American Society for Matrix Biology

President's Letter

Bill Parks

Dear Fellow Matrix Biologists,

A Call for Volunteers: Strengthening ASMB's Role in NIH Peer Review

For us in academic research, which represents the bulk of our membership, the importance of funding from the NIH can not be understated. Extramural funding is the researcher's life blood, providing us with the essential resource (i.e., money) needed to test our ideas, maintain our labs, hire personnel, and most importantly, train the next generation of investigators. As we all well know, the NIH is the principal source of that support, and securing grants from the NIH is critical to our success, advancement, recognition, and happiness. But other than budgetary constraints from Congress (we do, after all, have wars to deal with), the hurdle in getting a grant is peer review.

Although peer review is a tremendously valuable, time-proven mechanism for evaluating the merits of manuscripts and grant proposals (in fact, since the Royal Academy of Science began to use peer-review 350 years ago, no better process has been developed), the quality of the NIH grant peer review process depends much on the quality of the reviewers serving on study sections. I have no doubt that we can all relate our own horror stories on peer review. Many of the stories I have heard (or can tell) center on what the tormented soul believes is a lack of expertise by the reviewer or reviewers that sunk her or his proposal.

Matrix biology is well represented on several NIH study sections administered through the Center for Scientific Review (CSR: http://www.csr.nih.gov/Roster_proto/sectionI.asp), such as the Skeletal Biology Development and Disease (SBDD), Tumor Microenvironment (TME), and Intercellular Interactions (ICI) study sections. But representation within our field can be improved, especially by the inclusion of more senior investigators. Indeed, as this process benefits us all, I believe NIH-funded investigators have an obligation to serve on study section.

I was recently contact by Dr. Toni Scarpa, Director of the CSR, asking that ASMB provide a list of members who are willing to serve and who we (i.e., the Society) would recommend as reviewers. Dr. Scarpa requested that we identify "senior, experienced members… who [ASMB] endorses as being highly qualified" to review. I think this is a good idea. By providing CSR with a "pre-screened" list of established scientists who are willing to serve on study sections, we can be ensured that the Scientific Review Officers (SRO) will consider our members-i.e., peers with a good appreciation of what you propose-when they select reviewers. The criteria the CSR seeks are "experienced scientists who have received major peer-reviewed research support either from NIH or an equivalent agency, understand the grant review process, and are willing to serve as study section members."

So, please consider this request and serve on the study section. Sure, it requires effort, takes up time, and can be draining, but it is a rewarding and educational experience and you can contribute to a fundamentally important process of our profession (and don't forget the whopping NIH stipend!). If you are interested in serving as reviewers, please let me (parksw@uw.edu) or Jen (asmb@asmb.net) know.

Thank you for considering this request.

Bill

Bill Parks
ASMB President

Biennial Meeting of the American Society for Matrix Biology

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

Preliminary Schedule of Scientific Program

(Preliminary program - Subject to change – See www.asmb.net for full preliminary program)

Sunday, October 24, 2010

Guest Symposiums: TERMIS (Tissue Engineering & Regenerative Medicine International Society) & SFG (Society for Glycobiology)

President's Welcome & Keynote Lecture – Stem Cells, Extracellular Matrix, Tissue Morphogenesis & Cancer in Skin presented by: Elaine Fuchs, Rockefeller University, New York, NY

Monday, October 25, 2010

Plenary I: ECM-Cell Interactions & Signaling presented by: Richard Hynes, MIT, Mina Bissell, Lawrence Berkeley National Laboratory, and Martin Hemler, Harvard

Plenary II: ECM in Development presented by Senior Investigator Awardee Benoit de Cromburgghe, U.T. M. D. Anderson Cancer Center, Doug DeSimone, University of Virginia, and Rosa Serra, University of Alabama at Birmingham

Scientist Solutions Forum Demonstration & ASMB Business Meeting

Concurrents: Basement Membranes (chair Jeff Miner, Washington University School of Medicine); Wound Repair, Regeneration, & Fibrosis (chair Maria Trojanowska, Boston U.); Receptors (chair Ken Yamada, NIH); Proteases & Inhibitors (chair Suneel Apte, Cleveland Clinic Foundation); ECM Proteins and the Musculoskeletal System (chair, Marian Young, NIH)

Tuesday, October 26, 2010

Plenary III: ECM Disease Mechanisms presented by Junior Investigator Awardee Pyong Woo Park, Children's Hospital at Harvard, David Roberts, NIH, and Steven Shapiro, University of Pittsburgh

Plenary IV: ISMB (International Society for Matrix Biology) Guest Society Symposium chair Renato Iozzo, Thomas Jefferson University

Concurrents: Synthesis & Assembly (chair Dieter Reinhardt, McGill University); Neural Development & Disease (chair Sidney Strickland, Rockefeller University); Growth Factor Regulation (chair Lynn Sakai, Shriners Hospital); Angiogenesis (chair TBA); Engineered ECMs (chair Adam Engler, University of California, San Diego); Acquired, Acute, & Chronic Diseases (chair Pyong Woo Park, Children's Hospital at Harvard)

Wednesday, October 27, 2010

Concurrents: Invasion & Migration (chair Steve Weiss, University of Michigan); Proteoglycans and Glycobiology (chair Tom Wight, Benaroya Research Institute); Development & Morphogenesis (chair Christine Kern, Medical University of South Carolina); Genetic Diseases (chair Hans Peter Bächinger, Shriners Research Center); Matricellular Proteins (chair Amy Bradshaw, Medical University of South Carolina); Microenvironment in Stem Cell Biology & Cancer (chair Ralph Sanderson, Univ. of Alabama at Birmingham)

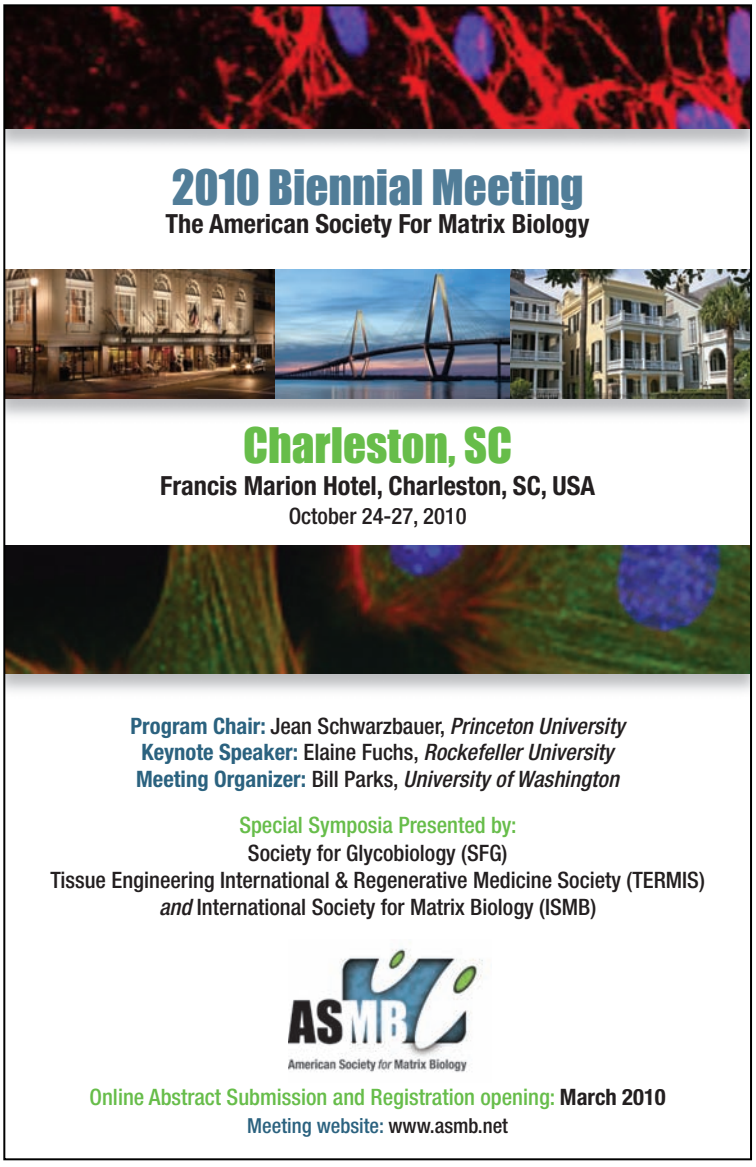
Tissue Engineering and Regenerative Medicine International Society (TERMIS) and ASMB Workshop

The Tissue Engineering and Regenerative Medicine International Society (TERMIS, http://www.termis.org) and ASMB are working together to hold a Guest Symposium on Sunday afternoon October 24, 2010 prior to the upcoming ASMB 2010 annual meeting. This workshop will explore the latest developments in synthetic extracellular matrices and how the properties of these fabricated biomaterials exploit the properties of extracellular matrices to play critical roles in cellular differentiation for tissue engineering. This symposium will be an excellent complement to the ASMB concurrent session on Engineered ECMs. In December 2008, the ASMB and TERMIS-NA began interactions as both meetings were both held in San Diego and members of each society were able to attend the reciprocal meeting at a discounted rate.

TERMIS promotes research and education in tissue engineering and regenerative medicine through meetings, fostering interaction and collaborations between members, and publications in journals such as Tissue Engineering. TERMIS consists of three Continental Chapters worldwide: Asia-Pacific (TERMIS-AP), Europe (TERMIS-EU) and North America (TERMIS-NA). These chapters hold separate regional conferences each year, coming together every three years for the World Congress Meeting (the next of which will be held in 2012). TERMIS also serves as an international forum to promote the informed discussion of challenges and therapeutic benefits of the application of tissue engineering and regenerative medicine technologies.

We look forward to the upcoming TERMIS – 2010 ASMB Symposium, and to a productive partnership.

Joanne Murphy-Ullrich, murphy@uab.edu, ASMB
Robert Sah, rsah@ucsd.edu, TERMIS



VOTE NOW!!

Online elections now open for 2010-2013 term ASMB Council Members. Vote via your invitation email today! Questions--email asmb@asmb.net. Candidates are:

Matthew Hoffman, NIDCR
Jim McCarthy, UMN
Maurizio Pacifici (Thomas Jefferson)
Ambra Pozzi (Vanderbilt)
Ralph Sanderson (UAB)
Phil Trackman (Boston Univ.)
Rocky Tuan (Univ. Pittsburgh)

Congratulations!

2010 Senior Investigator Awardee

Benoit de Crombrugghe,
UTMD Anderson Cancer Center

2010 Junior Investigator Awardee

Pyong Woo Park
Harvard Children's Hospital

Come hear them speak at the 2010 ASMB Meeting in Charleston, SC
October 24-27, 2010

Matricellular Proteins

A special issue of the *Journal of Cell Communication and Signaling* (volume 3 [3-4]; December 2009) provides a series of reviews focusing on the biology of matricellular proteins, an important class of extracellular proteins that includes the thrombospondins, tenascins, fibulins, SPARC, and osteopontin, among others. Although they do not play a primary structural role in the extracellular matrix, matricellular proteins modulate cell function by interacting with cell-surface receptors, proteinases, hormones, and other effector molecules, as well as with structural matrix proteins such as collagens. The table of contents is provided below. JCCS is an open-access journal, and these informative articles can be viewed and downloaded via the following link: http://www.springerlink.com/content/x266m21gk153/

Matricellular proteins: an overview
Paul Bornstein

The role of astrocyte-secreted matricellular proteins in central nervous system development and function
Cagla Eroglu

The interaction of Thrombospondins with extracellular matrix proteins
Kemin Tan and Jack Lawler

Thrombospondins function as regulators of angiogenesis
Paul Bornstein

Thrombospondins in the heart: potential functions in cardiac remodeling
Mark W. M. Schellings, Geert C. van Almen, E. Helene Sage, and Stephane Heymans

The role of thrombospondins in wound healing, ischemia, and the foreign body reaction
Themis R. Kyriakides and Susan MacLauchlan

Thrombospondin-2 and SPARC/osteonectin are critical regulators of bone remodeling
Anne M. Delany and Kurt David Hankenson

The role of SPARC in extracellular matrix assembly
Amy D. Bradshaw

SPARC functions as an inhibitor of adipogenesis
Jing Nie and E. Helene Sage

SPARC: a matricellular regulator of tumorigenesis
Shanna A. Arnold and Rolf A. Brekken

The many facets of the matricellular protein periostin during cardiac development, remodeling, and pathophysiology
Russell A. Norris, Ricardo Moreno-Rodriguez, Stanley Hoffman, and Roger R. Markwald

The role of tenascin-C in tissue injury and tumorigenesis
Kim S. Midwood and Gertraud Orend

The role of osteopontin in inflammatory processes
Susan Amanda Lund, Cecilia M. Giachelli, and Marta Scatena

The matricellular functions of small leucine-rich proteoglycans (SLRPs)
Rosetta Merline, Roland M. Schaefer, and Liliana Schaefer

Fibulin-5, an integrin-binding matricellular protein: its function in development and disease
Hiromi Yanagisawa, Marie K. Schluterman, and Rolf A. Brekken

Related Meetings Announcements

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

Developmental Vascular Biology Workshop IV

February 10-13, 2010 Asilomar, California

The next NAVBO Developmental Vascular Biology Workshop is being held February 10-13, 2010, at the Asilomar Conference Grounds on the scenic Monterey peninsula. This is the fourth installment of what has been a very highly regarded and very exciting series of meetings held every two years at this site, focusing on molecular control of vascular development, cell signaling pathways in angiogenesis and lymphangiogenesis, and mechanisms of patterning blood vessel growth and migration. The meetings are attended by researchers using a wide variety of different models, including mice, frogs, birds, fish, flies, and cell culture. Previous meetings have featured some of the latest, cutting-edge unpublished findings in vascular developmental biology, findings that have become major topics of widespread basic and clinical research study. The upcoming meeting is on track to be equally exciting and informative, with outstanding invited speakers representing many of the premiere research labs at the intersection of development and vascular biology. In addition to invited speakers, talks will be selected from the submitted abstracts. With two long poster sessions and even more time allotted for talks programmed from abstracts than in previous DVB meetings, there will be many opportunities for meeting attendees to present their research findings to other participants.

The meeting has been organized by Brant M. Weinstein of the National Institute for Child Health and Human Development and Dr. Richard O. Hynes of the Howard Hughes Medical Institute and Massachusetts Institute of Technology. The meeting is sponsored by the North American Vascular Biology Organization (NAVBO). NAVBO also sponsors the Vascular Matrix Biology and Bioengineering Workshop.

Early bird registration and abstract submission deadline is December 15. Preliminary program, additional information, registration and abstract submission are available at:

http://www.navbo.org/event/dvb

2010 Proteoglycan Gordon Research Conference

Development, Disease, & Therapeutics

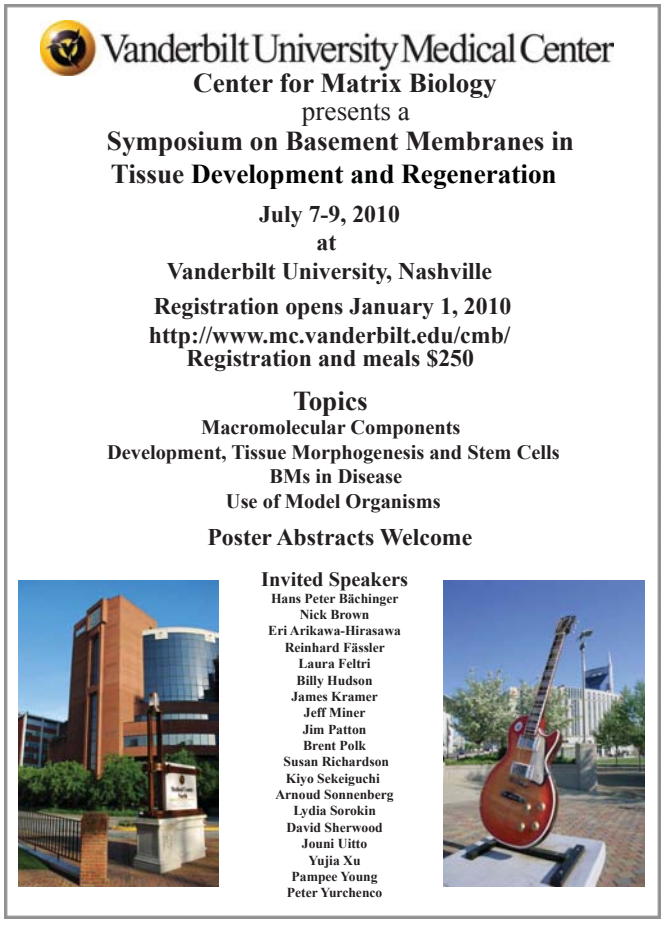
July 11-16, 2010 Andover, NH

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



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. This is the last ASMB newsletter for 2009--don't make it your last ASMB newsletter! RENEW TODAY

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 2009 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

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!

New Feature!
What's going on in the lab?

For each newsletter issue we will highlight the research in one or two member's labs. Current publications, research etc. along with photos. Enjoy this issue's feature on Marc McKee of McGill University.

Coalition of Heritable Disorders of Connective Tissue (CHDCT)

Contributed by Priscilla Ciccariello (CHDCT, Co-President)

The last several decades of medical progress have been marked by an increasingly close collaboration among researchers in different organizations that share a similar investigative focus. Less widely-recognized—though no less vital—have been the burgeoning relationships between these professional medical groups and the community of patients and their families that the research is apt to affect.

I feel fortunate to have been born at a moment in medical history when my family and I were able to participate in and benefit from these developments. After becoming aware that several of my children were affected by the Marfan syndrome, I became active in the National Marfan Foundation, and later also participated in the two related organizations referred to here. In 2002, in my role as President of the Coalition of Heritable Disorders of Connective Tissue (CHDCT), I attended the first national conference of the American Society for Matrix Biology in Houston, Texas. As CHDCT President at the time, I was elected to what I liked to refer to then as a "layman's position" on the ASMB Board.

Priscilla Ciccariello

The founders of the ASMB generously provided this representation as a way of acknowledging the partnership between patient and research, a concept whose importance had begun to be recognized about thirty years earlier. We can be confident that this outreach from both patients and researchers has enriched the prospect of NIH support, for even now, despite the vulnerability of Congressional support due to the current problematic financial outlook, there is an increased emphasis at the NIH on translational research—the transmission of medical findings from "the bench to the patient."

Founded in 1988, the CHDCT began testifying in Washington, D.C in 1994, offering oral and written testimony both in Congress and at the NIH, and emphasizing the need to build awareness of heritable disorders of connective tissue on a national level. Their goal was to press for research, visibility and increased understanding of these rare and complex disorders. The patients themselves testified, offering ethical and moral justification for basic research.

The awareness of this body of disorders was formally initiated in 1956, when Dr. Victor McKusick of Johns Hopkins Medical Center launched his first slim edition of Heritable Disorders of Connective Tissue, which was to see a number of revised editions through the years. Since then, there has been increased impetus for a basic understanding of connective tissue in general and heritable connective tissue disorders specifically.

The CHDCT grew in response to the need for research providing the strength of numbers. It includes groups that have their own membership-supported volunteer organizations, representing some twelve different disorders, which affect many millions of people. The Coalition, founded at the height of the growth of disease-specific voluntary health organizations, serves to strengthen the impact of these organizations through dissemination of information, conferences, and congressional testimony.

Running a parallel course with the ASMB—although, in this case, serving primarily to highlight the important research accomplishments in this field—the CHDCT has made its own mark. Among its most important accomplishments since its founding in 1988 are these: five NIH supported research symposia; support for other related conferences and symposia; CHDCT congressional testimony in support of connective tissue research since 1994; partnership with the ASMB since its founding; and in 2002, creation of a web site, http://www.chdct.org, which averages some 4,000 hits yearly. Recently, the CHDCT collaborated with the NIAMS on the revision and distribution of the brochure, Heritable Disorders of Connective Tissue (NIAMS, 2007).

The CHDCT's 2010 testimony is in the works, and the prospect of a future conference or symposium on heritable disorders of connective tissue is under consideration. We welcome the thoughts and input of the ASMB membership regarding these areas of interest. The CHDCT looks forward to continuing its long-standing partnership with the ASMB, and stands ready in support of the research and researchers that it represents.

For more information go to
http://www.niams.nih.gov/Health_Info/Connective_Tissue/default.asp

CHDCT members meeting with Senator Tom Harkin in ~1996. The group includes Joan Weiss (alliance of Genetic Support Groups--2nd from left) and Meg Caufield (Osteogenesis imperfecta--first row left). Together with several members of the Little People of America are three members of the National Marfan Foundation.

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

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

Tell Us What Your Lab is Doing!

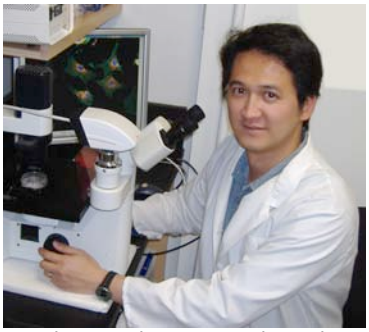
From the Laboratory of:
Marc D. McKee, Ph.D.
James McGill Professor
Faculty of Dentistry, Associate Dean (Research)
Faculty of Medicine, Department of Anatomy and Cell Biology
MUHC Medical Scientist, Department of Medicine
McGill University, Montreal, Quebec, Canada.

Graduate student William Addison (left) and Marc McKee

Addison WN, Masica DL, Gray JJ and McKee MD (2009) Phosphorylation-dependent inhibition of mineralization by osteopontin ASARM peptides is regulated by PHEX cleavage. *J. Bone Mineral Res.* In Press.

Chien Y-C, Masica DL, Gray JL, Nguyen S, Vali H and McKee MD (2009) Modulation of calcium oxalate dihydrate growth by selective crystal-face binding of phosphorylated osteopontin and poly-aspartate peptide showing occlusion by sectoral (compositional) zoning. *J. Biol. Chem.* In Press.

These two papers provide information on peptide sequences of osteopontin (OPN) and their post-translational modifications that regulate the mineralization-regulating functions of this extracellular matrix protein. We show for two different minerals – hydroxyapatite (bones and teeth) and calcium oxalate (kidney stones) – the potent inhibitory functions of a phosphorylated ASARM peptide (Acidic, Serine- and Aspartate-Rich Motif) and a polyAsp motif from OPN, respectively. We show that the OPN ASARM peptide is a substrate for PHEX enzyme, whose mutations cause X-linked Hypophosphatemia (XLH) showing extensive hypomineralization of the bone matrix (osteomalacia). We also provide peptide adsorption energy data for the peptides as determined by computational simulations using the RosettaSurface protocol.

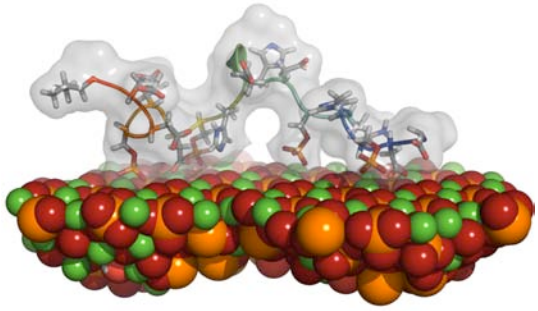


Graduate student Young-Ching Chien

Chien YC, Hincke MT, Gautron J, Vali H and McKee MD (2008) Ultrastructural matrix-mineral relationships and localization of osteopontin in avian eggshell, and effects of osteopontin on calcite growth in vitro. *J. Struct. Biol.*, 163:84-99.

Chien YC, Hincke MT and McKee MD (2009) Ultrastructure of avian eggshell during resorption following egg fertilization. *J. Struct. Biol.* 168:527-538.

Avian eggshell contains an abundant noncollagenous matrix network rich in osteopontin (OPN) that deposits on a collagenous shell membrane assembled in the shell gland of the hen's oviduct. This pair of papers on avian eggshell provides a reconciliation of how an extensive extracellular matrix protein network can co-exist with a crystalline array of calcite that exhibits a single-crystal X-ray diffraction pattern. We show that during formation of the eggshell, protein is occluded within growing calcite crystals at select crystallographic faces to form stratified lamellar sheets of matrix, or it is arranged as membranous sheets that define the boundaries of matrix/crystal compartments of the shell. During resorption of the shell that occurs from the inside-out during fertilized egg incubation to provide a source of calcium for the growing chick skeleton and to thin the shell for chick hatching, this protein network occluded within the calcite mineral phase serves as a conduit during mineral dissolution for the diffusion of calcium ions out of the shell and into the skeleton.



Computational modeling image of low-energy ASARM peptide configuration upon binding of hydroxyapatite mineral after sampling of 3.5 billion conformers.