International Society for Matrix Biology Newsletter

No. 4 - Aug 2006

Contents

From the President's Desk

ISMB at the Crossroads

It is a great honour to be voted in as the new president of ISMB. I look forward to working with the new Council comprising

Monique Aumailley, Cologne, Germany
Leena Bruckner-Tuderman, Freiburg, Germany
Jamie Fitzgerald, Portland OR, USA
Johanna Myllyharju, Oulu, Finland
Dieter Reinhardt, Montreal, Canada
Florence Ruggiero, Lyon, France
Lynn Sakai, Portland OR, USA
Klaus von der Mark, Erlangen, Germany
John Bateman, Melbourne, Australia.

Many thanks to the outgoing President John Bateman and Council Ruth Chiquet-Ehrismann, Benoit de Crombrugghe, Dick Heinegård, Martin Humphries, Renato Iozzo, Gerard Karsenty, Mats Paulsson, Taina Pihlajaniemi, Lydia Sorokin, Jouni Uitto, Michel van der Rest, Zena Werb, Kenneth Yamada and Peter Yurchenco for their valuable contributions

In fact Renato Iozzo does not really leave the Council as he is now the newly elected Vice-President of ISMB and as you may see we have promptly redrafted John Bateman back in the council. And of course we continue to have the valuable help of our super ever patient Secretary Peter Bruckner, who keeps us on our toes with his soul searching (see his comments in this issue - Personal Views section).

As I begin the presidency I realise that ISMB is at a critical stage in its development. One issue that was discussed a lot at Council was the future of ISMB, its role and its direction. Since ISMB was established some time ago we have seen changes in the field and in the international community of matrix biologists. For some time now awareness of the important role of the matrix in biological processes has become increasingly apparent. The matrix is no longer a mixture of macromolecules acting as "structural fillers" supporting cells in tissues. Matrix biology has long become more than the biochemical isolation and structural characterization of extracellular matrix (ECM) molecules. Rather the ECM has now clearly important roles instructive in development, growth and disease states for mediating and regulating availability of growth factors and morphogens, cell-matrix interactions. Nowadays publications on the functional and biological roles of the ECM appear in a wide range of journals serving different disciplines – clinical sciences, cell, molecular and developmental biology, cancer biology, neurobiology and so on. Societies for these fields often spring up to serve the scientific community. Often these societies' major role is in organizing regular conferences. In matrix biology there are several strong

and active national societies in different regions – such as in Europe, North America, Japan, Australia.

So the question arises about the need for ISMB and its role. In recent years our membership has not been growing and has in fact been declining (i.e. paid up members). So is ISMB a superfluous Society? Are many matrix biologists aware of the ISMB and what it can do? I strongly feel that ISMB does have a role to play internationally and that there is a need to develop a new vision/role for ISMB that is separate from that of the national societies. So I think the time has come to start a dialogue about increasing the relevance of ISMB to the matrix biologist by expanding the ISMB network across the world, developing its roles in facilitating interactions and collaborations across continents. It would be important to strengthen the role of ISMB in helping the careers of young matrix biologists through awards like the Rupert Timpl prize, travel grants to attend FECTS, ASMB meetings. And if we can increase the membership and raise some additional resources we can also envisage more awards and perhaps have short term training fellowships of 2-3 months for young scientists. ISMB could also help to sponsor attendance of young people from outside Asia Pacific region at the Pan Pacific Connective Tissue Societies meeting. These are just some ideas to start with.

But our ambitions to support these and other schemes will not be possible with the level of membership and financial situation. For example we will soon run out of money to support our current activities, the Rupert Timpl award and the travel bursaries to attend FECTS and ASMB meetings. We certainly don't have the resources to launch new schemes or fund bursaries to attend other meetings such as the forthcoming Pan Pacific Connective Tissue Societies meeting. While it's a key asset to have Matrix Biology as the ISMB official journal, we need more than that. So I am writing to ask for your support and help in working together helping to revitalise ISMB, perhaps raising some funds from industry- perhaps for a new award or different schemes to support the career development of our young researchers as well as promoting the field. First action that will help is joining ISMB if you haven't already done so and if you haven't paid your dues please do so! It is an easy step if you pay by credit card on-line (visit http://ismb.uni-muenster.de/PayMembFee.php for instructions). Please help recruit new members. And of course most important, regardless of whether you are a member or not, letting us know your views and ideas. I would like to recommend that this Newsletter become a forum for these discussions and Jamie Fitzgerald and Dieter Reinhardt are looking forward to hearing from you.

Best wishes

Kathy Cheah
President, ISMB

Meeting Announcements

American Society for Matrix Biology Biennial Meeting

To be held in Nashville, Tennessee from November 1st-4th, 2006. Meeting website: http://www.asmb.net/nationalmeeting/.

30th Annual meeting of the Matrix Biology Society of Australia and New Zealand.

To be held as part of the Australian Health and Medical Research Congress (from Nov 26th-Dec1st, 2006) MBANZ program is on November 27th and 28th. Details of program, registration and abstract submission can be found at: http://www.ahmrcongress.org.au/

Stem Cell Manchester meeting

The latest research and translation to clinical applications promoting a vigorous academic, clinical and commercial dialogue.
University of Manchester, UK
July 16th-18th, 2007
Organised by Tim Hardingham
Contact Sarah Farrar (sarah.farrar@manchester.ac.uk)

Gordon Research Conference on Collagen

To be held at Colby Sawyer College in New London, NH, July 22th-27th, 2007.
Chair: David E. Birk, Ph.D.
Vice Chair: Leena Bruckner-Tuderman, M.D., Ph.D.

Message from the organizers:
It is time to think about the program for this Conference. We would like to solicit your suggestions for session topics, including potential speakers, that you consider timely, important and, perhaps, neglected in recent conferences. This would help us in planning a conference that will be cover the current frontiers and most important recent developments in matrix biology. Please respond by email to: david.birk@jefferson.edu.

We value your input. Suggestions received in the near future will be those most useful in defining the session topics and assembling a preliminary program. The preliminary program will be posted on the GRC website and we welcome your input at any time leading up to the conference in July 2007. We look forward to hearing from you and seeing you in July 2007.

XIIIth International Symposium on Basement Membranes and Collagen IV Symposium in Honor of Klaus Kuhn

Center for Biochemistry, Medical Faculty, University of Cologne, Germany
September 19th-22nd, 2007
Email: bm-2007@uni-koeln.de
Website: http://www.BM2007.uni-koeln.de (under construction)

XXIst meeting of the Federation of European Connective Tissue Societies
To be held in Marseille, France
July 9th-13th, 2008
Chair: Phillippe Charpiot
philippe.charpiot@pharmacie.univ-mrs.fr
Vice-chair: Sylvie Ricard-Blum
s.ricard-blum@ibcp.fr

Rupert Timpl Award winner 2006

Elizabeth Canty (Wellcome Trust Centre for Cell-Matrix Research, University of Manchester) was selected by ISMB Council as the Rupert Timpl Award winner for 2006. Here she pictured with John Bateman (Past-President of ISMB) after her plenary presentation as the 2006 Rupert Timpl Laureate at the FECTS-ISMB meeting in Oulu.

The Rupert Timpl Award is made biannually by ISMB to a young scientist active in the field of matrix biology who has published the best paper during the preceding two years. Elizabeth was selected from a field of strong candidates for her paper published with Drs. Lu, Meadows, Shaw, Holmes and Kadler entitled "*Coalignment of plasma membrane channels and protrusions (fibripositors) specifies the parallelism of tendon"* published in Journal of Cell Biology, Vol. 165: pp 553-563 (2004).

This study used elegant three-dimensional reconstructions of EM images of the tendon cells to shed new light on the important question of how collagen fibrils are organized by cells into architecturally-precise networks. Elizabeth's paper was featured in "From the Editor's desk" Matrix Biology 23, 23-73 (2004).

Personal Views

Dear ISMB-member,

This is your secretary / treasurer calling. You know, this anonymous bureaucrat and rather ill-behaved individual who sends you reminders that it is about time that you finally pay your small obolus to ISMB. At last I can now contribute something more constructive and more interesting. We decided at the last FECTS / ISMB-meeting in Oulu to launch a campaign in the ISMB-Newsletter, called "Personal Views", for people to voice their opinions about ISMB. I offered to make the first contribution as part of a new drive to improve the spirit of ISMB and hopefully this letter may be provocative enough to trigger responses and promote discussion about the future of our society.

Let me start with the history of ISMB: When I took over from Michel van der Rest a number of years ago ISMB had more than 400 members and, at first glance, it seemed like a vigorous society. However, many members were inactive already for years, e.g. by not renewing their memberships. Since then, the membership steadily declined and currently we have 167 paying members. Then, I eliminated the names from my files of those who never responded for several years to my, initially very friendly, reminders. In this way, I have reduced the number of entries from more than 400 to 321, or roughly double the number of people who currently consider our society worth EUR 20,00 per year (This is what comes to ISMB - Elsevier gets the remainder of your membership fee for personal subscriptions to Matrix Biology). However, a rather large fraction of formerly active members apparently considers ISMB no longer necessary. And they certainly have a point in this. If I do not outright agree with them.

Maybe, my memories are playing tricks on me. But I think that ISMB was called into existence because the matrix community lacked an international organization. It was deemed necessary for securing good grants and to improve the reputation of the field such that our papers make it into the best journals.

May I speculate about some of the major objectives of the founders of ISMB? I don't want to be comprehensive. Rather, I'd like to pick a few points.

1). Before ISMB was born, Europe and Japan had FECTS, the Federation of European Connective Tissue Societies, which was not really a society but a loose organisation with a single activity: To organise a large meeting every other year. In part, the initiators of FECTS probably had in mind to create a counterbalance to the Collagen Gordon Conference which, in the meantime, has been so successful in generating "metastases" or, as you may rather think of them, spin-offs. In their spirit, FECTS-meetings were strongly Euro-centric and, thus, were not very suitable for the

ISMB manifesto of uniting matrix biologists of all nations. Also, scientific excellence was not necessarily the very prime objective. Instead, it was felt that young colleagues needed a special forum for communication without excessive peer pressure. However, more recent FECTS-meetings have morphed into truly international meetings of rather high scientific standard and have tried to bring together all matrix biologists. Curiously, some may say, the meetings more than ever attract especially young people and the quality of their contributions also seems on the rise. Although FECTS has yet to become a society (or a federation in a true sense), one of the goals of ISMB has largely been met.

2). And what about the other side of the big pond, the Atlantic? The US matrix biology scene knew the informal East-coast, West-coast, Mid-West...Connective Tissue Meetings, but no society dedicatedly promoting the interests of matrix biology as a field. We all know that North America now has ASMB which - Congratulations to our American colleagues! - has become the leading society in the field. We all wish for you (and, by implication, for all of us) that ASMB may prosper and become an ever stronger lobby for matrix biology. But, from the point of view of ISMB, one may say that there goes another reason for the society !

3). Together with the publisher, we owned the journal 'Matrix Biology'. The importance of that journal is rising steadily, mainly due to the merits of Bjorn Olsen, the editor-in-chief. ISMB, on the other hand, failed to meet the stipulations of the contract with Elsevier. The number of institutional subscriptions has not risen to the expectations of our strong financial partner. So, our contract will soon be terminated and ISMB will no longer be a beneficiary of Matrix Biology in the way Elsevier is. Nevertheless, Elsevier, as a commercial outfit, still has an interest in the label "Official Journal of the International Society for Matrix Biology". Should we consider this a success of ISMB?

4). The Rupert-Timpl-Award has been installed. Dear ISMB-member, did you know about this? If not, please, visit http://www.ismb.org. I have been administrating this award. There were 10 nominations of outstanding publications and the award went to a very worthy winner (see previous section). However, it was disappointing that these nominations came from just three ISMB-members which would disappoint this outstanding matrix biologist who gave the name. This award is given by a truly international society to young colleagues developing their careers. And, isn't this one of the important duties of us, the more experienced comrades in the struggle? Can I hope to obtain suggestions from more ISMB members in about one and a half years time?

5). Travel awards have been advertised by ISMB to the FECTS / ISMB-meeting in Oulu. But very few applications were received, did the message fail to reach potential beneficiaries? I can only speculate.

So, what is the conclusion? Let's be honest. Some missions have been achieved! And the others were unrealistic in the first place! Shall we disband ISMB !?

If we do not shape up, I'd rather answer with YES. I would prefer to be the secretary / treasurer of a society which actually has a purpose. Do you see one? Is it worth it? Whether you agree or disagree put pen to paper and write the next "Personal Views"! It is actually a bit of fun and merrily contrasting from our other writing experiences.

One final thought. Elsevier cares about institutional subscriptions to Matrix Biology and not at all about personal subscriptions. Besides, many ISMB-members do not bother to access their personal account of the journal on-line. So, why pay for this? If ISMB continues to exist or even to flourish, all of this should make us rethink our policy of compulsory personal subscriptions. It still should be offered to interested members, such as myself, with no easy access to the journal. At least in the past, Elsevier kept this option open. However, if we abandon the obligatory personal subscription, we could moderately raise the membership fee from a current EUR 20.00 to pay for such things as the Timpl-Award or the travel bursaries. A better investment? If we do not increase our income while keeping up our expenditures we shall be broke in a few years. So, would this be a viable idea? And could we decide on this in a written ballot rather than at the next General Assembly.

Tell Jamie and Dieter in your contribution for the next Newsletter!

Best wishes to you and your laboratory.

Peter Bruckner

Matrix Research Update

In Press Publications

Structural requirements for heparin/heparin sulfate binding to type V collagen
S. Richard-Blum, M. Beraud, Raynal, N., Farndale, R.W., Ruggerio, F.
The Journal of Biological Chemistry

Collagen-proteoglycan interactions participate in the regulation of matrix assembly and in cell-matrix interactions. We reported previously that a fragment (I824-P950) of the collagen a1(V) chain, HepV, binds to heparin via a cluster of three major basic residues R912, R918, R921 and two additional residues, K905 and R909 (Delacoux et al., 2000 J. Biol. Chem. 275: 29377-82). Here, we further characterized the binding of HepV and collagen V to heparin and heparan sulfate by surface plasmon resonance assays. HepV bound to heparin and

heparan sulfate with a similar affinity (KD ~ 18 and 36 nM respectively) in a cation-dependent manner and 2-O-sulfation of heparin was shown to be crucial for the binding. An octasaccharide of heparin and a decasaccharide of heparan sulfate were required for HepV binding. Studies with HepV mutants showed that the same basic residues were involved in the binding to heparin, to heparan sulfate and to the cell surface. The contribution of K905 and R909 was found to be significant. The triple-helical peptide GPC(GPP)5G904-R918(GPP)5GPC-NH2 and native collagen V molecules formed much more stable complexes with heparin than HepV and collagen V bound to heparin/heparan sulfate with a higher affinity (in the nanomolar range) than HepV. Heat and chemical denaturation strongly decreased the binding, indicating that the triple helix plays a major role in stabilizing the interaction with heparin. Collagen V and HepV may play different roles in cell-matrix interactions and in matrix assembly or remodeling mediated by their specific interactions with heparan sulfate.

Localisation of extracellular matrix receptors on the chondrocyte primary cilium

S. R. McGlashan, C. G. Jensen, C. A. Poole
Journal of Histochemistry and. Cytochemistry

A single primary cilium is found in chondrocytes and other connective tissue cells. We have previously shown that extracellular matrix (ECM) macromolecules such as collagen fibers closely associate with chondrocyte primary cilia, and their points of contact are characterised by electron-opaque plaques, suggesting a direct link between the ECM and the cilium. This study examines the expression of receptors for ECM molecules on chondrocyte primary cilia. Embryonic chick sterna were fluorescently labelled with antibodies against α and β integrins, NG2, CD44 and annexin V. Primary cilia were labelled using acetylated α-tubulin antibody. Expression of ECM receptors was examined on chondrocyte plasma membranes and their primary cilia using immunofluorescence and confocal microscopy. All receptors examined showed a punctate distribution on the plasma membrane. α2, α3 and β1-integrins and NG2 were also present on primary cilia, whereas annexin V and CD44 were excluded. The number of receptor-positive cilia varied from 8/50 for NG2 to 43/50 for β1-integrin. This is the first study to demonstrate the expression of integrins and NG2 on chondrocyte primary cilia. The data strongly suggest that chondrocyte primary cilia have the necessary machinery to act as mechanosensors, linking the ECM to cytoplasmic organelles responsible for matrix production and secretion.

Collagen XVI harbors an integrin α1β1 recognition site in its C-terminal domains

J. A. Elbe, A. Kassner, S, Niland, M. Morgelin, J, Grifka, S. Grassel
The Journal of Biological Chemistry

Collagen XVI is tissue-dependently integrated into distinct fibrillar aggregates, such as D-banded cartilage fibrils and fibrillin-1 containing microfibrils. In skin, distribution of collagen XVI overlaps that of the collagen-binding integrins, α1β1 and α2β1. Basal layer keratinocytes express integrin α2β1, whereas integrin α1β1 occurs in smooth muscle cells surrounding blood vessels, in hair follicles, and on adipocytes. Cells bearing the integrins α1β1 and α2β1 attach and spread on recombinant collagen XVI. Furthermore, collagen XVI induces the recruitment of these integrins into focal adhesion plaques, a principal step in integrin signaling. Of potential physiological relevance, these integrin-collagen XVI interactions may connect cells with specialized fibrils, thus contributing to the organization of fibrillar and cellular components within connective tissues. In cell-free binding assays, collagen XVI is more avidly bound by α1β1 integrin than by α2β1 integrin. Both integrins interact with collagen XVI via the A-domain of their α-subunits. A tryptic collagen XVI fragment comprising the collagenous domains 1-3 is recognized by α1β1 integrin. Electron microscopy of complexes of α1β1 integrin with this tryptic collagen XVI fragment or with full-length collagen XVI revealed a unique α1β1 integrin binding site within collagen XVI located close towards its C-terminal end.

Job Advertisements

Post-doctoral Position in Matrix Biology

University of Washington
Department: Orthopaedics & Sports Medicine
Location: Seattle, WA, USA
Start Date: Immediately

An NIH-funded post-doctoral position for research on the biochemistry/molecular biology of extracellular matrix. Our focus is on understanding mechanisms of collagen assembly in different skeletal tissues with an emphasis on the role of post-translational modifications, cross-linking mechanisms, fibril-associated proteins and studying the consequences of mutations that cause osteochondral defects. Candidates should have experience in protein isolation and analysis and basic techniques in molecular biology. Well-equipped laboratories with the opportunity to develop and practice mass spectrometric techniques tailored for matrix protein analysis. A motivated individual with a strong and appropriate background in the biological sciences is sought to work in a team environment. Salary related to experience within NIH guidelines. Applications with curriculum vitae, publications, one-page statement of career goals and names of three references by mail to Dr. David Eyre, Orthopaedic Research Laboratories,

University of Washington, Box 356500, Seattle, WA 98195-6500 or send by e-mail address to kaep@u.washington.edu. The University of Washington is an affirmative action, equal opportunity employer.

Person to contact:Ms. Kae Ellingsen
Email address: kaep@u.washington.edu

Post-doctoral fellowships in Developmental Biology and Biochemistry of Extracellular Matrix, Metalloproteases and Proteoglycans

Post-doctoral fellowships will be available in 2006 and 2007 to study the biology and biochemistry of ADAMTS proteases and MT1-MMP. ADAMTS proteases have been implicated in arthritis (aggrecanase), inherited connective tissue disorders, cell migration and angiogenesis and MT1-MMP is implicated in angiogenesis and skeletogenesis. Both are fast-moving and exciting fields. Ongoing projects include characterization of new knockout mice and phenotypes, proteomics for identification of substrates and intermolecular interactions, and interfaces with cell signaling mechanisms.

The laboratory will suit highly motivated new or recent PhD or MD/PhD graduates who are interested in augmenting or developing skills in mouse genetics, embryology, cell biology, enzymology and protein chemistry, including structural biology. The laboratory offers a stimulating and constructive environment for your professional development. The Lerner Research Institute has state of the art research facilities in a major clinical center, the Cleveland Clinic Foundation, and is affiliated with the adjacent Case Western Reserve University. Cleveland and its vicinity offer an affordable, high quality of life with outstanding recreational and cultural opportunities.

Representative publications: Koo, B-H, Longpre, J-M., Somerville, RPT, Alexander, J.P., Leduc, R.,Apte, SS. Cell surface processing of pro-ADAMTS9 by furin. J Biol Chem, 2006 281(18):12485-94; LeGoff C, Somerville, RPT, Kesteloot, F, Powell, K, Birk, D.E., Colige, A., Apte, S.S. Regulation of procollagen amino-propeptide processing during mouse embryogenesis by specialization of homologous ADAMTS proteases; Insights on collagen biosynthesis and dermatosparaxis. Development, 2006 133(8):1587-96; Oblander SA, Zhou Z, Galvez BG, Starcher B, Shannon JM, Durbeej M, Arroyo AG, Tryggvason K, ApteSS. Distinctive functions of membrane type 1 matrix-metalloprotease (MT1-MMP or MMP-14) in lung and submandibular gland development are independent of its role in pro-MMP-2 activation. Dev Biol. 2005 ;277:255-69. Somerville R P T, Longpre JM, Apel ED, Lewis RM, Wang LW, Sanes J, Leduc R, ApteSS. ADAMTS7B, the full-length product of the ADAMTS7 gene, is a chondroitin sulphate-proteoglycan containing a mucin domain. J Biol Chem.2004 279; 35159-35175

Contact: Suneel S. APTE, MD, PhD (aptes@ccf.org)

Postdoctoral Position

Division of Dermatology, Duke University Medical Center.

We are seeking candidates with a Ph.D for a postdoctoral position, available immediately. A strong background in molecular and cellular biology is essential. Experience in collagen biochemistry, baculoviral expression and protein purification is desirable. Candidates should be self-motivated and good communicators. Our laboratory uses cell culture, molecular biology techniques and baculoviral expression systems to investigate biochemical and molecular mechanisms of disorders of the extracellular matrix. Projects include expression and purification of lysyl hydroxylase isoforms, key modifying enzymes in collagen biosynthesis, to determine their kinetics and domain-specificity of collagen lysyl hydroxylation that defines the pattern of stable cross-link formation in collagen, and to examine their roles in collagen disorders such as Ehlers-Danlos syndrome and scleroderma. These studies are exciting in that they should lead to a better understanding of pathological matrix deposition in scleroderma with potential application to therapy of fibrotic diseases.

Salary will be based on the successful candidate's experience. There is an attractive benefit package.

Applicants should send a curriculum vitae and the names of three references to: Dr. H. Yeowell at Box 3135, Division of Dermatology, Duke University Medical Center, Durham, NC 27710, USA; or via email: yeowe001@mc.duke.edu. Duke University is an affirmative action and equal opportunity employer.

Postdoctoral Positions In Proteoglycan Research And Cancer

Thomas Jefferson University

Postdoctoral positions are available to investigate the biology of perlecan and decorin, two proteoglycans involved in tumor angiogenesis and tumor suppression, respectively. The candidates are sought to join a multi-disciplinary team of researchers involved in investigating the molecular mechanism by which these proteoglycans affect cell growth and tumor development (*J. Cell Biol.* **166**:97-109, 2004;*J. Biol. Chem.* **279**:6606-6612, 2004; *J. Biol. Chem.* **280**:32468-32479, 2005; *Nature Rev. Mol. Cell. Biol.* **6**:646-656, 2005.; Seidler et al, *J. Biol. Chem.* In press, 2006)

Requirements include a Ph.D. or an M.D./Ph.D. in biochemistry or cell biology. A molecular biology background is highly desirable. Send resume and three letters of reference to:

Renato V. Iozzo, M.D. Department of Pathology, Anatomy &Cell Biology, Thomas Jefferson University, 1020 Locust Street, Room 249 JAH, Philadelphia, PA 19107-6799, U.S.A. Fax (215) 923-7969
Email: Iozzo@mail.jci.tju.edu

Research Assistant Professor in Skeletal Biology

University of Hong Kong

Applications are invited for appointment as Research Assistant Professor in the Department of Biochemistry, tenable from as soon as possible. The appointment will initially be made on a three-year fixed-term basis, with the possibility of renewal.

This position is created under the Programme on Developmental Genomics and Skeletal Research (http://web.hku.hk/~aoebioc/), involving multi-disciplinary collaborations between scientists and clinicians, addressing key questions in Skeletal Biology and Disease. The appointee will help develop research aimed at contributing significantly to understanding the biology of osteochondro-progenitors and their niche. Applicants should have a Ph.D. degree with at least three years' postdoctoral experience and a proven excellent track record in relevant areas of research. Candidates with innovative ideas in applying new approaches/technolologies are encouraged to apply. Further information about the Department can be obtained at http://www.hku.hk/biochem/.

Starting annual salary for **Research Assistant Professorship** is around HK$487,320 (approx. US$1=HK$7.8) (subject to review from time to time at the entire discretion of the University). At current rates, salaries tax does not exceed 16% of gross income. The appointment will attract a contract-end gratuity and University contribution to a retirement benefits scheme, totalling up to 15% of basic salary, as well as leave, and medical/dental benefits.

The University of Hong Kong is at the international forefront of higher learning and research, with more than 100 teaching departments and sub-divisions of studies, and more than 60 research institutes and centres. It has over 20,000 undergraduate and postgraduate students from 48 countries. English is the medium of instruction. The University is committed to international standards for excellence in scholarship and research.

Further particulars and application forms (272/302 amended) can be obtained at https://extranet.hku.hk/apptunit/. Application and enquiries may be addressed to Professor Kathy Cheah, Head, Department of Biochemistry, The University of Hong Kong, Pokfulam Road, Hong Kong. Fax: (852) 2855 1254; e-mail: biochem@hkusua.hku.hk.
The University is an equal opportunity employer and is committed to a No-Smoking Policy

Assistant/Associate Professor Faculty Position

OHSU

The Department of Orthopaedics and Rehabilitation at Oregon Health and Science University is seeking a research scientist with expertise in biomechanical engineering related to skeletal tissues, for an Assistant/Associate Professor faculty position. This is a joint recruitment with the Bone and Mineral Unit in the Department of Medicine.

The successful applicant will be expected to establish a research program that complements basic and applied projects in bone and cartilage biology, as well as actively participating in the education and administrative programs of the Departments. S/he will direct an established biomechanics laboratory and will have opportunities for affiliation with the bioengineering programs of the OGI School of Science and Engineering.

To apply, please submit CV, a description of current research and future research interests and names and addresses of references to: Dr. Brian Johnstone, Mail code: OP31, Oregon Health and Science University, 3181 SW Sam Jackson Park Road, Portland, OR 97239 or email to johnstob@ohsu.edu. OHSU is an affirmative action and equal opportunity educator and employer.

Responsible Newsletter Editors

Jamie Fitzgerald: fitzgerj@ohsu.edu
Dieter Reinhardt: dieter.reinhardt@mcgill.ca

A selection of photos from the FECTS meeting held in the beautiful city of Oulu last month

Oulu City Hall Reception

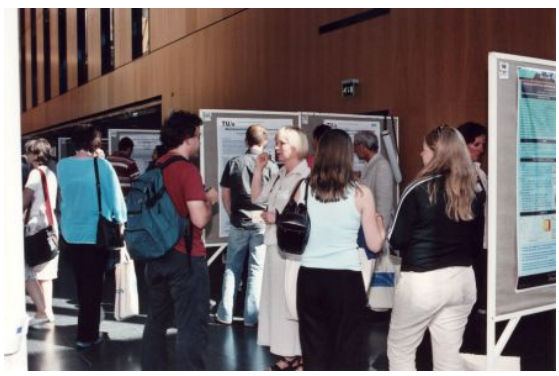


Plenary Talks




Workshop Talks


Poster sessions


Available online at www.sciencedirect.com
SCIENCE DIRECT
Matrix Biology 25 (2006) 200–201
MATRIX BIOLOGY
www.elsevier.com/locate/matbio

From the Editors Desk

Guest editorial letter: Molecular machines in the matrix?

In this letter to Matrix Biology, I wish to discuss the possible existence of molecular machines in the extracellular matrix and new approaches to elucidate them. My own frustrations have led me to conclude that the biological functions of the extracellular matrix can only partially be understood from studies of individual constituent molecules. In the past, many researchers have focused their attention on single proteins. As a result of such studies, key features of complex multifunctional proteins such as laminin, fibronectin and many others have been determined, including their domain organizations and three-dimensional structures. However, analyses of structures and properties of single molecules have frequently not led to a clear understanding of how the molecules may function within the matrix. As a consequence, research has turned to studies of interactions between matrix components and the assignment of interacting domains. This type of research has shown that the number of components interacting with, for example, laminin or fibronectin, is very large and that such a multiplicity of interactions is a general property of most matrix proteins. This has supported the idea that very many components form large assemblies, which are frequently named networks.

I wish to push the idea of networks a step further by hypothesizing that many of these networks are molecular machines with stringent arrangements of their building units in space acting in concert and along defined time courses. This idea is along the lines of Bruce Alberts who concluded from his work on signaling that "nearly every major process in a cell is carried out by assemblies of 10 or more protein molecules". He named these devices "protein machines" and wrote a vision article (Alberts, 1998) with the aim to "prepare the next generation of molecular biologists" for exploring them. His provocative reference: "In an era dominated by gene cloning, many of today's most distinguished scientists have been enormously productive without any quantitative skills" points to the need for more quantitative techniques.

Genomics, proteomics, genetics, classical biochemistry and molecular biology provide the basis for such work. However, the techniques of these fields lack the potential to map the detailed construction of a machine or network and the kinetic pathway of its function. Clearly, biophysical, structural and dynamic approaches are required. Novel biophysical techniques have already been developed for the elucidation of complex networks or machines. On a structural level, electron tomography is one such technique (Medalia et al., 2002). The elucidation of the complex arrangement of cadherins and their *cis*- and *trans*-contacts between the membranes of desmosomes is a beautiful example of the power of the method (He et al., 2003). Also, classical crystallography has been extended to larger and larger systems (Groll and Huber, 2005). For the elucidation of the dynamics with which a machine runs, I consider the various fluorescence resonance energy transfer methods (FRET, Wallrabe and Periasamy, 2005, single molecules FRET, Coban et al., in press) as very potent methods. I predict that a large number of related methods will be developed for the elucidation of molecular machines on a structural and dynamic level.

At present, molecular machines have been mainly studied in areas, which are not directly linked to the extracellular matrix. Classical examples are the rotary protein motors, which generate mechanical force by using intermolecular binding energy to capture favorable Brownian motions. Cytoskeletal "motors" like myosin V transport cargo along actin filaments. Different cargos can be connected to myosin V, giving rise to transport machines. Fascinating are also the intracellular molecular machines for protein degradation connected to the ubiquitin and proteasome dependent pathway. The 20S proteasome core particle is composed of 28 proteins. The list of well-known molecular machines also includes the reaction center of the photosynthetic system, the T4 DNA injection machine, the nuclear pore complex, the blood coagulation machine and several other systems.

Until now, only a few researchers in the matrix field have considered molecular machines as part of the extracellular matrix. It is known, however, that the integrins form large and well-defined complexes with cytosolic and extracellular components, show conformational changes and are activated and inactivated by many factors (Hynes, 2002). I feel that sophisticated structural and dynamic investigations will demonstrate a well-defined arrangement of the subunits in space and a concerted interaction. This may classify them as parts of a molecular machine. A beginning has been made with FRET measurements on integrins (de Virgilio et al., 2004). Another interesting example is the TGFbeta presenting fibrillin (Charbonneau et al., 2004), acting together with activating proteases and the TGFbeta receptor. However, new approaches to characterize large supramolecular structures and

0945-053X/$ - see front matter
doi:10.1016/j.matbio.2006.04.001

obtain dynamic information on their mutual interactions are clearly needed to move these and other ideas on molecular machines in the extracellular matrix from speculations to reality.

Acknowledgements

I am grateful for any comments concerning this letter.

References

Alberts, B., 1998. The cell is a collection of protein machines: preparing the next generation of molecular biologists. Cell 92, 291–294.

Charbonneau, N.L., Ono, R.N., Corson, G.M., Keene, D.R., Sakai, L.N., 2004. Fine tuning of growth factor signals depends on fibrillin microfibril networks. Birth Defects Res. C. Embryo Today 72, 37–50.

Coban, O., Lamb, D.C., Zaychikov, E., Heumann, H., Nienhaus, G.U., in press. Conformational heterogeneity in RNA polymerase observed by single pair FRET microscopy. Biophys. J. (Mar 31, Epub ahead of print).

de Virgilio, M., Kiosses, W.B., Shattil, S.J., 2004. Proximal, selective, and dynamic interactions between integrin alphaIIbbeta3 and protein tyrosine kinases in living cells. J. Cell Biol. 165, 305–311.

Groll, M., Huber, R., 2005. Purification, crystallization, and X-ray analysis of the yeast 20S proteasome. Methods Enzymol. 398, 329–336.

He, W., Cowin, P., Stokes, D.L., 2003. Untangling desmosomal knots with electron tomography. Science 302, 109–113.

Hynes, R.O., 2002. Integrins: bidirectional, allosteric signalling machines. Cell 110, 673–687.

Medalia, O., Weber, I., Frangakis, A.S., Nicastro, D., Gerisch, G., Baumeister, W., 2002. Macromolecular architecture in eukaryotic cells visualized by cryoelectron tomography. Science 298, 1–10.

Wallrabe, H., Periasamy, A., 2005. Imaging protein molecules using FRET and FLIM microscopy. Curr. Opin. Biotechnol. 16, 19–27.

Jürgen Engel
Department Biophysical Chemistry,
Biozentrum University of Basel,
CH 4056 Basel, Switzerland
E-mail address: juergen.engel@unibas.ch.