

ISMB NEWSLETTER

June 2010



Dear Fellow Matrix Biologists,
 I hope you all had a great spring.
 Matrix.....Matrix

This short essay will be focused on the definition of Matrix Biology. What does it really mean to you? Is there any common definition? Are there many definitions? And if so, why?

As you know, in the past the field of matrix biology has received some “illustrious” connotations such as slime, ground substance, loose connective tissue, mucous or amorphous (i.e. shapeless) substance, and so on
 According to Wikipedia... *“matrix (plural: matrices) is the material (or tissue) between animal or plant cells, in which more specialized structures are embedded..... Finger nails and toenails grow from matrices.....The molecules forming the “glue” between cells in connective tissues are summarily referred to as the extracellular matrix”*

Let’s find out what the concept of matrix biology is in 2010 for the younger (future) generation. To find a more rigorous (scientific?) definition of our field, I asked post-doctoral fellows, undergraduate and graduate students in my laboratory to send me a single paragraph with their definition of matrix biology using their own words. I thought that this might be a somewhat unbiased approach insofar as the members of my laboratory derive from three different continents (Europe, Asia and America), are well educated and are representative of the new generation of matrix biologists with most being in their early or late twenties. Below are some of their definitions:

- As humans get influenced by their surroundings so do cells. Matrix biology is a niche field of cell molecular biology which studies how the changes in the extracellular matrix, i.e. the microenvironment of the cells, influence the intracellular function and behavior of cells and vice-versa.
- Matrix biology can be considered as a vital and indissoluble link of union between the people (cells). I fancy it as a knot among people whereby each human being holds hand (ECM) of another human and so forth thus being symbolic of an existing harmony.
- The study of the extracellular matrix in both normal and disease states, and how key molecules communicate to regulate cell behavior.
- Matrix biology is concerned about the mysterious niche that nurtures our growth and development in our life history.
- Matrix biology is the study of a huge harbor, protecting the city, in which a lot of little boats and big ships are docking, leading to an immense flow of exchanges.

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- Matrix Biology is the study of the conditional environment of cells and the downstream effects that it has on the cells themselves.

- I see matrix biology as a structure-function relationship between the myriad of molecules comprising the cells' immediate environment and their subsequent interaction, and how the cell interprets these signals culminating and regulating various cellular functions. It is as much an ongoing conversation between the cells and the dynamic locale in which the cells reside (function) as it is structural.

- Matrix biology is like a great spider web, where every single node is essential for the formation of a complicated network. The center of the web, where the spider stay, is the cell that depends completely on the surrounding tissue.

- Matrix biology is a specialized area of studies focused on understanding the chemistry and biology of the extracellular microenvironment and how this influences cell behavior, in both physiological and pathological conditions. In recent years it has been recognized as a major discipline due to its interdisciplinary nature and to the realization that tissue complexity has to be taken into account to seek answers that are relevant in vivo. Matrix biology has gained even more importance since stem cell niche studies have taken the spotlight and tissue engineering is not any longer a dream.

- Matrix biology is an emerging field of biological studies focused on the understanding of complex protein and carbohydrate interactions that ultimately affect the behavior of cells, their growth characteristics and transcriptional activities. The extracellular matrix is like a building under constant construction, with walls of various thicknesses, glass windows, entrances and exits, all of which constrains and regulate cellular function.

I think that these diverse definitions are quite interesting, especially the anthropomorphic ones!

Matrix Biology Events and News

This is an even year and, thus, ISMB plays its essential role of sponsoring two major meetings, namely the FECTS meeting (<http://www.fects.eu/>) to be held in Davos, Switzerland, July 3-7, and the biennial ASMB meeting (http://www.asmb.net/2010_meeting.php) to be held in Charleston, South Carolina, October 24-27.

At the FECTS, the ISMB will give the coveted Rupert Timpl Award. The ISMB will give three travel awards for graduate students/postdocs and some of these will be selected for platform presentation. At the ASMB meeting, the ISMB will have a plenary session and will give the ISMB Distinguished Investigator Award, and again three travel fellowships selected from the internationals (non American) abstracts.

In the past months there have been several Matrix Biology meetings focusing on various aspects of our field, including "The extracellular matrix: from molecule to man", a joint meeting of the German and British Societies for Matrix Biology, held in Frankfurt, Germany, March 18-20. This meeting was organized by Liliana Schaefer and Hannes Eble from the German side, and by John Couchman and Graham Riley from the British side. The scientific sessions were outstanding and the meeting was important because it was the first joint meeting of the two societies. We hope that such meetings among European societies will continue and expand in the future. I have actively participated and functioned as the ISMB photographer (see the collection of pictures below).

The constitution of the ISMB stipulates that the three most senior members of the Council be replaced every year. In 2010, the Council members John Bateman, Yasunori Okada, and Lynn Sakai will step down. I wish to thank them for their valuable time and contribution to the society. I would like to express my congratulations to the new incoming council members which include Attila Aszódi, Danny Chan and Hans Peter Bächinger.

I hope you all have a fantastic summer.

Warmest regards to all,

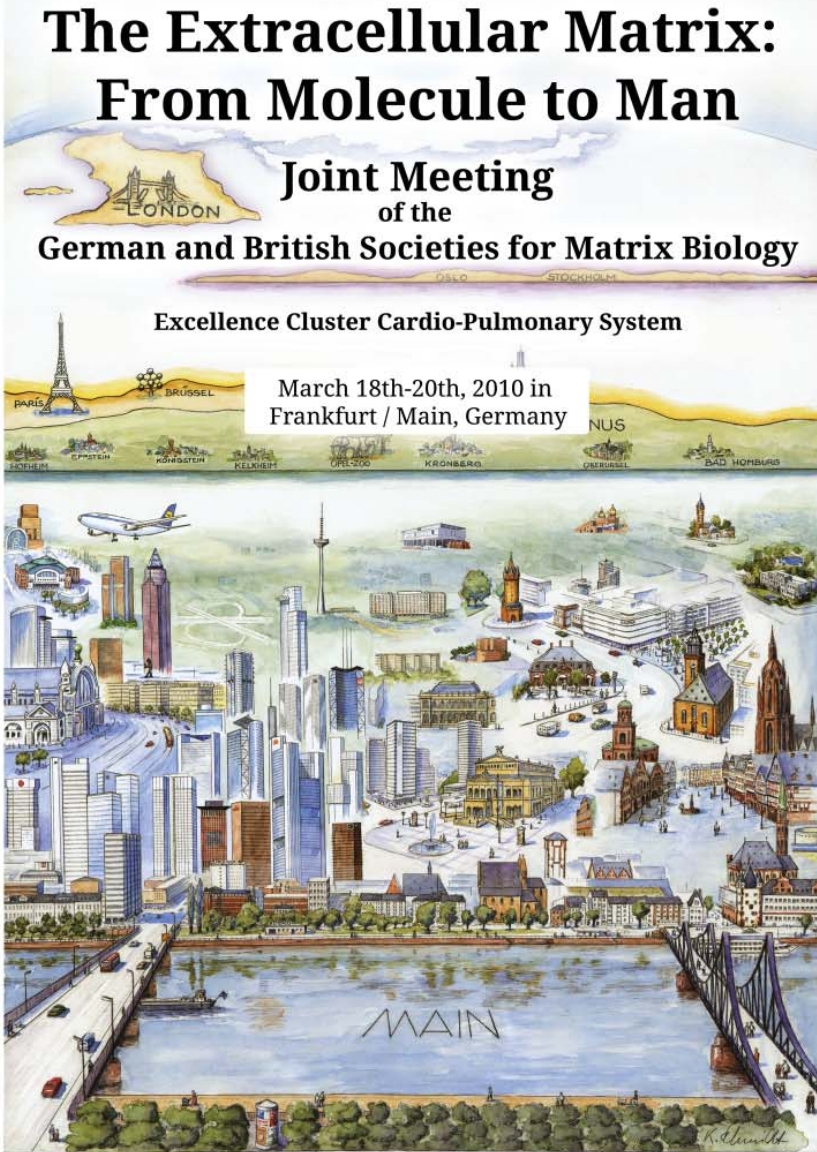
Renato V. Iozzo, M.D.
President ISMB

The Extracellular Matrix: From Molecule to Man

Joint Meeting
of the
German and British Societies for Matrix Biology

Excellence Cluster Cardio-Pulmonary System

March 18th-20th, 2010 in
Frankfurt / Main, Germany




Liliana Schaefer



Klaus von der Mark

Beate Eckes



The Davises

Roland Schaefer



John Couchman



Pyong Park:
Notice the two endogenous laser pointers

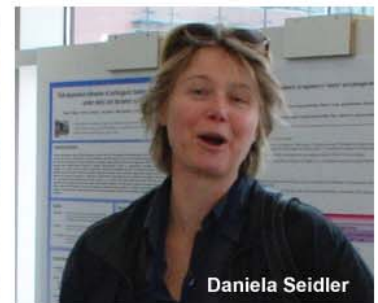


J. Fischer

RVI



Peter, our perennial
secretary treasurer



Daniela Seidler



Liliana is elected President of the German Connective Tissue Society





From the ISMB Secretary

You, the ISMB-members, have now designated the winners of the Rupert Timpl Award and the Distinguished Investigator Award. As you may know, the prize ceremony for the Rupert Timpl Award will take place on July 6, 2010, in Davos / Switzerland at the ISMB-sponsored 22nd meeting of the Federation of European Connective Tissue Societies (FECTS) (<http://www.fects.eu>) and the winner is Anika Lange (Martinsried), who received the prize for the paper "Integrin-linked kinase is an adaptor with essential functions during mouse development" which was published in Nature. Oct 15, 2009. (461:1002-10066). Anika showed in an elegant study involving several knock-in mice that integrin-linked kinase acts as an adaptor protein, mediating contacts (via parvins) between the beta subunits of integrins and the actin cytoskeleton, rather than as a kinase in signal pathways. She will present these and additional studies at the FECTS-meeting.

The Distinguished Investigator Award is a prize given for a whole lifetime oeuvre rather than a single, outstanding publication. You chose Bjorn Olsen from six candidates. We all know Bjorn's towering contributions to the field of matrix biology. He was one of the very early and decisive contributors to such milestones as the collagen fibril structures. Most remarkably, those discoveries were made when he still was a medical student at the department of anatomy at Oslo University. He then moved on to Philadelphia, later to Rutgers Medical School (now Robert Wood Johnson Medical School) in New Jersey and, finally, to Harvard Medical School in Boston. During all those years, he remained firmly convinced that matrix biology had a lot to offer to the best scientists. We all know and keep in high esteem his essays in Matrix Biology: From the editor's desk. Bjorn authored or co-authored well over 250 publications, among them many seminal papers and some of the best received reviews. The award will be presented to Bjorn at the biennial meeting of the American Society of Matrix Biology (http://asmb.net/2010_meeting.php), again co-sponsored by the ISMB. So, these are some of the places where your ISMB-money goes!

During the selection process, a number of subjects came up which I would like to present to you here. I hope that a public discussion of the issues will follow. Jamie and Dieter will be glad to publish your standpoints on the following subjects:

For both awards, Council nominates a number of candidates and the whole membership decides on the laureates – at least those that have settled their dues!! The founders of the prizes felt that the number of nominees should be kept at a reasonable level. But is this the best way to do this?

For example, you didn't have the choice to assign the Distinguished Investigator Award to a single woman among all these men! When I sent out reminders for the ballot, there were female members who complained about this and actively refrained from voting. Very few of us could rightfully disagree with their point! But how could this be remedied next time? Should the membership be asked to nominate? Could the problem of too many nominees be settled if the designation, rather than the nomination, became a task of the Council? Are there other ways to choose the laureates of what we all consider prestigious prizes? Do you have any comments on this?

I am sure that equal opportunity issues could be easily remedied by making the nomination of women compulsory for the Council. But would that solve all other aspects? We certainly need to discuss this, and maybe we could set up a discussion thread on our internet site?. For the time being, I await your e-mail contributions for distribution among the members.

Another minor issue: I think that - latest by spring of 2013 – time has come for me to hand over the post of the secretary / treasurer to someone else. I mention this early because my optimism about prospective volunteers forming long queues is rather dim. Anybody is welcome to nominate a friend. In this case, I am quite sure, the gender issue may be less important. Just as an aside, our constitution says nothing about the term length of this job! And the task may be a friend of yours who may not leave you as easily as others...

Peter Bruckner
ISMB Secretary/treasurer
peter.bruckner@uni-muenster.de



Meeting Announcements

**Gordon Research Conference on:
Signal Transduction By Engineered Extracellular Matrices**

Gordon-Kenan Research Seminar
June 26-27, 2010, University of New England, Biddeford, ME

Chairs: Jennifer L. Leight and Wesley R. Legant

The German and Swiss Societies of Matrix Biology invite you to the **XXII FECTS meeting** in Davos (Switzerland) July 3rd -7th, 2010.

The meeting includes plenary lectures, workshops with short talks selected from submitted abstracts, and poster sessions for individual scientific discussions.

Topics:

The role of the extracellular matrix in acquired and genetic diseases, cell therapy, stem cell research, biomaterials and biomechanics, inflammation and angiogenesis, tissue engineering and regenerative medicine.

Invited speakers:

Attila Aszodi, MPI Martinsried, Germany
Paolo Bonaldo, University of Padova, Italy
Georg Duda, Charite - Berlin, Germany
Donald Gullberg, University of Bergen, Norway
Martin Humphries, Wellcome Trust Centre for Cell-Matrix Research, UK
Renato V. Iozzo, Thomas-Jefferson University, USA
Cay Kielty, Wellcome Trust Centre for Cell-Matrix Research, UK
Magareta Müller, University of Heidelberg, Germany
Gillian Murphy, University of Cambridge, UK
Gertraud Orend, Inserm Strassbourg, France
David Ornitz, Washington University, USA
Wiltrud Richter, University of Heidelberg, Germany
Markus Ruegg, Biozentrum Basel, Switzerland
Lydia Sorokin, University of Münster, Germany
Rocky Tuan, University of Pittsburgh, USA
Fiona Watt, University of Cambridge, UK
Sabine Werner, University of Zürich, Switzerland
Atsuko Yoneda, University of Copenhagen, Denmark

Please note that the deadline for abstract submission was June 9th, 2010.

Abstracts sent after this deadline will not be published in the abstract book - nevertheless poster presentation will be possible.

Detailed information is provided on the FECTS – homepage (<http://www.fects.eu/>)

We look forward to welcome you in Davos!

Chairs: Prof Dr. Susanne Grässel and Prof. Dr. Johannes C. Schittny

See poster at the end of the Newsletter for more details.

Symposium on Basement Membranes in Tissue Development and Regeneration

July 7-9, 2010, Vanderbilt University, Nashville, TN

Registration opens January 1, 2010

<http://www.mc.vanderbilt.edu/cmb/> (see attached flyer)



**Gordon Research Conference on:
Proteoglycans - Development, Disease And Therapeutics**
July 11-16, 2010, Proctor Academy, Andover, NH
Chair: Marian F. Young and Robert J. Linhardt

**Gordon Research Conference on:
Transglutaminases In Human Disease Processes**

July 18-23, 2010. Davidson College, Davidson, NC
Chaired by: Richard Eckert and Kapil Mehta

Thrombospondins and Other Matricellular Proteins in Tissue Organization and Homeostasis

18 July-23 July 2010, Snowmass Village, Colorado, USA
Conference Organizers: David D. Roberts, NIH, and Joanne E. Murphy-Ullrich, UAB
FASEB Summer Research Conference, <http://src.faseb.org>
Contact: Julie Levin, jlevin@faseb.org

Matricellular proteins are non-structural proteins of the connective tissue that modulate cell functions through regulation of cell adhesion, growth factor activity, and signaling networks. Matricellular proteins, including thrombospondins, tenascins, SPARC, and the CCN family, have been implicated in a number of disease and developmental processes and represent novel therapeutic targets for major diseases. The program will include presentations by leading investigators, poster sessions, and short talks selected from the submitted abstracts. Major themes and session chairs:

- Structural biology and genetics of matricellular proteins
Deane F. Mosher University of Wisconsin
- Matricellular proteins in fibrosis and tissue remodeling
Joanne E. Murphy-Ullrich University of Alabama at Birmingham
- Neurobiology and developmental biology
Richard P. Tucker University of California at Davis
- Roles in injury and stress responses
David D. Roberts NIH
- Functions in musculoskeletal development and disease
Jacqueline T. Hecht University of Texas Medical School
- Roles in metabolic regulation
Olga I. Stenina Cleveland Clinic
- Carcinogenesis and tumor progression
Jack Lawler Harvard Medical School
- Cardiovascular disease and angiogenesis
William A Frazier Washington University St Louis
- Immunity and inflammation
Ruth Chiquet-Ehrismann Friedrich Miescher Institute

**Gordon Research Conference on:
Biom mineralization**

August 15-20, 2010, Colby-Sawyer College, New London, NH
Chair: Lia Addadi and Peter Fratzl

Biennial Meeting of the American Society for Matrix Biology.

Celebrating 10 years of ECM Connections! The meeting is set for October 24–27, 2010 in beautiful Charleston, SC. The Francis Marion Hotel will be providing the accommodations and meeting space and we are certain you will enjoy the charm of this prime location. Our Meeting Chair, Jean Schwarzbauer, has put together an amazing program committee and they are busily working on program topics and speakers. They have already identified a wonderful keynote speaker, Elaine Fuchs, from The Rockefeller University presenting “Stem Cells, Extracellular Matrix, Tissue Morphogenesis and Cancer in Skin”. We will also have Satellite symposiums presented by guest societies TERMIS, SFG and ISMB. More details will be forthcoming. Please check back regularly for updates on the website (www.asmb.net)



Get Connected! - Wellcome Trust Centre for Cell Matrix Research Symposium, Michael Smith Building, University of Manchester, UK, Monday 13 - Wednesday 15 September 2010

The organisers of the inaugural Wellcome Trust Centre for Cell Matrix Research meeting cordially invite you to register for Get Connected!, the 22nd meeting of the UK Adhesion Society and the Italian Associazione di Biologia Cellulare e del Differenziamento meeting.

This meeting will showcase fresh and exciting work from the fields of extracellular matrix, cell-matrix and cell-cell adhesions research. Our focus is to bring together young scientists who work in these fields and provide them with an opportunity to present their findings to their peers in a friendly and supportive environment.

We have put together an exciting programme including keynote lectures from Paola Defilippi, Elisabetta Dejana, Paul Martin, Ulrike Mayer, Jim Norman and Erik Sahai, and, a plenary lecture presented by Martin Schwartz. We will also be holding two special sessions. The first will enable scientists to participate in an informal discussion entitled: The Future of ECM Research. In the second, science Communicator of the Year 2009, Ceri Harrop and leading scientific journalist, Myc Rigulsford, will host a session aiming to highlight and develop the transferable skills of young scientists in communicating their research to lay audiences. There will also be a poster session. For further information and to register, visit: <http://ukadhesion.org>. We look forward to welcoming you in September!

The Organising Committee: Chloé Yeung, Douglas Dyer, Louise Kung and Luke Bonser, and their Italian collaborators: Virginia Morello and Giulia Germena

The **XXX Meeting of the Italian Society for the Study of Connective Tissues (SISC)** that will be held in Palermo on 27-29 October 2010?

Preliminary programme and information are available at: <http://www.siscpalermo2010.it/>

Meeting Report



Rare genetic diseases are in the current focus of the European Union health policy for two reasons. Collectively, rare diseases are estimated to affect > 6 % of the general population in the Union, and, therefore, represent a major health issue. Scientifically, they are rapidly emerging as ideal models to devise and test novel molecular therapies in preclinical settings and in pilot clinical trials. For these reasons, the multi-disciplinary Freiburg Center for Rare Diseases (FCRD) was founded in 2009 within the Freiburg University Medical Center. In FCRD clinical departments and science institutes collaborate on highly specialized molecular diagnostics, coordinated care of children and adults with rare genetic diseases, and on experimental research on rare diseases (www.uniklinik-freiburg.de/fzse, contact: fzse@uniklinik-freiburg.de).

The focus is on extracellular matrix and connective tissues diseases affecting the skin, the musculoskeletal system, the kidney, the lung, and the eye.

The initiators and the coordinators of FCRD, Bernhard Zabel, Andrea Superti-Furga, Hartmut Neumann and myself, have in the past coordinated a number of German and international research networks on rare diseases, and now merge their expertise in the FCRD to generate a multidisciplinary and highly synergistic clinical and research environment.

The University Medical Center also founded a diagnostic laboratory called MVZ (www.uniklinik-freiburg.de/mvz) for molecular genetics. So far, the MVZ offers mutation analyses of more than 150 genes involved in the pathology of rare genetic diseases, including a large number of connective tissue disorders. The laboratory works on a commercial basis, and the cost is covered mainly by the health insurance of the patients in Germany and abroad. After the mutations have been disclosed, the affected persons and their families are offered genetic counselling.

Translational research in FCRD relies on very well characterized patient cohorts generated by the clinical and diagnostic arms of the center. Currently, the research focuses on elucidation of common pathological mechanisms in matrix diseases in different tissues, identification of molecular targets for therapeutic intervention and translation into treatment applications. Some scientists in the FCRD specialize on design of clinical trial strategies for rare diseases with a low number of patients.

Now that the FCRD is well established and functional in a multidisciplinary setting, we are looking forward to collaborations with other centers to generate international networks of excellence on translational research on extracellular matrix diseases and – in hopefully not too distant future – on preclinical and clinical therapy trials.

Leena Bruckner-Tuderman, MD
bruckner-tuderman@uniklinik-freiburg.de



Matrix Research Update

Processing of Procollagen III by Meprins: New Players in Extracellular Matrix Assembly?

Daniel Kronenberg, Bernd Cem Bruns, Catherine Moali, Sandrine Vadon-Le Goff, Erwin Ernst Sterchi, Heiko Traupe, Markus Böhm, David J.S. Hulmes, Walter Stöcker and Christoph Becker-Pauly

J. Invest Dermatol, in press

Meprin α and β , a subgroup of zinc metalloproteinases belonging to the astacin family, are known to cleave components of the extracellular matrix, either during physiological remodeling or in pathological situations. Here we present a new role for meprins in matrix assembly, namely the proteolytic processing of procollagens. Meprin α and β both release the N- and C-propeptides from procollagen III, such processing events being critical steps in collagen fibril formation. In addition, both meprins cleave procollagen III at exactly the same site as the procollagen C-proteinases, including bone morphogenetic protein-1 (BMP-1) and other members of the tolloid proteinase family. Indeed, cleavage of procollagen III by meprins is more efficient than by BMP-1. Also, unlike BMP-1 whose activity is stimulated by procollagen C-proteinase enhancer proteins (PCPEs), the activity of meprins on procollagen III is diminished by PCPE-1. Finally, following our earlier observations of meprin expression by human epidermal keratinocytes, meprin α is also shown to be expressed by human dermal fibroblasts. In the dermis of fibrotic skin (keloids), expression of meprin increases and meprin begins to be detected. Our study suggests that meprins could be important players in several remodeling processes involving collagen fiber deposition.

Role of the netrin-like domain of procollagen C-proteinase enhancer-1 in the control of metalloproteinase activity.

Bekhouche M, Kronenberg D, Vadon-Le Goff S, Bijakowski C, Lim NH, Font B, Kessler E, Colige A, Nagase H, Murphy G, Hulmes DJ, Moali C.

J Biol Chem. 2010; 285(21):15950-9

The netrin-like (NTR) domain is a feature of several extracellular proteins, most notably the N-terminal domain of tissue inhibitors of metalloproteinases (TIMPs), where it functions as a strong inhibitor of matrix metalloproteinases and some other members of the metzincin superfamily. The presence of a C-terminal NTR domain in procollagen C-proteinase enhancers (PCPEs), proteins that stimulate the activity of astacin-like tolloid proteinases, raises the possibility that this might also have inhibitory activity. Here we show that both long and short forms of the PCPE-1 NTR domain, the latter beginning at the N-terminal cysteine known to be critical for TIMP activity, show no inhibition, at micromolar concentrations, of several members of the metzincin superfamily, including matrix metalloproteinase-2, bone morphogenetic protein-1 (a tolloid proteinase), and different ADAMTS (a disintegrin and a metalloproteinase with thrombospondin motifs) proteinases from the adamalysin family. In contrast, we report that the NTR domain within PCPE-1 leads to superstimulation of bone morphogenetic protein-1 activity in the presence of heparin and heparan sulfate. These observations point to a new mechanism whereby binding to cell surface-associated or extracellular heparin-like sulfated glycosaminoglycans might provide a means to accelerate procollagen processing in specific cellular and extracellular microenvironments.

Carcinomas contain an MMP-resistant isoform of type I collagen exerting selective support to invasion

Elena Makareeva, Sejin Han, Juan Carlos Vera, Dan L. Sackett, Kenn Holmbeck, Charlotte L. Phillips, Robert Visse, Hideaki Nagase, and Sergey Leikin.

Cancer Res. 2010 Jun 1;70(11):4366-74

Collagen fibers affect metastasis in two opposing ways, by supporting invasive cells but also generating a barrier to invasion. We hypothesized that these functions might be performed by different isoforms of type I collagen. Carcinomas are reported to contain $\alpha 1(I)3$ homotrimers, a type I collagen isoform normally not present in healthy tissues, but the role of the homotrimers in cancer pathophysiology is unclear. In this study, we found that these homotrimers were resistant to all collagenolytic matrix metalloproteinases (MMPs). MMPs are massively produced and utilized by cancer cells and cancer-associated fibroblasts for degrading stromal collagen at the leading edge of tumor invasion. The MMP-resistant homotrimers were produced by all invasive cancer cell lines tested, both in culture and in tumor xenografts, but they were not produced by cancer-associated fibroblasts, thereby comprising a specialized fraction of tumor collagen. We observed the homotrimer fibers to be resistant to pericellular degradation, even upon stimulation of the cells with pro-inflammatory cytokines. Further, we confirmed an enhanced proliferation and migration of invasive cancer cells on the surface of homotrimeric vs. normal (heterotrimeric) type I collagen fibers. In summary, our findings suggest that invasive cancer cells may utilize homotrimers for building MMP-resistant invasion paths, supporting local proliferation and directed migration of the cells while surrounding normal stromal collagen is cleaved. Because the homotrimers are universally secreted by cancer cells and deposited as insoluble, MMP-resistant fibers, they offer an appealing target for cancer diagnostics and therapy.



MOLECULAR MECHANISM OF TYPE I COLLAGEN HOMOTRIMER RESISTANCE TO MAMMALIAN COLLAGENASES

Sejin Han, Elena Makareeva, Natalia V. Kuznetsova, Angela M. DeRidder, Mary Beth Sutter, Wolfgang Losert, Charlotte L. Phillips, Robert Visse, Hideaki Nagase, and Sergey Leikin
J Biol Chem. 2010 May 12. [Epub ahead of print]

Type I collagen cleavage is crucial for tissue remodeling, but its homotrimeric isoform is resistant to all collagenases. The homotrimers occur in fetal tissues, fibrosis, and cancer, where their collagenase resistance may play an important physiological role. To understand the mechanism of this resistance, we studied interactions of $\alpha 1(I)3$ homotrimers and normal $\alpha 1(I)2\alpha 2(I)$ heterotrimers with fibroblast collagenase (MMP-1). Similar MMP-1 binding to the two isoforms and similar cleavage efficiency of unwound $\alpha 1(I)$ and $\alpha 2(I)$ chains suggested increased stability and less efficient unwinding of the homotrimer triple helix at the collagenase cleavage site. The unwinding, necessary for placing individual chains inside the catalytic cleft of the enzyme, was the rate limiting cleavage step for both collagen isoforms. Comparative analysis of the homo- and heterotrimer cleavage kinetics revealed that MMP 1 binding promotes stochastic helix unwinding, resolving the controversy between different models of collagenase action.

Lack of Cyclophilin B in Osteogenesis Imperfecta with Normal Collagen Folding

Aileen M. Barnes, M.S., Erin M. Carter, M.S., Wayne A. Cabral, B.A., MaryAnn Weis, B.S., Weizhong Chang, Ph.D., Elena Makareeva, Ph.D., Sergey Leikin, Ph.D., Charles N. Rotimi, Ph.D., David R. Eyre, Ph.D., Cathleen L. Raggio, M.D., and Joan C. Marini, M.D., Ph.D.
N Engl J Med 2010;362:521-8.

Osteogenesis imperfecta is a heritable disorder that causes bone fragility. Mutations in type I collagen result in autosomal dominant osteogenesis imperfecta, whereas mutations in either of two components of the collagen prolyl 3-hydroxylation complex (cartilage-associated protein [CRTAP] and prolyl 3-hydroxylase 1 [P3H1]) cause autosomal recessive osteogenesis imperfecta with rhizomelia (shortening of proximal segments of upper and lower limbs) and delayed collagen folding. We identified two siblings who had recessive osteogenesis imperfecta without rhizomelia. They had a homozygous start-codon mutation in the peptidyl-prolyl isomerase B gene (PPIB), which results in a lack of cyclophilin B (CyPB), the third component of the complex. The proband's collagen had normal collagen folding and normal prolyl 3-hydroxylation, suggesting that CyPB is not the exclusive peptidyl-prolyl cis-trans isomerase that catalyzes the rate-limiting step in collagen folding, as is currently thought.

Alternate protein kinase A activity identifies a unique population of stromal cells in adult bone.

Tsang KM, Starost MF, Nesterova M, Boikos SA, Watkins T, Almeida MQ, Harran M, Li A, Collins MT, Cheadle C, Mertz EL, Leikin S, Kirschner LS, Robey P, Stratakis CA.
Proc Natl Acad Sci U S A. 2010 May 11;107(19):8683-8

A population of stromal cells that retains osteogenic capacity in adult bone (adult bone stromal cells or aBSCs) exists and is under intense investigation. Mice heterozygous for a null allele of *prkar1a* (*Prkar1a*(+/-)), the primary receptor for cyclic adenosine monophosphate (cAMP) and regulator of protein kinase A (PKA) activity, developed bone lesions that were derived from cAMP-responsive osteogenic cells and resembled fibrous dysplasia (FD). *Prkar1a*(+/-) mice were crossed with mice that were heterozygous for catalytic subunit Calpha (*Prkaca*(+/-)), the main PKA activity-mediating molecule, to generate a mouse model with double heterozygosity for *prkar1a* and *prkaca* (*Prkar1a*(+/-)*Prkaca*(+/-)). Unexpectedly, *Prkar1a*(+/-)*Prkaca*(+/-) mice developed a greater number of osseous lesions starting at 3 months of age that varied from the rare chondromas in the long bones and the ubiquitous osteochondrodysplasia of vertebral bodies to the occasional sarcoma in older animals. Cells from these lesions originated from an area proximal to the growth plate, expressed osteogenic cell markers, and showed higher PKA activity that was mostly type II (PKA-II) mediated by an alternate pattern of catalytic subunit expression. Gene expression profiling confirmed a preosteoblastic nature for these cells but also showed a signature that was indicative of mesenchymal-to-epithelial transition and increased Wnt signaling. These studies show that a specific subpopulation of aBSCs can be stimulated in adult bone by alternate PKA and catalytic subunit activity; abnormal proliferation of these cells leads to skeletal lesions that have similarities to human FD and bone tumors.



Jobs

Post-doctoral position to work on extracellular matrix and proteases

An opening is available for a post-doctoral fellow with a career interest and background in extracellular matrix, proteases, cell biology or developmental biology. The laboratory currently works in the following areas:

1. Proteoglycan turnover by ADAMTS proteases and its biological implications: Several ADAMTS proteases cleave the core proteins of aggrecan and versican and are relevant to musculoskeletal and cardiovascular disease. This project investigates versican and aggrecan turnover in musculoskeletal, craniofacial and cardiovascular phenotypes of ADAMTS deficient mice, and the mechanisms of versican turnover by ADAMTS proteases. The project utilizes single and combinatorial mouse mutants, conditional gene targeting in mice, biochemistry and cell biology techniques.

2. ADAMTS molecules, fibrillin-1 networks and cell regulation: Several ADAMTS family members, e.g., ADAMTS10, ADAMTS17, ADAMTSL4, and ADAMTSL2, are mutated in disorders associated with fibrillin-1, a critical component of an extracellular network that regulates TGF-beta. These human and animal mutations have highlighted the potential role of ADAMTS proteins in fibrillin-rich tissues such as the zonule of the eye, and in regulating skeletal growth and skin/organ fibrosis. The project utilizes single and combinatorial mouse mutants, protein chemistry, intermolecular interaction assays and cell biology techniques.

More information, including recent publications, is available at <http://www.lerner.ccf.org/bme/apte/>. Please send a curriculum vitae and the names and contact information (telephone and email) of three references to: aptes@ccf.org



Meeting Announcements



Dear Colleagues,

on behalf of the German and Swiss Societies of Matrix Biology
we invite you to the

XXII FECTS-Meeting
Davos (Switzerland) July 3rd -7th, 2010

Invited speakers

Attila Aszodi, Georg Duda, Martin Humphries, Renato V. Iozzo, Cay Kiely,
Margareta Müller, Gillian Murphy, David Ornitz, Wiltrud Richter, Markus Ruegg,
Lydia Sorokin, Rocky Tuan, Fiona Watt, Sabine Werner, Paolo Bonaldo,
Donald Gullberg, Atsuko Yoneda and Gertraud Orend

Workshop Topics

Stem cells and stem cell niches, Extracellular matrix during inflammation, Connective tissue and development, Cell-cell and cell-matrix interaction, Tissue regeneration and repair, Molecules and supramolecular complexes in the extracellular matrix, Extracellular matrix: Sources and reservoir of biomolecules, Synthesis and remodeling of extracellular matrix, Extracellular matrix in angiogenesis and tumor biology, Extracellular matrix in the musculoskeletal system, Extracellular matrix in skin and wound healing, Endothelial and epithelial barriers, Biomechanical forces, Hot Topics in extracellular matrix research

Please find additional information on <http://www.facts.eu/>

Please note that the deadline for abstract submission was June 9th, 2010.
Abstracts sent after this deadline will not be published in the abstract book
- nevertheless poster presentation will still be possible.

We look forward to welcome you in Davos!

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CH-3012 Bern, Switzerland
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presents a

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Tissue Development and Regeneration**

July 7-9, 2010

at

Vanderbilt University, Nashville

Registration opens January 1, 2010

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Registration and meals \$250

Topics

Macromolecular Components

Development, Tissue Morphogenesis and Stem Cells

BM's in Disease

Use of Model Organisms

Poster Abstracts Welcome



Invited Speakers

**Hans Peter Bächinger
Nick Brown
Eri Arikawa-Hirasawa
Reinhard Fässler
Laura Feltri
Billy Hudson
James Kramer
Jeff Miner
Jim Patton
Brent Polk
Susan Richardson
Kiyo Sekeiguchi
Arnoud Sonnenberg
Lydia Sorokin
David Sherwood
Jouani Uitto
Yujia Xu
Pampee Young
Peter Yurchenco**





7th International Conference on Proteoglycans
Sydney, Australia
16th – 21st October 2011

<http://www.gsbme.unsw.edu.au/proteoglycan2011>

Convenors

John Whitelock (Sydney)
Amanda Fosang (Melbourne)

Australian Committee

Craig Freeman (Canberra)
Deirdre Coombe (Perth)
James Melrose (Sydney)
Megan Lord (Sydney)

International Committee

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Sally Stringer (Manchester, UK)
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Tony Day (Manchester, UK)
Hideato Watanabe (Aichi, Japan)
Sarah Knox (Bethesda, USA)
Daisy Shum (Hong Kong)
Jacob van den Born (Netherlands)

G'day!

Come down under in October 2011 and join us at the 7th International Conference on Proteoglycans in Australia's famous harbour-side city, Sydney; home of extravagant wildlife and a relaxed beach culture that enjoys plenty of sunshine and tasty BBQs.





Get Connected!

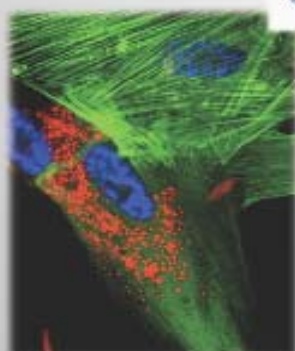
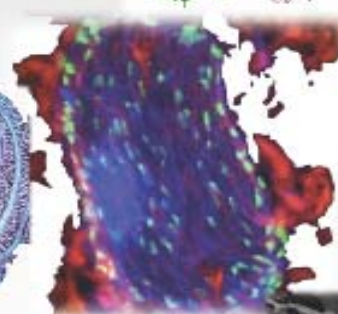
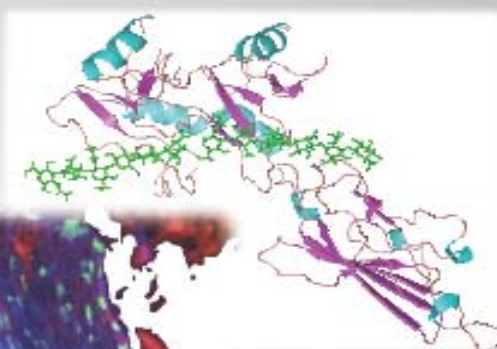
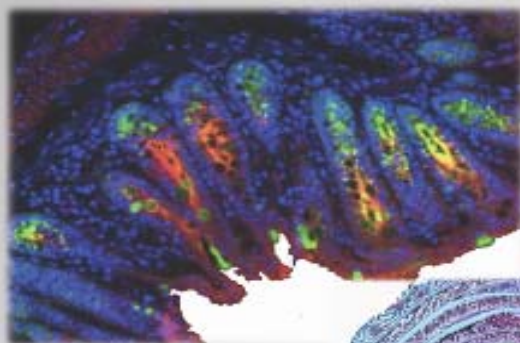
The First Wellcome Trust Centre for Cell Matrix Research Conference 2010

In association with the 22nd UK Adhesion Society Meeting
and the Italian Associazione di Biologia Cellulare e del Differenziamento

13th-15th September 2010

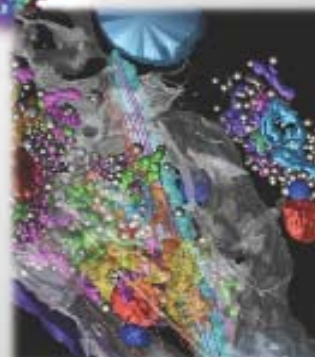
Michael Smith Building, University of Manchester

<http://ukadhesion.org>



Invited speakers include:

Paolo Defilippi
Elisabetta Dejana
Paul Martin
Ulrike Mayer
Jim Norman
Erik Sahai
Martin Schwartz



Registration and abstract submission open from 14th May 2010

Deadline: 6th August 2010

We look forward to welcoming you to **Get Connected!** in Manchester



Lonza

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