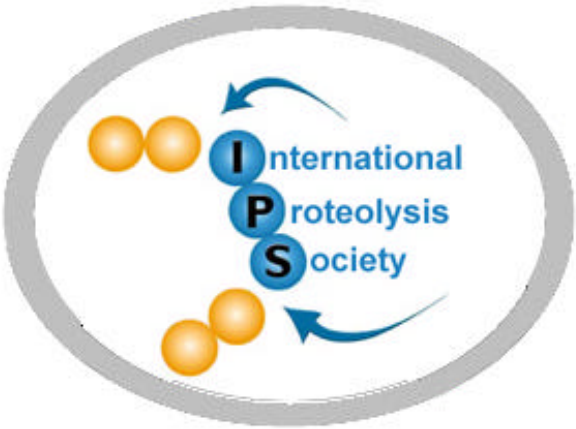
Quick Cuts



International Proteolysis Society Newsletter

QC2 - April 2002

- articles about the 2nd IPS meeting, postgraduate workshops, and honorary IPS members (Nobuhiko Katunuma and Hans Fritz)
- information about publication of papers from the IPS meeting
- list of protease meetings and Keystone meeting report
- information about the 3rd IPS meeting to be held in Nagoya, Japan
- obituary - John Jeffrey
- job advertisement

Reports from the 2nd IPS meeting

The 2nd General Meeting of the International Proteolysis Society was held October 31st - November 4th, 2001.

The 2nd General Meeting of the IPS, held in conjunction with the International Conference on Proteinase Inhibitors (ICPI), took place in the Bavarian town of Freising between 31st October and 4th November 2001. Despite taking place so soon after the terrible events of September 11th, over 430 scientists from 31 countries – senior researchers and doctoral students, academics and industrial scientists, chemists, biologists and physicians – converged on Freising for five days of intense proteolytic activity.

The location proved a stroke of genius – near enough to Munich to allow short excursions into the Bavarian capital, yet only a short ride to the airport – as long as one didn't get a taxi that went via the other Marriott hotel situated in downtown Munich! The town of Freising, with its open marketplace to which participants inevitably gravitated and its variety of cafes, bars and restaurants, was highly conducive to informal contacts. For the most part, the weather played along too, with the autumn sun complementing the medieval architecture.

For those accustomed to Hans-Fritz-organised-meetings, the packed program will have come as no surprise. A total of 109 lectures packed into 12 3½ hour sessions may have seemed a daunting prospect. Yet the lectures were well attended, and were often followed by lively debate. Time keeping was essential, and various methods were resorted to in order to keep the speakers within their limits – including one chair demanding a beer for every minute overtime (a win-win situation for him at least).

The sheer scope of the meeting precludes a comprehensive description of the presentations. The twelve sessions, organised along functional lines (table 1), included two novel topics – 'Plant Proteinases/Inhibitors' and 'Proteinases in the Postgenomic Era'. Coming late after dinner on the second evening, the plant session was less well attended than it should have been, which was a shame – interesting insights were given into the complex interrelationships in the repertoire of proteolytic enzymes and inhibitors developed by plants and insects in order to outwit each other – a case of 'you are what you eat'.

The final session, devoted to implications of the draft genome, highlighted some of the problems facing the search for new proteinases and inhibitors linked to pathological situations. In this context, the report that limited cathepsin D proteolysis of fibronectin generates novel 'cryptic proteinase' fragments resulted in considerable discussion, suggesting that a wide range of undiscovered proteolytic activities may still be waiting to be found. Bridging the gap between the biochemical and the physiological aspects of proteolysis remained a *leitmotif* of the meeting, and new strategies for the design of chemical entities to test proteinase substrate specificities and inhibition profiles were presented.

Table 1. The 12 sessions of the Meeting

Membrane-associated Proteinases/Proteolysis	Novel Biological Functions and Structure-Function Relationships
Processing and Degradation	Wound Healing, Tissue Remodeling, Angiogenesis
Pathogen Invasion and Host Defense	Tumor Invasion and Metastasis
Plant Proteinases/Inhibitors	Design and Medical Application of Inhibitors
Development, Differentiation, Apoptosis	Drug Discovery and New Technologies
Degeneration in the Nervous System	Proteases in the "Postgenomic" Era

The level of presentation was excellent, and special praise must go to Christian Sommerhoff for managing the technical aspects so professionally – often a stumbling block at meetings in the electronic era. Many made use of the new possibilities provided by computer presentations, culminating in the spectacular animation of the anthrax lethal factor structure. Not to be forgotten are the 214 posters that were presented – and if I have one criticism to make of the meeting, it is a lack of 'quality viewing time' – after a complete day of talks, the bar is much more welcoming than the poster room!

The meeting finished with a Bavarian evening, complete with alpine bell ringers and fire buglers. But the evening was multicultural – being banished to the 'young people's room' (thanks, Marianne), the author found himself at the Swedish table, where the game of 'bästa bordet' (=best table) was unveiled to an unsuspecting proteolytic community. Briefly, a 'volunteer' is persuaded to sit on the table, and the table is lifted into the air. Attempts to persuade the new IPS President to 'volunteer' failed miserably, however, but maybe next time. Finally, the Japanese choir prepared the ground for the next IPS meeting in Nagano, for which we wish them every success. In the meantime, thanks go to the Munich organisers (Hans Fritz, Marianne Jochum, Wolfram Bode and Christian Sommerhoff) and their assistants for the excellent time (scientific and otherwise) in Freising.

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Kinetics postgraduate course

Prior to the 2nd International Proteolysis Congress two post graduate courses on Kinetics and Crystallography were arranged. The two of us attended the kinetic course taught by the eminent kineticists, Professor Werner Machleidt (LMU, Munich, Germany), Professor Christian Sommerhoff (LMU, Munich, Germany) and Professor Guy Salvesen (Burnham Institute, La Jolla, USA).

We gathered in front of the Department of Clinical Chemistry and Clinical Biochemistry at the Ludwig-Maximilians-Univesität, Munich. We were treated to lunch and coffee and afterwards Christian held a lecture about the secrets of protein chemistry. Christian talked about the basics of peptidase and inhibitor kinetics, substrate kinetics, Km and kcat as well as different instrumental approaches for performing kinetic experiments. Werner held a lecture in pre-steady state kinetics with reversible and irreversible inhibitors and finally Guy informed us about the practical work to come. The point was to let us participants work *"in vivo"* with kinetics and feel the rate constants and Ki values *in our hands*.

After the theoretical lectures we were split in to two groups. One group went to Werner's laboratory to do pre-steady state kinetics and the other stayed in Christians laboratory to do inhibitor/substrate kinetics.

Werner gave us four different enzymes and an inhibitor and we were to determine which inhibitor we were working with. We had to start with a titration to determine the inhibitor concentration and furthermore decide if the inhibition was reversible or not. With the excellent instructions of Werner and his wife (Dr Irmgard Assfalg-Machleidt) we were all very successful and could easily conclude that we were working with the irreversible inhibitor E64. Guy and Christian took care of steady-state kinetics dealing with substrate competition and reversible inhibitors. We were again divided in two to groups where Christian's teams worked with tryptases and Guy's team worked with caspases.

Completely exhausted after the first long and intense day, a *real* Bavarian dinner was served for us in a true Bavarian atmosphere. This was a fine getting-to-know-people arrangement and the Weiss bier was very tasty. At the tables people discussed seriously the mysteries of kinetics. It didn't seem as difficult as first anticipated and as the hours went on and the bier became even more tasty the kinetics became crystal clear.

The next day the groups switched teachers. After another intense day we thanked our teachers, their families, and the technicians properly and went off to the conference in Freising, all happy and looking forward to understanding *everything* about kinetics during the lectures the following days.

However, this was not the end of the story. The last day of the conference our three musketeers arranged an "after-conference" session for those of us who hadn't understood everything. For 2 hours we analysed the results we had obtained some days earlier. We were given the opportunity to ask all the stupid questions we did not dare to ask during the lectures and we were given a "flow scheme" titled "Kinetics for dummies".

Again the discussion about slow binders and tight binders was taken up as well as the importance of spending money on substrates. This conclusion tied the course together.

The idea of postgraduate courses before international meetings is a good one for several reasons: it gives a great opportunity to make friends before and during the meeting, it gives a chance to engage specialists in the field plus you have the chance to freshen up your skills in an important and complex field. The hands-on concept of the course was a good introduction and motivation to this complicated area. Additionally it took place in a very good atmosphere among all the graduate students and other course participants.

Bjarne Vincents
Carl-Michael Nathanson
Department of Clinical Chemistry, Lund University, Sweden

Crystallisation/ structure analysis postgraduate course

Our group arrived at the Max Planck Institute for Biochemistry outside of Munich on the morning before the 2001 IPS meeting was to begin. We were greeted outside by Dr. Wolfram Bode, whose frantically motioning arms signalled immediately that we were both welcome, and late. The course began with a general overview of crystallography given by Manuel Than. The presentation was quite helpful as it lay the groundwork for the path that the course was to take.

Following this we were shown some of the equipment used in crystal preparation and analysis. Then the hands-on session began. We were given proteinase K samples and buffer preparations with which we set up crystal trials. We were cautioned that we were starting at an unfair advantage; protein preparation can often be one of the most laborious tasks of any crystallographer.

That evening we were treated to a delightful Bavarian dinner in downtown Munich. Dr. Bode made several suggestions about food and beer . . . err I mean, beverage, selections. This was a great meal as it allowed us to get to know the other students in the course in a relaxed setting. These would be people with whom we would continuously interact for the duration of the conference.

The following morning our group returned to the Max Planck where we were given another informative lecture by Klaus Maskos. We got hands-on experience in fishing out crystals, freezing them in liquid nitrogen and mounting them for diffraction. We were then taken to view the diffraction patterns created from some of the better crystals that had been formed from our trials set up the previous day. Once again, a word of caution: it usually is not so easy! Following this, we were taken to the computer lab where various crystallographers helped us to view and manipulate some of the structures that they were currently working on.

This course was excellent as it allowed us to get a feeling for various stages of crystallography; from trials to data analysis. For most of us, it was a first exposure to the “art” of crystallography and we came to appreciate the study of structural biology. This course also allowed us to make contacts with the researchers at the Max Planck Institute, as well as other attendees of the IPS meeting.

Kelly Boatright
Hwain Shin
The Burnham Institute/University of California, San Diego

IPS Honorary Membership

Awards of Honorary IPS membership were made to Nohubiko Katunuma (Tokushima, Japan) and Hans Fritz (Munich, Germany).

Professor Nobuhiko Katunuma

Professor Nobuhiko Katunuma is one of the pioneers in the broad spectrum of proteolysis. Nobuhiko – his friends call him Nobo – has contributed tremendously to developing our understanding of intracellular proteolysis in general, and lysosomal cysteine proteinases and their natural protein and synthetic inhibitors in particular. Last year, Nobo celebrated his 75th birthday. He remains a simple man with unbelievable energy, a great sense of humour and high motivation for his research. Simply, Nobuhiko Katunuma is a great personality with a strong character, and a respected scientist.

Nobuhiko graduated from School of Medicine at Nagoya University. After completing his PhD thesis in medical sciences, he worked as a postdoc with Professor Hugo Theorell at the Nobel Institute in Stockholm. In 1959 he was appointed Assistant Professor at the Institute for Protein Research, Osaka University. In 1963 he moved to his favourite place Tokushima, where he started his highly successful scientific career as Professor of School of Medicine at Tokushima University. Later he served as Dean and from 1982 until 1992 he was also Director of the Institute for Enzyme Research at the same University. During this period of nearly thirty years at the Tokushima University he studied the enzymes involved in vitamin B-6 metabolism. His discovery of mitochondrial glutamic-oxalacetic transaminase, studies on regulation of the urea cycle, and on glutaminase isozymes and their role in carcinogenesis in liver cells, all constitute important contributions to biochemistry. Important too were his studies on the metabolism of pyridoxal enzymes and their limited proteolysis by serine proteases under *in vivo* conditions. Nobuhiko and co-workers found the acceleration of protein turnover rates of pyridoxal enzymes in vitamin B-6 deficient animals, and discovered the protease which inactivates the apo-proteins of these pyridoxal enzymes by limited proteolysis. He suggested that apo-protein formation is an initial step in the degradation of these enzymes *in vitro* and *in vivo*. He has many more publications to his credit, involving characterization of serine proteases.

I first met Nobuhiko in Reinhardsbrunn in Germany, in the late seventies, when we both attended the International Conference of Intracellular Protein Catabolism, organized by colleagues from Halle. I was impressed by his energy and boundless interest for proteinases and their inhibitors. He showed a profound interest in lysosomal cysteine proteinases and their endogenous inhibitors. We both immediately established personal contact, which later turned into fruitful collaboration – also competition, let us say "friendly competition" as Nobo likes to call it. Indeed our two groups worked on the same proteins from different species, his on rat and mine on human. Professor Katunuma's early studies of cathepsins B and L, the first primary structures of rat cathepsin B and H, the role of lysosomal enzymes in intracellular proteolysis and the development of cysteine proteases inhibitor derivatives of E-64 are all well known. Simultaneously Nobuhiko established broad international collaborations, including a personal friendship with Professor Helmut Holzer in Freiburg, where some of his students worked as postdocs.

At the meeting in Tokushima in 1982, which Nobuhiko organized together with the well known Professor Hamao Umezawa, he presented for the first time a partial sequence of rat cystatin. I was fortunate to have been invited to this meeting and, listening to his lecture, I found that our studies on endogenous protein inhibitors, cystatins and stefins, were confirmed by his independent findings. From this time on, our laboratories established a collaboration which resulted in more than 10 publications and is still very active. Nobuhiko has regularly attended the Brdo meetings on proteolysis in Slovenia from 1987 when the meetings started. Collaboration between him, our group and Drs. Wolfram Bode and Robert Huber resulted in the first crystal structure of cathepsin B.

In 1992 Nobuhiko retired, although still full of energy, intellectual power and ideas. He therefore embarked on his second career, now as Professor and Director of the Institute for Health Sciences, Tokushima Bunri University – again in Tokushima. From 1999 he has been President of the whole University. Although heavily involved in administrative duties, he was able, due to his personality, to establish a new, laboratory with an active group of young researchers, among whom Nobuhiko is always very happy to be working. In this new position his participation was crucial to the development of new cysteine protease inhibitors, derivatives of E-64 and the CLIK inhibitors. He has published many other studies on the roles of trypsin-type and chymotrypsin-type proteases, the role of cysteine proteases in bone resorption and their possible therapeutic use as drugs for different pathological states.

Nobuhiko's scientific interest has been connected mostly to medical and biomedical research. He was always an enthusiastic supporter of young students and always gave them credit for their successful work and achievement. Talking to him is always an exciting and intellectually stimulating experience, as he is continually coming up with new ideas. For these reasons, Nobuhiko has collected around him many brilliant students who became internationally recognized scientists, such as Drs. Ishikawa, Kido, Kominami, Kuroda, Matsuda, Saheki, Tsuboji and others.

The several hundred publications published over the years have earned him the highest distinctions as, for example, the "National Violet Ribbon Decoration for Scientists and Artists" and the "Second Degree National Medal", both from Empera, not to mention many other international awards.

Outside science Nobuhiko has many interests, including music, mountains and sword fencing or 'kendo'. I have known him for years as a kendo fanatic and many scientists have enjoyed his excellent performances during the international conferences that he organized. He boasts the high seventh master degree in kendo. In Slovenia, he particularly likes the Venetian port of Piran on the Adriatic coast, where we both enjoy the pleasant atmosphere, the blue sea and his favourite seafood, scampi.

Nobuhiko has many friends around the world who, I am convinced, wish him on-going success in his research and many, many more years of exuberant life.

Vito Turk, Ljubljana

HANS FRITZ: A life devoted to proteinases and their inhibitors

Born in 1935 in a small town in the Bavarian Swabien, Hans' childhood was much influenced by the close contact to nature, by the neighbourhood to mountains, and – last not least – by the discovery of penicillin by Fleming, what directed him to study chemistry at the Technical University of Munich (TUM). During his Ph.D. thesis (1961 – 1963), where he worked on peptide synthesis, Hans first got in contact with proteins. Wholeheartedly devoted to Southern Bavaria by his Alpine hobbies montaineering, climbing and skiing, he in 1963 did not follow the advice of his Ph.D. supervisor, Friedrich Weygand, to start a career in one of the big German chemical companies, but joined Eugen Werle in his Munich Institute for Clinical Chemistry and Clinical Biochemistry at the Ludwig-Maximilians-University (LMU). Werle´s Institute already had a long tradition in proteinase and proteinase inhibitor research, with a strong focus on the kallikrein-kinin system, which had been discovered in 1925 and extensively described by E.K. Frey, H. Kraut and E. Werle (see: Das Kallikrein-Kinin-System und seine Inhibitoren. Ferdinand Enke-Verlag, Stuttgart 1968).

At the beginning, Hans focussed his research on natural protein proteinase inhibitors. Together with his students and coworkers, Hans found, described and isolated a number of inhibitory proteins in human and animal tissues and secretions such as pancreas, submandibular and sex glands, sea anemonaes, snails and medical leeches. Without any conditions, he provided many colleagues with these proteins, setting up fruitful worldwide collaborations and friendships. His major achievement at that time was the introduction of affinity chromatography for the rapid and simple isolation of inhibitors and subsequently also of proteinases. In 1970, Hans, together with Harald Tschesche (whom he had inspired also to work on proteinase inhibitors), organized the "International Research Conference on Proteinase Inhibitors" in Munich, his first international proteinase meeting, which was attended by the 27 scientists representing the inhibitor community at that time, including Robert Huber, Jim Travis, Michael Laskowskis Jr. and Sr. (for the lectures, see the Proceedings of the International Research Conference on Proteinase Inhibitors, Munich, November 4-6, 1970. H. Fritz, H. Tschesche (eds.). Walter de Gruyter, Berlin-New York 1971). Shortly thereafter, Hans, together with colleagues, organized the 2nd "International Conference on Proteinase Inhibitors" (with a number of remarkable lectures referenced in: Proteinase Inhibitors, Proceedings of the 2nd International Research Conference - Bayer Symposium V, held at Grosse Ledder near Cologne, FRG, October 16-20, 1973; H. Fritz, H. Tschesche, L.J. Greene, E. Truscheit (eds.) Springer-Verlag Berlin-Heidelberg-NewYork 1974), which was attended this time by 51 noted scientists, reflecting the rapid increase of interest in proteinase inhibitors. Both inhibitor conferences initiated long term contacts and collaborations between colleagues worldwide such as Alan Barrett, Joseph Bieth, Robert Huber (joined later by Wolfram Bode), Michael Laskowski Jr., Clarence Ryan, Elliot Shaw and Jim Travis.

Until the late 80s, Hans Fritz concentrated primarily on the biochemistry, structure, occurrence, function, pharmacological behaviour and therapeutic potential of proteinase inhibitors, among them the Pancreatic Secretary Trypsin Inhibitor from man and from other species, the Dog Submandibular gland Inhibitor, HUSI-I/SLPI/MPI (a PMN elastase inhibitor) and HUSI-II (an acrosin inhibitor) from human seminal plasma; the trypsin/plasmin/acrosin inhibitors from pigs and guinea pigs; hirudin (a thrombin inhibitor), the bdellins (trypsin/plasmin/acrosin inhibitors) and eglin c (a PMN elastase inhibitor) from medicinal leeches; and the trypsin-plasmin-kallikrein inhibitor aprotinin (also known as BPTI) from bovine mast cells as well as aprotinin homologues from sea anemonae, snails and as part of the inter-α-trypsin inhibitor.

Remaining in the tradition of Eugen Werle, Hans Fritz focussed his research also on components of the kallikrein-kinin system, especially on tissue-kallikreins and their natural substrates, the kininogens: isolation and characterisation of t-kallikreins from human and animal sources, their cellular localization, and elucidation (in collaboration with H. Tschesche and W. Bode) of their primary and tertiary structure; identification of the α_1-proteinase inhibitor as a progressive t-kallikrein inhibitor, investigation of biochemical and pharmacological aspects of the therapeutic t-kallikrein administration in humans to improve fertility by increasing the sperm number and motility, and to stimulate glucose uptake and thus energy metabolism in muscles. Hans and his team also extensively studied the participation of t-kallikrein and of plasma kallikrein in inflammatory reactions via excessive kinin liberation or kininogen consumption, and of therapeutically administered aprotinin in experimental models and in clinical studies to block kallikrein.

In a search for target proteinases of the seminal plasma inhibitors, Hans´ team (at that time including doctoral student Wolf-Dieter Schleuning) identified and isolated acrosin from boar and human spermatozoa, which they characterized biochemically, structurally and functionally and identified as a kinin-liberating enzyme. They showed that the sperm-induced zona pellucida dissolution of the ovum and thus fertilization *in vitro* could be prevented by synthetic acrosin inhibitors, and proved the presence of all components of the kallikrein-kinin system in seminal plasma and the involvement of kinins in sperm motility and migration.

In 1974, Hans Fritz became Professor for Clinical Chemistry at the Medical Faculty of LMU, in 1977 he was appointed head of the newly established Department for Clinical Chemistry and Clinical Biochemistry at the Surgery Clinic at the LMU, and in 1978 he became independent Associate Professor, with full responsibility for future-directed teaching and research and for an experimental animal station and the clinical chemistry routine laboratory. Therefore, besides doing his own research, Hans had to increasingly take care of running clinical chemistry courses for medical students, for organising and setting up new laboratory facilities, for integrating the surgeons in the research activities of the Department, for organizing the Munich collaborative research center/SonderForschungsBereich (SFB51) of the German Research Foundation/Deutsche ForschungsGemeinschaft as vice-chair and chairman (1977-82), and – last not least – for orchestrating the Munich proteinase/inhibitor research in the SFB207 “Basic aspects and clinical significance of extracellular limited proteolysis” (1983-1996). In these SFBs, the projects are peer-reviewed every 3 years, requiring tremendous efforts of the chairman and his crew to organize research collaborations and to direct research.

Due to this growing organisational engagement, research had to be done more and more by Hans’ coworkers, whom he supported in every respect. He had hired a number of creative and highly motivated colleagues, who had complete freedom to persue their own research. Among them, Edwin Fink, responsible for the routine laboratory work of the Clinic, studied from 1967 onwards functional aspects of the kallikrein-kinin system, the structure, function and genomic organization of Kazal-type inhibitors (PSTI, HUSI-II, bdellin and bdellastasin), and more recently the involvement of metalloproteinases in cancer cell invasion. Werner Müller-Esterl, starting in 1975 as a medical student and continuing in 1979 as full time researcher, became engaged in the structural determination of the sperm acrosin and of the multidomain and multifunctional kininogens, which soon became his favourite molecules to study structure-function relationships on the protein level, and in the elucidation of their genomic organization. Werner became interested in epitope mapping with highy specific anti-peptide antibodies, what eventually made him interested in the kinin receptors, which became his major research projects when he in 1989 became Chair of the Institute for Pathobiochemistry at the Johannes-Gutenberg University in Mainz.

Marianne Jochum joined Hans in 1978 to establish intensive collaborations with clinicians, primarily with surgeons and anesthesiologists, in Munich and other German clinics. She became especially engaged in the elucidation of pathomechanisms in severe inflammatory conditions such as polytrauma and ARDS, multiple organ failure and SIRS, sepsis and peritonitis, and developed a number of clinical assays (e.g. a PMN elastase-α_1PI ELISA) for inflammatory mediators derived from cells, tissues and humoral systems, and made new therapeutic approaches and clinical studies towards the application of proteinase inhibitors and antioxidants. In 1991, Marianne Jochum became Professor for Pathobiochemistry; since 1997

she has lead the newly founded SFB 469 "Induction and inhibition of proteolysis-induced processes in inflammation and cancer" in Munich, and in 2001 she was appointed head of the Department when Hans Fritz retired.

In 1987, Ennes Auerswald introduced the cloning techniques, which he had learnt at the Bayer Company, to the Department. Besides the preparation of several aprotinin-type inhibitors, kininogen domains, and leech-derived proteinase inhibitors such as antistasin, bdellastasin and the leech-derived tryptase inhibitor (LDTI), Ennes designed and expressed a number of bifunctional protein inhibitors and cystatin mutants with distinct preferences for papain-like cathepsins and for calpain, elucidated their structure-function relationships in collaboration with his colleagues at the SFBs 207 and 469, in particular Werner Machleidt (kinetics) and Wolfram Bode (tertiary structures), and cloned, expressed and characterized (in close collaboration with W. Machleidt) μ-calpain.

In 1989, Christian Sommerhoff, a Research Fellow from the Cardiovascular Institute at the University of California at San Francisco, joined the Department. Christian focussed his research on mast cell tryptases and leech-derived tryptase (LDTI) and kallikrein (hirustasin) inhibitors, primarily on their function (e.g. in keratinocyte proliferation) and pathological (e.g. tryptase in psoriasis) or therapeutic (synthetic and natural inhibitors in cell and animal models) potential. Structural studies, based on the successful yeast expression of various tryptase species and made in collaboration with Wolfram Bode, revealed that human β-tryptase is a cage-like tetramer, with the active centers directed to the inner pore, restricting access to very small protein inhibitors (such as LDTI) and to a small number of protein substrates. More recently, the structural basis of the apparent inactivity of the α-tryptase was elucidated. Based on these structures, currently highly potent synthetic tryptase inhibitors are being developed within the SFB 469 research network (in particular together with Luis Moroder). In 2001, Christian became C3-Professor for Clinical Biochemistry.

In 1987, the veterinary doctor Heinz-Peter Scheuber joined the Department as a coworker and official "animal protection" representative of the LMU. Under his guidance, a modern animal station was established, which offered coworkers and surgical colleagues excellent conditions for experimental animal studies. These facilities allowed, e.g., the surgeon Matthias Siebeck to study pathomechanisms in severe inflammatory conditions and to develop new therapeutic approaches with proteinase inhibitors, antioxidants and kinin and PAF receptor antagonists.

Due to the Department's interdisciplinary research including chemistry, biology and medicine, Hans Fritz invited several colleagues from all over the world to spend some time in Munich, and attracted a number of their students for training in special techniques, sent e.g. from Ljubljana (Vito Turk), Sao Paulo (Claudio Sampaio) or Habana (Maria Chavez). Utilising his excellent contacts to colleagues in the Munich area, Hans was also particularly able to mediate contacts to other research institutions working inside but also outside of the SFB networks. The Department's output in diploma, dissertation and habilitation theses was thus high. Many colleagues from abroad interested in the basic and applied research going on in the Department or in collaborating SFB-projects (e.g. Claudio Sampaio, Eric Whalley, John Cheronis, Vito Turk, Jim Travis, Kanti Bhoola, Koichi Suzuki, Domenico Regoli, John Stewart) stayed for some time to do experimental work there, to plan common projects or to discuss topics of mutual interest.

Particularly noteworthy is Hans Fritz´ permanent engagement in the organization of numerous international meetings, both as chief or as co-organizer. Besides the aforementioned Proteinase Inhibitor meetings in 1970 and 1973, he cared for the KININ Conferences in Munich (1981, 1991, 2000), Guarujá/Brazil (1993), Denver/USA (1995), Durban/South Africa (1997), Nara/Japan (1999), and for a special KININ meeting in Munich in 1988, where he in addition introduced the E.K. Frey/E.Werle Foundation of the Henning L. Voigt Family, becoming also head of the board. This Foundation became a major sponsor for all of these KININ Conferences, and awarded the E.K.Frey/E. Werle Commemorative gold Medal for important life-long contributions to kinin research and the Promotion Prizes for more recent outstanding research work. Hans was also co-organizer of the BRDO Conferences on "Proteinase Inhibitors and Biological Control" established in 1987 by Vito Turk in BRDO near Ljubljana/Slovenia (reviewed e.g. in Biological Chemistry Hoppe-Seyler. Vol 369 (Suppl.), May 1988), which take place periodically since that time. Another periodically organized series of meetings on proteinases and inhibitors with a long tradition were the Conferences on Intracellular Protein Catobolism orginally established in the former German Democratic Republic by Hanson and Aurich. As a longtime member of the International Committee on Proteolysis (ICOP), Hans in October 1990, i.e. shortly after the German reunification, organized a memorable ICOP conference in Wildbad-Kreuth near Munich, where for the first time also extracellular proteolysis became a major topic. Hans was one of the leading scientists transforming ICOP into the International Proteolysis Society (IPS), and it was also because of Hans' engagement that the 2nd General Meeting of the (IPS), in association with the International Conference on Protease Inhibitors (ICPI), could be held in Freising near Munich in November 2001, again with Hans as a co-chair.

Hans had his deepest devotions to the "Winter Schools on Proteinases and their Inhibitors - Recent Developments", originally established together with Vito Turk in 1981 aimed at training German and Slovenian students in the English presentation and discussion of their results to be held alternatively in Slovenia or Germany. Since about 1990, this school occured with always a few international colleagues present early every year in Tiers/Southern Tyrol, located in the scenic Dolomite Alps in front of the majestic Rosegarden. These Winter Schools offer a unique opportunity for undergraduate and postgraduate students as well as junior scientists to present their ideas and projects in a relaxed atmosphere and to discuss them with leading experts in the field, often leading to valuable new collaborations and friendships.

All in all, Hans enjoys a highly successful past, as author or co-author of more then 420 publications in peer-reviewed journals and meeting reports, co/editor of 16 congress proceeding volumes, reviewer for various journals, and executive editor of Biological Chemistry. He received two major awards for his scientific work and is proud to be Associate Member of the Josef Stefan Institute in Ljubljana since 1985. He still keeps close contacts to the Department and his colleagues in Munich, Martinsried and abroad. We hope that he will continue to keep the proteinase-and-inhibitor community alive, but we wish him also now enough free time for his hobbies mountaineering and skiing, and for his granddaughters, relatives and many friends throughout the world.

Wolfram Bode, Martinsried, April 12, 2002

Publication of papers from the IPS meeting

Papers from the 2nd IPS meeting will be published in two IPS highlight issues of Biological Chemistry in the next few months. Thanks to Hans Fritz (Munich) for co-ordinating this.

Proteolysis meetings 2002/03

3rd International Symposium on Serpin Biology, Structure and Function
Chicago, IL, USA
June 2-5, 2002
Organizers: Peter Gettins, Philip Patston, and Steve Olson

Gordon Conference on Proteolytic Enzymes and Their Inhibitors
Colby-Sawyer College, New Hampshire, USA
July 7-12, 2002
Organizers: Jim McKerrow (Chair), Nancy Thornberry (Vice-chair)

16th International Congress of the International Society for Fibrinolysis and Proteolysis
Munich, Germany
September 8-13, 2002
Organizer: Manfred Schmitt

3rd International Conference on Cysteine Proteinases and their Inhibitors
Portoroz, Slovenia
September 14-18, 2002
Organizer: Vito Turk

We plan to discuss biochemical and structural aspects of cysteine proteases and their inhibitors, their functional characteristics and mechanisms of action. We will cover topics including the role of cysteine proteases and their inhibitors in apoptosis, tumour growth and progression, antigen presentation, genetic disorders of these molecules, plant defence system, insects and parasites, viral

and bacterial diseases. Any presentations discussing new ideas and perspectives in our field are encouraged.

Our aim is to have about 35 lectures, of which some will be short presentations, and a poster session with sufficient time for discussions of results presented. We can accept up to 130 active participants. Those of you under the age of 30 will be charged a reduced fee. At the moment, we expect the regular registration fee to be about 500 EUR (450 USD) and the reduced fee about 380 EUR (350 USD). The fee will cover accommodation in an international 3*+ hotel on a shared room, full board basis. Juniors will be accommodated in a 3* hotel only a few steps away. Transportation from/to Ljubljana airport or railway station will be provided free of charge.

The venue of the conference is Histrion Hotel, located 10 min walk from both the medieval town of Piran (to the north) and the town of Portoroz (to the south), which is the major tourist resort on the Slovenian Adriatic coast.

Registration forms are available from the conference homepage or from the organisers by E-mail, fax or air-mail. The deadline for registration and abstract submission will be June 30, 2002.

Updated information will be available on the conference homepage at the address
http://bio.ijs.si/conf/p2002.html

To contact the organisers by E-mail, please send inquiries to: P2002@ijs.si. Boris Turk and myself are the persons behind this contact address. If you feel you have to contact the principal organiser, Professor Vito Turk, you can reach him by E-mail at Vito.Turk@ijs.si. Of course you can also send fax inquiries - the number is +386 1 257 3594. Full addresses and phone numbers of the organisers are available from the conference homepage. Do not hesitate to get in touch with us for any additional information. We will contact you again (*unless you want to be removed from the list – see above*) in mid-April to keep you up to date with news about the Portoroz conference.

With best regards, Marko Dolinar (for the organisers)

Proteases, Extracellular Matrix and Cancer, American Association for Cancer Research Special Conference in Cancer Research, Hilton Head Island, South Carolina, USA
October 9-13
Organizers: Yves deClerck and Ruth Muschel

Amererican Association for Cancer Research conference on Proteases, Extracellular Matrix and Cancer
October, 2002.
Website address http://www.aacr.org/4311z.asp

Two symposia at the Annual Biochemical Society Symposium
London, UK December 16-18, 2002
"Proteases and the Regulation of Biological Processes" (3 days) in Honour of Alan Barrett. Organizers: J Saklatvala, Hideaki Nagase, and Guy Salvesen
"Proteasome interactions with viral and cellular proteins" (1 day)
Organizers: Jennifer Rivett and Martin Allday

Vth International proteasome Workshop, Clermont-Ferrand, France, April 27-29, 2003
Organisers: Yves Briand < Yves.BRIAND@univ-bpclermont.fr> and Didier Attaix

Please send details/ contacts/ web addresses of future meetings.

Keystone Symposium on Proteolytic Enzymes as Therapeutic Targets

The 2002 Keystone Symposium on Proteolytic Enzymes as Therapeutic Targets was held Feb. 3-8 in Keystone, Colorado, under the leadership of Robert Heinrikson and Jan Potempa. Sessions included an opening address by Charles Esmon on the regulation of blood doagulation pathways; protease targets in Alzheimer's Disease (AD); a workshop on aspartyl proteases and approaches to AD therapy; the ups and downs of proteinase inhibitor-based therapy of viral infections; caspases as therapeutic targets; a workshop on cysteine, serine, and metalloproteases; secreted protease in cancer; exopeptidases; targeting bacterial and parasitic proteases; and selected aspects of intracellular proteolysis.

Highlights included Dennis Selkoe's discussion of the presenilins and their role in the cell biology of Amyloid Precursor Processing, Alex Loukas's discussion of proteases from hookworms, Peter Dragovich's presentation on new inhibitors of the rhinovirus 3C
protease and their promise for treatment of the common cold and Nancy Thornberry's overview of the caspase field. Also of note later in the week: Lynn Matrisian gave an excellent discussion on the role of proteases in cancer metastasis, Bonnie Sloane showed beautiful pictures of cell surface proteases, Brian Matthew presented a discussion of methionine aminopeptidases, and Hans-Ulrich DeMuth contributed an analysis of the
role of inhibition of DPIV on glucose metabolism, The week took a decidedly dark turn when Michael Curtis scared everyone with pictures of *porphyromonas gingivalis*, Michael James told a harrowing tale of the experiment that just made it in time, Jim McKerrow
presented a chilling discussion of parasites that use proteases in their attack on humans. The week concluded on a high note as Wolfgang Baumeister discussed the 26S proteasome, Wolfram Bode gave an excellent presentation on the relationship between a number of enzymes, and Ed Madison discussed the role of transmembrane proteases in cancer. In addition, a number of short presentations were included. All of these added to the quality of the conference proceedings.

The weather was spectacular, the company was congenial, the discussion was lively, and the science on a very high level.

Ben Dunn, Florida

3rd International Proteolysis Society meeting

The next IPS general meeting will be held in Nagoya, Japan in November 2003. The chairman of the organizing committee is Professor Shigehiko Mizutani in Nagoya University. See flyer circulated with QC2 for more details.

Obituary - John Jeffrey

John Jeffrey, my scientific mentor, passed away of a stroke on November 24, 2001. He was 64 years old. John was a pioneer in matrix metalloproteinase biology and the following briefly encapsulates his contributions to the field and to the scientific development of others whom he touched.

John was born in Worcester, Massachusetts on May 3, 1937. He attended Classical High School in Worcester and graduated from College of the Holy Cross. John obtained his Ph.D. from Georgetown University in Biochemisty, the degree awarded with "distinction". He then became a Research Fellow in the laboratory of Jerome Gross at Harvard. John was in this laboratory with Charles LaPierre at the time of the breakthrough discovery that launched the matrix metalloproteinase field – the finding that explants of tadpole tail (as part of metamorphosis) degraded a collagen matrix – and the demonstration of the first vertebrate collagenase.

In 1967, John left Harvard to join Arthur Eisen at Washington University School of Medicine to build a scientific unit in Dermatology. Under John's and Arthur's stewardship, this enterprise would become a world recognized center of matrix metalloproteinase biology. In the ensuing two decades, John would direct or participate in the scientific training of many individuals who would become leaders at this and other institutions – George Stricklin, Tom Koob, Gene Bauer, Jouni Uitto, Bob Mecham, Bernadette Tyree, Mark Udey, Bill Parks, Jo Seltzer, and myself. He would rise through the ranks of the institution, becoming a Full Professor in the Department of Medicine, and one of its few tenured PhD's.

John was recruited to Albany Medical College in 1991 as a Professor of Medicine and Biochemistry. Respect for his scientific talent was rapidly recognized and in 1996 he was named Chairman of the Department of Biochemistry. Despite these administrative responsibilities, John continued in his two favorite roles – publishing original science and the training of pre-doctoral and post-doctoral students. While in Albany, 11 such individuals received their training in John's laboratory.

John's contributions to science were prodigious. He authored 130 original scientific articles. Most of these were in highly prestigious journals, including 20 in the *Journal of Biological Chemistry*. John's biological instincts were inspiring. His favorite system to study was post-partum uterine involution, the subject of an RO-1 grant for which John received continuous funding for 31 years and a Merit Award without ever altering a single word of the grant's title ("Hormonal Regulation of Collagenase in the Uterus"). John often pointed out that post-partum uterine involution represents the single most massive physiologic resorptive process in the animal. Among his scientific achievements were defining and characterizing the collagenase (collagenase-3, MMP-13) responsible for postpartum uterine involution in rodents, identifying the roles of relaxin, serotonin, and the estrogen/progesterone axis in collagen degradation accompanying this process, and providing the first in-depth kinetic analysis of mammalian collagenase action.

In the words of Bill Parks, John's life in science was "inspirational". In the words of another colleague, Connie Brinckerhoff, John was "such a very nice man". Indeed, John taught many of us as much about life as about science. For John, science was the study of life but not the entirety of life itself. He freely advised that the amount of work one does should be proportional to the amount one celebrates life. John is survived by his wife of 29 years, Ann, and by the many individuals whom he touched. Rest in peace, my friend and mentor.

Howard G. Welgus, M.D.
Executive Director, Inflammation Discovery Research
Pfizer Global R&D
Ann Arbor, Michigan

Post-Doctoral positions

Post-Doctoral positions available in Metalloproteinase Degradomics, Department of Biochemistry and Molecular biology, University of British Columbia.

Two 3-year post-doctoral positions are now open funded by the Protein Engineering Networks of Centres of Excellence, Canada. Start date is negotiable, but the positions are available immediately. The projects entail genetic and proteomic screening for novel metalloproteinase substrates (eg see Science 2000, 289, 1202-1206) by yeast 2-hybrid, novel exosite scanning, and ICDC techniques. Mass spectroscopic experience is not required. For further information check our web site: www.clip.ubc.ca, or contact Prof Christopher Overall at chris.overall@ubc.ca, +1 (604) 822-2958.

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COMING IN FUTURE ISSUES

- Highlights - Recently published/ in press articles of interest to the proteolysis field.
- Meeting reports

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Your newsletter

Please send any information for *Quick Cuts* by email to Jennifer Rivett <j.rivett@bristol.ac.uk>. Anticipated circulation of QC3, September 2002.

The International Proteolysis Society web site is http://www.protease.org.