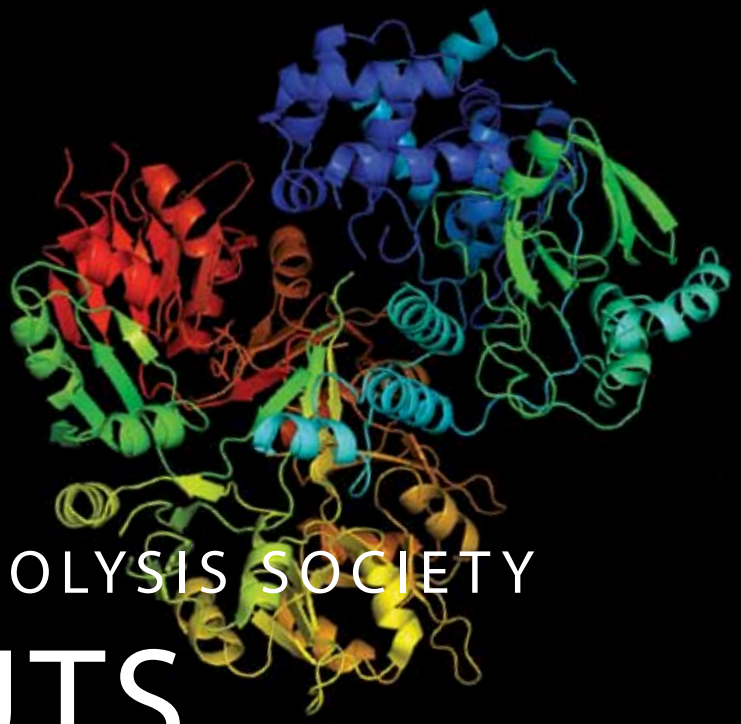
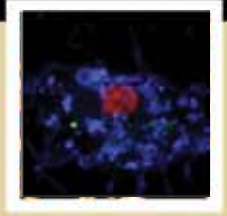
FEB 2013

IN THIS ISSUE:



INTERNATIONAL PROTEOLYSIS SOCIETY

QUICKCUTS


THE PREMIER RESOURCE
FOR ALL YOUR IMPORTANT PROTEASE QUESTIONS

A Message From the President:

I hope you all had a succesfull year and are making preparations to attend the IPS meeting organized by Ed Sturrock in South Africa (October 20-24, 2013, http://www.ips2013.org/). The highly successful IPS meeting in 2011 and was recently covered in a Sept. 2012 Highlight issue of Biological Chemistry with an introduction of Guy Salvesen and Matt Bogyo.

I would like to take this opportunity to remind everyone to renew their IPS membership at http://www.protease.org/index.html (the last membership period ended in 2012). Membership lasts for 2 years and gives you a significant registration discount for IPS 2013, access to our newsletter and the ability to post job and meeting listings on our website. The IPS largely depends on funds raised through membership fees. These fees primarily go towards supporting travel awards for members-in-training to attend the general meeting.

The current issue of QuickCuts contains new job listings, meeting announcements, and a list of important protease papers published in the past year. Please feel free to send feedback to me (boris.turk@ijs.si). Ideas and suggestions from our members are always welcome. This is your society, and the more active you are in helping to shape the direction it goes, the more successful it will be. Thanks again for your support. Looking forward to seeing you all in South Africa in October.

Boris Turk, IPS President

COUNCIL OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

In Memorium – Professor Israel Schechter (1935-2012)

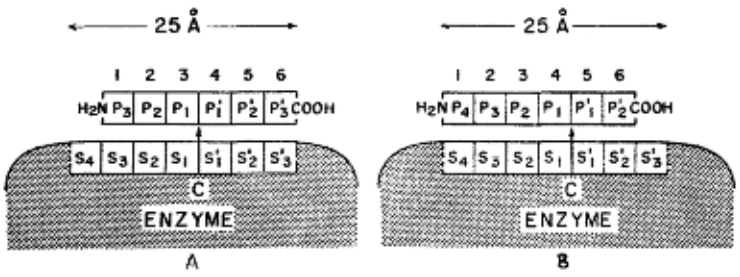
"The Father of Protease Biochemistry"

by Vivian Hook, University of California, San Diego

This article celebrates the life of Professor Israel Schechter, M.D., Ph.D., who many consider the "father of protease biochemistry," for his key contributions to understanding protease active site mechanisms. His hypothesis regarding protease subsite interactions with peptide and protein substrates provided the foundation for current protease biochemistry research. Professor Schechter was a great experimentalist and had a deep understanding of science in all its venues. His scientific accomplishments led the field to utilize knowledge of fundamental protease catalytic mechanisms for design of effective drugs for treatment of AIDS, hypertension, kidney diseases, viral infections, and numerous diseases.

The structure and function of the active sites of enzymes and antibodies were the main scientific interests of Professor Schechter. In the 1960's, synthetic polymers of amino acids were used to characterize the physical properties of enzymes, revealing that the active site of proteases was larger than expected and, importantly, interactions occur in regions remote from the catalytic site. The large active site was divided into subsites and a system for its mapping was set up, known as the Schechter-Berger nomenclature. Professor Schechter's article published in 1967 describing the protease active site map is the seminal report of the protease-substrate interactions, and is highly cited (Schechter and Berger, 1967, BBRC 27, 157-162). *Nature* had laudable comments on the article.

The idea of a large protease active site, proposed by Professor Schechter, was initially unacceptable by several leading scientists. He was looking for a chemist in order to synthesize the series of peptides required to validate the hypothesis. Prof. Arie Berger, an experienced chemist, was interested in the concept that led to the fruitful collaboration. Subsequently, predictions of the model were confirmed by X-ray crystallography of enzyme-inhibitor complexes in the 1970's. The model and nomenclature – S1, S2,… for subsites of the active site and P1, P2,… for substrate residues reacting with corresponding subsites – has stood the test of time for more than 50 years, and is used today in basic and pharmaceutical research to develop inhibitors and drugs. Also in the 1970's, Professor Schechter investigated the exciting field of molecular biology and disease mechanisms. During the 1990's, the field's renewed interest in proteases led to successful development of protease inhibitors for treatment of AIDS and hypertension. As a result, Professor Schechter resumed his interest in proteases. Most recently, Professor Schechter initiated search for proteases as therapeutic targets for Alzheimer's disease, and investigated new cathepsin proteases that cleave the beta-secretase site of APP (amyloid precursor protein) with comparisons to the BACE1 beta-secretase (Schechter and Ziv, 2011, Biol. Chem. 392, 555-569). Professor Schechter proposed that further studies of cathepsins are deserving of evaluation as therapeutic targets for Alzheimer's disease.



Schechter and Berger, "On the Active Site of Proteases" *Biochem Biophys Res Comm*. 1967. 20:157-162.

Professor Schechter was born in 1935 in Haifa, Israel. He was trained as medical physician, receiving his M.D. at the Hebrew University and Hadassah Medical School in Jerusalem, and in science as a biochemist, receiving his Ph.D from the Weizmann Institute of Science. After completing his military service, he joined the Dept. of Chemical Immunology at the Weizmann Institute of Science in Rehovot and was Professor for many years; he was also a visiting scientist at the NIH, Columbia University and the Massachusetts Institute of Technology.

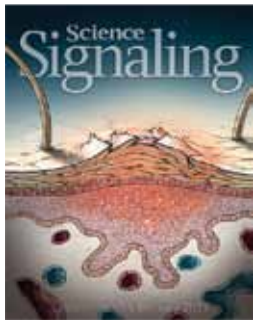
Professor Schechter's love for science and keen motivation for deciphering enzyme mechanisms opened the protease field for bold opportunities in developing new therapeutic targets for human diseases. The world is a better place because he was here, and he will be missed.

IMPORTANT PROTEASE PAPERS I

Research Publications

PROTEOMICS & BIOINFORMATICS

auf dem Keller U, Prudova A, Eckhard U, Fingleton B, Overall CM.



Systems-Level Analysis of Proteolytic Events in Increased Vascular Permeability and Complement Activation in Skin Inflammation.

Science Signaling. 2013. 6, rs2, 1-15: DOI: 10.1126/scisignal.2003512.

From the Cover...

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auf dem Keller U and Overall CM.

CLIPPER—An Add-on to the Trans-Proteomic Pipeline for the Automated Analysis of TAILS N-terminomics Data.

Biol. Chem. 2012. Epub ahead of print.

Jefferson T, Auf dem Keller U, Bellac C, Metz VV, Broder C, Hedrich J, Ohler A, Maier W, Magdolen V, Sterchi E, Bond JS, Jayakumar A, Traupe H, Chalaris A, Rose-John S, Pietrzik CU, Postina R, Overall CM, Becker-Pauly C.

Systems-Level Analysis of Proteolytic Events in Increased Vascular Permeability and Complement Activation in Skin Inflammation.

Cell Mol Life Sci. 2013 70:309-33.

Song J, Hao Tan H, Perry AJ, Akutsu T, Webb GI, Whisstock JC, and Pike RN.

PROSPER: an integrated feature-based tool for predicting protease substrate cleavage sites.

PLoS One 2012. 7:e50300.

O'Donoghue AJ, Eroy-Reveles AA, Knudsen GM, Ingram J, Zhou M, Statnekov JB, Greninger AL, Hostetter DR, Qu G, Maltby DA, Anderson MO, Derisi JL, McKerrow JH, Burlingame AL, Craik CS.

Global identification of peptidase specificity by multiplex substrate profiling.

Nat Methods. 2012. 9:1095-100.

PROTEASE STRUCTURES

Sivaraman KK, Oellig CA, Huynh K, Atkinson SC, Poreba M, Perugini MA, Trenholme KR, Gardiner DL, Salvesen G, Drag M, Dalton JP, Whisstock JC, McGowan S.

X-ray crystal structure and specificity of the *Plasmodium falciparum* malaria aminopeptidase PfM18AAP.

J Mol Biol. 2012. Sep 28;422(4):495-507.

McGowan S, Buckle AM, Mitchell MS, Hoopes JT, Gallagher DT, Heselpoth RD, Shen Y, Reboul CF, Law RH, Fischetti VA, Whisstock JC, Nelson DC.

X-ray crystal structure of the streptococcal specific phage lysin PlyC.

Proc Natl Acad Sci U S A. 2012. 31:12752-7.

RHOMBOID PROTEASES

Vosyka O, Vinothkumar KR, Wolf EV, Brouwer AJ, Liskamp RM, Verhelst SHL.

Activity-based probes for rhomboid proteases discovered in a mass spectrometry-based assay.

Proc. Natl. Acad. Soc. U.S.A. 2013, doi: 10.1073/pnas.1215076110

Zhou Y, Moin SM, Urban S and Y Zhang.

An internal water-retention site in the rhomboid intramembrane protease GlpG ensures catalytic efficiency.

Structure 2012. 20: 1255-1263.

Baker RP and S Urban.

Architectural and thermodynamic principles underlying intramembrane protease function.

Nat. Chem. Biol. 2012 8: 759-768.

Moin SM and S Urban.

Membrane immersion allows rhomboid proteases to achieve specificity by reading transmembrane segment dynamics.

eLife, 2012. 1: e00173. (DOI 10.7554/eLife.00173).

PROTEASE MECHANISMS/ INHIBITORS

Gersch M, Gut F, Korotkov VS, Lehmann J, Böttcher T, Rusch M, Hedberg C, Waldmann H, Klebe G, and Sieber SA.

The Mechanism of Caseinolytic Protease (ClpP) Inhibition.

Angew Chem Int Ed Engl. 2013, in press.

Stein ML, Beck P, Kaiser M, Dudler R, Becker CF, and Groll M.

One-shot NMR analysis of microbial secretions identifies highly potent proteasome inhibitor.

Proc Natl Acad Sci U S A. 2012 109:18367-183671.

CONTINUED NEXT PAGE ▶

IMPORTANT PROTEASE PAPERS II

Research Publications

Valverde IE, Lecaille F, Lalmanach G, Aucagne V, and Delmas AF.

A biologically active bis-triazolo analogue of cystatin A through successive peptidomimetic alkyne/azide ligations.

Angew. Chem. Int. Ed. 2012 51:718 –722.

Masuyer G, Schwager SLU, Sturrock ED, Isaac RE, and Acharya KR.

Molecular recognition and regulation of human angiotensin-I converting enzyme (ACE) activity by natural inhibitory peptides.

Scientific Reports. 2012; 2:717. doi: 10.1038/srep00717

Petrillo T, O'Donohoe C, Howe N, Malthouse JPG.

The importance of tetrahedral intermediate formation in the catalytic mechanism of the serine proteases chymotrypsin and subtilisin.

Biochemistry 2012, 51: 6164-6170.

Ceruso M, Howe N, and Malthouse JPG.

Mechanism of the binding of Z-L-tryptophan and Z-L-phenylalanine to thermolysin and stromelysin-1 in aqueous solutions.

Biochimica et Biophysica Acta. 2012. 1824: 303-310.

Salameh MA, Soares AS, Alloy A, Radisky ES.

Presence versus absence of hydrogen bond donor Tyr-39 influences interactions of cationic trypsin and mesotrypsin with protein protease inhibitors.

Protein Sci. 2012. 21:1103-12.

Minond D, Cudic M, Bionda N, Giulianotti M, Maida L, Houghten RA, Fields GB.

Discovery of Novel Inhibitors of A Disintegrin And Metalloprotease 17 (ADAM17) Using Glycoslyated and Non-Glycosylated Substrates.

J. Biol. Chem. 2012. 287:36473-36487.

Matúz K, Mótyán, J, Li, M, Wlodawer A, and Tőzsér, J

Inhibition of XMRV and HIV-1 proteases by pepstatin A and acetyl-pepstatin.

FEBS J. 2012. 279:3276-3286.

Duncan RC, Mohlin F, Taleski D, Coetzer TH, Huntington JA, Payne RJ, Blom AM, Pike RN, and Wijeyewickrema LC.

Identification of a catalytic exosite for complement component C4 on the serine protease domain of C1s.

J. Immunol. 2012. 189:2365-2373.

Pilla E, Moller U, Sauer G, Mattiroli F, Melchior F, Geiss-Friedlander R.

A novel SUMO1-specific interacting motif in Dipeptidyl peptidase 9 (DPP9) that is important for enzymatic regulation.

J. Biol. Chem. 2012. 284:27211–27219.

PROTEASES INVOLVED IN PATHOGENESIS

Stura EA, Le Roux L, Guitot K, Garcia S, Bregant S, Beau F, Vera L, Collet G, Ptchelkine D, Bakirci H, Dive V.

Structural framework for covalent inhibition of *Clostridium botulinum* neurotoxin A by targeting Cys165.

J. Biol. Chem. 2012, 287:33607-14.

Rieux A, Gras S, Lecaille F, Niepceron A, Katrib M, Smith NC, Lalmanach G, and Brossier F.

Eimeripain, a Cathepsin B-Like Cysteine Protease, Expressed Throughout Sporulation of the Apicomplexan Parasite *Eimeria tenella*.

PLoS One 2012. 7(3): e31914.

Jusko M, Potempa J, Karim AY, Ksiazek M, Riesbeck K, Garred P, Eick S, and Blom AM.

A metalloproteinase karilysin present in the majority of *Tannerella forsythia* isolates inhibits all pathways of the complement system

J. Immunol. 2012. 188:2338-2349.

Kantyka T, Pyrc K, Gruca M, Smagur J, Plaza K, Guzik K, Zeglen S, Ochman M, Potempa J.

Staphylococcus aureus Proteases Degrade Lung Surfactant Protein A Potentially Impairing Innate Immunity of the Lung.

J Innate Immun. 2012 Dec 11. [Epub ahead of print]

Adams CM, Eckenroth BE, Putnam EE, Doublié S, Shen A.

Structural and Functional Analysis of the CspB Protease Required for *Clostridium* Spore Germination.

PLoS Pathog. 2013 Feb;9(2):e1003165.

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IMPORTANT PROTEASE PAPERS III

Research Publications

Aleshin, A. E., Drag, M., Gombosuren, N., Wei, G., Mikolajczyk, J., Satterthwait, A. C., Strongin, A. Y., Liddington, R. C. and Salvesen, G. S.

Activity, specificity, and probe design for the smallpox virus protease K7L.

J. Biol. Chem. 2012. 287:39470-39479.

Zdzalik M, Karim AY, Wolski K, Buda P, Wojcik K, Brueggemann S, Wojciechowski P, Eick S, Calander A, Jonsson I, Kubica M, Polakowska K, Miedzobrodzki J, Wladyka B, Potempa J, and Dubin G.

Prevalence of genes encoding extracellular proteases in *Staphylococcus aureus* – important targets triggering immune response in vivo

FEMS Immunol Med Microbiol 2012. 1-10.

Li H, Ponder EL, Verdoes M, Asbjornsdottir KH, Deu E, Edgington LE, Lee JT, Kirk CJ, Demo SD, Williamson KC, Bogyo M.

Validation of the proteasome as a therapeutic target in *Plasmodium* using an epoxyketone inhibitor with parasite-specific toxicity.

Chem Biol. 2012.19:1535-45.

CASPASES

Boucher D, Blais V, and Denault JB.

Caspase-7 uses an exosite to promote poly(ADP ribose) polymerase 1 proteolysis.

Proc. Natl. Acad. Soc. U.S.A. 2012. 109:5669-5674.

Puri AW, Broz P, Shen A, Monack DM, Bogyo M.

Caspase-1 activity is required to bypass macrophage apoptosis upon *Salmonella* infection.

Nat Chem Biol. 2012. 8:745-7

LEGUMAIN

Haugen MH, Johansen HT, Pettersen SJ, Solberg R, Brix K, Flatmark K, and Maelandsmo GM.

Nuclear legumain activity in colorectal cancer.

PLoS One 2013. 8(1):e52980.

Edgington LE, Verdoes M, Ortega A, Withana NP, Lee J, Syed S, Bachmann MH, Blum G, Bogyo M.

Functional imaging of legumain in cancer using a new quenched activity-based probe.

J Am Chem Soc. 2013. 135:174-82.

CATHEPSINS

Arampatzidou M, Schütte A, Hansson GC, Saftig P, and Brix K.

Effects of cathepsin K deficiency on intercellular junction proteins, luminal mucus layers, and extracellular matrix constituents in mouse colon.

Biol. Chem. 2012. 393:1391-1403.

Dauth S, Schmidt MM, Rehders M, Dietz F, Kelm S, Dringen R, and Brix K.

Characterization and metabolism of astroglia-rich primary cultures from cathepsin K-deficient mice.

Biol. Chem. 2012. 393:959-970.

Laurent-Matha ||V, Huesgen PF, Masson O, Derocq D, Prébois C, Gary-Bobo M, Lecaille F, Rebière B, Meurice G, Oréar C, Hollingsworth RE, Abrahamson M, Lalmanach G, Overall CM, and Liaudet-Coopman E.

Proteolysis of cystatin C by cathepsin D in the breast cancer microenvironment.

FASEB J. 2012. 26: 5172–5181.

Sage J, Leblanc-Noblesse E, Nizard C, Sasaki T, Schnebert S, Perrier E, Kurfurst R, Brömme D, Lalmanach G, Lecaille F.

Cleavage of nidogen-1 by cathepsin S impairs its binding to basement membrane partners.

PLoS One 2012. 7(8): e43494.

Barry ZT and Platt MO.

Cathepsin S cannibalism of cathepsin K as a mechanism to reduce type I collagen degradation.

J. Biol. Chem. 2012. 287(33):27723-30.

Gole B, Huszthy PC, Popović M, Jeruc J, Ardebill SY, Bjerkvig, R, Lah Turnšek T.

The regulation of cysteine cathepsins and cystatins in human gliomas.

Int. J. Cancer 2012. 13:1779-1789.

Torkar A, Bregant S., Deve LL, Novinec M, Lenarčič B, Lah Turnšek T, Dive V.

A novel photoaffinity-based probe for selective detection of cathepsin L active form.

ChemBioChem. 2012. 13:2616-2621.

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IMPORTANT PROTEASE PAPERS IV

Research Publications

Verdoes M, Edgington LE, Scheeren FA, Leyva M, Blum G, Weiskopf K, Bachmann MH, Ellman JA, Bogyo M.

A nonpeptidic cathepsin S activity-based probe for non-invasive optical imaging of tumor-associated macrophages.

Chem Biol. 2012. 19:619-28.

Caglič D, Repnik U, Jedeszko C, Kosec G, Miniejew C, Kindermann M, Vasiljeva O, Turk V, Wendt KU, Sloane BF, Goldring MB, Turk B.

The proinflammatory cytokines interleukin-1α and tumor necrosis factor α promote the expression and secretion of proteolytically active cathepsin S from human chondrocytes.

Biol Chem. 2013. 1:307-16.

METALLOPROTEASES

Bertini I, Fragai M, Luchinat C, Melikian M, Toccafondi M, Lauer JL, Fields GB.

Structural Basis for Matrix Metalloproteinase 1-Catalyzed Collagenolysis.

J. Am. Chem. Soc. 2012. 134:2100-2110.

Czarny B, Stura EA, Devel L, Vera L, Lajeunesse E, Beau F, Calderone V, Fragai M, Luchinat C, Dive V.

Molecular determinants of a selective matrix metalloprotease-12 inhibitor: Insights from crystallography and thermodynamic studies.

J. Med. Chem. 2013. Jan 23. [Epub ahead of print]

Nury C, Bregant S, Czarby B, Berthon F, Cassar-Lajeunesse E, Dive V.

Detection of endogenous matrix metalloprotease-12 active form with a novel broad-spectrum photoaffinity probe.

J. Biol. Chem. 2012. Dec 27. [Epub ahead of print]

Batra J, Robinson J, Soares AS, Fields AP, Radisky DC, Radisky ES.

Matrix metalloproteinase-10 (MMP-10) interaction with tissue inhibitors of metalloproteinases TIMP-1 and TIMP-2: binding studies and crystal structure.

J. Biol. Chem. 2012. 287:15935-46.

Castro MM, Cena J, Cho W-J, Walsh MP, and Schulz R.

Matrix metalloproteinase (MMP)-2 proteolysis of calponin-1 contributes to vascular hyporeactivity in endotoxemic rats.

Arterioscler. Thromb. Vasc. Biol. 2012 32:662-668.

Batra J, Robinson J, Mehner C, Hockla A, Miller E, Radisky DC, Radisky ES.

PEGylation extends circulation half-life while preserving in vitro and in vivo activity of tissue inhibitor of metalloproteinases-1 (TIMP-1).

PLoS One. 2012. 7:e50028.

Ali MAM, Chow AK, Kandasamy AD, Fan X, West LJ, Crawford BD, Simmen T, and Schulz, R.

Mechanisms of cytosolic targeting of matrix metalloproteinase-2.

J. Cell. Physiol. 2012. 227:3397-3404. [Highlighted page V.]

Ali MAM, Stepanko A, Fan X, Holt A, and Schulz R.

Calpain inhibitors exhibit matrix metalloproteinase-2 inhibitory activity.

Biochem. Biophys. Res. Commun. 2012. 423:1-5.

Sariahmetoglu M., Skrzypiec-Spring M, Youssef N, Jacob-Ferreira AL, Sawicka J, Holmes C, Sawicki G, and Schulz R.

Phosphorylation status of matrix metalloproteinase-2 in myocardial ischemia-reperfusion injury.

Heart. 2012. 98:656-662.

Detry B, Erpicum C, Paupert J, Blacher S, Maillard C, Bruyère F, Pendeville H, Remacle T, Lambert V, Balsat C, Ormenese S, Lamaye F, Janssens E, Moons L, Cataldo D, Kridelka F, Carmeliet P, Thiry M, Foidart JM, Struman I, Noël A.

Matrix metalloproteinase-2 governs lymphatic vessel formation as an interstitial collagenase.

Blood. 2012. 119:5048-56.

THERAPEUTICS/ DIAGNOSTICS

Park K, Li AW, Platt MO.

Patient specific proteolytic activity of monocyte-derived macrophages and osteoclasts predicted with temporal kinase activation states during differentiation.

Integrative Biol. 2012. 4(12):1459-69.

Hockla A, Miller E, Salameh MA, Copland JA, Radisky DC, Radisky ES.

PRSS3/Mesotrypsin Is a Therapeutic Target for Metastatic Prostate Cancer.

Mol Cancer Res. 2012. 10:1555-66.

Reviews, Books, Websites and Jobs

REVIEWS

Huesgen PF and Overall CM.

N- and C-terminal Degradomics Approaches for Plant Protease Substrate Identification.

Front Pharmacol. 2012. 3:133.

Lange P and Overall CM.

The TAILS of Proteins: Protein Termini Tell Tales of Proteolysis and Protein Function.

Curr. Opin. Chem. Biol. 2013. Epub ahead of print

Knapinska A and Fields GB.

Chemical biology for understanding matrix metalloproteinase function.

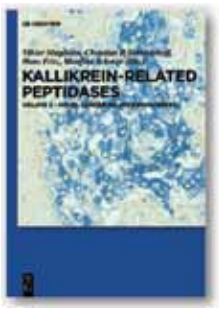
ChemBioChem 2012. 13:2002-2020.

BOOKS

Magdolen V, Sommerhoff CP, Fritz H, Schmitt M (Eds.)

Kallikrein-related peptidases: Novel cancer-related biomarkers.

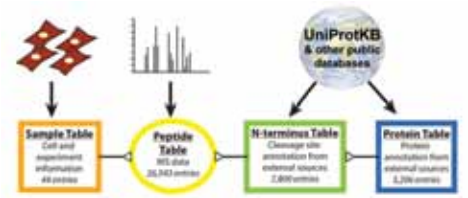
ISBN 13: 9783110303582
ISBN 10: 3110303582



NEW PROTEASE WEBSITES

Degrabase 1.0: non-biased description of all possible capsase substrates in healthy and apototic human cells.

http://wellslab.ucsf.edu/degrabase/index.htm

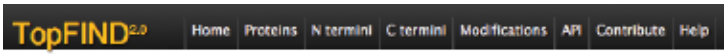


Cascleave: computational identification of caspase substrate cleavage sites

http://sunflower.kuicr.kyoto-u.ac.jp/~sjn/Cascleave/webserver.html

TopFIND: The **T**ermini **o**riented **p**rotein **F**unction **I**nferred **D**atabase is an integrated knowledgebase focused on protein termini, their formation by proteases and implications for protein function.

http://clipserve.clip.ubc.ca/topfind



PROSPER: an integrated feature-based tool for predicting protease substrate cleavage sites using machine learning techniques.

http://lightning.med.monash.edu.au/PROSPER/

JOB LISTINGS

Postdoctoral position - Mass Spectrometry-based Proteomics

We are seeking a motivated individual to join the laboratory of Dr. Markus Hardt as an NIH- and DOD-funded postdoctoral fellow to study the role of proteases and peptides in cancer pain using mass spectrometry-based proteomics approaches in conjunction with functional studies. Research experience in mass spectrometry, proteomics, biochemistry and neurobiology is preferred. You will be responsible for independent projects and will publish in peer-reviewed journals. You will also have the opportunity to travel to scientific meetings to present your research results.

The laboratory is in the Department for Applied Oral Sciences, The Forsyth Institute (a Harvard Affiliate), located at 245 First Street, Cambridge, MA, 02142. The Forsyth Institute is the world's leading organization dedicated to research and education in oral, craniofacial, and related biomedical science. Postdoctoral researchers in our laboratory have Harvard appointments at the Harvard School of Dental Medicine. Our benefits package includes health, dental and vision insurance, generous tuition reimbursement, and flexible spending accounts. Please visit our website (www.forsyth.org) to learn more .

Qualified applicants should possess a Ph.D. or related degree with a strong background in analytic chemistry, biochemistry and/or mass spectrometry. Salary will be commensurate with experience. Please provide a cover letter, curriculum vitae, and contact information for three references to humanresources@forsyth.org. The position will be available to start on or after March 1, 2013. (Affirmative Action/Equal Oppty. Employer M/F/H/V).

MEETING ANNOUNCEMENTS

MEETINGS

2013 Gordon Research Conference on Matrix Metalloproteinases: Crucial components of molecular networks and disease pathways

May 19-24, 2013 at Il Ciocco Tuscany Resort, Barga, Italy.

http://www.grc.org/programs.aspx?year=2013&program=matrix

Chair: Suneel S. Apte, Cleveland Clinic, USA

Vice-Chair: M. Sharon Stack, University of Notre Dame, USA

Proteases co-evolved with their substrates as integral components of specific networks or pathways in development and homeostasis. Elucidating their role in disease, resulting either from loss of function or over-expression, requires a sophisticated understanding within the context of these networks. Furthermore, successful development of novel therapies relies on an integrated, multidisciplinary approach to investigating such networks and pathways.

The 2013 GRC on Matrix Metalloproteinases will develop these themes in the context of major functional networks, and will be inclusive of multiple organ/biological systems and a variety of disease pathways. The conference will feature fundamental and applied research on all aspects of MMPs, ADAM, ADAMTS, and astacin metalloproteinases, as well as their natural and synthetic inhibitors to highlight general principles as well as specific properties. The role of these metalloproteinases in molecular maturation and turnover in diverse biological systems and models is a major focus. In addition, disease-causing protease mutations, proteolytic mechanisms in acquired diseases, protease regulatory mechanisms at all levels, structural biology, developmental biology, genetics, and therapeutics will constitute the broad scope of the meeting.

The associated **Gordon Research Seminar** will be held **May 18-19, 2013**. The GRS will be chaired by **Sean Gill** (U. Western Ontario) with **Alisha Mendonsa** (Vanderbilt University) as vice chair.

Abstracts must be submitted by **April 21, 2013.**

5th International Symposium on Kallikreins (ISK)

Sept. 28 - Oct. 1, 2013 at the Chelsea Hotel, Toronto, CA

http://www.kallikreinsymposium2013.com/

Chair: Eleftherios Diamandis, University of Toronto, Ontario, Canada

30th Winter School on Proteinases and Inhibitors

Feb 27 - March 3, 2013 at Tiers, South Tyrol, Italy.

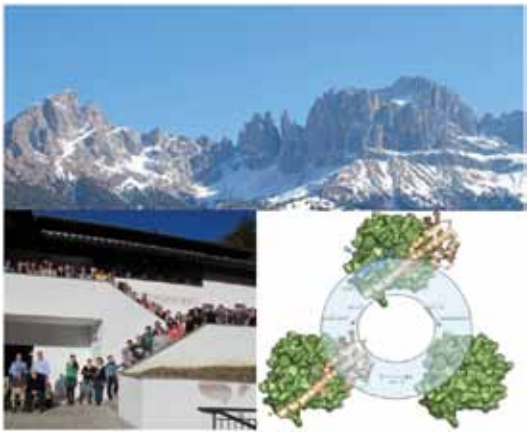
http://www.uni-alzburg.at/portal/page?_pageid=146,2185983&_dad=portal&_schema=PORTAL

Organizing Committee: Klaudia Brix, Christian Sommerhoff, Boris Turk, Hans Brandstetter

Founded by Hans Fritz and Vito Turk more than three decades ago, the **annual** Winter School provides a scientifically stimulating and personally outstandingly open atmosphere to researchers on proteolytic enzymes.

By its tradition, the Winter School provides a forum primarily to young scientists allowing them to present their exciting and /or intriguing results for discussion with leading experts. The exceptional success story of the Winter School also relates to the beautiful scenery of the Tiers valley which serves as an ideal incubator for scientific exchange.

The splendid spirit of the Winter School in Tiers attracts scientists from Europe and worldwide, covering diverse and vibrant fields of protease research.



2014 Gordon Research Conference on Proteolytic Enzymes & Their Inhibitors

June 22-27, 2014 at Il Ciocco Tuscany Resort, Barga, Italy.

http://www.grc.org/programs.aspx?year=2014&program=protenz

Chair: James C. Whisstock, Monash University, Australia

Vice-Chair: Johanna A. Joyce, Sloan-Kettering, USA

The Gordon Research Seminar (GRS) will take place June 21-22, 2014 at the same location.

Gordon Research Conferences

THE 8TH GENERAL MEETING OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

International Proteolysis Society

CONFERENCE
Sunday 20 – Thursday 24 October 2013

WORKSHOPS
Saturday 19 & Sunday 20 October 2013

CONFERENCE VENUE
Spier Estate, Cape Town

WORKSHOP VENUE
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REGISTRATION
Registration and accommodation booking forms are available online
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