NOV. 2014

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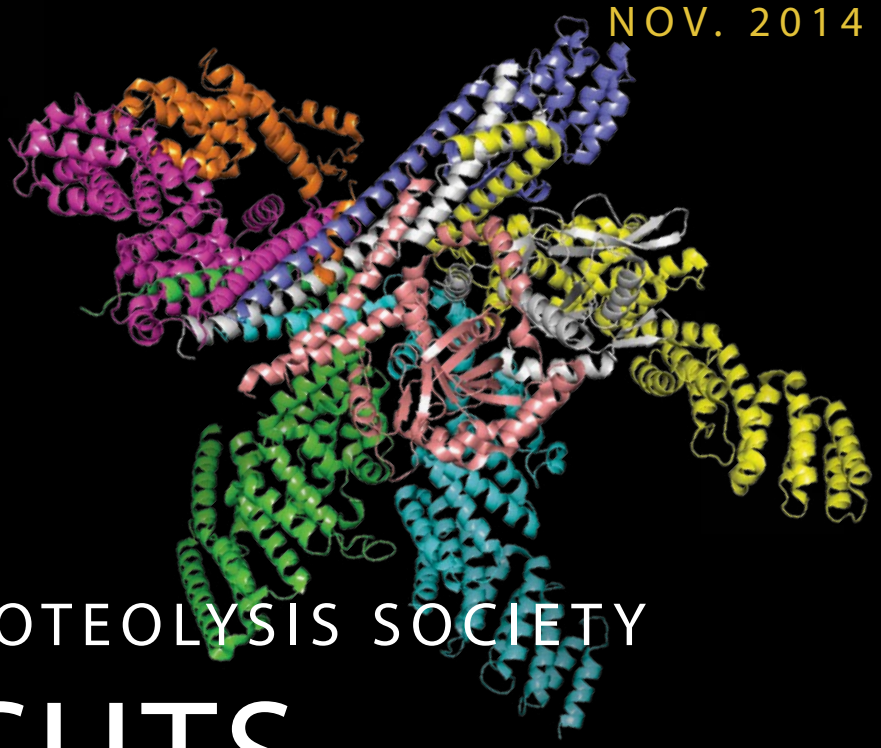
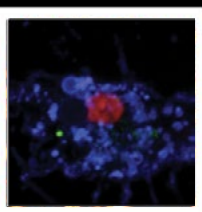


INTERNATIONAL PROTEOLYSIS SOCIETY

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

Proteases always have company: a friendly cofactor that cuddles up and nudges (or catapults!) them into action, a nasty inhibitor that keeps them from wildly reeking havoc in their playground, or perhaps it's quite friendly and is just looking out to keep everything safe, a frightened substrate getting ready to head down that dark one way street, never to return to its original identity – or is it an enlightened substrate volunteering to transform itself into a beautiful product, going on to an exciting new journey? Hard to say.

My point is perspective. Good to have one and better to have several! As we study our cherished proteases, keep some perspective and awareness of not only about what they are doing, but also what they are *not* doing. Whom are they talking to and whom *aren't* they talking to – protease social media is undoubtedly very active and complex! Speaking of social media, the IPS is now on LinkedIn (https://www.linkedin.com/groups/International-Proteolysis-Society-7411541/about).

In addition to our regular features, in this issue we highlight the first international protease meeting held in South America. I had the great pleasure of attending this meeting in São Carlos, Brazil, along with several other IPS councilors and members.

We are also inviting nominations for honorary Lifetime Members of the IPS to be presented at IPS2015. Candidates should have an extensive record of accomplishments in the protease field and be IPS members. Please send names and a short case for support to Henning Stennicke (ipssecretary@gmail.com). A list of our Lifetime Members can be found at http://protease.org/LifetimeMembers.html.

Please remember to renew your membership for the Jan 2015-Dec 2016 period. Most of our membership dues go to support members-in-training travel awards for our general meeting. We have implemented new membership software , which should make the process effortless and more transparent Want a tax break this year – send in your dues in 2014!! We are a nonprofit organization.

Judith Clements and her team are ramping up for IPS2015, which will be held in Penang, Malaysia from the October 4-8, 2015. This will be a great meeting and will include training workshops for young scientists.

As always, please send suggestions to any of us on the council – we want to hear from you! Thanks for your support of the IPS!!

Bob Lazarus, IPS President Email: lazarus.bob@gene.com

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IMPORTANT PROTEASE PAPERS I

Research Publications

AGONISTS & INHIBITORS

Gable JE, Lee GM, Jaishankar P, Hearn BR, Waddling CA, Renslo AR, Craik CS.

Broad-spectrum allosteric inhibition of herpesvirus proteases.

Biochemistry. 2014. 53:4648-60.

Mistry N, Drinkwater N, Ruggeri C, Kannan Sivaraman K, Loganathan S, Fletcher S, Drag M, Paiardini, A, Avery VM, Scammells PJ, McGowan S.

A Two-pronged Attack: Dual Inhibition of M1 and M17 Metalloaminopeptidases by a Novel Series of Hydroxamic acid-based Inhibitors.

J Med Chem. 2014. epub ahead of print.

Kannan Sivaraman K, Paiardini A, Sienczyk M, Ruggeri C, Oellig CA, Dalton JP, Scammells PJ, Drag M, and McGowan S.

Synthesis and Structure-Activity Relationships of Phosphonic Arginine Mimetics as Inhibitors of the M1 and M17 Aminopeptidases from *Plasmodium falciparum*.

J Med Chem. 2013. 56: 5213-5217.

Landgraf KE, Steffek M, Quan C, Tom J, Yu C, Santell L, Maun HR, Eigenbrot C, and Lazarus RA.

An Allosteric Switch for pro-HGF/Met Signaling Using Zymogen Activator Peptides.

Nat Chem Biol. 2014. 10:567-573.

Wolf EV, Zeißler A, Vosyka O, Zeiler E, Sieber S, Verhelst SHL.

A new class of rhomboid protease inhibitors discovered by activity-based fluorescence polarization.

PLoS One 2013. 8: e72307.

Cleary J, Doherty W, Evans P, Malthouse JP.

Hemiacetal stabilization in a chymotrypsin inhibitor complex and the reactivity of the hydroxyl group of the catalytic serine residue of chymotrypsin.

Biochim Biophys Acta. 2014.1844:1119-27.

PROTEASES PROBES

Verdoes M, Oresic Bender K, Segal E, van der Linden WA, Syed S, Withana NP, Sanman LE, Bogyo M.

Improved quenched fluorescent probe for imaging of cysteine cathepsin activity.

J Am Chem Soc. 2013. 135:14726-14730.

Tajon CA, Seo D, Asmussen J, Shah N, Jun YW, Craik CS.

Sensitive and Selective Plasmon Ruler Nanosensors for Monitoring the Apoptotic Drug Response in Leukemia.

ACS Nano. 2014. Sep 3. epub ahead of print.

Bachovchin DA, Koblan LW, Wu W, Liu Y, Li Y, Zhao P, Woznica I, Shu Y, Lai JH, Poplawski SE, Kiritsy CP, Healey SE, DiMare M, Sanford DG, Munford RS, Bachovchin, WW, Golub TR.

A high-throughput, multiplexed assay for superfamily-wide profiling of enzyme activity.

Nat Chem Biol. 2014. 10:656-663.

Haedke UR, Frommel SC, Hansen F, Hahne H, Kuster B, Bogyo M, Verhelst SHL.

Phosphoramidates as novel activity-based probes for serine proteases.

ChemBioChem. 2014. 15: 1106-1110.

PROTEASES IN PATHOGENESIS

Li H, van der Linden WA, Verdoes M, Florea BI, McAllister FE, Govindaswamy K, Elias JE, Bhanot P, Overkleeft HS, Bogyo M.

Assessing subunit dependency of the Plasmodium proteasome using small molecule inhibitors and active site probes.

ACS Chem Biol. 2014. 9:1869-1876.

Loveday EK, Diederich S, Pasick J, Jean F.

Human microRNA-24 modulates highly pathogenic avian-origin H5N1 influenza A virus infection in A549 cells by targeting secretory pathway furin.

J Gen Virol. 2014. (in press).

Cruz R, Huesgen P, Riley SP, Wlodawer A, Faro C, Overall CM, Martinez JJ, Simões I.

RC1339/APRc from *Rickettsia conorii* Is a Novel Aspartic Protease with Properties of Retropepsin-Like Enzymes.

PLoS Pathog. 2014. 10:e1004324.

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IMPORTANT PROTEASE PAPERS II

Research Publications

Gras S, Byzia A, Gilbert FB, McGowan S, Drag M, Silvestre A, Niepceron A, Lecaille F, Lalmanach G, Brossier F.

Aminopeptidase N1 (Et-ApN1), a M1 metalloprotease of the apicomplexan parasite *Eimeria tenella* participates in parasite development

Eukaryot. Cell. 2014. 13: 884-895.

SUBSTRATE PROFILING

Poreba M, Mihelic M, Krai P, Rajkovic J, Krezel A, Pawelczak M, Klemba M, Turk D, Turk B, Latajka R, Drag M.

Unnatural amino acids increase activity and specificity of synthetic substrates for human and malarial cathepsin C.

Amino Acids. 2014. 46:931-943.

Byzia A, Haeggström JZ, Salvesen GS, Drag M.

A remarkable activity of human leukotriene A4 hydrolase (LTA4H) toward unnatural amino acids.

Amino Acids. 2014. 46:1313-1320.

Kasperkiewicz P, Poreba M, Snipas SJ, Parker H, Winterbourn CC, Salvesen GS, Drag M.

Design of ultrasensitive probes for human neutrophil elastase through hybrid combinatorial substrate library profiling.

Proc Natl Acad Sci U S A. 2014. 111:2518-2523.

Poreba M, Kasperkiewicz P, Snipas SJ, Fasci D, Salvesen GS, Drag M.

Unnatural amino acids increase sensitivity and provide for the design of highly selective caspase substrates.

Cell Death Differ. 2014. 21:1482-1492.

O'Donoghue AJ, Jin Y, Knudsen GM, Perera NC, Jenne DE, Murphy JE, Craik CS, Hermiston TW.

Global substrate profiling of proteases in human neutrophil extracellular traps reveals consensus motif predominantly contributed by elastase.

PLoS One. 2013. 8:e75141.

PROTEOMICS & SYSTEMS BIOLOGY

Schlage P, Egli FE, Nanni P, Wang LW, Kizhakkedathu JN, Apte SS, auf dem Keller U.

Time-resolved analysis of the matrix metalloproteinase 10 substrate degradome.

Mol Cell Proteomics. 2014. 13: 580-593.

Huesgen PF, Alami M, Lange PF, Foster LJ, Schröder WP, Overall CM, Green BR.

Proteomic amino-termini profiling reveals targeting information for protein import into complex plastids.

PLoS One. 2013 8:e74483.

Fahlman RP, Chen W, Overall CM.

Absolute proteomic quantification of the activity state of proteases and proteolytic cleavages using proteolytic signature peptides and isobaric tags.

J Proteomics. 2014. 100:79-91.

Lange PF, Huesgen PF, Nguyen K, Overall CM.

Annotating N termini for the human proteome project: N termini and Nα-acetylation status differentiate stable cleaved protein species from degradation remnants in the human erythrocyte proteome.

J Proteome Res. 2014. 13:2028-2044.

Fortelny N, Cox JH, Kappelhoff R, Starr AE, Lange PF, Pavlidis P, Overall CM.

Network analyses reveal pervasive functional regulation between proteases in the human protease web.

PLoS Biol. 2014. 12:e1001869.

STRUCTURE

Lingaraju GM, Bunker RD, Cavadini S, Hess D, Hassiepen U, Renatus M, Fischer ES, Thomä NH.

Crystal structure of the human COP9 signalosome.

Nature. 2014 12:161-165.

CATHEPSINS

Liszewski MK, Kolev M, Le Friec G, Leung M, Bertram PG, Fara AF, Subias M, Pickering MC, Drouet C, Meri S, Arstila TP, Pekkarinen PT, Ma M, Cope A, Reinheckel T, Rodriguez de Cordoba S, Afzali B, Atkinson JP, Kemper C.

Intracellular complement activation sustains T cell homeostasis and mediates effector differentiation.

Immunity. 2013. 39:1143-1157.

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IMPORTANT PROTEASE PAPERS III

Research Publications

Tholen M, Hillebrand LE, Tholen S, Sedelmeier O, Arnold SA, Reinheckel T.

Out-of-frame start codons prevent translation of truncated nucleo-cytosolic cathepsin L in vivo.

Nat Commun. 2014. 5:4931 doi: 4910.1038/ncomms5931.

Muller S, Faulhaber A, Sieber C, Pfeifer D, Hochberg T, Gansz M, Deshmukh SD, Dauth S, Brix K, Saftig P, Peters C, Henneke P, Reinheckel T.

The endolysosomal cysteine cathepsins L and K are involved in macrophage-mediated clearance of Staphylococcus aureus and the concomitant cytokine induction.

FASEB J. 2014. 28: 162-175.

Bengsch F, Buck A, Gunther SC, Seiz JR, Tacke M, Pfeifer D, von Elverfeldt D, Sevenich L, Hillebrand LE, Kern U, Sameni M, Peters C, Sloane BF, Reinheckel T.

Cell type-dependent pathogenic functions of overexpressed human cathepsin B in murine breast cancer progression.

Oncogene 2014. 33: 4474-4484.

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

Hu HY, Vats D, Vizovisek M, Kramer L, Germanier C, Wendt KU, Rudin M, Turk B*, Plettenburg O*, Schultz C*

In vivo imaging of mouse tumors by a lipidated cathepsin S substrate.

Angew Chem Intl Ed. 2014. 53:7669-7673.

Novinec M, Korenc M, Caflisch A, Ranganathan R, Lenarcic B, Baici A.

A novel allosteric mechanism in the cysteine peptidase cathepsin K discovered by computational methods.

Nat Commun. 2014. 5:3287. doi: 10.1038/ncomms4287.

Kasabova M, Joulin-Giet A, Lecaille F, Gilmore BF, Marchand-Adam S, Saidi A, Lalmanach G.

Regulation of TGF β1-driven differentiation of human lung fibroblasts: emerging roles of cathepsin B and cystatin C

J Biol Chem. 2014. 289:16239-16251.

Zhao P, Lieu T, Barlow N, Metcalf M, Veldhuis N, Jensen D, Kocan M, Sostegni S, Haerteis S, Baraznenok V, Henderson I, Lindstrom E, Guerrero-Alba R, Valdez-Morales E, Liedtke W, McIntyre P, Vanner SJ, Korbmacher C, Bunnett NW.

Cathepsin S causes inflammatory pain via biased agonism of PAR2 and TRPV4.

J Biol Chem. 2014. In press.

Floyel T, Brorsson C, Nielsen LB, Miani M, Bang-Berthelsen CH, Friedrichsen M, Overgaard AJ, Berchtold LA, Wiberg A, Poulsen P, Hansen L, Rosinger S, Boehm BO, Ram R, Nguyen Q, Mehta M, Morahan G, Concannon P, Bergholdt R, Nielsen JH, Reinheckel T, von Herrath M, Vaag A, Eizirik DL, Mortensen HB, Storling J, and Pociot F.

CTSH regulates beta-cell function and disease progression in newly diagnosed type 1 diabetes patients.

Proc Natl Acad Sci U S A. 2014. 111: 10305-10310.

Mikhaylov G, Klimpel D, Schaschke N, Mikac U, Vizovisek M, Fonovic M, Turk V, Turk B*, Vasiljeva O.*

Selective targeting of tumor and stromal cells by a nanocarrier system displaying lipidated cathepsin B inhibitor.

Angew Chem Int Ed Engl. 2014. 53:10077-10881.

LEGUMAIN

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

Simvastatin inhibits glucose uptake and legumain activity in human myotubes.

PLOS ONE. 2014. 9:e85721.

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. 2014. epub ahead of print.

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IMPORTANT PROTEASE PAPERS IV

Research Publications

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

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

Bioorg & Med Chem. 2014. 22:3309-3315.

ECE-1 and ACE

Whyteside AR, Turner AJ, Lambert DW.

Endothelin-converting enzyme-1 (ECE-1) is post-transcriptionally regulated by alternative polyadenylation.

PLoS One 2014. 9:e83260.

Douglas RG, Sharma RK, Masuyer G, Lubbe L, Zamora I, Acharya KR, Chibale K, Sturrock ED.

Fragment-based design for the development of N-domain-selective angiotensin-1-converting enzyme inhibitors.

Clin Sci. 2014. 126:305-313.

Kido-Nakahara M, Buddenkotte J, Kempkes C, Ikoma A, Cevikbas F, Akiyama T, Nunes F, Seeliger S, Hasdemir B, Mess C, Buhl T, Sulk M, Muller FU, Metze D, Bunnett NW, Bhargava A, Carstens E, Furue M, Steinhoff M.

Neural peptidase endothelin-converting enzyme 1 regulates endothelin 1-induced pruritus.

J Clin Invest. 2014. 124:2683-2695.

Kramer GJ, Mohd A, Schwager SL, Masuyer G, Acharya KR, Sturrock ED, Bachmann BO.

Interkingdom pharmacology of angiotensin-I converting enzyme inhibitor phosphonates produced by actinomycetes.

ACS Med Chem Lett. 2014. 5:346-351.

Clarke NE, Belyaev ND, Lambert DW, and Turner AJ.

Epigenetic regulation of angiotensin-converting enzyme 2 (ACE2) by SIRT1 under conditions of cell energy stress.

Clin Sci. 2014. 126:507-516.

Yates CJ, Masuyer G, Schwager SLU, Mohd A, Sturrock ED, Acharya KR.

Molecular and Thermodynamic Mechanisms of the Chloride Dependent Human Angiotensin-I Converting Enzyme (ACE).

J Biol Chem. 2014. 289:1798-1814.

Jensen DD, Halls ML, Murphy JE, Canals M, Cattaruzza F, Poole DP, Lieu T, Koon HW, Pothoulakis C, Bunnett NW.

Endothelin-converting Enzyme 1 and beta-Arrestins Exert Spatiotemporal Control of Substance P-induced Inflammatory Signals.

J Biol Chem. 2014. 289:20283-20294.

Patel VB, Clarke N, Wang Z, Fan D, Parajuli N, Basu R, Putko B, Kassiri Z, Turner AJ, Oudit GY.

Angiotensin II induced proteolytic cleavage of myocardial ACE2 is mediated by TACE/ADAM-17: a positive feedback mechanism in the RAS.

J Mol Cell Cardiol. 2014. 66:167-176.

MATRIX METALLOPROTEASES

Marchant DJ, Bellac CL, Moraes TJ, Wadsworth SJ, Dufour A, Butler GS, Bilawchuk LM, Hendry RG, Robertson AG, Cheung CT, Ng J, Ang L, Luo Z, Heilbron K, Norris MJ, Duan W, Bucyk T, Karpov A, Devel L, Georgiadis D, Hegele RG, Luo H, Granville DJ, Dive V, McManus BM, Overall CM.

A new transcriptional role for matrix metalloproteinase-12 in antiviral immunity

Nat Med. 2014. 20:493-502.

Mehner C, Hockla A, Miller E, Ran S, Radisky DC, Radisky ES.

Tumor cell-produced matrix metalloproteinase 9 (MMP-9) drives malignant progression and metastasis of basal-like triple negative breast cancer.

Oncotarget. 2014. 5:2736-2749.

Batra J, Soares AS, Mehner C, Radisky ES.

Matrix metalloproteinase-10/TIMP-2 structure and analyses define conserved core interactions and diverse exosite interactions in MMP/TIMP complexes.

PLoS One. 2013. 8:e75836.

Marino G, Huesgen PF, Eckhard U, Overall CM, Schröder WP, Funk C.

Family-wide characterization of matrix metalloproteinases from *Arabidopsis thaliana* reveals their distinct proteolytic activity and cleavage site specificity

Biochem J. 2014. 457:335-346.

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IMPORTANT PROTEASE PAPERS V

Research Publications

Proteases and Pathologies

Kebede MA, Oler AT, Gregg T, Balloon AJ, Johnson A, Mitok K, Rabaglia M, Schueler K, Stapleton D, Thorstenson C, Wrighton L, Floyd BJ, Richards O, Raines S, Eliceiri K, Seidah NG, Rhodes C, Keller MP, Coon JL, Audhya A, Attie AD.

SORCS1 is necessary for normal insulin secretory granule biogenesis in metabolically stressed β-cells.

J Clin Invest. 2014. epub ahead of print

Kasabova M, Joulin-Giet A, Lecaille F, Saidi A, Marchand-Adam S, Lalmanach G.

Human cystatin C: a new biomarker of idiopathic pulmonary fibrosis?

Proteomics Clin. Appl. 2014. 8:447-453.

Kerridge C, Belyaev ND, Nalivaeva NN, Turner AJ.

The Aβ-clearance protein transthyretin, like neprilysin, is epigenetically regulated by the amyloid precursor protein intracellular domain.

J Neurochem. 2014. 130: 419-431.

Kauder SE, Santell L, Mai E, Wright LY, Luis E, N'Diaye EN, Lutman J, Ratti N, Sa SM, Maun HR, Stefanich E, Gonzalez LC, Graham RR, Diehl L, Faubion WA Jr, Keir ME, Young J, Chaudhuri A, Lazarus RA, and Egen JG.

Functional Consequences of the Macrophage Stimulating Protein 689C Inflammatory Bowel Disease Risk Allele.

PLoS One. 2013. 8:e83958.

Happy Birthday to the 1964 club!!

A fun fact we discovered at the Gordon Research Conference this year is the existence of an exclusive 1964 club!

Our esteemed protease colleagues including (from left to right) Rob Pike, F. Xavier Gomis-Rűth, Jim Huntington, Boris Turk and Hans Brandstetter were all born in 1964 and therefore are all turning 50 this year!

Happy birthday to all! 1964 was a good year for protease biology!

CONTINUED NEXT PAGE

Protease Reviews

Research Publications

Drinkwater N & McGowan S.

From crystal to compound: structure-based antimalarial drug discovery.

Biochem J 2014. 461: 349-369

Douglas RG, Ehlers MR, Sturrock ED.

The anti-fibrotic peptide Ac-SDKP: opportunities for ACE inhibitor design.

Clin Exp Pharmacol Physiol. 2013. 40:535- 41.

Wang W, Liu Y, Lazarus RA.

Allosteric inhibition of BACE1 by an exosite-binding antibody.

Curr Opin Struct Biol. 2013. 23:797-805.

Sanman LE & Bogyo M.

Activity-based profiling of proteases.

Annu Rev Biochem. 2014. 83:249-73.

Tajon C, Jun YW, Craik CS.

Single-molecule sensing of caspase activation in live cells via plasmon coupling nanotechnology.

Methods Enzymol. 2014. 544:271-97.

McGowan S.

Working in concert: the metalloaminopeptidases from *Plasmodium falciparum*.

Curr Opin Struct Biol. 2013. 23: 828-835.

Sojka D, Franta Z, Caffrey CR, Mares M, and Kopacek P.

New insights into the machinery of blood digestion by ticks.

Trends Parasitol. 2013. 29:276-285.

Kessler E & Safrin M

Elastinolytic and proteolytic enzymes.

Pseudomonas. Methods and protocols (Filloux A and Ramos J-L eds). Methods Mol Biol. 2014. 1149:135-169.

Lalmanach G, Saidi A, Marchand-Adam S, Lecaille F, Kasabova M.

Cysteine cathepsins and cystatins: from ancillary tasks to prominent status in lung diseases.

Biol. Chem. 2014. doi: 10.1515/hsz-2014-0210.

Hamson EJ, Keane FM, Tholen S, Schilling O, and Gorrell MD.

Understanding Fibroblast Activation Protein (FAP): substrates, activities, expression and targeting for cancer therapy.

PROTEOMICS – Clinical Applications. 2014. 8:454-463.

Dong Y, Harrington BS, Adams MN, Wortmann A, Stephenson SA, Lisle J, Herington A, Hooper JD, Clements JA.

Activation of membrane bound proteins and receptor systems: a link between tissue kallikrein and the KLK-related peptidases

Biol Chem. 2014. 1:977-90.

Seidah NG, Awan Z, Chrétien M, and Mbikay M.

PCSK9: a key modulator of cardiovascular health.

Circ. Res. 2014. 4114:1022-1036.

Salameh MA, Radisky ES.

Biochemical and structural insights into mesotrypsin: an unusual human trypsin.

Int J Biochem Mol Biol. 2013. 4:129-39.

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Now in Press in *Biological Chemistry*

A Message from Boris Turk, Executive Editor.

Biological Chemistry, the oldest existing journal in the field starting back in 1877, is proud to publish a collection of excellent papers from the proteolysis field in a Highlight issue dedicated to the IPS 2013 meeting in Cape Town. This issue is a reflection of the tight connection between the journal and IPS, a link established many years ago with the help of Hans Fritz, Executive Editor of the journal at that time. As a result, a Highlight issue linked to an IPS meeting has been published regularly since IPS2001 in Freising, Germany. Since proteolysis has always been one of the highlight topics of the journal, I encourage you to submit your works to Biological Chemistry.

- (For more info see: http://www.degruyter.com/view/j/bchm).

HIGHLIGHT: THE PROTEASE WEB

Sturrock, E. and Sommerhoff, C.P.

A major strength of the biennial IPS meeting is its systematic and thematic coverage of proteases and their networks. The proteases featured in this issue function not only as protein hydrolysing enzymes, but also as elegant signalling molecules making them highly attractive drug targets. The reviews and research articles in this Highlight issue span the role of proteases in cardiovascular, gastrointestinal and communicable diseases, and cancer; proteases in fertilization and immunity, inflammation and apoptosis; and the development of inhibitors for therapeutic intervention.

The upcoming IPS2015 meeting will be organized in Penang, Malaysia, Oct. 4-8, 2015 by Judith Clements &James Whisstock from Australia. It will be preceded by 6th International Symposium on Kallikreins & Kallikrein-Related Peptidases in Brisbane, Australia (Sept. 29-Oct. 2, 2015). Visit www.protease.org for more information .

Masuyer G, Yates CJ, Sturrock ED, & Acharya KR. Angiotensin-I converting enzyme (ACE): structure, biological roles, and molecular basis for chloride ion dependence.

Naicker P & Sayed Y. Non-B HIV-1 subtypes in sub-Saharan Africa: impact of subtype on protease inhibitor efficacy.

Davidovich P, Kearney CJ, & Martin SJ. Inflammatory outcomes of apoptosis, necrosis and necroptosis.

Bernstein KE, Gonzalez-Villalobos RA, Giani JF, Shah K, Bernstein E, Janjulia T, Koronyo Y, Shi PD, Koronyo-Hamaoui M, Fuchs S, Shen XZ. Angiotensin-converting enzyme overexpression in myelocytes enhances the immune response.

Steinberger J, Skern T. The leader proteinase of foot-and-mouth disease virus: structure-function relationships in a proteolytic virulence factor.

Ehlers MR. Immune-modulating effects of alpha-1 antitrypsin.

Stöcker W, Karmilin K, Hildebrand A, Westphal H, Yiallouros I, Weiskirchen R, Dietzel E, Floehr J, Jahnen-Dechent W. Mammalian gamete fusion depends on the inhibition of ovastacin by fetuin-B.

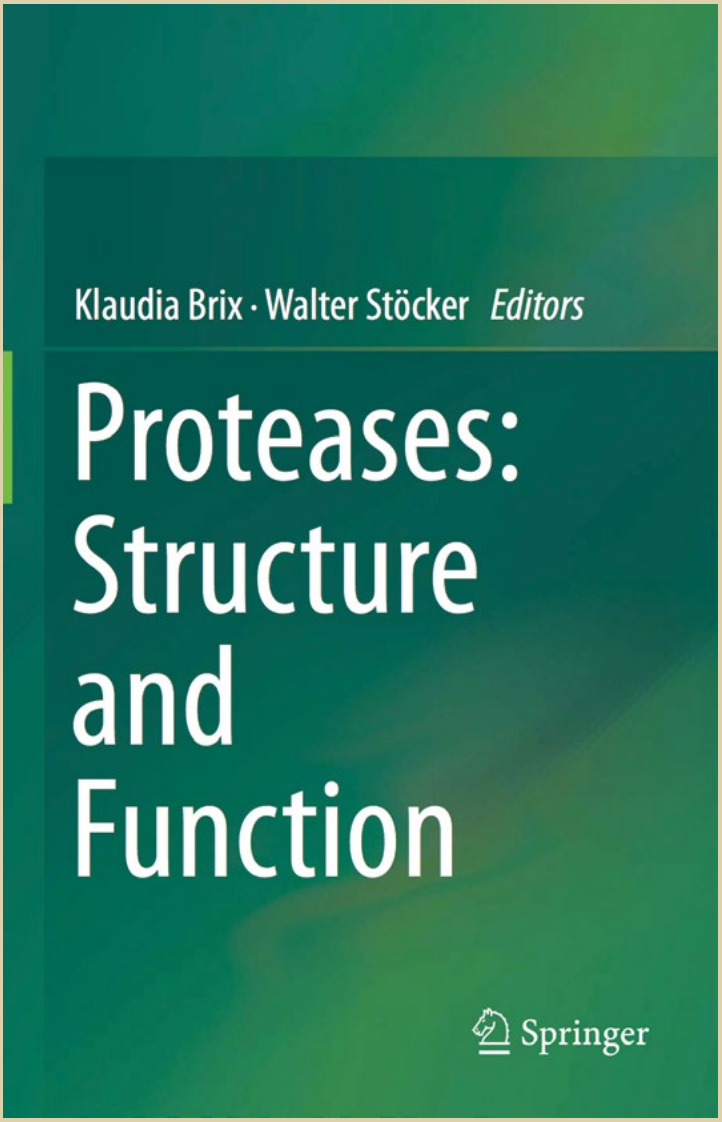
Tamhane T, Arampatzidou M, Gerganova V, Tacke M, Illukkumbura R, Dauth S, Schaschke N, Peters C, Reinheckel T, Brix K. The activity and localization patterns of cathepsins B and X in cells of the mouse gastrointestinal tract differ along its length.

Bruney L, Conley KC, Moss NM, Liu Y, Stack MS. Membrane-type I matrix metalloproteinase-dependent ectodomain shedding of mucin16/ CA-125 on ovarian cancer cells modulates adhesion and invasion of peritoneal mesothelium.

Pomowski A, Ustok FI, Huntington JA. Homology model of human prothrombinase based on the crystal structure of Pseutarin C.

Flütsch A, Schroeder T, Barandun J, Ackermann R, Bühlmann M, Grütter MG. Specific targeting of human caspases using designed ankyrin repeat proteins.

Ahmad J, Bird PI, Kaiserman D. Analysis of the evolution of granule associated serine proteases of immune defence (GASPIDs) suggests a revised nomenclature.



1. Protease Families, Evolution, & Mechanism of Action
Neil D. Rawlings

2. Kinetics of the Interaction of Peptidases with Substrates & Modifiers
Antonio Baici, Marko Novinec, & Brigita Lenarcic

3. Compartmentalization of Proteolysis
Klaudia Brix, Christopher J. Scott, & Margarete M.S. Heck

4. Cathepsins: Getting in Shape for Lysosomal Proteolysis
Ann H. Erickson, Ciro Isidoro, Lukas Mach, & John S. Mort

5. Limited and Degradative Proteolysis in the Context of Posttranslational Regulatory Networks:
Current Technical and Conceptional Advances
Stefan Tholen, Maria Magdalena Koczorowska, Zon Weng Lai, Joern Dengjel, & Oliver Schilling

6. Exploring Systemic Functions of Lysosomal Proteases:
The Perspective of Genetically Modified Mouse Models
Martina Gansz, Ursula Kern, Christoph Peters, & Thomas Reinheckel

7. Astacins: Proteases in Development and Tissue Differentiation
Walter Stocker & F. Xavier Gomis-Ruth

8. Proteases in Death Pathways
Andreas Flutsch & Markus G. Grutter

9. ADAM Proteases in Physiology and Pathophysiology: Cleave to Function in Health or to Cause Disease
Joachim Grotzinger & Stefan Rose-John

10. Protease in the Nervous System
Holger Cynis, Stefan F. Lichtenthaler, Leona Wagner, & Hans-Ulrich Demuth

11. Proteases in the Mammalian Digestive System
S. Gaylen Bradley, Toni M. Antalis, & Judith S. Bond

12. Calpains in Health &Disease
John Anagli, Kevin K.W. Wang, Yasuko Ono, & Hiroyuki Sorimachi

13. Metalloproteinases in Cartilage Matrix Breakdown: The Roles in Rheumatoid Arthritis & Osteoarthritis
Hideaki Nagase & Gillian Murphy

14. MMP-Mediated Collagen Remodeling and Vessel Functions
Agne`s Noel & Nor Eddine Sounni

15. Proteases in Cancer: Significance for Invasion and Metastasis
Bonnie F. Sloane, Karin List, Barbara Fingleton, and Lynn Matrisian

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Gordon Research Conference on Proteolytic Enzymes & their Inhibitors

Row 1: Laura Edgington, Antoine Dufour, Johanna Joyce, James Whisstock
Row 2: Ian Smith, Christopher Overall, Klaudia Brix, Judith Clements, Sheena McGowan, Irit Sagi, Veronica Anania, Peilong Lu, Dan Ma, Sinisa Urban, Desiree Wunsch, Stephanie Smith, Ioannis Manolaridis
Row 3: Anthony O'Donoghue, Taisuke Tomita, Maria Dahmen, Margarete M Heck, Bonnie Sloane, Robert Pike, Cliff Luke, James Huntington, Henry Maun, Marcin Drag, Titia Sixma, Piet Gros, Dylan Edwards, Hans Brandstetter, Henrik Ostergaard, Manu Platt, Denise Monack
Row 4: Kamiar Moin, Lakshmi Wijeyewickrema, Cameron Fyfe, Dion Kaiserman, Adrian Herington, Matthew Cullen, Anne Wiemhoefer, Larissa Hillebrand, Keith Cross, Laila Huq, Anna Byzia, Marcin Poreba, Paulina Kasperkiewicz, Adam Lesner, Joanne Lemieux , Galia Blum, Edward Sturrock
Row 5: Ana Oliveira, Solange Serrano, Bruno Martoglio, Walter Stoecker, Ingrid De Meester, Kevin Dagbay, Mariusz Madej, Dominika Staniec, Jan Potempa, Magdalena Widziolek, Mark Gorrell, Stig Linder, Gregg Fields, Steve Weiss, Thomas Reinheckel, Hendrika Duivenvoorden, Janna Hachmann, Margaret Gall, Hui Zhang

The 2014 Gordon Research Conference on Proteolytic Enzymes & their Inhibitors was held at the beautiful Il Ciocco resort in Italy. This year's conference had 138 delegates from 22 countries and an excellent gender balance of 75 male to 63 female participants. The weather was kind and on the following pages are some of the social photos of the event.
We look forward to the 2016 conference!
2016 Chair: Johanna Joyce; Co-chair Matt Bogyo.

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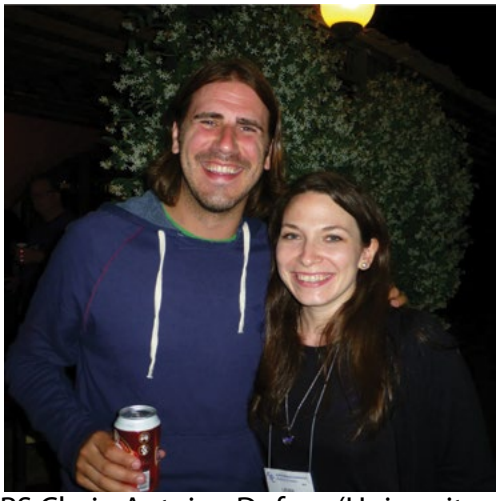
Gordon Research Seminar on Proteolytic Enzymes & their Inhibitors

The second GRS on Proteolytic Enzymes and their Inhibitors organized by Antoine Dufour (Chair) and Laura Edgington (Associate Chair) took place on June 21-22nd in Il Ciocco, Italy. It featured several thought provoking oral presentations, two dynamic poster sessions and a career panel with Chris Overall (University of British Columbia), Bruno Martoglio (Novartis), Bonnie Sloane (Wayne State University) and Margarete Heck (University of Edinburgh).



GRS Chair: Antoine Dufour (University of British Columbia) and Associate Chair: Laura Edgington (LaTrobe University)

Il Ciocco Resort, Italy

Looking forward to 2016!!

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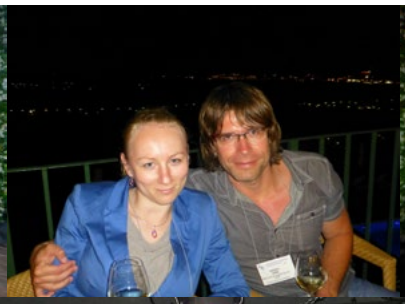
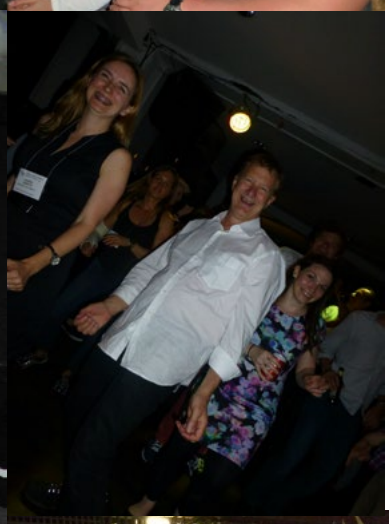
GRC / GRS Proteolytic Enzymes & their Inhibitors - 2014!



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GRC / GRS Proteolytic Enzymes & their Inhibitors - 2014!

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Brazilian Symposium on Chemistry and Physiology of Proteases and their Inhibitors

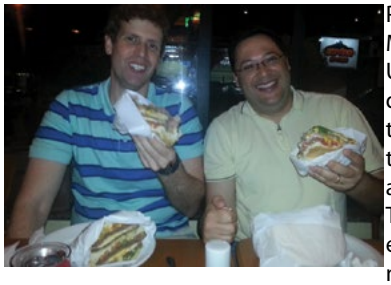
The Chemistry Department of the Federal University of São Carlos in the State of São Paulo, Brazil, hosted the "Brazilian Symposium on the Chemistry and Physiology of Proteases and their Inhibitors" from September 28–30, 2014. The meeting was organized by Dr. Paulo Cezar Vieira (UFSCar, São Carlos, Brazil), Dr. Dieter Brömme (UBC, Vancouver, Canada) and Dr. Richele P. Severino (UFG, Catalão, Brazil).

Organizers Paulo, Richele and Dieter

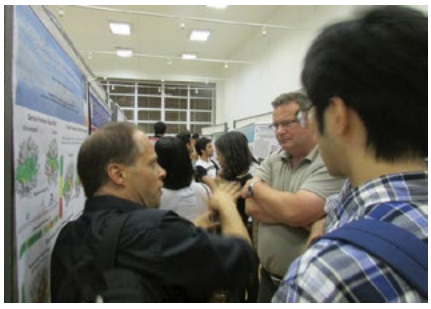
This was the first protease conference organized in Brazil to combine the expertise of chemists, biochemists, structural biologists as well as pharmacists to discuss novel protease inhibitors, proteases, and their pharmaceutical relevance. The 2-day symposium focused on the following topics: (i) Proteases in diseases and as drug targets, (ii) Chemistry of novel inhibitors and substrates, (iii) Proteases and infectious diseases, and (iv) Natural product and endogenous protease inhibitors. The symposium had 122 attendees including undergraduate and graduate students, post-doctoral fellows, and other researchers from different states in Brazil. The scientific program comprised invited speakers from Canada, USA, Germany, and Brazil who delivered 20 invited lectures and 9 short lectures from selected abstracts. There was also a poster session with 36 poster presentations.

The president of the Brazilian National Research Council for Science and Technology, Dr. Glaucius Oliva, participated in the opening ceremony. The opening plenary lecture by Dr. Michael N. G. James (University of Alberta, Canada), on the topic "What can avian ovomucoids teach us about serine peptidase specificity?"

Participants had a fantastic evening at the closing Brazilian BBQ with plenty of BBQ meats as well as plenty of Caipirinhas, Brazil's national cocktail, made by the students with their own special Cachaça.



PhD student Bruno Salu & postdoc Marlon Vilela de Brito (both UNIFESP, São Paulo, Brazil) out for dinner with a group of others – they are each holding just half of the BIG sandwich, which was actually even bigger than it looks. Their trypsin had a major workout – either that or Brazilian trypsin is the most efficient protease ever!



Klaus Leidl (University of Innsbruck, Austria) has IPS Vice President Thomas Reinheckel (Albert-Ludwigs-University Freiburg, Germany) in deep thought at the poster session while PhD student Simon Law (UBC, Canada) looks on. The poster was on local dynamics of serine protease recognition – Klaus' hands were doing some local dynamics as well!

At the end of the symposium, all of the participants agreed that the event was a great success in bringing together scientists and students to discuss this important topic for the first time in Brazil. It is expected that this conference will act as a catalyst to promote the collaboration of protease scientists within Brazil and their partners abroad and that in the future other symposia on proteases will be held in Brazil.

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THE 9TH GENERAL MEETING OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

International Proteolysis Society

Meeting Announcement

Kinin Symposium & Related Peptide Receptors

28 June – 1 July, 2015

Foz do Iguaçu city, Brazil

The scientific program will cover all fields involving the kallikrein-kinin system highlighting the newest involvement of this system with physiological and pathological conditions. The meeting will also approach peptide receptors to increase and improve the relationships between researchers from correlated domains.

We look forward to seeing you at the world famous Iguaçu waterfalls!

Local Organizing Committee

João Batista Calixto, Chairman
João Bosco Pesquero, Vice-Chairman
Hudson Sousa Buck, Secretary
Tânia Araujo Viel, Treasurer
Maria Martha Campos, Scientific Coordinator
Giles Alexander Rae, Scientific Coordinator

The meeting will be held at the Rafain Palace Hotel & Convention Center (www.rafainpalace.com.br).

Iguaçu Falls is located where the Iguaçu River tumbles over the edge of the Paraná Plateau, 23 kilometers (14 mi) upriver from the Iguaçu's confluence with the Paraná River. Numerous islands along the 2.7-kilometer-long (1.7 mi) edge divide the falls into numerous separate waterfalls and cataracts, varying between 60 to 82 meters (197 to 269 ft) high. The number of these smaller waterfalls fluctuates from 150 to 300, depending on the water level. About half of the river's flow falls into a long and narrow chasm called the Devil's Throat. The Devil's Throat is U-shaped, 82 meters high, 150 m wide, and 700 m long (269×492×2,297 ft) (http://en.wikipedia.org/wiki/Iguazu_Falls).

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40th Lorne Conference on Protein Structure and Function

Sunday 8th - Thursday 12th February, 2015 · Mantra Lorne, Lorne, Victoria

CONFIRMED INTERNATIONAL SPEAKERS

Wolfgang Baumeister,
Max Planck Institute of Biochemistry, Germany
Senyon Choe,
The Salk Institute for Biological Studies, USA
Deborah Fass,
Weizmann Institute of Science, Israel
Albert Heck
Biomolecular Mass Spectrometry and Proteomics, Netherlands
Colin Kleanthous,
University of Oxford, UK
Susan Lea,
University of Oxford, UK
Christopher Overall
University of British Columbia, Canada
Sabine Petry,
Princeton University, USA
Nikolaus Pfanner,
University of Freiburg, Germany
Venki Ramakrishnan,
MRC Laboratory of Molecular Biology, UK
Helen Saibil,
Birkbeck College, UK
Brenda Schulman,
St. Jude Children's Research Hospital, USA
Janet Smith,
University of Michigan, USA
JoAnne Stubbe,
Massachusetts Institute of Technology, USA
Jim Wells,
UCSF Mission Bay, USA
Eva Wolf,
Ludwig-Maximilians-Universität (LMU), Germany
Beili Wu,
Chinese Academy of Sciences, China
Ry Young,
Texas A&M University, USA

KEY DATES

Oral Abstract & Earlybird Registration Deadline – Friday 31st October, 2014
Poster Abstract Deadline – Friday 5th December, 2014

www.lorneproteins.org

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GEORG-AUGUST-UNIVERSITÄT
GÖTTINGEN

PhD Student Position
University of Goettingen, Germany

A major interest in our lab is studying the biochemistry and cellular biology of Dipeptidyl peptidases (DPPs) – a small group of amino-dipeptidases that have the unique ability to cleave a peptide bond after proline residues. Members of this family have important roles in regulating the activity of peptide hormones, neuropeptides and the immune system. The aim of the proposed PhD project is to characterize novel interaction partners of DPP9, a rate-limiting enzyme for cleavage of proline-containing peptides in the cytosol that is essential for neonatal survival. The functions of these interactions will be studied using molecular and biochemical approaches as well as microscopy and cell culture work.
For more information on the lab look into:
http://www.uni-bc.gwdg.de/bio_1/Friedlaender/index-RF.html

We offer an open position for a Ph.D. student in the Center for Biochemistry and Molecular Cell Biology in Goettingen, Germany. The position will be financed for three years by the Deutsche Forschungsgemeinschaft (DFG).

We are looking for a motivated, hard working and talented Ph.D. applicant who is curious and open for new challenges. A good understanding in biochemistry and experience in cell culture and molecular biology is an advantage. The successful candidate will join a young and still growing independent group in a stimulating and dynamic working environment with highly interacting groups and excellent research facilities. The University of Goettingen is an equal opportunities employer and places particular emphasis on fostering career opportunities for female scientists.

If you are interested, please send your applications containing your curriculum vitae, certificates and a cover letter summarizing relevant work experience and motivation to rgeiss@gwdg.de. Alternatively applications can be send by mail to: Dr. Ruth Geiss-Friedlander, Department of Biochemistry I, Georg-August University of Göttingen, Humboldtallee 23, 37073 Goettingen, Germany.

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INTERNATIONAL PROTEOLYSIS SOCIETY

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