American Society for Matrix Biology

President's Letter

Expanding the Society's Value to You and Your Role in the Society

Bill Parks

Since its inception in 2001, the principal function of the ASMB has been to organize the biennial meeting. The value of this meeting to our members cannot be understated. The ASMB meeting has emerged as the matrix-centric meeting in North America, and it provides an open venue for students, postdocs, fellows, and junior faculty to present their work and to interact with established investigators. Speaking for myself, I very much look forward to the ASMB meeting, not only because I get to see many friends, but also to hear a lot of incredibly good science. This year's meeting will be no exception and promises to be truly outstanding. I applaud Jean Schwarzbauer and the rest of the Program Committee for putting together an exciting meeting loaded with interesting topics and great speakers (please check out the program here).

By organizing the meeting, ASMB provides value to you, the membership, but I think we-the Society-should always be looking to do more; that is, to provide more bang for your dues buck. For this year's meeting, we have expanded the Travel Awards that will be given to trainees in recognition of outstanding research, and we recently established merit-based Minority Scholarships that will be awarded to eligible students and postdocs. In addition to these, ASMB will recognize-as done in previous meetings- the accomplishments of an established researcher and a promising, up-and-coming new investigator. The 2010 ASMB Senior Investigator and Junior Investigator Awardees, which were nominated by the membership and elected by the Council, will be Benoit De Crombrugghe, MD Anderson, in recognition of his many seminal contributions to our understanding of ECM gene regulation, and Pyong W. Park, Harvard, who is developing a productive research program on proteoglycans in immunity.

In addition, we have expanded our interaction with related societies, thereby providing our members with further avenues for interactions with investigators working in complimentary areas. At the 2008 meeting, we began a successful relationship with the International Society of Matrix Biology, providing them with a Plenary Session that they program and use for presentation of several prestigious awards. For the 2010 meeting, we have established two new relationships, with the Society for Glycobiology and TERMIS (Tissue Engineering & Regenerative Medicine International Society), both of whom have organized satellite sessions that will be held just hours before the official start of our meeting. These relationships are simply great, and our hope is to expand them in the future, such as by organizing joint meetings.

These examples are but just some of the ways that I hope you agree that ASMB is enriching your involvement and career in matrix biology (other ideas are brewing). But providing value can be and should be a two-way street. To paraphrase John F. Kennedy, "Ask not what ASMB can do for you, ask what you can do for ASMB."

One thing you can do is to add to the ASMB meeting program. As we have done at previous meetings, we will provide space and time for programming 6 Special Interest Groups (SIGs), which are announced elsewhere in this newsletter. I strongly encourage you to take advantage of this opportunity. In particular, our hope is that junior members of the society will organize sessions on a focused topic that they feel needs to be represented and will be of interest to many. As stated in the SIG announcement, please send your ideas to me.

Another way you can participate–and one I hope you do consider–is to contribute to the content and impact of the ASMB web site, and there are two areas I wish to emphasize. One, the web site includes a Links page that lists a variety of topic-specific sites, such as for information on integrins or metalloproteinases or java tools on what filters can be used with specific fluorophore (very nice!). However, I have no doubt that there are many more sites that provide practical information for matrix biologists. Thus, if you run across a particularly useful, interesting, or fun site, please forward the link to us* and we will add it. (In this case, "us" is Jen Holland.)

Two, we hope to build a gallery of images accessible only to ASMB members. But in order to do this, we need images, and we need images from you. So, if you have some slick, matrix-related immunofluorescence or stained images, please send them to us. With your approval, your images will be included in the rotating display embedded in the fixed sidebar that is part of essentially all pages. Let the world admire your work!

I thank you for reading this letter, and I do hope you will consider ways to contribute to the ASMB. See you in Charleston!

Bill Parks
ASMB President

Request for Proposals

Special Interest Groups (SIGs)

American Society for Matrix Biology
Biennial Meeting, October 24-27, 2010
Charleston, SC

What are SIGs?

Special Interest Groups (SIGs), which are an adjunct to the official program for the 2010 ASMB meeting, should be centered on a fairly focused topic. The overall goals of the SIGs are to provide opportunity for investigators working in closely similar areas to exchange new data and ideas and to allow students, postdocs, and junior investigators to present their work and receive feedback from leaders in the field.

What is the Format of SIGs?

Each SIG will have a 60-min block. The format of the SIGs is flexible and can be adjusted to fit the ideas and goals of the organizers. Typically, the format of SIGs has been similar to other sessions, with 1 (or more) Discussion Leaders and 3-4 speakers, but any format is OK. Although a "Big Name" can be included as a speaker, the bulk of presentations should be those doing the work.

When and Where will the SIGs be Held?

Space and time has been reserved for 6 SIGs during the ASMB meeting. These sessions will be held from 6 to 7 PM on Monday, October 25, 2010, and Tuesday, October 26, 2010 at the meeting hotel.

How do I Submit my Proposal? By When?

SIG proposals should include the overall topic and format and the names and affiliations of the discussion leaders and speakers (if appropriate). Send your 1 page proposal to Bill Parks (parksw@uw.edu).

Proposals are due August 1, 2010

Take Advantage of the Early Bird Registrations Rates!
Register for the ASMB Meeting NOW!

http://www.asmb.net/2010_registration.php

Biennial Meeting of the American Society for Matrix Biology

October 24-27, 2010 • Francis Marion Hotel • Charleston, South Carolina

Organizers: *William Parks, Jean Schwarzbauer*

Sunday, October 24th

1:00-3:00 pm Guest Symposium I
Presented by TERMIS (Tissue Engineering & Regenerative Medicine International Society)
Chair: **Robert Sah,** UCSD

Mimicking ECM Regulation of Growth Factor Signaling
William Murphy, University of Wisconsin

Dynamic Shear-influenced Collagen Self-Assembly and Corneal Tissue Engineering
Jeffrey Ruberti, Northeastern University

How the Matrix Controls the Myofibroblast to Control the Matrix
Boris Hinz, University of Toronto

Tooth Tissue Engineering
Pam Yelick, Tufts University

3:30-5:30 pm Guest Symposium II
Presented by SFG (The Society for Glycobiology)
Chair: **Robert Haltiwanger,** Stony Brook University

Glycosylation of Thrombospondin Type 1 Repeats
Robert Haltiwanger, Stony Brook University

Proteoglycans in Vascular Biology
Jeff Esko, UCSD

Novel Post-Translational Processing of Dystroglycan: Insights from Muscular Dystrophy Patients
Kevin Campbell, University of Iowa

Proteoglycan Codes in Embryonic Development
Joseph Yost, University of Utah School of Medicine

7:00-7:15 pm President's Welcome
William Parks, University of Washington

7:15-8:00 pm Keynote Lecture
Stem Cells, Extracellular Matrix, Tissue Morphogenesis and Cancer in Skin
Elaine Fuchs, Rockefeller University

Monday, October 25th

8:30-10:00 am Plenary I: ECM-Cell Interactions and Signaling

Cell-Matrix Interactions in Tumor Progression
Richard Hynes, MIT

Dynamic Reciprocity Between the ECM and DNA Machinery: A Progress Report
Mina Bissell,
Lawrence Berkeley National Laboratory

Tetraspanin CD151 Facilitates Laminin-Specific Tumor Cell Behavior
Martin Hemler, Harvard

10:30-12:00 pm Plenary II: ECM in Development

Transcriptional Control of Cartilage and Bone Homeostasis
Senior Investigator Awardee:
Benoit de Crombrugghe,
U.T.M.D. Anderson Cancer Center

Matrix, Mechanical Forces and Morphogenesis
Doug DeSimone, University of Virginia

Regulation of Cell Fate in the Skeleton
Rosa Serra, UAB

12:00-12:30 pm Business Meeting and Forum Demonstration

12:30-2:30 pm Poster Session I Lunch

2:30-4:00 pm Concurrent A: Basement Membranes
Basement Membranes and Kidney Function: Laminin Rules
Chair/Speaker: **Jeff Miner,** Washington Univ. School of Medicine

Concurrent B: Wound Repair, Regeneration, and Fibrosis
Molecular Control of Stromal Remodeling
Chair/Speaker: **Maria Trojanowska,** Boston Univ.

Concurrent C: TBA

4:30-6:00 pm Concurrent D: Receptors
Dynamics of Integrin-Based Migration
Chair/Speaker: **Ken Yamada,** NIH

Concurrent E: Proteases and Inhibitors
ADAMTS Proteolysis of Versican
Chair/Speaker: **Suneel Apte,** Cleveland Clinic Foundation

Concurrent F: ECM Proteins and the Musculoskeletal System
Key Roles of Proteoglycans and their Partners in Skeletal Homeostasis and Disease
Chair/Speaker: **Marian Young,** NIH

Tuesday, October 26th

8:30-10:00 am Plenary III: ECM Disease Mechanisms

Syndecan-Pathogen Interactions in Infectious Diseases
Junior Investigator Awardee:
Pyong Woo Park, Children's Hospital at Harvard

New Functions of Thrombospondin-1 and its Receptor CD47 in Responses to Stress
David Roberts, NIH, NCI

Elastases in Health and Disease: The Matrix and Beyond
Steven Shapiro, University of Pittsburgh

10:30-12:00 pm Plenary IV: ISMB Guest Symposium
Chair: **Renato Iozzo**, Thomas Jefferson University

Presentations by ISMB's Distinguished Investigator and Travel Awardees.

12:00-2:00 pm Poster Session II Lunch

2:00-3:30 pm Concurrent G: Synthesis and Assembly
Fibrillin Assembly Mechanisms
Chair/Speaker: **Dieter Reinhardt,** McGill University

Concurrent H: Neural Development and Disease
The Role of Laminin in Excitotoxic Neurodegeneration
Chair/Speaker: **Sidney Strickland,** Rockefeller Univ.

Concurrent I: Angiogenesis
New Insights into Activation of the Angiogenic Switch
Chair/Speaker: **Kayla Bayless,** Texas A&M Health Science Center

4:00-5:30 pm Concurrent J: Growth Factor Regulation
Extracellular Interactions that Fine Tune Growth Factor Signaling: Structure/Function Studies Using New Fbn1 Mutant Mouse Models
Chair/Speaker: **Lynn Sakai,** Shriners Research Center, Portland

Concurrent K: Engineered ECMs
Dynamic, Engineered Matrices Improve Cell Differentiation: Lessons from Developmental Biology
Chair/Speaker: **Adam Engler,** UCSD

Concurrent L: Acquired, Acute, and Chronic Diseases
Chair: **Pyong Woo Park,** Children's Hospital at Harvard
Role of Hyaluronan in Diabetic Pathologies
Speaker: **Vincent Hascall,** Cleveland Clinic Foundation

Wednesday, October 27th

8:30-10:00 am Concurrent M: Invasion and Migration
3-D Extracellular Matrix Remodeling and the Linked Control of Nuclear Function
Chair/Speaker: **Steve Weiss,** University of Michigan

Concurrent N: Proteoglycans and Glycobiology
Versican: A Key ECM Regulator of Cellular Phenotype
Chair/Speaker: **Tom Wight,** Benaroya Research Inst.

Concurrent O: Development and Morphogenesis
ADAMTS Cleavage of Versican is Critical for Cardiac Valve Morphogenesis
Chair/Speaker: **Christine Kern,** MUSC

10:30-12:00 pm Concurrent P: Genetic Diseases
Genetic Diseases Caused by Defects in the Collagen Folding Machinery
Chair/Speaker: **Hans Peter Bächinger,** Shriners Research Center, Portland

Concurrent Q: Matricellular Proteins
SPARC: A Critical Player in ECM Assembly
Chair/Speaker: **Amy Bradshaw,** MUSC

Concurrent R: Microenvironment in Stem Cell Biology and Cancer
Heparanase Regulation of the Tumor Microenvironment: Mechanism and Therapy
Chair/Speaker: **Ralph Sanderson,** UAB

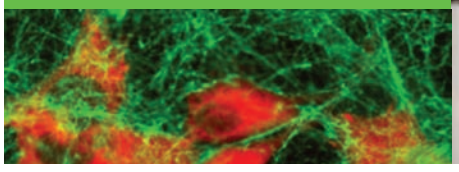
ASMB
American Society for Matrix Biology

October 24-27, 2010
Francis Marion Hotel
Charleston, SC

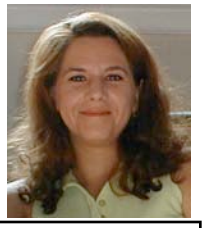
2010

Online registration and abstract submission now open!
www.asmb.net

Meeting website: www.asmb.net



Tell Us What Your Lab is Doing!



Rosa Serra, Ph.D.

From the laboratory of Rosa Serra, Ph.D.

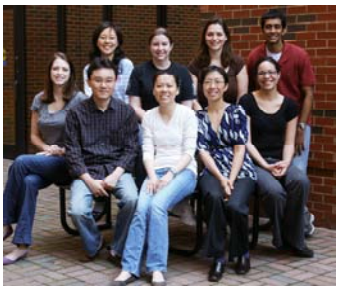
Professor of Cell Biology, University of Alabama at Birmingham
Birmingham, AL USA

Sohn P, Cox M, Chen D, Serra R Molecular profiling of the developing mouse axial skeleton: A role for Tgfbr2 in the development of the intervertebral disc. BMC Developmental Biology 10(1):29, 2010.

Seo H-S, Serra R Deletion of Tgfbr2 in Prx1-cre expressing limb mesenchyme results in defects in the development of the long bone and joints. Developmental Biology 310:304-316, 2007.

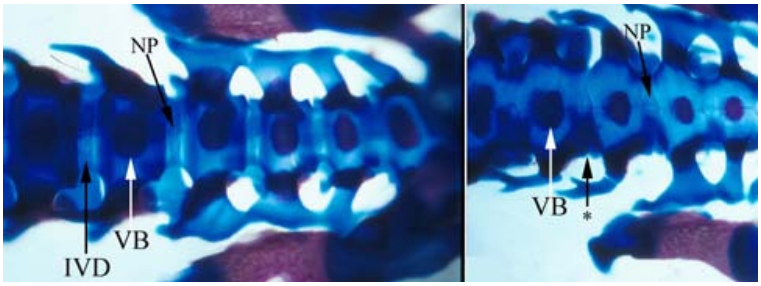
Baffi, MO, Slattery E, Sohn P, Moses HL, Chytil A, Serra R Conditional Deletion of the TGF-β Type II Receptor in Col2a Expressing Cells Results in Defects in the Axial Skeleton Without Alterations in Chondrocyte Differentiation or Embryonic Development of Long Bones. Developmental Biology, 276:124-142, 2004

The goal of this project is to study the role of TGFβ in developing connective tissues of the skeleton, including intervertebral disc (IVD) and joint interzone, and then use this information in tissue repair and engineering strategies. Previously, we showed using genetically engineered mouse models that the TGF-ß Type II receptor (Tgfbr2) is required for development and maintenance of the IVD. More recently, we showed that TGF-ß promotes differentiation of sclerotome, an embryonic pluripotent mesenchymal cell, into annulus cells of the IVD. Cultures treated with TGF-ß1 displayed spindle shaped morphology with diffuse Alcian blue staining characteristic of cells in the IVD whereas BMP treated cells displayed typical cartilage staining and morphology. Microarrays were used to compare gene expression in cultures that were untreated or treated with BMP4 or TGF-ß1and to determine the molecular phenotype of the cells. Treatment with BMP resulted in the induction of genes associated with chondrogenesis including Sox5, Sox9, and Aggrecan. None of these genes were up-regulated in TGF-ß treated sclerotome. Instead the expression of genes that are normally enriched in IVD and tendon relative to cartilage, including Fibromodulin, Adamtsl2, Versican, and Scleraxis, were up-regulated. Comparison of the global gene expression profiles in IVD and vertebrae with the genes that were up-regulated by TGF-ß suggested that TGF-ß promotes differentiation of IVD at the molecular level. Several of the genes identified in this screen represent transcription factors that could act as master regulators of annulus differentiation, similar to the role of Sox9 in cartilage.



Current lab members: Wen Jiang, Megan Cox, Sarah Baxley, Girish Ramaswamy, Elizabeth Mitchell, Hwa-seon Seo, Ying Wang, Jessica Perez. Not shown, Phil Sohn.

We also addressed the role of Tgfbr2 in limb development in vivo using Prx1Cre-mediated LoxP recombination in mouse embryos. Surprisingly, early limb development including mesenchymal condensation and early chondrocyte differentiation occurred normally in Tgfbr2 depleted mice. However depletion of Tgfbr2 in limb mesenchyme resulted in fusion of the joints in the phalanges later in development. Analysis of markers for joint development indicated that the joint was specified properly but that cells in the interzone, the transient connective tissue that will form the joint, were not maintained. Furthermore, there was an unexpected increase in the number and intensity of Alcian blue stained chondrogenic nodules when limb cells from Tgfbr2-null mice were grown in micromass cultures relative to cultures from control limbs suggesting Tgfbr2 normally limits chondrogenesis in vitro. Together the results suggest that Tgfbr2 is required for normal development of the skeleton and that Tgfbr2 acts to limit chondrogenesis and maintain differentiation of connective tissues like the interzone and intervertebral disc.



Loss of IVD in Col2aCre;Tgfbr2 mutant mice. Alcian blue/ alizarin red stained skeletons from control (left) and mutant (right) mice at E17.5 days. The annulus fibrosus of the IVD is replaced with red staining mineralized tissue.

Important Annual Meeting Announcements

TBA Concurrent Sessions

The ASMB 2010 meeting program includes 18 Concurrent sessions. 17 of these sessions have been programmed and will focus on defined topics. One concurrent session is "to be announced". We plan to develop the focus for this session based on submitted abstract topics. It may be used to fill in a gap in the program or to highlight late-breaking research. If you have suggestions for this session topic, send them to Jean Schwarzbauer (jschwarz@princeton.edu).

Society for Glycobiology (SfG) Guest Symposium

Due to the many common interests of ASMB and the Society for Glycobiology, the leadership of both societies have initiated joint events to highlight and increase these links at our respective meetings. This fall the Society for Glycobiology is sponsoring a guest symposium at the beginning of the ASMB meeting in Charleston, South Carolina. The symposium will highlight the roles of glycans in the interactions and function of extracellular matrix components. Presentations will include the role of O-fucosylation on thrombospondin type 1 repeats (Robert Haltiwanger), roles of proteoglycans in vascular biology (Jeff Esko) and embryonic development (Joseph Yost), and the roles of O-glycans on α-dystroglycan in interaction with matrix and congenital muscular dystrophies (Kevin Campbell). These talks should have broad appeal to members of the matrix biology community. ASMB hosted a similar symposium at the 2009 Society for Glycobiology meeting last November. Jeff Esko, Barbara Mulloy, Renato Izzo, and Jean Schwarzbauer gave excellent presentations. We look forward to continuing similar interactions between the two societies well into the future.

Related Meeting Information

Thrombospondins and other Matricellular Proteins in Tissue Organization and Homeostasis

July 18-23, 2010 Snowmass, Colorado

2010 FASEB Summer Research Conference. Organizers: David D. Roberts, Chair; Joanne Murphy-Ullrich, Co-Chair

Hyaluronan 2010

June 6-11, 2010 Kyoto, Japan

International Society for Hyaluronan Sciences
8th International Conference, Kyoto, Japan
Conference organizers:
Koji Kimata (Aichi Medical University)
Masaki Yanagishita (Tokyo Medical & Dental University)
Bryan Toole (Medical University of South Carolina)
For details, please visit: http://www.ishas.org

2010 Proteoglycan Gordon Research Conference

Development, Disease, & Therapeutics

July 11-16, 2010 Andover, NH

The goal of the 2010 Gordon Research Conference on Proteoglycans will be to bring together leading national and international scientists to present their latest findings in proteoglycan research. Topics that will be discussed include mechanisms regulating the production and assembly of the proteoglycans core proteins as well as their turnover. The role of proteoglycans in development, skeletal pathology, cancer, stem cells, regenerative medicine, inflammation, cardiovascular disease, and angiogenesis will also be addressed. The most recent progress within these areas with attention to the generation of both novel tracking assays and treatment regimens for diseases caused by abnormal proteoglycan function will be presented. Particular emphasis will be given to new insights into basic molecular mechanisms and to translational efforts designed to understand the role of proteoglycans in human disease as well as their use in prevention and novel therapeutics.
Chair: Marian Young, Co-chair, Robert Linhardt
To view details on this conference please go to the following website:
http://www.grc.org/programs.aspx?year=2010&program=proteoglyc

8th International Symposium for Marfan Syndrome and Related Disorders.

Sept 11-14, 2010 Arlie Center, VA

The National Marfan Foundation (NMF) along with the University of Washington Collagen Diagnostic Laboratory are hosting the 8th International Symposium for Marfan Syndrome and Related Disorders. This meeting will take place at the Airlie Center in Warrenton, VA, from Sept. 11 – 14, 2010. Abstract deadline is June 11, 2010. Submissions should be sent to abstract@marfan.org. For more detailed information on the program and abstract submission guidelines, visit Conference and Events at www.marfan.org.

Save the Date!
New Gordon Conference
Lung Development, Injury, & Repair
August 14-19, 2011 Salve Regina Univ.
Newport, RI

Lung diseases present a huge global health burden with over 600 million people worldwide affected by diseases such as COPD and pulmonary fibrosis. Furthermore, acute lung injury is a common response to infection with many emerging pathogens. Despite the huge health burden, there are relatively few, if any therapeutic agents that improve survival for these diseases. Because injury and repair often utilize similar pathways, understanding the common biological principles will facilitate developing innovative treatments for lung disease. This conference will emphasize mechanisms in lung development, injury and repair and focus on new advances in these fields such as microRNA, systems biology, and bioengineering. By bringing together a diverse and outstanding group of investigators together to present the most up-to-date advances in these related fields, we hope to encourage creative and multidisciplinary approaches that will ultimately facilitate development of innovative and effective therapies.

For more information,
http://www.grc.org/programs.aspx

Sixth European Elastin Meeting
June 28-July 2, 2010 Maratea, Italy

It is for us a great honor to announce that the Sixth European Elastin Meeting 2010 will be held in Maratea, on the Italian Tyrrhenian Sea, and will be organized by the University of Basilicata. The program will cover the most recent advances in all aspects of elastin biology. In addition to a strong scientific program, the informal atmosphere of the meeting is designed to facilitate informal scientific discussion and the establishment of collaborations.The scientific program will consist of invited talks, of oral contributions selected from the submitted abstracts and of poster presentations. More information can be found at:http://www.unibas.it/utenti/pepe/Home_Elastin2010/index.htm

A Symposium on Basement Membranes in Tissue Development and Regeneration
July 7-9, 2010
Vanderbilt University, Nashville, TN

Abstract submission site now open
To Register and submit abstract please go to
http://www.mc.vanderbilt.edu/cmb/ or
http://www.asmb.net/meeting_signup.php?meeting_id=3
25 abstracts will be chosen for oral presentations
Great Scientific program with world leaders as speakers
Abstract deadline is June 1, 2010
Questions on program : Roy Zent roy.zent@vanderbilt.edu

Registration Questions
Jennifer Holland
FASEB Managed Society Services
9650 Rockville Pike
Bethesda, MD 20814
jholland@faseb.org
P: 301.634.7814
F: 301.634.7455

Vanderbilt University Medical Center
Center for Matrix Biology
presents a
Symposium on Basement Membranes in Tissue Development and Regeneration
July 7-9, 2010
at
Vanderbilt University, Nashville
Registration and abstract submissions now open
http://www.mc.vanderbilt.edu/cmb/
Registration and meals $250

Topics
Macromolecular Components
Development, Tissue Morphogenesis and Stem Cells
BMs in Disease
Use of Model Organisms

Keynote Speaker
Karl Tryggvason

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 Sekiguchi
Arnoud Sonnenberg
Lydia Sorokin
David Sherwood
Jouni Uitto
Yujia Xu
Pampee Young
Peter Yurchenco

Check out the New and Improved ASMB Website

www.asmb.net

Website Features

- Society information, including bylaws, history, Council members, etc.
- Complete ASMB awards information including criteria, applications and history
- Historical information about past ASMB meetings
- Career opportunities as posted on our new forum site with Scientist Solutions
- Other meetings listings
- Links to other resources such as partnering societies
- Newsletter archive
- Image Gallery

ASMB business

- Join/Renew your membership
- Manage and update your ASMB record
- Search our member database
- Link to Scientist Solutions forums
- Post related meetings
- Post job opportunities (under forums)
- Manage your *Matrix Biology* journal subscription

Need help navigating the new website?
Email asmb@asmb.net and we'll be happy to assist!

Don't Forget to Renew!

Your participation in our Society is the most important contribution you can make to helping increase awareness of research and opportunities in extracellular matrix biology.

With the help of your membership dues, we have added professional management of the society and provided students and postdoctoral fellows with travel awards to our national meeting. In the coming year, your dues will be at work to improve our website. We urge you to pay your dues so we can continue to add programs that benefit matrix biology.

The 2010 Annual Dues are $90 for regular membership and $50 for students/postdoctoral fellows. Dues can be paid any time via the ASMB website: http://www.asmb.net/

Alternatively, checks can be sent to the administrative office: ASMB, 9650 Rockville Pike, Bethesda, MD 20814.

Advantages of Membership:

- Discounts on *Matrix Biology* subscriptions (print and online)
- Discounts on Biennial Meeting registration
- Access to online forums and image galleries
- Receive society newsletters with article reviews and summaries
- Partner links to numerous other societies and valuable scientific resources
- Opportunities to submit abstracts for biennial meeting presentations
- Biennial meeting award eligibility
- Eligibility to run for Council positions and help direct the Society
- Access to list and view career opportunities within the community
- Make valuable professional connections with junior and senior researchers

Thank you to our sustaining members!

William Parks, *University of Washington*
Renato Iozzo, *Thomas Jefferson University*
Kenneth Yamada*, NIH, NIDCR*
Robert Mecham, *Washington University*
Peter Yurchenco, *UMDNJ-RW Johnson Medical School*

JOB OPENINGS

Postdoctoral Position to Study Mouse Genetic Models of Retinal Degeneration

A postdoctoral position is available to study a novel mouse genetic model of retinal degeneration at the UCSF School of Medicine in San Francisco. Mice with mutations in the Col4a1 gene have clinical, histological, molecular and ultrastructural hallmarks of Age-Related Macular Degeneration (AMD). We are using genetic and cell biological approaches (modifier screens, conditional mutations and mutant allelic series) to characterize the pathology and determine the primary disease mechanism(s). The goal is to identify key molecular mechanisms that may be targeted with therapeutic interventions in human patients. Interested individuals should have a published track record in genetics and molecular biology. Candidates with experience in vision research, matrix biology and mouse genetics are preferred.

Interested individuals should email the following to GouldD@vision.ucsf.edu: 1) their CV; 2) a statement of research experience; 3) a statement of career goals; 4) contact information for two references.

Doug Gould, PhD.
Departments of Ophthalmology and Anatomy
Institute for Human Genetics, UCSF School of Medicine
10 Koret Way, Room K235
San Francisco, CA, 94143

Postdoctoral Position to Study Mouse Genetic Models of Cerebrovascular Disease

A postdoctoral position is available to study a novel mouse genetic model of cerebrovascular disease at the UCSF School of Medicine in San Francisco. We have previously determined that mutations in the Col4a1 gene in mice and in human patients can cause porencephaly (Gould et al. Science, 2005) and predispose to a spectrum of cerebrovascular phenotypes including hemorrhagic stroke (Gould et al. New Engl J Med, 2006). More recently, COL4A1 mutations have been identified in several families with cerebrovascular disease.

The successful candidate will use genetic and cell biological approaches (modifier screens, conditional mutations and mutant allelic series) to characterize the pathology and determine the primary disease mechanism(s). The goal is to identify key molecular mechanisms that may be targeted with therapeutic interventions in human patients. Interested individuals should have a published track record in genetics and molecular biology. Candidates with experience in vascular biology, matrix biology and mouse genetics are preferred. Interested individuals should send their CV, a statement of research experience, a statement of career goals and contact information for two references to GouldD@vision.ucsf.edu.

Doug Gould, PhD.
Departments of Ophthalmology and Anatomy
Institute for Human Genetics, UCSF School of Medicine
10 Koret Way, Room K235
San Francisco, CA, 94143

Post-doctoral Research Opportunity. Department of Orthopaedic Surgery and Department of Cell Biology and Physiology, Washington University in St. Louis

Studies involve gene expression in connective tissues, cartilage repair, osteoarthritis, and angiogenesis. Specific studies are on type II collagen functions, the transcription factors C/EBP and NF-kB, and the role of chemokines in skeletal development and disease. Position available immediately. Contact Dr. Linda Sandell, sandell@wustl.edu.

Interesting Science

Gabapentin receptor alpha2delta-1 is a neuronal thrombospondin receptor responsible for excitatory CNS synaptogenesis.

Eroglu C, Allen NJ, Susman MW, O'Rourke NA, Park CY, Ozkan E, Chakraborty C, Mulinyawe SB, Annis DS, Huberman AD, Green EM, Lawler J, Dolmetsch R, Garcia KC, Smith SJ, Luo ZD, Rosenthal A, Mosher DF, Barres BA. Cell (2009) 139:380-92.

The Barres laboratory previously identified a novel activity of astrocyte-secreted Thrombospondin-1 (TSP-1) in promoting excitatory synaptogenesis by CNS neurons (Christopherson et al (2005), Cell 120, 421-33). The Eroglu et al. paper constitutes a major follow-up that identifies both a mechanism of potential applicability to all mammalian TSPs and implicates TSPs in a new clinical context.

The authors map the synaptogenic activity of TSP-1 and TSP-1 to their EGF domains and demonstrate that other TSP family members (all of which contain EGF domains) have synaptogenic activity in vitro. Very few ligands are known for the EGF domains of TSPs and, building from a reported interaction with the vWF_A domain of αM integrin, the authors identify α2δ-1, a non-essential subunit of the L-type calcium channel, as a receptor on retinal ganglion cells that binds TSP-1 or -2 and is required for synaptogenic activity. This interaction is mediated by the vWF_A domain of α2δ-1 and the role of α2δ-1 is separable from the status of calcium channel levels or function. The significance of the interaction is confirmed by studies in vivo in which over-expression of α2δ-1 in CNS neurons increased the numbers of VGlut-2-positive excitatory synapses without altering the numbers of neurons.

This part of the Eroglu et al. paper opens up many new questions for thrombospondin and ECM biology: because α2δ-1 is widely expressed outside the CNS, could this receptor be a general binding partner of TSPs in many tissues? Are there other vWF_A domain proteins that interact with the EGF domains of TSPs? Are there other EGF domain-containing adhesion proteins (eg, tenascin is also upregulated after CNS injury) that bind α2δ1?

Clear biochemical evidence is presented for the α2δ1/TSP interaction, yet, because the synaptogenic activity of α2δ1 can be recapitulated by its extracellular domain alone, it is possible that other interacting proteins are required for intracellular signaling of synapse organization. Notably, TSP-1 acts to increase synapse number in vitro but the synapses formed are not fully active and lack post-synaptic cell surface AMPA receptors. Interestingly, a very recent independent study of the synaptogenic activity of TSP-1 on immature hippocampal neurons has implicated neuroligin, a transmembrane synaptic cell adhesion molecule, as a necessary binding partner for this activity of TSP-1 (Xu et al., Nat Neurosci. epub Nov 15 2009). This study did not define the TSP domain necessary for the interaction or include in vivo analyses, nevertheless the data underscore the possibility that TSP/α2δ1 might be part of a larger molecular assembly at neuronal cell surfaces.

The Eroglu et al. paper also brings TSP biology into the arena of clinical neuroscience. α2δ-1 is the receptor for two widely-prescribed medications for epilepsy and neuropathic pain, gabapentin and pregabalin. The mechanism of action of these drugs has remained unclear but appears to be independent of calcium channel function. The authors demonstrate that gabapentin interferes with the EGF domain/α2δ1 interaction in vitro and blocks TSP activity at the level of new synapse formation. In a barrel cortex plasticity assay (an in vivo model for synaptic plasticity), normal plastic remodeling in wild-type mice was blocked by gabapentin treatment. TSP-1/2 double knockout mice had similar deficiencies in remodeling. These data suggest that one action of gabapentin is to interfere with the TSP/α2δ1 interaction and thereby the formation of excitatory synapses. This would imply that the TSP/α2δ1 interaction should be strictly regulated in vivo: indeed, TSP-1 and -2 are essentially absent from adult mammalian brain but are up-regulated after acute injury. The TSP field began with the study of TSP-1 in platelets: this paper signposts CNS injury and pain as fruitful areas for the future.

Contributed by Josephine Adams, University of Bristol

New Publications (contributed by ASMB members)

*Contributed by Rolf A. Brekken, PhD (*rolf.brekken@utsouthwestern.edu)

1) Arnold SA, Rivera LB, Miller AF, Carbon JG, Dineen SP, Castrillon DH, Xie Y, Sage EH, Puolakkainen P, Bradshaw AD, and Brekken RA. (2010) Lack of host SPARC enhances vascular function and accelerates metastasis in an orthotopic murine model of pancreatic carcinoma. Disease Models and Mechanisms 3:57-72. PMID: 20007485
Summary:
Utilizing subcutaneous tumor models, we previously validated SPARC (secreted protein acidic and rich in cysteine) as a key component of the stromal response, where it regulated tumor size, angiogenesis and extracellular matrix deposition. In the present study, we demonstrate that pancreatic tumors grown orthotopically in Sparc-null (Sparc*/*) mice are more metastatic than tumors grown in wild-type (Sparc+/+) littermates. Tumors grown in Sparc*/* mice display reduced deposition of fibrillar collagens I and III, basement membrane collagen IV and the collagen-associated proteoglycan decorin. In addition, microvessel density and pericyte recruitment are reduced in tumors grown in the absence of host SPARC. However, tumors from Sparc*/* mice display increased permeability and perfusion, and a subsequent decrease in hypoxia. Finally, we found that tumors grown in the absence of host SPARC exhibit an increase in alternatively activated macrophages. These results suggest that increased tumor burden in the absence of host SPARC is a consequence of reduced collagen deposition, a disrupted vascular basement membrane, enhanced vascular function and an immune-tolerant, pro-metastatic microenvironment.

2) Schluterman MK, Chapman SL, Korpanty G, Ozumi K, Fukai T, Yanagisawa H and Brekken RA. (2010) Loss of endogenous fibulin-5 inhibits pancreatic tumor growth by increasing the level of ROS in the tumor microenvironment. Disease Models and Mechanisms (in press) PMID: 20197418.
Summary:
Tumor survival depends in part on the ability of tumor cells to transform the surrounding extracellular matrix (ECM) into an environment conducive to tumor progression. Matricellular proteins are secreted into the ECM and impact signaling pathways that are required for pro-tumorigenic activities such as angiogenesis. Fibulin-5 (Fbln5) is a matricellular protein that was recently shown to regulate angiogenesis; however, its effect on tumor angiogenesis and thus tumor growth is currently unknown. We report that the growth of pancreatic tumors and tumor angiogenesis is suppressed in Fbln5-null (Fbln5*/*) mice compared with wild-type (WT) littermates. Furthermore, we observed an increase in the level of reactive oxygen species (ROS) in tumors grown in Fbln5*/* animals. Increased ROS resulted in elevated DNA damage, increased apoptosis of endothelial cells within the tumor, and represented the underlying cause for the reduction in angiogenesis and tumor growth. In vitro, we identified a novel pathway by which Fbln5 controls ROS production through a mechanism that is dependent on b1 integrins. These results were validated in Fbln5RGE/RGE mice, which harbor a point mutation in the integrin-binding RGD motif of Fbln5, preventing its interaction with integrins. Tumor growth and angiogenesis was reduced in Fbln5RGE/RGE mice, however treatment with an antioxidant rescued angiogenesis and elevated tumor growth to WT levels. These findings introduce a novel function for Fbln5 in the regulation of integrin-induced ROS production and establish a rationale for future studies to examine whether blocking Fbln5 function could be an effective anti-tumor strategy, alone or in combination with other therapies.

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*Contributed by Gunjan Agarwal (*Gunjan.Agarwal@osumc.edu)

1. Sivakumar S and Agarwal G. The Influence of Discoidin Domain Receptor 2 on the Persistence Length of Collagen Type I Fibers, Biomaterials 2010 (in press)

2. Flynn LA, Blissett AR, Calomeni EP and Agarwal G Inhibition of Collagen Fibrillogenesis by Cells Expressing Soluble Extracellular Domains of DDR1 and DDR2. J Mol Biol. 2010 395(3):533-43

3. Blissett AR, Garbellini D, Calomeni E, Mihai C, Elton TS and Agarwal G. Regulation of Collagen Fibrillogenesis by Kinase-Dead DDR2, J. Mol Biol. 2009 Jan 23; 385(3) 902-911.

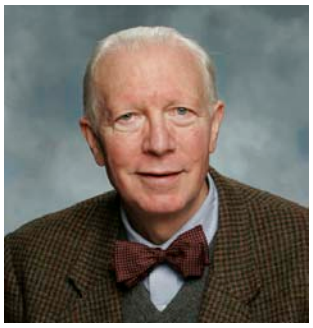
In Memoriam

In Memoriam: Bob Trelstad

From the Office of Peter S. Amenta, MD, PhD, Dean, UMDN J-Robert Wood Johnson Medical School.

It is with great sadness that I inform you that Robert L. Trelstad, MD, passed away on February 16, 2010. Dr. Trelstad worked tirelessly to build academic and clinical programs throughout the university and the state. His leadership resulted in the development and growth of the Department of Pathology and Laboratory Medicine as we know it today. His accomplishments were only matched by his collegiality and collaborative nature. He will be greatly missed in our community, nationally and internationally.

Dr. Trelstad began his career at UMDNJ-Robert Wood Johnson Medical School as professor and chair, Department of Pathology and Laboratory Medicine in 1981. He served as chair of the department for 17 years. It was my honor and privilege to work for him and with him. In 1998, Dr. Trelstad became the acting director and the Harold L. Paz, MD, Professor of Developmental Biology at the Child Health Institute of New Jersey. For seven years, he served a pivotal role in the funding, planning and construction of the new facility.



Bob Trelstad

Dr. Trelstad received his medical degree in 1966 from Harvard Medical School, cum laude, Alpha Omega Alpha. He completed an internship and residency in pathology at Massachusetts General Hospital and was an assistant professor of pathology at Harvard Medical School. He was appointed to associate professor at Harvard Medical School in 1977 before joining Robert Wood Johnson Medical School.

For more than 30 years, Dr. Trelstad contributed greatly to the scientific community. In the 1970s, he served as a member of the Corneal Task Force of the National Eye Institute, and as a member of a number of National Institutes of Health (NIH) study sections including cell biology and pathobiological chemistry. He served on the external review committee for the laboratory on developmental biology and craniofacial anomalies. During the 1980s, he served the NIH as a member of the panel on congenital anomalies and acquired defects. As a member of the executive council of the American Society for Cell Biology and as president of the Society for Developmental Biology he played pivotal roles in the growth and maturation of the organizations. He was a member of the Research Peer Review Committee for the American Heart Association, served on the Scientific Advisory Board for the Shriners Hospital for Crippled Children and was a member of Fogarty International Awards Review Group for the NIH.

Dr. Trelstad served on numerous editorial boards, including the Journal of Cell Biology. He was an associate editor of at least eight journals and was a member of the editorial advisory board of at least three other journals. He was the editor-in-chief of Keyboard Publishing, Inc., one of the first ventures in the area of online publications.

Dr. Trelstad authored more than 175 publications in journals as prestigious as Nature, The Journal of Cell Biology, The New England Journal of Medicine and The Journal of Biochemistry. He published studies in developmental biology, collagen morphogenesis and biochemistry and basement membrane assembly. He also co-authored chapters in leading pathology textbooks on tissue repair and regeneration. Dr. Trelstad was an investigator or principal investigator on 25 different research grants.

His educational accomplishments were well recognized by his peers. In 1992, Dr. Trelstad was the recipient of the National Distinguished Teaching Award in Basic Sciences from Alpha Omega Alpha and the Association of American Medical Colleges, now known as the Alpha Omega Alpha Robert J. Glaser Distinguished Teacher Awards.

In 2007, he received the Edward J. Ill Outstanding Medical Educator Award which is presented annually to a medical educator who has made outstanding contributions to graduate and/or undergraduate medical education in New Jersey. He was recognized as an educational visionary and a leader, advocating and promoting the use of computers in medical education and the deployment of computers and technology in meeting the education mission of one of the nation's largest health education systems.

Please join me in expressing our condolences to his wife, Barbara, his entire family, friends and colleagues.

In Memoriam: Leena Peltonen

From Lynn Sakai, Shriners Hospital. and Darwin Prockop, Texas A&M Health Science Center

The passing of Leena Peltonen on March 11, 2010, came as very sad and surprising news. Memorials written by the Academy of Finland, the Broad Institute, and the Wellcome Trust Sanger Institute are available for reading on the internet. These memorials describe Leena's many contributions to human molecular genetics, her mentoring of some 70 Ph.D. students, her multiple honors including the Finnish honorary title of "Academician of Science," and the many leadership roles that she performed. From these memorials, we see that Leena is remembered primarily as a "visionary geneticist." Leena was also an accomplished matrix biologist. For many of us in matrix biology, Leena was a dear friend and wonderful colleague, someone who grew up in the famous matrix biology environments of Rutgers and Helsinki. One of Leena's first papers was on "thermal stability of type I and type III procollagens from normal human fibroblasts and from a patient with osteogenesis imperfecta." This manuscript was published in *PNAS* in January, 1980. Later that year, a paper by Peltonen, Palotie and Prockop on "A defect in the structure of type I procollagen in a patient who had osteogenesis imperfecta: excess mannose in the COOH-terminal propeptide" also appeared in *PNAS*. These publications were among the first to demonstrate that mutations that altered the structure of collagen were a cause of skeletal diseases. Therefore, they helped usher in the explosion of research on genetic diseases of collagens and other components of the extracellular matrix as the genes were isolated in the years that followed.

Leena Peltonen

During her early years, Leena worked primarily on types I and II collagens, on their gene structures and protein processing, and on the enzymes that modify collagens. She also contributed specifically to many of the heritable disorders of connective tissue (Osteogenesis imperfecta, Ehlers-Danlos syndrome, Menkes syndrome, the chondrodysplasias, and Epidermolysis bullosa). However, Leena's most notable accomplishment in matrix biology was mapping the locus for the Marfan gene. Using linkage analysis with polymorphic gene markers, Leena and Kati Kainulainen, Leena's M.D., Ph.D. student, first showed that the Marfan gene is located on chromosome 15, publishing their data in the *N. Engl. J. Med.* in 1990. Kati and Leena also identified the second and third mutations discovered in fibrillin-1 in individuals with the Marfan syndrome (published in *PNAS* in 1992) and were also the first to show "mutations in the fibrillin gene responsible for dominant ectopia lentis and neonatal Marfan syndrome" (*Nature Genetics*, 1994). During the next few years, Leena and other students went on to characterize additional novel mutations in FBN1 in the Marfan syndrome.

An obituary published in the April 15 issue of *Nature* closes by stating that "Leena Peltonen's drive, radiance and inimitable style were as impressive as her achievements." Darwin Prockop has these memories of Leena: "During her years at Rutgers, Leena quickly demonstrated her flair for research and leadership. She was a leader in setting one remarkable record: She, Aarno and their friends attended more Broadway and off-Broadway shows in a two year period than any other postdoctoral fellows in the history of the school and probably in the history of NIH sponsored research. And, of course, Leena always had style, not just the smashing new dress for every scientific presentation. Many years ago I was lucky enough be invited to convocation for Ph.D. graduates of the University of Oulu. I will never forget the joy she radiated as she and Aarno (her husband), in their formal ware and high hats, swept the floor at 2 or 3 in the morning dancing the Palinase, the ballroom dance made famous at the Russian imperial court."

I will always remember when Leena made a detour home through Portland after a meeting in Miami where Victor McKusick had told Leena that we had just mapped the gene for fibrillin-1 to her chromosome 15 locus for Marfan syndrome. She called and asked if she could stop by on her way home to Finland to talk with me. It was winter (January or February, 1991) and cold, and my first glimpse of Leena waiting for me outside of the Heathman Hotel was of her in a beautiful fur coat with a matching fur hat. And, she had on a red dress. Needless to say, I found Leena charming and persuasive, as well as elegant and stylish, and we agreed to collaborate. Who could resist Leena?* Leena and Kati later wrote quite graciously about our intersecting pathways in the "elucidation of the gene defect in Marfan syndrome: success by two complementary research strategies" (*FEBS*, 1992). It was a pleasure to have known Leena Peltonen and an honor to have worked with her at a watershed moment in the history of Marfan research, catalyzed in no small measure by Leena's energy, vision, and generosity of spirit.

** At the 2nd International Symposium on the Marfan Syndrome, held in San Francisco in 1992, Leena's group and my group went to lunch at a very nice Italian restaurant. When we walked in, the restaurant was very crowded, and we were being turned away when Leena then said, "Oh, but we have come all the way from Finland, just to eat at your restaurant!" Miraculously, we were escorted in and seated at a large table in a beautiful atrium! One of her students said appreciatively to me that Leena could always make impossible things happen. This story is now lab lore in Portland, along with at least two other stories about Leena that live on in our oral histories.*