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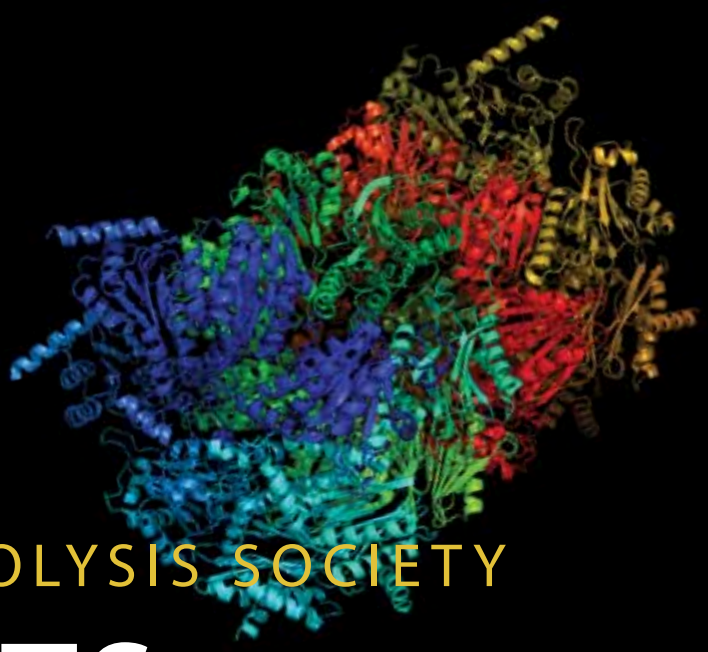
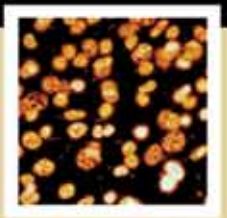
IN THIS ISSUE:



INTERNATIONAL PROTEOLYSIS SOCIETY

QUICKCUTS


THE PREMIER RESOURCE
FOR ALL YOUR IMPORTANT PROTEASE QUESTIONS

COUNCIL OF THE INTERNATIONAL PROTEOLYSIS SOCIETY

A Message From the President:

In October 2011, we had our 7th General Meeting of the Society in San Diego organized by Guy Salvesen, Matt Bogyo and their colleagues. I would like to thank Matt and Guy on the behalf of the Society for all the hard work it took to organize an excellent meeting and for the great hospitality. You can read more about it in the complete meeting report in this issue. At the Meeting we welcomed Chris Overall and Jim Powers among our Lifetime members, whose careers are outlined in the articles that follow. The meeting will be also highlighted in a special issue of Biological Chemistry, a journal that has a special relationship with our Society since many years.

The next General Meeting of the Society will be held near CapeTown in South Africa by Ed Sturrock and his colleagues. Mark October 20-24, 2013 in your calendar for this exciting meeting! You can read more about this meeting and others, such as the GRC Conference on Proteolytic Enzymes and Their Inhibitors on the following pages, as well as about the other protease related meetings in the near future, the first. In addition, you can find more information about the exciting articles from the proteolysis field that were published recently, as well as about some job adverts.

I would also like to formally welcome all our new Council members, whose names you can read on the left side. Just to remind you, there are four Council members representing your region with half of the Council being replaced every two years.

I hope you will find this issue enjoyable to read - we are excited that QuickCuts is back to life again. Please feel free to send feedback to me about the newsletter by emailing boris.turk@ijs.si. It is great to get ideas and suggestions from our members. Please remember that 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 of the IPS. See you all in Italy in June and for sure in October 2013 in South Africa.

Boris Turk - IPS President

Seventh General Meeting of the International Proteolysis Society

iPS2011 was held at a beach-side resort in San Diego, USA from October 16-20, 2011. Although it was unseasonably cold and cloudy, conference attendees were rewarded with exciting research talks and posters and lively and engaging scientific discussions. Pool and beach activities helped the over 350 participants from 23 countries unwind, while dinners on the beach provided a lovely backdrop to the stimulating conference organized by former IPS president, Matthew Bogyo, and Lifetime IPS member, Guy Salvesen.

Hilton San Diego Resort and Spa, San Diego, CA

The 7th general meeting was preceded by training workshops for students and postdocs to get practical training in "Protease Kinetics," "Structural Biology" and "Imaging." The meeting opened on Sunday evening with James Whisstock presenting elegant new data on the structure of plasminogen. Roger Tsien, recipient of the Nobel Prize in Chemistry in 2008, delivered the keynote address. He described protease-based imaging strategies that could aid surgeons in the important task of finding tumor margins.

The first session focused on the role of proteases in "Cancer and Cell Survival." Agnès Nobel presented some gorgeous microscopy data that shed light on the contribution of collagenases to cancer progression and lymphangiogenesis. Karen McLuskey reported the first crystal structure of a metacaspase, providing insight into their mechanism of substrate recognition and proteolysis. Oakley Olson, a graduate student in Johanna Joyce's lab, described how cathepsin inhibition during chemotherapy can enhance tumor cell death by reducing the function of protective macrophages. In a similar vein, Berta Cesar showed that proteolytic processing of CDCP1 enhances tumor survival, implicating CDCP1 as a potential target for developing therapies to prevent metastatic disease.

A second focus of the morning was on "Immunity and Host-Pathogen Interactions." Vishva Dixit of Genentech described the discovery of a non-canonical inflammasome activation pathway that signals through Caspase-11. He also showed that the widely used caspase-1 deficient mice are in fact knock-outs of both *caspase-1* and *caspase-11*. Aaron Puri, a graduate student in Matt Bogyo's lab, described the development of improved Caspase-1 activity-based probes (ABPs) that he has used to uncover cross-talk between pyroptotic and apoptotic cell death in infected macrophages. Continuing with the theme of proteases that regulate macrophage function during infection, Thomas Reinheckel presented his group's recent work implicating cathepsins in modulating macrophage activation in innate and adaptive responses to bacterial pathogens. Hans-Ulrich Demuth of ProBioDrug showed that inhibitors of glutaminyl cyclase, which regulates the stability of the chemokine MCP-1, reduce the pathology associated with proinflammatory diseases like colitis and atherosclerosis.

On the pathogen side of the interface, Renier van der Hoon described how protease inhibitors produced by plant pathogens have convergently evolved to inhibit defensive plant cysteine proteases. Jim McKerrow gave a thought-provoking talk on the evolution of cysteine and serine proteases from single celled organisms to vertebrates and showed how species-specific differences in proteases can be exploited to develop antiparisitic protease inhibitors. Aimee Shen described how ABPs can be used to study the allosteric activation mechanism of a protease conserved in bacterial toxins and how their cognate inhibitors can prevent toxin activity in cells.

During lunch, Ze'ev Ronai organized a workshop on "Targeting Ubiquitin-Proteasome Components." This was followed by the first poster session, which featured ~100 posters.

Michael Wolfe started the evening session on "Neurobiology and Degeneration" by describing how the lipid microenvironment modulates the proteolytic activities of γ-secretase. Mark Kindy showed that the Alzheimer's disease phenotype of cathepsin B and BACE1 knockout mice varies depending on the disease model used, a difference that arises from differences in their respective substrate specificities. Janko Kos examined the role of a different Cathepsin, CatX, in regulating inflammation-induced neurodegeneration through its proteolytic inactivation of γ-enolase, which normally enhances cell survival and neuritogenesis. Related to neuronal repair, Monica Driscoll described the non-apoptotic, regenerative roles for caspases in *C. elegans* during neural injury, which dually function in regulating cell death and cell survival. A similar role in protecting cells from death was revealed for Serpinb6 by Dion Kaiserman, a fellow in Phillip Bird's lab, who showed how this protease inhibitor can prevent hearing loss by protecting cells from aberrant proteolysis. Francois Jean revealed that novel S1P subtilase inhibitors can prevent SREBP cleavage by S1P to reduce lipid droplet biogenesis and stop HCV infection of hepatoma cells .

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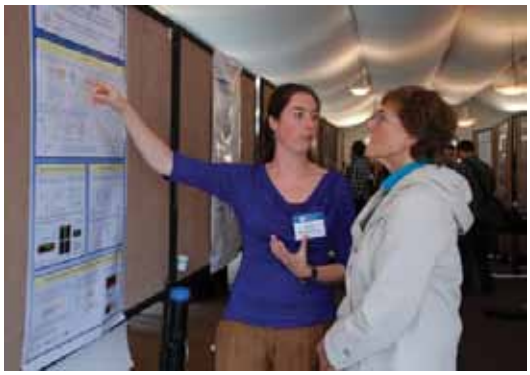
On Day 2, Sheena McGowan opened the morning session on "Mechanisms of Pathogenesis" by presenting the first structures of *Plasmodium falciparum* aminopeptidases alone and in complex with novel protease inhibitors. Alexander Wlodawer presented the structure of a previously uncharacterized aspartic protease from the XMRV virus, which has been associated with prostate cancer, alone and in complex with inhibitors. Jan Potempa described how a conserved C-terminal domain found in *Porphyromonas gingivalis* gingipains regulates their secretion and proteolytic activation by a novel secretion system, termed "Periogate." Wilhelmina Huston reported the recent identification of a novel activation mechanism for *Chlamydia trachomatis* DegP/HtrA protease, a key virulence factor, that is mediated by its chaperone function. Gilles Lamanach examined the role of Cathepsin S in modulating the antimicrobial activity of lung surfactant protein (SP-A) in cystic fibrosis.

The "Proteosome and Ubiquitin-like Modifiers" session was opened by Kenji Tanaka, who gave an overview of his work on immunoproteasomes and the recently described thymoproteasome, which may play a role in thymic selection. Craig Leach of Progenra described the development of novel proteasome inhibitors and assays that target deubiquitylases (DUBs). Continuing the discussion of DUBs, Oscar Huang of Genentech showed how DUBA activity is uniquely regulated by phosphorylation, while Margarete Heck revealed that the metalloprotease Invadolysin genetically interacts with a histone DUB to regulate chromatin modification in *Drosophila*. Yuushi Okumura of Hiroshi Kido's group reported on the effect of Type II transmembrane serine proteases MSPL and TMPRSS14 on avian flu virus infectivity, and Birgitta Tomkinson examined the endopeptidase activity and kinetics of the large tripeptidyl-peptidase (TPP II) subtilisin-like complex.



In Session 6, Ben Turk took us "Beyond the Active Site" by describing a novel screen for inhibitors that target the exosite of anthrax lethal factor. Continuing the theme of exosite-mediated inhibition of proteases, Weiru Wang of Genentech examined the structural basis by which a human antibody (anti-BACE1) inhibits β-secretase activity using an allosteric mechanism that affords high selectivity. Adam Renslo described the identification of novel caspase inhibitors that specifically recognize the enzyme-substrate complex and thus do not directly compete for the active site. Dmitriy Minond reported on the development of exosite-binding glycosylated substrates of ADAM proteases that may facilitate screening for ADAM inhibitors. Rob Pike described the identification of residues that form an exosite for complement component C4 that can also bind heparin. Gregg Fields examined the structural basis using NMR by which a select group of matrix metalloproteinases (MMPs) cleave the highly stable triple-helical regions of collagen.

Session 7 focused on "Therapeutic Strategies." Yoshiaki Kiso described the design and synthesis of novel classes of aspartic acid inhibitors that inhibit the β-secretase active site. Irit Sagi reported on the development of a novel immunization strategy that uses molecular mimicry of TIMPs to produce selective and inhibitory antibodies against metalloproteases. Olga Vasiljeva described the use of ferri-liposomes as an MRI-visible drug delivery system that target cysteine cathepsins in tumors and simultaneously allow drug distribution to be monitored. Evette Radisky showed how novel mesotrypsin inhibitors can prevent cancer growth and invasion, while Erik Lindstrom of Medivir described the characterization of a selective, orally active cathepsin K inhibitor that inhibits bone and cartilage resorption. Azza Eissa, a student in Eleftherios Diamandis lab, presented her work on the identification of kallikrenin-specific small molecule inhibitors through high-throughput screening that can block KLK activity in human epidermis.

In Session 9, the focus was on "Hunting for Substrates." Francis Impens, a postdoc with Kris Gevaert, described their progress developing methods for mapping new N- and C-termini, in particular for the elusive substrates of carboxypeptidases. He also reported the use of N-terminal COFRADIC to determine the substrate specificity of calpains in lung cells. Ding Xue described a novel strategy for identifying CED3 caspase substrates in *C. elegans* using a GFP-based genetic screen for suppressors of constitutively active CED3. Emily Crawford, a student in Jim Wells group, reported on their use of subtiligase N-terminal labeling enrichment to identify and compare caspase cleavages in human, mice, *Drosophila*, and *C. elegans*. Anna Prudova, a postdoc in Chris Overall's lab, described the use of TAILS, an N-terminal labeling strategy, to identify the in vivo substrates of cysteine cathespins in pancreatic cancer in collaboration with Johanna Joyce's group. Ulrich auf dem Keller showed how his group has used TAILS to identify proteolytic signatures in acute wound-healing.

A lunch workshop on "Publishing and FASEB Societies" was organized by Sharon Schendel of the Biochemical Journal and Judith Bond, President of FASEB. This was followed by the second poster session of IPS 2011.

From substrate discovery, we moved to "Drug/Probe discovery." Marcin Drag started off Session 9 reporting on the use of unnatural amino acids in combinatorial substrate libraries to identify better substrates for a variety of protease families. Anthony O'Donaghue, a postdoctoral fellow in Charles Craik's lab, described the development of a novel synthetic peptide

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library that can be used to profile the substrate specificity of many protease classes using LC-MS/MS. Oliver Voskya, a student in Steven Verhelst's lab, reported on the development of a MALDI-based screening method to identify new inhibitors and ABPs for rhomboid proteases, which have previously been refractory to high-throughput assays. Herman Overkleeft described the development of ABPs and inhibitors that target specific catalytic activities within the constitutive proteasome. Montse Morell, a postdoc in Matt Bogyo's lab, reported on a novel strategy for covalently labeling specific MMPs by engineering probe-sensitive MMP variants. Vincent Dive presented the crystal structures of MMP-12 in complex with novel inhibitors that reveal an unusual binding mode from previous structures.

On Day 5 of IPS2011, Jim Huntington opened the morning session on "Cardiovascular Disease and Homeostasis" by describing the structural basis by which thrombin is activated from a super-zymogen state and the re-zymogenized upon serpin binding. Ed Sturrock characterized the function of a familial point mutation in controlling the shedding and plasma levels of ACE, a blood pressure-regulating protease. Maria Arampatzidou, a student in Klaudia Brix's lab, described her work examining the role of secreted cathepsin B in regulating ECM turnover rates and maintaining intestinal homeostasis. Kai Kessenbrock, a postdoc in Zena Werb's lab, showed how MMP-3 regulates mammary stem cell activity by antagonizing Wnt signaling. Katsuya Hirasaka examined how the interaction between uncoupling protein 3 (UCP3) and thioredoxin 2 (Trx2) leads to Trx2 processing and modulates ROS production in mitochondria.

In Session 11, the focus was on "Proteolysis and Signaling." Hiroyuki Sorimachi described how proteolytic and non-proteolytic activites of calpain 3 regulates Ca2+-efflux and muscular dystrophy. Nabil Seidah elucidated the physiological functions of proprotein convertases via substrate identification. He also shared an important lesson that elevated expression levels of a protein in specific tissues do not necessarily reveal its role in disease. Matthew Freeman described how the pseudoprotease iRhom2 is required for TNFα-converting enzyme (TACE) activation and proposed that rhomboidlike membrane proteins may broadly regulate the fate of single-pass transmembrane proteins. Christoph Becker-Pauly reported on the use of proteomics to identify substrates of Meprin metalloproteases, such as ADAM10 (which in turn releases meprin β from the membrane). Bram van Raam, a postdoc in Guy Salvesen's lab, showed how RIP kinases are cleaved by caspase-6 in a caspase-8 independent manner during intrinsic apoptosis.

After a lunch workshop on "Approaches to the Development of Drugs in the Coagulation System," the last session focused on "Cancer and Metabolism." Klaudia Brix revealed how cell-type and tissue specific production of cysteine cathepsins modulates diverse processes ranging from tissue homeostasis to cancer. Sharon Stack described how kallekrein processing of cadherins may potentiate metastatic dissemination. Mark Gorell reported on how loss of the cell surface protease fibroblast activation protein (FAP) renders mice resistant to obesity and liver injury. Christian Ries described a novel form of proMMP-9 processing that produces an aberrant glycoform enriched in leukemic cells. Cindy Lim, a student in Xin Chen's lab, revealed that the amino-peptidase Slamdance plays a previously unappreciated role in establishing the stem cell niche in *Drosophila* testis. Galia Blum concluded the scientific meeting by describing the development of novel quenched activity-based probes that can be used for both non-invasive imaging and photo-dynamic therapy.

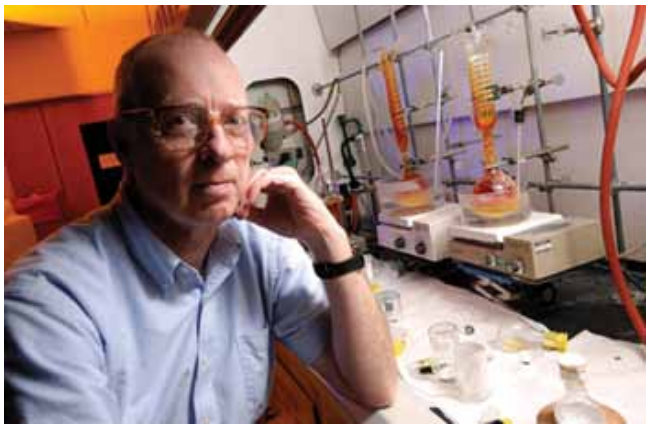
Amidst a lively atmosphere at the Awards banquet, the IPS celebrated the significant contributions to the protease community of the 2011 Lifetime Achievement Award recipients, Chris Overall and James Powers. The Herbert Tabor Young Investigator Award was awarded to Ulrich auf dem Keller, for his work on wound healing, and a number of student travel grants were awarded. Lastly, Ed Sturrock, the next IPS conference organizer, announced that Capetown, South Africa will be the future site os IPS2013. Overall, IPS2011 was distinguished by its outstanding talks, excellent posters, and open exchange of ideas and knowledge between members of our protease society.

Above: Matt Bogyo Ulrich auf dem Keller, Guy Salvesen, and Judith Bond. Left: Chris Overall and Jim Powers

James Powers – Insight through Inhibition

by Juliana Asgian, Vertex Pharamaceuticals

Talking about Dr. James Powers's accomplishments is an effortless task, because he had so many, but I will start with a short biography. He received his BS degree in chemistry from Wayne State University in 1959 and his PhD in organic chemistry from MIT in 1963. He began his teaching career at UCLA where he taught for four years. He became interested in enzymes and studied chymotrypsin, trypsin and elastase at the University of Washington in Seattle from 1967 to 1970. Then Dr. Powers joined the faculty of Georgia Institute of Technology in 1970 and is currently a Regents Professor Emeritus in the School of Chemistry and Biochemistry at Georgia Tech in Atlanta, GA. He was Georgia Tech's first biochemist.



For more than 40 years, Dr. Powers' research has focused on the design and synthesis of synthetic protease inhibitors, for use in treating diseases such as emphysema, arthritis, stroke, and peripheral neuropathy, among others. His persistent contributions to the field of proteases are unsurpassed.

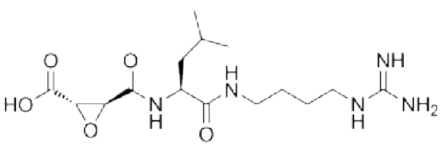
Dr. Powers synthesized his first protease inhibitor (para-nitrophenyl cyanate) in 1965 which resulted in a 1972 paper on the x-ray structure of carbamyl chymotrypsin. His research group was also responsible for synthesis of the first peptide chloromethyl ketone for a serine protease, the first specific inhibitor for neutrophil elastase in 1973. This inhibitor has been used by hundreds of other investigators, and for many years, was the reference compound for standardizing animal models of emphysema in testing drug candidates. His research also resulted in the development of peptide azapeptides as active site titrants for serine proteases, the discovery of peptide hydroxamates as specific inhibitors for metalloproteases, development of peptide thioesters as substrates for serine proteases, and the discovery of several classes of heterocyclic inhibitors for serine proteases including benzoxazinones and isocoumarins.

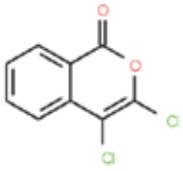
Dichloroisocoumarin (DCI) is probably the best synthetic inhibitor developed in the Powers laboratory and is a general inhibitor for most serine proteases. In addition, his research group has also developed peptide phosphonates as irreversible serine protease inhibitors, allyl sulfones as cysteine protease inhibitors, and alpha-ketoacids, esters, and amides as transition-state inhibitors for serine and cysteine proteases. Recently, he has worked on aza-peptide epoxides and aza-peptide Michael acceptors as irreversible inhibitors for cysteine protease such as caspases, legumain, gingipains and related enzymes. Over the years, Dr. Powers has provided samples of a variety of synthetic protease inhibitors to hundreds of other investigators.

Dr. Powers has published papers involving all the major classes of proteases and his research group has synthesized thousands of novel synthetic protease inhibitors and activity-based probes. He is the author of more than 200 research publications, and 35 book chapters and reviews. His research is heavily cited, as thousands of scientists follow his accomplishments, recognizing the value of his work as an idea generator. He has 37 patents with several still pending. He was the recipient of multiple awards during his career including the 1999 Distinguished Professor Award, Georgia Tech's highest academic honor. In 1980, together with James Travis, he started the Proteolytic Enzymes & Their Inhibitors section of the Gordon Research Conference. He is co-founder of a start-up biotech company, Axona, which is developing novel treatments for peripheral neuropathy.

An avid walker, experienced rock climber and mountaineer, he has led many student expeditions and backpacking trips through Outdoor Recreation Georgia Tech, a student-operated recreation program. A dedicated high pointer, he has climbed the highest peak in 49 states, leaving the highest point (Alaska) as a future challenge.

I think one of Dr. Powers major accomplishments is guiding so many students in their beginning years as future Scientists, including myself. He did this with great passion and a spirit of ethics and logic. A great innovator, research pioneer, and outstanding teacher, Jim has definitely been an inspiration to many!





Chris Overall – Research at the "Cutting" Edge

by Ulrich Aum dem Keller, ETH Zurich

Without a doubt, Chris Overall's research has always been at the forefront of his field, ever since he became interested in proteolysis after his move from Australia to Canada in 1985. As the first J.L. Eustace Scholar and an Associate Researcher with Jaro Sodek in the Department of Dentistry at the University of Toronto, Chris studied teeth and their adjacent surroundings, the gingiva. Since this tissue is particularly prone to collagen remodeling, his research very soon focused on the characterization of matrix metalloproteinases (MMPs), the protease family that still accompanies Chris in his stellar scientific career. More than twenty important publications arose from Chris's PhD thesis, and he made outstanding contributions to the understanding of the expression, mechanism and regulation of these important enzymes as crucial mediators of periodontal tissue remodeling.

In 1989 Chris moved to the University of British Columbia, Vancouver, where he first worked as an M.R.C. Centennial Fellow with the future Nobel laureate Michael Smith and then started his own laboratory as an Assistant Professor in 1992. While quickly moving up the career ladder to become an Associate Professor in 1994, and Full Professor in 2000, Chris's laboratory elucidated the sophisticated mechanisms of MMP activity in more and more detail. A particular focus was the function of the catalytically inactive C-terminal hemopexin domain in mediating substrate specificity. This knowledge together with Chris's exceptional ability to combine the development of new methods with their application to urgent biological questions led to the break-through discovery that MMPs specifically modulate chemokine activity by proteolytic processing published in Science in 2000. This finding pushed the whole field into a new direction and profoundly changed the view of how MMPs can regulate both inflammation and carcinogenesis. These insights came at a time of desperation and perplexity after myriads of MMP inhibitor cancer trials had failed. However, this crucial methodological approach, termed exosite scanning, was only the first of numerous technical inventions conceived by Chris to facilitate new discoveries in the protease field. For these contributions, Chris was named Canada Research Chair in Metalloproteinase Proteomics and Systems Biology in 2001.

When the human genome sequence became available - opening up what we might call the era of 'omics' and systems biology - Chris was again at the cutting edge and among the first to bring and extend these emerging concepts to the protease world. By coining the term 'degradomics' and extending it to a novel framework for protease research in a landmark Nature Review with Carlos Lopez-Otin in 2002, Chris laid the foundation for a new field in proteolysis research.

Thanks to the significant contributions of his laboratory, we are closer than ever to what might have sounded like an utopian vision: the description of all proteases that are expressed at a given time in a cell, tissue or organism (the protease degradome) and their substrate repertoires (substrate degradome). This became possible through the development of a whole array of systems biology technologies: the CLIP-CHIP™ cDNA microarray for the analysis of proteolysis related genes; Proteome-derived, database-searchable peptide libraries for identifying protease cleavage sites (PICS) for the comprehensive characterization of protease cleavage specificities; and Terminal Amine Isotopic Labeling of Substrates (TAILS) for the system-wide discovery of physiological protease substrates in complex proteomes. Once again, by bringing these approaches to the protease community, Chris was one of the pioneers in revolutionizing how proteases are studied and extended our understanding of proteases from blunt tissue bulldozers to precise signaling scissors.

Impressively, apart from his outstanding science Chris still finds time to share incredible travel experiences with his two sons, to grill a salmon for his team on Keats Island or to take it up to Cypress Mountain for skiing with an awesome view of the English Bay. Overall, we are tremendously lucky to have Chris in our community of protease researchers as a fellow scientist, a great mentor and a good friend.

IMPORTANT PROTEASE PAPERS I

Research Publications

PROTEOMICS

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Proteomic identification of protease cleavage sites characterizes prime and non-prime specificity of cysteine cathepsins B, L, and S.

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Nucleic Acids Res. 2012 40:D351-61.

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Nat Methods. 2011 8:703-4.

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System-Wide Proteomic Identification of Protease Cleavage Products by Terminal Amine Isotopic Labeling of Substrates.

Nat Protoc. 2011 6:1578-1611.

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Factor Xa Subsite Mapping by Proteome-Derived Peptide Libraries Improved Using WebPICS, a Resource for Proteomic Identification of Cleavage Sites.

Biol Chem. 2011 392:1031-7.

Hardt, M, Lam D, Dolan J, Schmidt B.

Surveying Proteolytic Processes in Human Cancer Microenvironments by Microdialysis and Activity-Based Mass Spectrometry.

Proteomics Clin Appl. 2011. 5: 636–643

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Mol Cell Proteomics. 2011 10(9):M111.009233.

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The Structural Basis for Matrix Metalloproteinase 1 Catalyzed Collagenolysis.

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

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Activation of legumain involves proteolytic and conformational events, resulting in a context- and substrate-dependent activity profile

Acta Crystallogr F. 2012. 68:24-31

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Angew. Chem. Int. Ed. 2012. 51: in press.

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Structural evidence for standard-mechanism inhibition in metallopeptidases from a complex poised to re-synthesize a peptide bond.

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Cell. 2012. 148: 727–738.

Li M, Gustchina A, Matúz K, Tözsér J, Namwong S, Goldfarb NE, Dunn BM, Wlodawer A.

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FEBS J., 2011. 278:4413-4424

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BBA - Proteins and Proteomics, 2012, 1824:207-223

Huang OW, Ma X, Yin J, Flinders J, Maurer T, Kayagaki N, Phung Q, Bosanac I, Arnott D, Dixit VM, Hymowitz SG, Starovasnik MA, Cochran AG.

Phosphorylation-dependent activity of the deubiquitinase DUBA.

Nat Struct Mol Biol. 2012. 19:171-5

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The X-ray Crystal Structure of Full-length Human Plasminogen.

Cell Reports. 2012. March 8.

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Alkyne derivatives of isocoumarins as clickable activity-based probes for serine proteases

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

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Bioorg Med Chem Lett. 2012. 22:916-9.

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Hydroxyureas as noncovalent proteasome inhibitors.

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Exploiting nature's rich source of proteasome inhibitors as starting points in drug development.

Chem Commun. 2012. 48:1364-78

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Tumor necrosis factor signaling requires iRhom2 to promote trafficking and activation of TACE.

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PROTEASE POT POURRI

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IMPORTANT PROTEASE PAPERS IV

Research Publications

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IMPORTANT PROTEASE PAPERS V

REVIEWS

The January 2012 Issue of Biochimica et Biophysica Acta (BBA) - Proteins and Proteomics "Proteolysis 50 years after the Discovery of the Lysosome," edited by Vito Turk, features 24 review articles.

http://www.sciencedirect.com/science/journal/15709639/1824/1

The majority of these are from IPS members, a few of which are highlighted below:

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Cysteine cathepsins: From structure, function and regulation to new frontiers.

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BOOKS

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Proteinases as Drug Targets.

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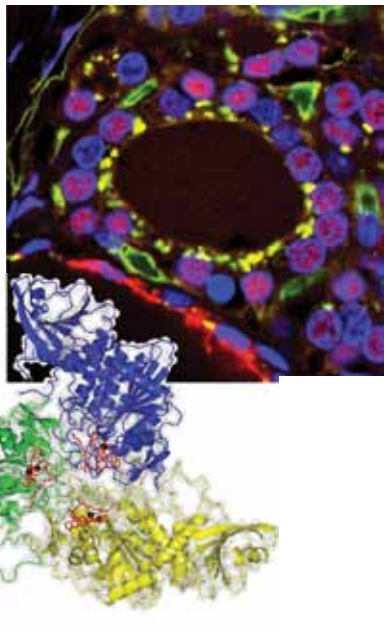

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Proteases as Drug Targets
Proteases and Pathogenesis
Proteases and Inhibitors
- Speakers: To be selected from submitted abstracts
- Keynote Speakers:
  Johanna Joyce: "Cathepsin proteases at the cutting edge of cancer"
- Mentorship Component:
  "A Small World", a career panel showcasing international training and career development

k.brix@jacobs-university.de
sheena.mcgowan@monash.edu

GRC 2012, Klaudia Brix (Chair) & James Whisstock (Vice Chair), preliminary program
http://www.grc.org/programs.aspx?year=2012&program=protenz

- The Active Site of Proteases
  Klaudia Brix // Wolfram Bode / Antonio Baici / Guy S. Salvesen / Bonnie F. Sloane
- Animal Models for Studies on Proteolysis
  Christoph Peters // Annik Prat / Agnès Noel / Margarete M. S. Heck / John W. M. Creemers / Stephanie Dauth / N.N. / N.N.
- Networking in Proteolysis From Molecules to Complex Systems
  Walter Stöcker // James C. Whisstock / Christopher M. Overall / Irit Sagi / N.N.
- Proteolysis in Signaling Events
  Nabil G. Seidah / Judith Clements // Matthew Freeman / Sin Urban / Rob Pike / N.N.
- Proteases in Infectious and Tropical Diseases
  James McKerrow / Sheena McGowan // Doron C. Greenbaum / Jan Potempa / Aimee Shen / N.N.
- Proteases in Wound Healing, Metastasis, Fibrotic Diseases
  Bonnie F. Sloane / Thomas Reinheckel // Dieter Brömme / Johanna Joyce / Daniel H. Madsen / Mark Gorrell / Boris Turk
- Protease Inhibitors and Their Biological Significance
  F. Xavier Aviles / Henning Stennicke // F. Xavier Gomis-Rüth / James A. Huntington / Daniel Lawrence
- Proteases and Inhibitors in Translational Approaches
  Bob Lazarus / Hans-Ulrich Demuth // Matthew S. Bogyo / Christopher Scott / Galia Blum / N.N. / N.N.
- Perspectives in Proteolysis
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