMILY?

The conference venue has on-site

Infant services (cots & strollers)
Cool Zone Kids Club
Kids Passport
Adventure Zone (playground)
Waterslides & children pools
Baby-sitting & child-care available

Nearby (20 mins car)

Penang butterfly farm
Escape Theme Park
Teluk ahang Fishing Village



VISAS & TRAVEL

Please check your travel arrangements carefully!
The closest airport is Penang. Transfers to/from
the conference centre are easy. For more info,
see [www.ips2015.org/venue-and-location/
getting-there/](http://www.ips2015.org/venue-and-location/getting-there/)

WANT MORE INFORMATION?

Check out www.ips2015.org

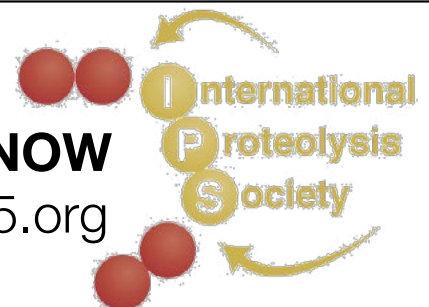
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James Whisstock | james.whisstock@monash.edu



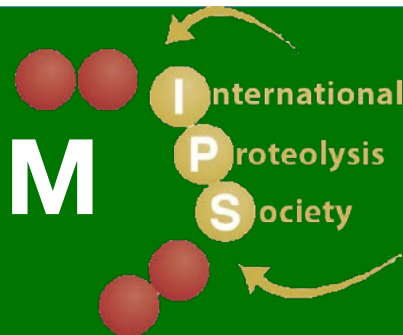
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EARLY CAREER FORUM

3 – 4 October, 2015



Want to present
your research?
IPS 2015!!

Need a break
from the lab?
YOU need to come to Penang!!

ARE YOU A GRAD STUDENT OR EARLY CAREER RESEARCHER?

Want new friends &
collaborators?
3-4 October, Penang

Need to actually get outside &
remind yourself what sunshine is?
Come to Penang!!

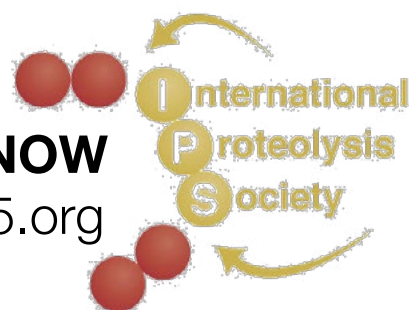
Not sure if your future is in
Industry or Academia?
**IPS 2015 ECR Forum
Penang!!**

Need more convincing?

www.ips2015.org/ecr-forum/

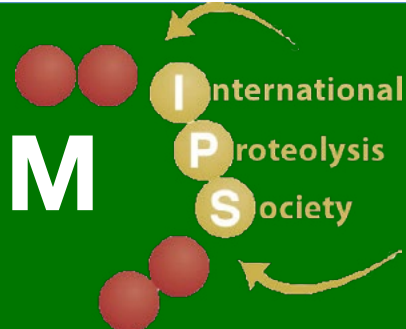
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EARLY CAREER FORUM

3 – 4 October, 2015

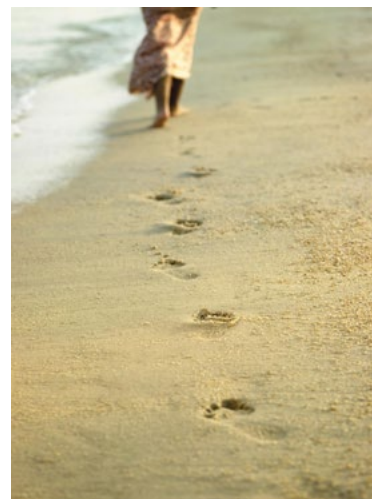


The IPS 2015 committee is keen for our younger scientists to present their fantastic research and contribute to the protease community. Therefore our dedicated EARLY CAREER FORUM will be held immediately before IPS 2015 at the same venue. On offer will be training workshops, a keynote address from a leading industry scientist and oral presentations. We aim to make this a fun and relaxed environment where you can make new friends and colleagues, learn some new skills and tell us about all your hard work!

TRAINING WORKSHOPS

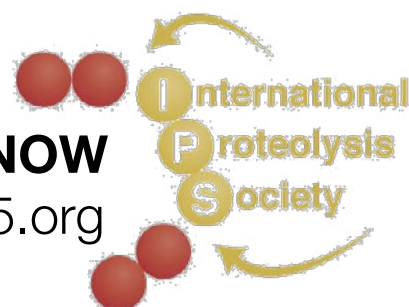
- Practical Protease Kinetics I & II
- Imaging I & II
- Degradomics
- Genetically modified mice

The training workshops will be 'dry' sessions and take place at the conference centre. They will have a practical focus with real problems & data analysis. The aim of the workshops is to provide practical skills that can be used in your future research careers.



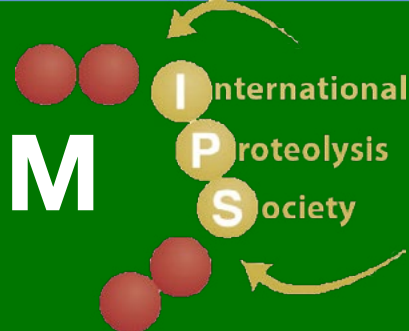
A proud sponsor of the Early Career Forum

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EARLY CAREER FORUM

3 – 4 October, 2015



ORAL PRESENTATIONS AVAILABLE

We are keen to hear all about your research! So there will be an opportunity to present your research to the Forum in our rapid fire scientific session!

Reflections on my path and research adventures along the way

BOB LAZARUS

Principal Scientist, IPS President
Early Discovery Biochemistry
Genentech Inc



Bob has spent the last 30 years working in industry and maintaining extensive links and collaborators within academia. He epitomizes the aims of the IPS to maintain strong connections between academia and industry. Have you ever wondered about a research career in industry? Come along and hear what Bob has to say in his keynote address at the IPS 2015 Early Career Forum.

Bob's talk will be followed by a Q & A session between attendees and our senior tutors on site.

EARLY BIRD REGISTRATION CLOSES

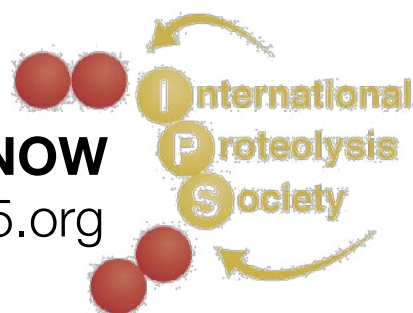
26 JUNE, 2015

Delegates will need to arrive in Penang on Friday 2 October as the program will start on the morning of the 3rd.

You can find IPS on



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Meeting Reports:

32nd Winter School, Tiers (Feb 25 - Mar 1, 2105)

Following a long-standing tradition, 120 scientists from all continents gathered in Tiers (South Tyrol) with the spectacular surroundings of the Italian Alps. Reflecting the Winter School character, talks are mostly given by young scientists (PhD students and postdocs) and organized in topical sessions, covering pathogens, immunity, cancer, neurodegeneration, metalloproteases, substrates & enzyme mechanisms, inhibition, and technology. Each session was introduced by two senior scientists in a press release style, often with very funny choreographic sketches.



The Thursday night session with the InhibiTiers Allstar Band served as an illustrative example for what enzyme catalysis is all about: Co-localization and molecular crowding, overcoming activation barriers, assisted by (liquid) co-factors. The hiking tours on Saturday afternoon were guided by Hans Fritz, the founder of the Winter school, and Thomas Reinheckel, but there were also perfect conditions for skiing and sightseeing in Bozen including Ötzi the Iceman. The unsurpassed highlight of the meeting was the unique Fritzi award ceremony on Saturday evening ("everybody can win an Oscar, but only Tiers participants can win a Fritzi") which was moderated by the masters of ceremonies Guy Salvesen, Ed Sturrock and James Whisstock. Beyond words. Oxford turned out to be the most successful participating lab this year, earning both the Best Talk Award (Pernille Søgaard) and the Paparazzo Award (Yoshi Itoh). You don't want to miss the meeting next year, www.uni-salzburg.at/tiers.

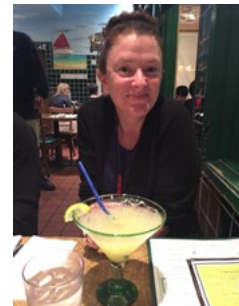
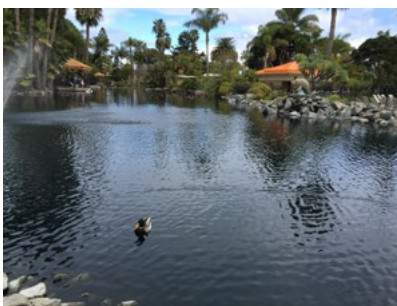
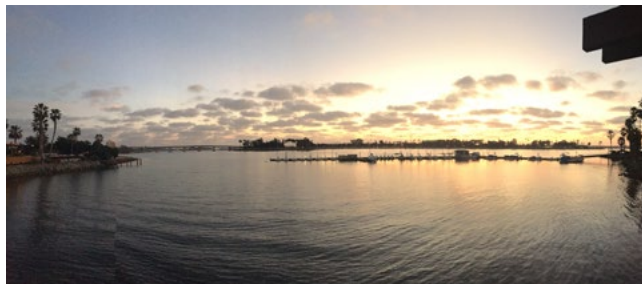


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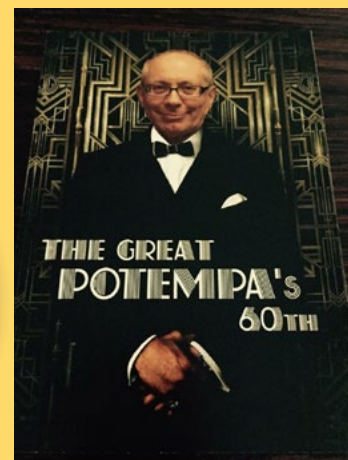
Meeting Reports:

GTCBio Meeting - Protease Inhibitors in Drug Discovery, San Diego (26-27 Feb, 2015)

The inaugural GTCbio meeting for protease inhibitors in drug discovery was held in late February. Held at the Paradise Point Resort & Spa in San Diego, the meeting attracted speakers from both academia and industry. The meeting had a large number of local attendees from the wealth of institutes and biotech located on the west coast as well as international speakers. Speakers discussed their latest research covering protease inhibitors under development for the treatment of cancer, infectious diseases, alzheimer's and cardiovascular disease. The opening day shared plenary keynote speakers from concurrent meetings and the evening poster session provided a social opportunity to meet other enzymologists from the joint meetings. For more info on the GTCBio meeting, check out <https://www.gtcbio.com/conferences/protease-inhibitors-drug-discovery-overview>.



We heard a rumour of a very special birthday.....



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IMPORTANT PROTEASE PAPERS I

Research Publications

AGONIST & INHIBITORS

Drinkwater N, Bamert, RS, Kannan-Sivaraman, K, Paiardini, A & McGowan S.

X-ray crystal structure of the orally available aminopeptidase inhibitors, Tosedostat, bound to the antimalarial drug targets PfA-M1 and PfA-M17

Proteins. 2015. 83:789-795

Paiardini, A, Bamert, RS, Kannan Sivaraman, K, Drinkwater, N, Mistry, S, Scammells PJ & McGowan, S.

Screening the Medicines for Malaria Venture "Malaria Box" against the Plasmodium falciparum aminopeptidases, M1, M17 and M18"

PLoS ONE. 2015. 10:e0115859

Conroy, T, Guo, JT, Elias, N, Cergol, KM, Gut, J, Legac, J, Khatoon, L, Yang, L, McGowan, S, Rosenthal, PJ, Hunt, NH & Payne, RJ.

Synthesis of Gallinamide A Analogues as Potent Falcipain Inhibitors and Antimalarials.

J. Med. Chem. 2014. 57: 10557-10563

Dubiella C, Cui H, Gersch M, Brouwer AJ, Sieber SA, Krüger A, Liskamp RM, Groll M.

Selective inhibition of the immunoproteasome by ligand-induced crosslinking of the active site.

Angew Chem Int Ed Engl. 2014. 53: 11969-73.

Gersch M, Famulla K, Dahmen M, Göbl C, Malik I, Richter K, Korotkov VS, Sass P, Rübnsamen-Schaeff H, Madl T, Brötz-Oesterhelt H, Sieber SA.

AAA+ chaperones and acyldepsipeptides activate the ClpP protease via conformational control

Nat Commun. 2015. 6: 6320.

Ono Y, Shindo M, Doi N, Kitamura F, Gregorio CC, and Sorimachi H.

The N- and C-terminal autolytic fragments of CAPN3/p94/calpain-3 restore proteolytic activity by intermolecular complementation.

Proc Natl Acad Sci USA. 2014. 111: E5527-5536.

PROTEASE PROBES

Serim S, Baer P, Verhelst SH

Mixed Alkyl Aryl Phosphonate Esters as Quenched Fluorescent Activity-Based Probes for Serine Proteases.

Org Biomol Chem 2015. 13: 2293-2299.

Eitelhuber AC, Vosyka O, Nagel D, Bogner M, Lenze D, Lammens K, Schlauderer F, Hlahla D, Hopfner KP, Lenz G, Hummel M, Verhelst SH, Krappmann D.

Activity-based probes for detection of active MALT1 paracaspase in immune cells and lymphomas.

Chem Biol 2015. 22: 129-138.

Garenne T, Saidi A, Gilmore BF, Niemiec E, Roy V, Agrofoglio LA, Kasabova M, Lecaille F, and_Lalmanach G.

Active site labeling of cysteine cathepsins by a straightforward diazomethylketone probe derived from the N-terminus of human cystatin C

Biochem Biophys Res Comm 2015. 460:250-254.

Bikker FJ, Koop G, Leusink NB, Nazmi K, Kaman WE, Brand HS and Veerman EC.

Tailor made plasmin substrates as potential diagnostic tool to test for mastitis.

Vet Res Commun. 2014. 38:271-277

PROTEASES IN PATHOGENESIS

Arya, T, Ravikumar Reddi, R, Kishor, C, Ganji, RJ, Bhukya, S, Gumpena, R, McGowan, S, Drag, M & Addlagatta, A.

Identification of the Molecular Basis of Inhibitor Selectivity between the Human and Streptococcal Type I Methionine Aminopeptidases

J Med Chem. 2015.58:2350-2357

O'Donoghue AJ, Knudsen GM, Beekman C, Perry JA, Johnson AD, DeRisi JL, Craik CS, Bennett RJ.

Destructin-1 is a collagen-degrading endopeptidase secreted by Pseudogymnoascus destructans, the causative agent of white-nose syndrome.

Proc Natl Acad Sci U S A. 2015 In press

SUBSTRATE PROFILING

Szabó A, Salameh MA, Ludwig M, Radisky ES, and Sahin-Tóth M.

Tyrosine sulfation of human trypsin steers S2' subsite selectivity towards basic amino acids.

PLoS One. 2014. 9: e102063.

Pendlebury D, Wang R, Henin RD, Hockla A, Soares AS, Madden BJ, Kazanov MD, and Radisky ES.

Sequence and conformational specificity in substrate recognition: several human Kunitz protease inhibitor domains are specific substrates of mesotrypsin.

J Biol Chem. 2014. 289: 32783-32797.

IMPORTANT PROTEASE PAPERS II

Baker RP and Urban S.

Cytosolic extensions directly regulate a rhomboid protease by modulating substrate gating.

Nature. 2015. 523 (In press).

Urban S and Moin SM.

A subset of membrane-altering agents and g-secretase modulators provoke nonsubstrate cleavage by rhomboid proteases.

Cell Reports. 2014. 8: 1241-1247.

PROTEOMICS & SYSTEMS BIOLOGY

Gersch M, Hackl MW, Dubiella C, Dobrinevski A, Groll M, Sieber SA.

A mass spectrometry platform for a streamlined investigation of proteasome integrity, posttranslational modifications, and inhibitor binding.

Chem Biol. 2015. 22: 404-11.

Buch F, Kaman WE, Bikker FJ, Yilamujiang A and Mithöfer A.

Nepenthesin protease activity indicates digestive fluid dynamics in carnivorous nepenthes plants.

PLoS One. 2015. 10: e0118853.

Fortelny N, Yang S, Pavlidis P, Lange PF, and Overall CM.

Proteome TopFIND 3.0 with TopFINDER and PathFINDER: database and analysis tools for the association of protein termini to pre- and post-translational events.

Nucleic Acids Res. 2015. 43:D290-297

Barré O, Dufour A, Eckhard U, Kappelhoff R, Béliveau F, Leduc R, and Overall CM.

Cleavage specificity analysis of six type II transmembrane serine proteases (TTSPs) using PICS with proteome-derived peptide libraries.

PLoS One. 2014. 9(9):e105984.

Huesgen PF, Lange PF, Rogers LD, Solis N, Eckhard U, Kleifeld O, Goulas T, Gomis-Rüth FX, and Overall CM.

LysargiNase mirrors trypsin for protein C-terminal and methylation-site identification.

Nat Methods. 2015. 12(1):55-8.

Kern U, Wischnewski V, Biniossek ML, Schilling O, & Reinheckel T.

Lysosomal protein turnover contributes to the acquisition of TGFβ-1 induced invasive properties of mammary cancer cells.

Mol Cancer. 2015. 14: 39 ff.

STRUCTURE

Pathak M, Wilmann P, Awford J, Li C, Hamad BK, Fischer PM, Dreveny I, Dekker LV, Emsley J.

Coagulation factor XII protease domain crystal structure.

J Thromb Haemost. 2015. 13(4):580-91.

Harper S, Gratton HE, Cornaciu I, Oberer M, Scott DJ, Emsley J, Dreveny I.

Structure and catalytic regulatory function of ubiquitin specific protease 11 N-terminal and ubiquitin-like domains.

Biochemistry. 2014 ;53(18):2966-78.

Skala W, Utzschneider DT, Magdolen V, Debela M, Guo SH, Craik CS, Brandstetter H, Goettig P.

Structure-Function Analyses of Human Kallikrein-related Peptidase 2 Establish the 99-Loop as Master Regulator of Activity.

J Biol Chem. 2014. 289:34267-83.

CATHEPSINS

Tamhane T, Arampatzidou M, Gerganova V, Tacke M, Illukkumbura R, Dauth S, Schaschke N, Peters C, Reinheckel T, and Brix K

The activity and localization patterns of cathepsins B and X in cells of the mouse gastrointestinal tract differ along its length.

Biol. Chem. 2014. 395: 1201-1219. COVER PAGE

Jílková A, Horn M, Rezáčová P, Marešová L, Fajtová P, Brynda J, Vondrášek J, McKerrow JH, Caffrey CR, Mareš M.

Activation route of the *Schistosoma mansoni* cathepsin B1 drug target: structural map with a glycosaminoglycan switch.

Structure. 2014 Dec 2;22(12):1786-98.

Andrault PM, Samsonov SA, Weber G, Coquet L, Nazmi K, Bolscher JGM, Lalmanach AC, Jouenne T, Brömme D, Pisabarro MT, Lalmanach G, and Lecaille F.

The antimicrobial peptide LL-37 is both a substrate of cathepsins S and K and a selective inhibitor of cathepsin L

Biochemistry. 2015. 54 : 2785–2798.

Sharma V, Panwar P, O'Donoghue AJ, Cui H, Guido RV, Craik CS, Brömme D.

Structural requirements for the collagenase and elastase activity of cathepsin K and its selective inhibition by an exosite inhibitor.

Biochem J. 2015. 465:163-73.

CONTINUED NEXT PAGE

IMPORTANT PROTEASE PAPERS III

Tholen M, Wolanski J, Stolze B, Chiabudini M, Gajda M, Bronsert P, Stickeler E, Rospert S, and Reinheckel T.

Stress-resistant Translation of Cathepsin L mRNA in Breast Cancer Progression.

J Biol Chem. 2015. (In Press)

LEGUMAIN

Dall E, Fegg JC, Briza P, Brandstetter H.

Structure and Mechanism of an Aspartimide-Dependent Peptide Ligase in Human Legumain.

Angew Chem Int Edit. 2015. 54:2917-21.

Haugen MH, Boye K, Nesland JM, Pettersen SJ, Egeland EV, Tamhane T, Brix K, Maeldandsmo GM, Flatmark K

High expression of the cysteine proteinase legumain in colorectal cancer - Implications for therapeutic targeting.

Eur. J. Cancer. 2015. 51: 9-17.

Smith R, Solberg R, Jacobsen LL, Voreland AL, Rustan R, Thoresen GH, Johansen HT.

Simvastatin inhibits glucose uptake and legumain activity in human myotubes.

PLOS ONE. 2014. 9(1):e85721.

Smith R, Åstrand AO, Nguyen LM, Elvestrand T, Hagelin G, Solberg R, Johansen HT, Rongved P.

Synthesis of a novel legumain-cleavable colchicine prodrug with cell-specific toxicity.

Bio & Med Chem. 2014. 22(13):3309-15.

Solberg R, Smith R, Almlöf M, Tewolde E, Nilsen H, Johansen HT.

Legumain expression, activity and secretion are increased during monocyte-to-macrophage differentiation and inhibited by atorvastatin.

Biol Chem. 2015. 396(1):71-80.

ADAMS

Dong F, Eibach M, Bartsch JW, Dolga AM, Schlomann U, Conrad C, Schieber S, Schilling O, Biniossek ML, Culmsee C, Strik H, Koller G, Carl B, and Nimsky C.

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