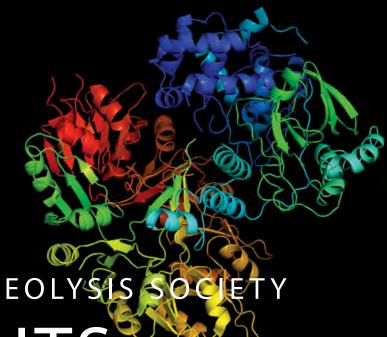
IN THIS ISSUE:

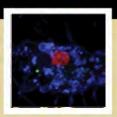
- Membership Renewal Reminder
- Important Protease Papers
- IPS 2013 Schedule
- Meeting announcements
- Job Listings



INTERNATIONAL PROTEOLYSIS SOCIETY

QUICKCUTS







THE PREMIER RESOURCE FOR ALL YOUR IMPORTANT PROTEASE QUESTIONS

A Message From the President:

Our general meeting, which will be held in Cape Town, South Africa from October 20 to 24 is quickly approaching. Ed Sturrock and colleagues have made an extremely exciting program including a one day training course for young protease scientists, and it is not too late to register! At the meeting, we will also elect new councilors as well as decide where the next meeting in the Australasia region will be. Find more information about the meeting on the meeting webpage (http://www.ips2013.org/).

I would like to take this opportunity to remind you that your last membership fee expired at the end of 2012. Thanks to those who have already paid the 2013/14 membership fee: we have been able to provide travel grants to 26 talented students and postdocs to attend the 2013 meeting. You can also get the info on how to pay through our web site (http://www.protease.org/index.html).

As always, the current issue of QuickCuts contains new job listings, information about the IPS 2013 meeting and announcements of other protease-related meetings. The number is significantly higher than previous times, so proteolysis is clearly becoming a very exciting field. Finally, this issue contains an extensive list of important protease papers that have come out in the past 6 months.

Thanks again for your support of the IPS. and thanks to our sponsors. Looking forward to seeing you in South Africa in October.

Boris Turk, IPS President

COUNCIL OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

Boris Turk - President of the Council

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Sin Urban

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

IMPORTANT PROTEASE PAPERS I

Research Publications

PROTEASES & CANCER

Loessner D, Rizzi SC, Stok KS, Fuehrmann T, Hollier B, Magdolen V, Hutmacher DW, and Clements JA.

A bioengineered 3D ovarian cancer model for the assessment of peptidase-mediated enhancement of spheroid growth and intraperitoneal spread.

Biomaterials. 2013. 34:7389-400.

Mirigian LS, Makareeva E, Koistinen H, Itkonen O, Sorsa T, Stenman UH, Salo T, and Leikin S.

Collagen degradation by tumor-associated trypsins.

Arch Biochem Biophys. 2013 535:111-114.

Anti-cancer Agents

LeBeau AM, Duriseti S, Murphy ST, Pepin F, Hann B, Gray JW, VanBrocklin HF, and Craik CS.

Targeting uPAR with antagonistic recombinant human antibodies in aggressive breast cancer.

Cancer Res. 2013. 73:2070-81.

Merchant M*, Ma X*, Maun HR*, Zheng Z*, Peng J, Romero M, Huang A, Yang NY, Nishimura M, Greve J, Santell L, Zhang YW, Su Y, Kaufman DW, Billeci KL, Mai E, Moffat B, Lim A, Duenas ET, Phillips HS, Xiang H, Young JC, Vande Woude GF, Dennis MS, Reilly DE, Schwall RH, Starovasnik MA, Lazarus RA, and Yansura DG.

Monovalent antibody design and mechanism of action of onartuzumab, a MET antagonist with anti-tumor activity as a therapeutic agent.

Proc Natl Acad Sci USA. 2013 110:E2987-96 #Authors with equal contribution

Walsh MP, Duncan B, Larabee S, Krauss A, Davis JP, Cui Y, Kim SY, Guimond M, Bachovchin W, and Fry TJ.

Val-BoroPro Accelerates T Cell Priming via Modulation of Dendritic Cell Trafficking Resulting in Complete Regression of Established Murine Tumors.

PLoS One, 2013, 8:e58860.

Nakahata AM, Mayer B, Neth P, Hansen D, Sampaio MU and Oliva MLV.

Blocking the Proliferation of Human Tumor Cell Lines by Peptidase Inhibitors from Bauhinia Seeds.

Planta Medica, 2013, 79:227-235.

**See "Legumain" section for more papers related to Cancer.

PROTEASES & PATHOGENESIS

Child MA, Hall CI, Beck JR, Ofori LO, Albrow VE, Garland M, Bowyer PW, Bradley PJ, Powers JC, Boothroyd JC, Weerapana, E, and Bogyo, M.

Small-molecule inhibition of a depalmitoylase enhances *Toxoplasma* host cell invasion.

Nat Chem Biol. 2013. Aug 11. Doi: 10.1038/nchembio.1315.

Gloeckl S, Ong V, Patel P, Tyndall JDA, Timms P, Beagley K, Allan J, Armitage C, Turnbull L, Whitchurch C, Merdanovic M, Ehrmann M, Powers J, Oleksyszyn J, Verdoes M, Bogyo M, and Huston W.M

Identification of a serine protease inhibitor which causes inclusion vacuole reduction and is lethal to *Chlamydia trachomatis*.

Mol Microbiol. 2013. 89(4):676-89.

PROTEASES & DEVELOPMENT

Dietzel E, Wessling J, Floehr J, Schafer C, Ensslen S, Denecke B, Rosing B, Neulen J, Veitinger T, Spehr M, Tropartz T, Tolba R, Renné T, Egert A, Schorle H, Gottenbusch Y, Hildebrand A, Yiallouros I, Stocker W, Weiskirchen R, and Jahnen-Dechent W.

Fetuin-B, a Liver-Derived Plasma Protein Is Essential for Fertilization.

Developmental Cell. 2013. 25:106-112.

Vass S and Heck MM.

Perturbation of Invadolysin Disrupts Cell Migration in Zebrafish (*Danio rerio*).

Exp Cell Res. 2013. 319:1198-212.

Tonami K, Hata S, Ojima K, Ono Y, Kurihara Y, Amano T, Sato T, Kawamura Y, Kurihara H, and Sorimachi H.

Calpain-6 Deficiency Promotes Skeletal Muscle Development and Regeneration.

PLoS Genet. 2013 9:e1003668.

Ono Y, Iemura S, Novak SM, Doi N, Kitamura F, Natsume T, Gregorio CC, and Sorimachi H.

PLEIAD/SIMC1/C5orf25, a Novel Autolysis Regulator for a Skeletal-Muscle-Specific Calpain, CAPN3, Scaffolds a CAPN3 Substrate, CTBP1.

J Mol Biol. 2013 425:2955-2972.



IMPORTANT PROTEASE PAPERS II

Research Publications

PROTEASES & AUTOPHAGY

Thomes PG, Ehlers RA, Trambly CS, Clemens DL, Fox HS, Tuma DJ, and Donohue TM.

Multilevel regulation of autophagosome content by ethanol oxidation in HepG2 cells.

Autophagy. 2013. 9:63-73.

Wolfe DM, Lee JH, Kumar A, Lee S, Orenstein SJ, Nixon RA.

Autophagy failure in Alzheimer's disease and the role of defective lysosomal acidification.

Eur J Neurosci 2013 37:1949-1961.

STRUCTURAL STUDIES OF PROTEASES

Lechtenberg BC, Murray-Rust TA, Johnson DJ, Adams TE, Krishnaswamy S, Camire RM, and Huntington JA.

Crystal structure of the prothrombinase complex from the venom of *Pseudonaja textilis*.

Blood. 2013 Jul 18. [Epub ahead of print]

Zhang Y*, Zhou L*, Rouge L, Phillips AH, Lam C, Liu P, Sandoval W, Helgason E, Murray J, Wertz IE, and Corn JE.

Conformational stabilization of Ubiquitin yields potent and selective inhibitors of USP7.

Nat Chem Biol. 2013. 9: 51-58. *Authors with equal contribution

Phillips AH*, Zhang Y*, Cunningham CN, Zhou L, Forrest WF, Liu PS, Steffek M, Lee J, Tam C, Helgason E, Murray JM, Kirkpatrick DS, Fairbrother WJ, and Corn JE.

Conformational dynamics control ubiquitin-deubiquitinase interactions and influence in vivo signaling.

Proc Natl Acad Sci USA. 2013. 110:11379-11384. *Authors with equal contribution

Eckhard U, Schönauer E, and Brandstetter H.

Structural basis for activity regulation and substrate preference of clostridial collagenases G, H, and T.

J Biol Chem. 2013. 288:20184-20194.

de Vera IMS, Smith AN, Dancel MCA, Huang X, Dunn BM, and Fanucci GE.

Elucidating a Relationship between Conformational Sampling and Drug Resistance in HIV-1 Protease.

Biochemistry 2013 52(19):3278-3288.

de Vera IMS, Blackburn ME, and Fanucci GE.

Correlating conformational shift induction with altered inhibitor potency in a multidrug resistance HIV-1 protease variant.

Biochemistry 2012 51:7813-5.

Huang X, de Vera IMS, Blackburn ME, Kear JL, Carter JD, Rocca JR, Simmerling C, Dunn BM, and Fanucci GE.

Inhibitor-Induced Conformational Shifts and Ligand Exchange Dynamics for HIV-1 Protease Measured by Pulsed EPR and NMR Spectroscopy.

J Phys Chem B 2012 116:14235-14244.

Dall E and Brandstetter H.

Mechanistic and structural studies on legumain explain its zymogenicity, distinct activation pathways, and regulation.

Proc Natl Acad Sci USA. 2013. 110:10940-10945.

Solomonson M, Huesgen PF, Wasney GA, Watanabe N, Gruninger RJ, Prehna G, Overall CM, and Strynadka NC.

Structure of the mycosin-1 protease from the mycobacterial ESX-1 protein type VII secretion system.

J Biol Chem. 2013. 288:17782-90.

Yongqing T, Wilmann PG, Reeve SB, Coetzer TH, Smith Al, Whisstock JC, Pike RN, and Wijeyewickrema LC.

The X-ray Crystal Structure of Mannose-binding Lectinassociated Serine Proteinase-3 Reveals the Structural Basis for Enzyme Inactivity Associated with the Carnevale, Mingarelli, Malpuech, and Michels (3MC) Syndrome.

J Biol Chem. 2013. 288:22399-407.

Batra J, Szabó A, Caulfield TR, Soares AS, Sahin-Tóth M, and Radisky ES.

Long-range electrostatic complementarity governs substrate recognition by human chymotrypsin C, a key regulator of digestive enzyme activation.

J Biol Chem. 2013. 288:9848-9859.

Ferreira RD, Zhou D, Ferreira JG, Silva MC, Silva-Lucca RA, Mentele R, Paredes-Gamero EJ, Bertolin TC, Dos Santos Correia MT, Paiva PM, Gustchina A, Wlodawer A and Oliva MLV.

Crystal Structure of Crataeva tapia Bark Protein (CrataBL) and Its Effect in Human Prostate Cancer Cell Lines.

PLoS One. 2013 8:e64426

IMPORTANT PROTEASE PAPERS III

Research Publications

SUBSTRATE PROFILING OF PROTEASES

Paper of the Week:

Wilson CH, Indarto D, Doucet A, Pogson LD, Pitman MR, McNicholas K, Menz RI, Overall CM, and Abbott CA.

Identifying natural substrates for dipeptidyl peptidases 8 and 9 using terminal amine isotopic labeling of substrates (TAILS) reveals in vivo roles in cellular homeostasis and energy metabolism.

J Biol Chem 2013, 288:13936-49.

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, and Becker-Pauly C.

The substrate degradome of meprin metalloproteases reveals an unexpected proteolytic link between meprin β and ADAM10.

Cell Mol Life Sci. 2013 Jan;70(2):309-33.

Small JL, O'Donoghue AJ, Boritsch EC, Tsodikov OV, Knudsen GM, Vandal O, Craik CS, and Ehrt S.

Substrate specificity of MarP, a periplasmic protease required for resistance to acid and oxidative stress in *Mycobacterium tuberculosis*.

J Biol Chem. 2013. 288:12489-12499.

Corvo I, O'Donoghue AJ, Pastro L, Pi-Denis N, Eroy-Reveles A, Roche L, McKerrow JH, Dalton JP, Craik CS, Caffrey CR, and Tort JF.

Dissecting the Active Site of the Collagenolytic Cathepsin L3 Protease of the Invasive Stage of Fasciola hepatica.

PLoS Negl Trop Dis. 2013. 7:e2269.

CHEMICAL INHIBITORS OF PROTEASES

Poplawski, SE, JH Lai, Y Li, Z Jin, Y Liu, W Wu, Y Wu, Y Zhou, JL Sudmeier, DG Sanford, and WW Bachovchin.

Identification of Selective and Potent Inhibitors of Fibroblast Activation Protein and Prolyl Oligopeptidase.

J Med Chem. 2013. 56: 3467-77.

Jansen K, Heirbaut L, Cheng JD, Joossens J, Ryabtsova O, Cos P, Maes L, Lambeir A-M, De Meester I, Augustyns K, and Van der Veken P.

Selective Inhibitors of Fibroblast Activation Protein (FAP) with a (4-Quinolinoyl)-glycyl-2-cyanopyrrolidine Scaffold.

Torkar A, Lenračič B, Lah T Turnšek, Dive V, and Devel L.

Identification of new peptide amides as selective cathepsin L inhibitors: the first step towards selective irreversible inhibitors?

Bioorg Med Chem Lett. 2013. 23:2968-2973.

Strålberg F, Henning P, Gjertsson I, Kindlund B, Souza PPC, Persson E, Abrahamson M, Kasprzykowski F, Grubb A, and Lerner UH.

Cysteine proteinase inhibitors regulate human and mouse osteoclastogenesis by interfering with RANK signaling.

FASEB J. 2013. 27:2687-2701.

Wallin H, Abrahamson M, and Ekström U.

Cystatin C properties crucial for uptake and inhibition of intracellular target enzymes.

J Biol Chem. 2013. 288:17019-17029.

Schlauderer F, Lammens K, Nagel D, Vincendeau M, Eitelhuber AC, Verhelst SHL, Kling D, Chrusciel A, Ruland J, Krappmann D, and Hopfner KP.

Structural analysis of phenothiazine derivatives as allosteric inhibitors of the MALT1 paracaspase.

Angew Chem Int Ed Engl. 2013. [Epub ahead of print]

ACTIVITY-BASED PROBES

Xiao J, Broz P, Puri AW, Deu E, Morell M, Monack DM, and Bogyo M.

A coupled protein and probe engineering approach for selective inhibition and activity-based probe labeling of the caspases.

J Am Chem Soc. 2013. 135:9130-9138.

Morell M, Nguyen Duc T, Willis AL, Syed S, Lee J, Deu E, Deng Y, Xiao J, Turk BE, Jessen JR, Weiss SJ, and Bogyo M.

Coupling protein engineering with probe design to inhibit and image matrix metalloproteinases with controlled specificity.

J Am Chem Soc. 2013. 135: 9139-9148.

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

Functional Imaging of Legumain in Cancer Using a New Quenched Activity-Based Probe.

J Am Chem Soc. 2013. 135:174-182.

IMPORTANT PROTEASE PAPERS IV

Research Publications

Serim S, Mayer SV, and Verhelst SHL.

Tuning Activity-Based Probe Selectivity for Serine Proteases by On-Resin 'Click' Construction of Peptide Diphenyl Phosphonates.

Org Biomol Chem. 2013 11: 5714-5721.

METALLOPROTEASES

Becker-Pauly C and Rose-John S.

TNFα cleavage beyond TACE/ADAM17: matrix metalloproteinase 13 is a potential therapeutic target in sepsis and colitis.

EMBO Mol Med. 2013. 5:970-2.

Broder C and Becker-Pauly C.

The metalloproteases meprin α and meprin β : unique enzymes in inflammation, neurodegeneration, cancer and fibrosis.

Biochem J. 2013. 450(2): 253-264.

Broder C, Arnold P, Vadon-Le Goff S, Konerding MA, Bahr K, Müller S, Overall CM, Bond JS, Koudelka T, Tholey A, Hulmes DJS, Moali C, and Becker-Pauly C.

Metalloproteases meprin α and meprin β are C- and N-procollagen proteinases important for collagen assembly and tensile strength.

Proc Natl Acad Soc USA. 2013. 110:14219-24.

Chen F, Radisky ES, Das P, Batra J, Hata T, Hori T, Baine AM, Gardner L, Yue, MY, Bu G, Del Zoppo G, Patel TC, and Nguyen JH.

TIMP-1 attenuates blood-brain barrier permeability in mice with acute liver failure.

J Cereb Blood Flow Metab. 2013 33:1041-1049.

Bautista-López NL, Morillo CA, López-Jaramillo P, Quiroz R, Luengas C, Silva SY, Galipeau J, Lalu MM, and Schulz R.

Matrix metalloproteinase-2 and -9 as diagnostic markers in the progression to Chagas cardiomyopathy.

Am Heart J. 2013. 165:558-566.

Castro MM, Fuah J, Ali MAM, Sung M, Schulz J, Kondo MY, Fan X, Holt A, and Schulz R.

Inhibitory effects of caspase inhibitors on the activity of matrix metalloproteinase-2.

Biochem Pharmacol. 2013. 86:469-475.

Jacob-Ferreira Al, Kondo MY, Baral PK, James MNG, Holt A, Fan X, and Schulz R.

Phosphorylation status of 72 kDa MMP-2 determines its structure and activity in response to peroxynitrite.

PLOS ONE 2013. 8:e71794.

Ali MAM, Kandasamy AD, Fan X, and Schulz R.

Hydrogen peroxide-induced necrotic cell death in cardiomyocytes is independent of matrix metalloproteinase-2.

Toxicology In Vitro. 2013. 27:1686-1692.

**Note the metalloprotease activity-based probe on pg. 4.

LEGUMAINS

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

Nuclear legumain activity in colorectal cancer.

PLoS One. 2013. 8:e52980.

Berven L, Johansen HT, Solberg R, Kolset SO, and Samuelsen ABC.

Autoactivation of prolegumain is accelerated by glycosaminoglycans.

Biochimie. 2013. 95:772-781.

**Note the legumain structure on pg. 3 and legumain activity-based probe on pg. 4.

CATHEPSINS

Lecaille F, Naudin C, Sage J, Joulin-Giet A, Courty A, Andrault P-M, Veldhuizen R, Possmayer F, and Lalmanach G.

Specific cleavage of the lung surfactant protein A by human cathepsin S may impair its antibacterial properties.

Int J Biochem Cell Biol. 2013 45: 1701-1709.

Sage J, De Quéral D, Leblanc-Noblesse E, Kurfurst R, Schnebert S, Perrier E, Nizard C, Lalmanach G, and Lecaille F.

Differential expression of cathepsins K, S and V between young and aged Caucasian women skin epidermis.

Matrix Biol. 2013 (in press) doi:10.1016/j.matbio.2013.07.002

IMPORTANT PROTEASE PAPERS V

Research Publications

CALPAINS

Hata S, Kitamura F, and Sorimachi H.

Efficient expression and purification of recombinant human μ-calpain using an *Escherichia coli* expression system.

Genes Cells 2013. 18:753-63.

**Note calpains and their role in development on pg. 2.

PROPROTEIN CONVERTASES

Luna SYG, Zhang J and Seidah NG.

PCSK9 Prosegment Chimera as Novel Inhibitors of LDLR Degradation.

PloS One. 2013. 8:e72113.

Canuel M, Susan-Resiga D, Sun X, Asselin M-C, Prat A, Paramithiotis E, and Seidah NG.

Proprotein convertase subtilisin/kexin type 9 (PCSK9) can mediate degradation of the low density lipoprotein receptor-related protein 1 (LRP-1).

PLoS One. 2013. 8:e64145.

Guillemot J, Canuel M, Essalmani R, Prat A, and Seidah NG.

The proprotein convertase PC7 is the sheddase of human transferrin receptor 1: implication in iron homeostasis.

Hepatology. 2013. 57:2514-2524.

Essalmani R, Susan-Resiga D, Chamberland A, Asselin M-C, Canuel M, Constam D, Creemers JWM, Day R, Gauthier D, Lazure C, Prat A and Seidah NG.

Hepatocyte furin is the major in vivo convertase of angio-poietin like 3 and endothelial lipase.

J Biol Chem. 2013. 288:26410-8.

KALLIKREINS

de Souza LR, M Melo P, Paschoalin T, Carmona AK, Kondo M, Hirata IY, Blaber M, Tersariol I, Takatsuka J, Juliano MA, Juliano L, Gomes RA, Puzer L.

Human tissue kallikreins 3 and 5 can act as plasminogen activator releasing active plasmin.

Biochem Biophys Res Commun. 2013 433:333-337.

Ferreira JG, Diniz PMM, de Paula C AA, Lobo YA, Paredes-Gamero EJ, Paschoalin T, Nogueira-Pedro A, Maza PK, Toledo MS, Suzuki E and Oliva MLV.

The impaired viability of prostate cancer cell lines by the recombinant plant kallikrein inhibitor.

J Biol Chem. 2013. 288:13641-13654.

Dong Y, Stephens C, Walpole C, Swedberg JE, Boyle GM, Parsons PG, McGuckin MA, Harris JM, and Clements JA.

Paclitaxel resistance and multicellular spheroid formation are induced by kallikrein-related peptidase 4 in serous ovarian cancer cells in an ascites mimicking microenvironment.

PLoS One. 2013. 8:e57056.

COMPLEMENT

Wijeyewickrema LC, Perry AJ, Wilmann PG, Gunzburg MJ, D'Andrea L, Irving JA, Pang SS, Duncan RC, Wilce JA, Whisstock JC, and Pike RN.

A molecular switch governs the interaction between the human complement protease C1s and its substrate, complement C4.

J Biol Chem. 2013 288:15821-9.

Wijeyewickrema LC, Yongqing T, Tran TP, Thompson PE, Viljoen JE, Coetzer TH, Duncan RC, Kass I, Buckle AM, Pike RN.

Molecular determinants of the substrate specificity of the complement-initiating protease, C1r.

J Biol Chem. 2013 288:15571-80.

**Note complement component structure on pg. 3.

REVIEWS

Nixon RA.

The role of autophagy in neurodegenerative disease

Nat. Med. 2013 19(8):983-997.

Butler GS and Overall CM.

Matrix metalloproteinase processing of signaling molecules to regulate inflammation.

Periodontol 2000. 2013. 63:123-48.

Dufour A and Overall CM.

Missing the target: matrix metalloproteinase antitargets in inflammation and cancer.

Trends Pharmacol Sci. 2013 34:233-42.

Rogers L and Overall CM.

Proteolytic post translational modification of proteins: proteomic tools and methodology.

Mol Cell Proteomics. 2013 Jul 25. [Epub ahead of print]

Tajnšek U, Motaln H, Levičar N, Rotter A, Lah T, Turnsek U.

The duality of stem cells: double edged sword in tumour evolution and treatment.

Resende R, Ulrich AH (eds). Trends in stem cell proliferation and cancer research.

OUICKCUTS | 6

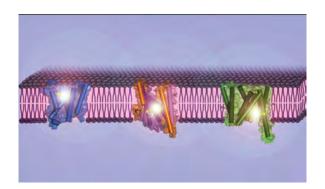
Special Issue: Intramembrane Protease Review

INTRODUCTION

Urban S.

Mechanisms and cellular functions of intramembrane proteases.

Biochim. Biophys. Acta - Biomembr. 2013 1838:1–4.



PART I: CELLULAR FUNCTIONS

Rawson RB.

The Site-2 Protease.

Biochim. Biophys. Acta - Biomembr. 2013 1828:5–11.

Schneider JS, and Glickman MS.

Function of site-2 proteases in bacteria and bacterial pathogens.

Biochim Biophys Acta - Biomembr. 2013. 1838:12–18.

Jurisch-Yaksi N, Sannerud R, and W Annaert.

A fast growing spectrum of biological functions of y-secretase in development and disease.

Biochim Biophys Acta - Biomembr. 2013. 1828:19–31.

Voss M, Schröder B, and Fluhrer R.

Mechanism, specificity, and physiology of signal peptide peptidase (SPP) and SPP-like (SPPL) proteases.

Biochim Biophys Acta - Biomembr. 2013. 1828:32–43.

Bergbold N, and Lemberg MK.

Emerging role of rhomboid family proteins in mammalian biology and disease.

Biochim. Biophys. Acta - Biomembr. 2013 1838:44–52.

Rather P.

Role of Rhomboid Proteases in Bacteria.

Biochim Biophys Acta - Biomembr. 2013. 1828:53–58.

Morohashi Y, and Tomita T.

Protein trafficking and maturation regulates intramembrane proteolysis.

Biochim Biophys Acta - Biomembr. 2013. 1828:59–65.

PART II: BIOCHEMICAL MECHANISMS

Brooks CL, and Lemieux MJ.

Untangling structure-function relationships in the rhomboid family of intramembrane proteases.

Biochim Biophys Acta - Biomembr. 2013. 1828:66–76.

Kroos L, and Akiyama Y.

Biochemical and Structural Insights into Intramembrane Metalloprotease Mechanisms.

Biochim. Biophys. Acta - Biomembr. 2013 1828:77–89.

Toward the structure of presenilin/γ-secretase and presenilin homologs.

Biochim Biophys Acta - Biomembr. 2013. 1828:90–101.

PART III: THERAPEUTIC STRATEGIES

Golde TE, Koo EH, Felsenstein KM, Osborne BA, Miele L. Gamma-Secretase Inhibitors and Modulators.

Biochim Biophys Acta - Biomembr. 2013. 1828:102–111.

The roles of intramembrane proteases in protozoan parasites.

Biochim. Biophys. Acta - Biomembr. 2013. 1828:112–119.

Chan EYL, and McQuibban GA.

The mitochondrial rhomboid protease: its rise from obscurity to the pinnacle of disease-relevant genes.

Biochim Biophys Acta - Biomembr. 2013 1828:120–129.

PART IV: EMERGING TOPICS

Roles of Regulated Intramembrane Proteolysis in Virus Infection and Antiviral Immunity.

Biochim Biophys Acta - Biomembr. 2013. 1828:130–136.

Adam Z.

Emerging roles for diverse intramembrane proteases in plant biology.

Biochim Biophys Acta - Biomembr. 2013. 1828:137–140.

Kinch LN, and Grishin NV.

Bioinformatics perspective on rhomboid intramembrane protease evolution and function.

Biochim Biophys Acta - Biomembr. 2013. 1828:141–147.

http://www.sciencedirect.com/science/journal/00052736/28/12

THE 8TH GENERAL MEETING OF THE 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

IIDMM, University of Cape Town

REGISTRATION

Registration and accommodation booking forms are available online www.ips2013.org

ENQUIRIES

Deborah McTeer - Onscreen Conferences conference@onscreenav.co.za - www.ips2013.org



Programme Outline

SUNDAY 20th OCTOBER

15:00 - 17:00 Registration

17:00 Opening and Welcome

Vishva Dixit (Genentech Inc., San Francisco, USA) "Inflammatory caspases: Trouble in paradise"

Opening Reception

MONDAY 21st OCTOBER

Proteases in Immunity

Chris Overall (University of British Columbia, Vancouver, Canada)

"A nuclear MMP in viral Infection regulates gene transcription and substrate expression"

Phillip Bird (Monash University, Clayton, Australia)

"A new role for Granzyme B - in lymphocyte trafficking"

Protease Inhibitors for Therapeutic Intervention

James McKerrow (University of California, San Francisco, USA

"What parasite proteases teach us about molecular evolution and drug development"

Dieter Brömme (University of British Columbia, Canada)

"To inhibit or not to inhibit: What to do when a protease drug target also exhibits vital functions?"

Proteases, Cell Signalling and Metabolism

Klaudia Brix (Jacobs University Bremen, Germany)

"Effects of cysteine cathepsin-deficiencies on the auto-regulation of the thyroid gland"

TUESDAY 22nd OCTOBER

Proteases in Cancer and Metastasis

Johanna Joyce (Memorial Sloan-Kettering Cancer Center, New York, USA)

"Investigating proteases in the metastatic tumour microenvironment"

Proteases in Cell Death

Seamus Martin (Smurfit Institute, Trinity College, Dublin, Ireland)

THE EMBO LECTURE ON PROTEASES IN CELL DEATH

"Arming & disarming the alarmins: Proteolytic processing of members of the extended IL-1 family"

Intracellular Proteolytic Systems

Guy Salvesen (Sanford Burnham Institute, San Diego, USA)

"The fuzzy logic of SUMO signaling"

David Komander (University of Cambridge, UK)

"OTULIN - a new human deubiquitinase involved in NFkB signaling that uses substrateassisted catalysis"

Biannual Meeting of the International Proteolysis Society

WEDNESDAY 23rd OCTOBER

Proteases in Developmental Biology

Walter Stöcker (Johannes Gutenberg University, Mainz, Germany)

"Mammalian gamete fusion depends on the inhibition of ovastacin by fetuin B"

Atsuko Sehara (University of Kyoto, Japan)

"Roles of ADAM proteases in development of zebrafish"

Proteases and Pathogens 1

Yasien Sayed (University of Witwatersrand, South Africa)

"South African HIV-1 subtype C protease: Structural and functional insights"

Matt Bogyo (Stanford University, Stanford, USA)

"Targets in parasite pathogens"

Proteases in Cardiovascular Disease

James Huntington (University of Cambridge, UK)

"In search of the Holy Grail - An antithrombotic that doesn't cause bleeding"

Ken Bernstein (Cedars-Sinai Medical Center, Los Angeles, USA)

"Angiotensin-converting enzyme: New functions for an established protease"

THURSDAY 24th OCTOBER

Membrane-Associated Proteolysis and Neurological Disorders

Bart De Strooper (Leuven Institute for Neuroscience & Disease)

THE EMBO LECTURE ON PROTEASES IN ALZHEIMER'S DISEASE

Taisuke Tomita, Univ. of Tokyo

"Mechanistic insight of the gamma-secretase-mediated intramembrane cleavage"

New Approaches to the Design of Proteolytic Inhibitors

Irit Sagi (The Weizmann Institute of Science, Rehovot, Israel)

"Generating molecular understanding of selective protease action"

Proteases and Pathogens 2

Sheena McGowan (Monash University, Clayton, Australia)

"The in's and out's of the malarial aminopeptidase PfA-M1"

Kelly Chibale (University of Cape Town, South Africa)

"Integrated use of computational tools and medicinal chemistry: Towards antimalarial inhibitors of the cysteine protease Falcipain-2"

Awards Banquet and Entertainment

FOR FURTHER INFORMATION PLEASE CONTACT:

Deborah McTeer

Onscreen Conferences & Events

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Advanced Confocal Microscopy For Protease Imaging on Live and Fixed Cells **Edith Elliott, Bonnie Sloane and Kami Moin**

In this workshop theoretical and practical principles of confocal microscopy for live or fixed specimens, will be covered, with special emphasis on the imaging of proteases. Topics will include: live cell imaging; hanging drop and other 3D cell culture techniques; cell and tissue handling and fixation techniques; FRET and FRAP; useful free software downloads. Practical experience will include hands-on image capture and data processing, and spinning disc (to be supplied by Zeiss) and LSM 510 confocal pulsed infrared laser 2-photon imaging (NLO) and handling and labelling of various tissues.

Lecture and practical sessions and workshop registration will be held in the Confocal and Light Microscope Imaging Facility

Structural Biology

Trevor Sewell

In this workshop trainees will learn, discuss and apply principles of structural biology using X-ray crystallography with a focus on the mechanism and specificity of metalloproteases. Topics include: interpreting diffraction patterns and maps to produce an atomic model; using biochemistry to validate structural models; and molecular modelling and docking.

The workshop will be hosted by the Institute of Infectious Disease and Molecular Medicine (IIDMM) at the University of Cape Town, a postgraduate research institute located at the base of Table Mountain.

Practical Protease Kinetics

Christian Sommerhoff and Guy Salvesen

In this workshop trainees will discuss and apply principles of theoretical and practical enzyme kinetics with a special focus on proteases. Topics include e.g. substrate and inhibitor kinetics, steady-state, presteady-state and transient approaches, inhibitor mechanisms, slow versus fast binding, hardware and software.

The workshop will be hosted by the Institute of Infectious Disease and Molecular Medicine (IIDMM) at the University of Cape Town, a postgraduate research institute located at the base of Table Mountain.

MEETING ANNOUNCEMENTS

MEETINGS

5th International Symposium on Kallikreins and **Kallikrein-related Peptidases (ISK)**

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

http://www.kallikreinsymposium2013.com/

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

Toronto is the biggest and most diverse city in Canada and is home to many world-renowned scientists and medical professionals. The Symposium presentations will take place at the Li Ka Shing Knowledge Institute of St. Michael's Hospital, and our host hotel will be the Chelsea Toronto Hotel in the heart of downtown.

We have a very exciting program this year that features talks from international experts on topics including:

- Biochemical, structural, and functional aspects of kallikreins and kallikrein-related peptidases
- The role of kallikreins in skin and inflammatory diseases; kallikrein signaling
- Genetic and epigenetic regulation
- Kallikreins as cancer biomarkers and their roles in tumor initiation and progression.

We also have a special section on the role of kallikreins in the clinic with interesting up-to-date developments for pathologists, urologists and oncologists. Our program is accredited by the Royal College of Physicians and Surgeons of Canada (RCPSC Section 1 for Canadian physicians/specialists) and also for American attendees (AMA Category 1) and international attendees (EACCME credits).

In addition to the scientific program, we are planning several social and sightseeing events for our attendees including an opening mixer, gala dinner, and trips to Niagara Falls and Ontario wineries.

We look forward to seeing you in September!



30th Winter School on Proteinases and Inhibitors

Feb 26 - March 2, 2014 at Tiers, South Tyrol, Italy.

http://www.uni-salzburg.at/index.php?id=25444

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

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

The Winter School has traditionally provided a forum primarily for young scientists to present their exciting and/or intriguing results for discussion with leading experts. In addition, the beautiful scenery of the Tiers valley serves as an ideal incubator for scientific exchange.

The Winter School in Tiers attracts scientists worldwide and covers diverse and vibrant fields of protease research.

Participate and enjoy this unique event by registering today and sending your abstract by January 15, 2014.



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

Gordon Research Seminar (GRS): June 21-22, 2014

Chair: Antoine H. Dufour

Associate Chair: Laura E. Edgington



7TH INTERNATIONAL SYMPOSIUM ON SERPIN **BIOLOGY, STRUCTURE AND FUNCTION**

MARCH 29 - APRIL 2, 2014

Registration and Information: www.meduniwien.ac.at/serpins2014

Location of the Meeting: Hotel Krallerhof *****, Leogang, Austria

Nearest Airport:

Salzburg Airport W. A. Mozart (SZG)

Submission of Abstracts:

Abstract submission will open soon

International Advisory Commitee:

Peter Andreasen (DK), Pat Becerra (USA), Phil Bird (AU), Stephen Bottomley (AU), Robin Carrell (UK), Frank Church (USA), Paul Coughlin (AU), Paul Declerck (BE), Peter Gettins (USA), Jim Huntington (UK), Mike Kanost (USA), Alex Lucas (USA), Joost Meijers (NL), Steven Olson (USA), Maki Onda (JP), Cynthia Peterson (USA), Rob Pike (AU), Jan Potempa (USA), Hermann Ragg (DE), Jean-Marc Reichhart (FR), Tom Roberts (AU), Rick Sifers (USA), Gary Silverman (USA), Dudley Strickland (USA), James Whisstock (AU), and Ming Zhang (USA).









7™INTERNATIONAL SYMPOSIUM ON SERPIN BIOLOGY, STRUCTURE AND FUNCTION

SERPINS 2014

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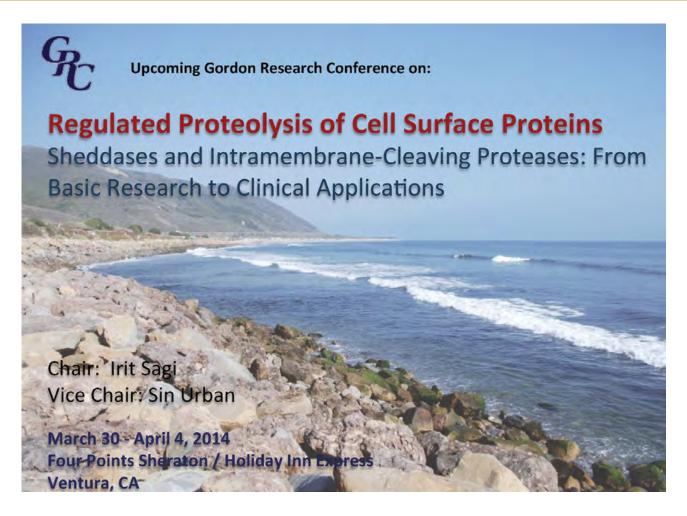
For further information please contact us



Serpins 2014 Congress Office Department of Vascular Biology Schwarzspanierstr. 17, 1090 Vienna, AT serpin2014@meduniwien.ac.at



CONTINUED NEXT PAGE



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

Regulated proteolytic release of proteins from the membrane provides cells with information essential for controlling cell fate specification, maintaining organelle homeostasis, and sustaining tissue-specific functions. Dysregulation of membrane proteolysis underlies many pathologies including Alzheimer's disease, Parkinson's disease, allergies, obesity, cardiac hypertrophy, inflammation, autoimmune diseases and cancer. Some of the world's deadliest pathogens also rely upon these proteolytic cascades to infect hosts, causing diseases including malaria, tuberculosis, cholera and hepatitis C virus infection. Thus many sheddase and intramembrane proteases are attractive targets for therapeutic intervention.

Focusing efforts on membrane proteolytic reactions that impact physiological and pathologic conditions, this meeting will bring together experts from diverse disciplines to discuss frontier projects, emerging experimental strategies and most recent advancement in understanding sheddase and intramembrane protease activities in health, disease, and therapy.

- Advancing our Understanding of ADAMs and iCLiPs Networks and Molecular Mechanisms (Marcia Moss/ Chris Overall/ Michael Wolfe)
- ADAMs and iCLiPs in Development and Beyond (Matthew Freeman/ Carl Blobel)
- ADAM- and iCLiP-Dependent Signaling Pathways (Stefan Rose-John/ Rama Khokha/ Paul Saftig)
- Structural Biology of iCLiPs and Sheddases (Charles Sanders/ Nicoleta Bonder/ Joanne Lemieux)
- Regulation of Ectodomain Shedding and RIP (Christian Haass)
- iCLiP and Shaddase Substrate Identification (Stefan Lichtenthaler/ Jim Wells /Stefan Lichtenthaler)
- iCLiP and Shaddase Modulators and Drug Discovery (Bart De-Strooper)
- iCLiPs and Shaddases in Infectious Diseases (Mike Glickman)
- iCLiPs and Shaddases: From Bench to Bedside (Patrick May)

XIVth International Symposium on Proteinases, **Inhibitors and Biological Control**

Portorož, Slovenia, September 6-10, 2014



Contact: boris.turk@ijs.si barbara.vrtacnik@ijs.si veronika.stoka@ijs.si









Post-Doctoral Fellow position Role of the proprotein convertases in cardiovascular and neurological diseases

Limited proteolysis of precursor proteins is one of the major mechanisms regulating the activation of various growth factors, receptors, polypeptide hormones, and infectious agents. The major processing enzymes found in the secretory pathway include the 9 proprotein convertases (basic amino acid specific PCs; 7 of them are known), SKI-1, as well as PCSK9. These enzymes are implicated in various pathologies including cancer, cardiovascular complications and viral infections. The Biochemical Neuroendocrinology Laboratory at the IRCM (Montreal, Canada) invites applications from qualified individuals wishing to pursue postdoctoral studies in an exciting program combining the fields of enzymology, protein chemistry, proteomics, molecular and cellular biology towards the elucidation of the ex vivo and in vivo functions of the above enzymes, with particular emphasis on PC7.

Post Doctoral Fellow to work on the cellular and *in vivo* functions of PC7 The applicant should not have more than 2-years post-doctoral training and be versed in the techniques of enzymology, cellular and molecular biology and immunocytochemistry

- Biosynthesis and cellular studies of PC7, its substrates and its mutants.
- Identification of new endogenous substrates by proteomics and array approaches in cells and knockout animals.
- Analysis of transgenic and knockout mice and their phenotypes
- Structure-function, domain definition.
- Development of cellular silencing techniques for the elimination of selected protein substrates.
- Kinetic analyses, combinatorial library screens and structural studies.

A postdoctoral stipend is available, especially for applicants interested in cardiovascular and neuropsychiatric conditions including anxiety and fear, which are regulated by PC7. The successful applicant will be encouraged to apply for a post-doctoral fellowship. Experience in molecular biology, cellular biology and trafficking analysis would be advantageous. Located in downtown Montreal, the IRCM features state-of-the-art research facilities and equipment.

Please submit a curriculum vitae, comprising your publication list (at least one publication in a high impact journal and another submitted) and three reference names and their coordinates to:

> Dr. Nabil G. Seidah, Director Laboratory of Biochemical Neuroendocrinology, IRCM, 110 Pine Ave, West Montreal, QC, H2W 1R7, Canada

Tel: (514) 987-5609 Email: seidahn@ircm.gc.ca; Website: http://www.ircm.gc.ca/seidah

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