A PUBLICATION OF THE AMERICAN SOCIETY FOR MATRIX BIOLOGY SUMMER 2008, VOLUME 7, NO. 2

ASMB Newsletter

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President's Letter


Renato Iozzo

Dear Fellow Matrix Biologists,

I hope you had a great winter and spring!

We have been very busy in fund raising, organizing the San Diego meeting and the Special Interest Groups (there is still time to propose additional sessions). I would like to ask that you submit a brief proposal to Don Senger (dsenger@caregroup.harvard.edu) for the SIGs. With the input of the fund raising committee, we have raised over $52,000 so far and we hope that the NIH grant will be funded. We now have a record number of membership renewals which is close to 350! However, there are several members who have not yet renewed their memberships. Please, **RENEW NOW!** Everything can be easily done on line by going to www.asmb.net.

Obviously, the main event since the winter 2008 newsletter is the activation and implementation of new rules for evaluating the NIH grants. To see the full report, visit:www./enhancing-peer-review.nih.gov/meetings/EnhancingPeerReviewACD2-21-08.pdf. Below are my personal opinions which do not necessarily reflect the ASMB standing, just my thoughts and comments. I will focus on just a few points with the idea to start a dialogue with all of you. Your e-mails will not be edited and will be published in the next newsletter of the ASMB.

1. **Each application should be reviewed by 4 independent reviewers.**
This is not a great idea since NIH receives ~80,000 proposals/year and since there are ~290,000 scientists in the Unites States. One can make a simple calculation that this is not going to work well and smoothly.

2. **Each grant is a new grant; no need to address the previous critique of the study section.**
This is also not a great idea. It makes little sense to me: what would the role of a study section be? Is not one of the mandates to try to improve, redirect a given grant? Also, the next submission of the same grant might or might not be improved at all. This scheme will encourage multiple submissions of mediocre grants that need to be evaluated by 4 scientists. Is our system ready for this avalanche of new grants?

3. **New investigators should be evaluated separately with separate criteria.**
This is also not a good idea. By definition, a new investigator is a given researcher who has never obtained NIH funding before. Thus, a Nobel prize-winner from Europe, for example, moves to the United States because of forced retirement at the age of 65. He/she will apply to NIH as a "new investigator". Is this fair?

4. **Past productivity is less important than innovation.**
This, to me, is the most unusual concept. Don't we judge a stock from previous performance? Is just the simple writing of a crazy, unproved, unfunded idea more valuable than extension of previously published work? Why do we publish and why is there so much pressure on publishing in the best journals if we cannot use this "productivity" to continue important research?

It is also strange that the intramural programs of the NIH (earlier this year I was one of the outside reviewers for an intramural research program) base the future funding of a given program almost exclusively on past accomplishments. Essentially, the funding of an intramural program (equivalent to extramural RO1) is based on the summation of research accomplishment (i.e., productivity) during the preceding four years. Why does the federal government use two sets of rules for the intramural and extramural funding?

From our ASMB side, we need to make a data base of matrix biology scientists who are willing to serve on study sections. Below is an important e-mail I received from

Tony Scarpa, the CSR director. I would like to share this request with you. And I am hopeful that several of our members will volunteer to be on study sections. Please, send the required information directly to me at iozzo@mail.jci.tju.edu and I will compile the list.

Warmest regards to all,

Renato Iozzo
President ASMB

Renato Iozzo
Renato,

As you know, the quality of NIH's peer review process depends mightily on the quality of the reviewers serving on our study sections. Several of your fellow society presidents and other leaders of scientific organizations have sent us screened lists of volunteers from their membership who they recommend as reviewers. We greatly appreciate their help and are **writing to ask for your assistance in identifying senior, experienced members of your society willing to volunteer to serve as NIH reviewers who you endorse as being highly qualified.**

By providing CSR with a **pre-screened** list of senior scientists who volunteer to be study section members, you are ensuring that CSR's SROs (Scientific Review Officers) consider your members when they select reviewers.

We would appreciate any help you can provide in:

- asking your members if they are interested in serving as reviewers,
- collecting that information in the attached format,
- screening it for appropriate senior-level experience, then
- sending it to CSR as your recommended list of reviewers.

The attached template requests information including name, institution, e-mail address, Web address, area of expertise, the most appropriate study section or Integrated Review Group, if known, and recent funding sources. In our Registry, we will also indicate that your society recommended this reviewer.

Our criteria are straightforward. We seek reviewers who:

- are experienced senior scientists,
- 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.

We would like this to be an ongoing process in which you send us names of volunteer reviewers to include in our CSR Registry of Volunteer Reviewers, and at the end of the year we provide you with information on how many of your volunteer reviewers actually served on study sections.

Any help you can provide in assembling and screening a list of qualified, senior-level, volunteer reviewers would be greatly appreciated. Please send the annotated template to Diane Stassi, the Chair of our CSR Registry of Volunteer Reviewers, at RecruitReviewers@csr.nih.gov

Thank you and best wishes,

Toni Scarpa and Diane Stassi

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voice: 301-435-2514
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ASMB Elections Summary

The ASMB Council would like to thank everyone for voting in the 2008 ASMB Elections. We had an excellent response which speaks to the growing strength of our society and interest by our members.

The ASMB Nominating Committee, led by Past President, Linda Sandell, would like to thank everyone on the ballot for their dedication to our society and the board looks forward to their future participation. The new board members are as follows:

Secretary/Treasurer (thru 2011)
Joanne Murphy-Ullrich

Councilors (thru 2011)
Amy Bradshaw
Jean Schwarzbauer
Jeff Davidson
and
David McQuillan, ex officio, Industry Representative


Joanne Murphy-Ullrich


Amy Bradshaw


Jean Schwarzbauer


Jeff Davidson


David McQuillan

The ASMB Council has just completed its spring Council meeting and along with these new members, we have some wonderful visions and projects for the coming year for the society.

As always, please feel free to contact our administrative office at asmb@faseb.org if you have any questions, comments or ideas about the society.

New Directions

Along with many other society details, the ASMB council recently discussed the state and direction of the societies committees. We have a number of groups focused on different areas of interest to our society. In the interest of obtaining new perspective and direction for these various interests, we welcome new membership in the committees listed below. Each group lists a brief description of their focus. Please feel free to contact asmb@faseb.org or Linda Sandell (sandelll@wudosis.wustl.edu) if you have any questions or interest in joining one of these groups and, in doing so, helping the progress of ASMB and the science of Matrix Biology.

COMMITTEE MISSION STATEMENTS

NOMINATIONS COMMITTEE:

The directive of the nominations committee is to prepare the slate of candidates annually for elections as needed. The committee is chaired by the Past-President and comprised of three current council members and three members-at-large, appointed ad hoc. Consideration should be given to the proposed nominees areas of specialty to ensure a broad representation of associated areas within the Council. This slate is to be presented to the Board for approval prior to opening official elections for the general membership. The Chair of this committee is responsible for contacting the nominees to confirm their interest and availability in running for the office and for follow-up post election with results. The Chair is also responsible for providing new Board members with an introduction to their duties either via email communications, conference call or at the next society meeting.

MEMBERSHIP COMMITTEE:

The directive of the membership committee is to monitor the current society membership levels and to develop plans to recruit new members. They may utilize the newsletter, available ad space in the associate journal or any other medium including the membership email list for blasts. The chair is to report activity and membership trends at the annual ASMB Council meeting along with current committee actions.

SCIENTIFIC ADVISORY COMMITTEE:

The advisory committee's directive is to provide ASMB with expert advice on matters pertaining to the science and areas affecting the society's interest as a whole. Areas may include grants and funding procedures, developments in research or any other area in which the council, as a whole, sees fit to require expert advice and consultation. The committee oversees the long range planning for the biennial meeting and oversees the awards that are given at the meeting.

NEWSLETTER COMMITTEE:

The directive of the newsletter committee is to facilitate a gathering of submissions for the ASMB newsletter. The committee is headed by an Editor (Chair) and Co-Editor (Vice-Chair) with members appointed. The newsletter is published electronically and sent to the current membership 3 times per year. The editors along with any assistance available will review submissions, compile appropriate material and draft the newsletter into an appropriate and consistent format. A draft of the completed newsletter is to be sent to the society President for final approval before general distribution.

WEBSITE COMMITTEE:

The directive of the website committee is to periodically review the current society website and ascertain what updates or enhancements are required. The committee is also responsible for formulating plans for new website development as approved by the Board to keep the website current with regards to programming and capacity. New endeavors of the website committee may be recommended to the Board.

NIH COMMITTEE:

The NIH committee directive is to keep the society informed on relevant issues and act on behalf of the society, with Council and President approval, for matters pertaining to NIH

issues that effect scientists in our field. The committee should research current issues and report to the council on relevant findings; making recommendations on any actions required to maintain the interest of the society.

PUBLICATIONS COMMITTEE:

The publication committee directive is to manage the publications of the society under policies determined by the council. They are to provide advice and consent on the appointment of the editor of the associated journal(s) and render an annual financial report and statistical data regarding the publications. The committee may act on its own in bringing recommendations to the council for review of the direction of publications and new ideas for future development. The committee will include individuals who have served as editors or associate editors of scientific publications.

STRATEGIC PLANNING COMMITTEE:

The Strategic planning committee directive is to provide the vision, framework and strategies for the development of the society as it grows. The committee should provide support, ideas and advice in facilitating the maintenance and growth of the society with regards to education, economic, and membership development or any other area(s) that require this support throughout the society. This committee should review the strategic planning documents annually and bring to the Council items that require attention. A yearly report and action plan will be made at the annual Council meeting.

Welcome New 2008 Members

ASMB welcomes these new members who have joined us since January 2008
Stacey Schutte, Georgia Institute of Technology
Peter Roughley, Shriners Hospital
Linda Gutierrez, Wilkes University
Tracy Gwyther, Worcester Polytechnic Institute
Qian Zheng, Avon Products Inc.
Colette Inkson, University of Manchester
Kun Yuan, University of Alabama at Birmingham
Ri-ichiroh Manabe, Osaka University
Carl Blobel, Weill Cornell
Carol Feghali-Bostwick, University of Pittsburgh
Mandy Plumb, University of Aberdeen
Roberto Perris, University of Parma
Maria Fragiadaki, Imperial College London
Shawn Pyott, University of Washington
Malgorzata Wiweger, Leiden Uni. Medical Center
Ruth Lupu, Northwestern University
Francoise Coustry, UT Medical School, Houston
Kiran Nistala, Mount Sinai School of Medicine

2008 ASMB Annual Dues

Your 2008 Annual Dues are NOW past due – You can renew and pay via the ASMB website at www.asmb.net. As members, you will receive a discount on the meeting and access to reduced fees or no cost for other ASMB activities. For 2008, Regular membership is $90 and $50 for Students/ Postdoctoral Fellow. We need your continued support in the ASMB and we encourage you to RENEW NOW!

Scientists in the Spotlight

Ken Yamada has won the Distinguished Scientist award from the American Association for Dental Research, which is awarded once every two years to a scientist who has contributed "outstanding research of particular significance in any of the fields related to oral science." The award comes with a plaque, cash prize, and travel funds. Ken is an ASMB Council member and Chief of the Laboratory of Cell and Developmental Biology, NIDCR, NIH, and he studies cell-matrix interactions, migration, and development.

Renato Iozzo has been appointed Honorary Professor in the School of Life Sciences at the University of Manchester, UK. This is in recognition for the successful training and mentoring of 20 undergraduate students from the University of Manchester during the past decade. Most of these trainees have pursued graduate studies in numerous institutions around the world including Rockfeller University in New York, Oxford, Cambridge, Imperial College London, University of Manchester, University of Sydney in Australia, and Thomas Jefferson University.

Mina Bissell has been named the winner of the 2008 Medal of Honor in Basic Research from the American Cancer Society (ACS). The award, the highest honor bestowed by the ACS, will be presented to Dr. Bissell at the organization's annual meeting in New York on November 21st.

Related Meetings Announcements

Workshop: Vascular Biology and Bioengineering II

March 16-19, 2009 Whistler, British Columbia

Cecilia Giachelli of the University of Washington, an ASMB Member, along with colleagues Michelle Bendeck, University of Toronto, Elaine C. Davis, McGill University and Themis R. Kyriakides, Yale University, are organizing this second workshop of its type. The aims of this one of a kind interdisciplinary workshop are to provide a forum for basic and clinical researchers in vascular matrix biology, regenerative medicine and bioengineering to share their recent and novel science and to promote communication and exchange of ideas and concepts between traditional vascular matrix biologists, cardiovascular regenerative medicine researchers and cardiovascular tissue engineers. Our program is characterized by the presentation of cutting edge research in areas like vascular matrix remodeling and repair, matrix genetics and development, stem cell biology, vascular scaffolds, engineering biomaterials, tissue engineering, angiogenesis, mechanobiology, regenerative matrices and matrix calcification. The preliminary program and additional information about this workshop can be found on NAVBO's web site - www.navbo.org/VMBB2009. Those who wish to participate are encouraged to submit an abstract; abstracts will be accepted for oral and poster presentations.

5th International Workshop on the CCN (Cyr61, CTGF, NOV) Gene Family

October 18-22,2008 Toronto, Canada

For more information, please contact Annick Perbal, Administrative Secretary of the International CCN Society, or visit the Society's Web site http://ccnsociety.com.

5th European Meeting on Elastin

July 16-19, 2008 Alcalá de Henares , Spain

The 5th European conference on elastin will be held in Alcalá de Henares, Spain form July 16-19. The meeting will cover all aspects of elastin biology, including microfibrils, proteases, elastin-related diseases, and tissue development. The meeting is being organized by Dr. Julia Buján (mjulia.bujan@uah.es). Further information can be found at: www.elastin2008.fgua.es

XXIst FECTS Meeting

July 9-13, 2008 Marseille, France

This meeting will address all topics related to matrix biology and will include plenary lectures by invited speakers, short talks selected from submitted abstracts, and poster presentations. The scientific committee is chaired by Philippe Charpiot (philippe.charpiot@pharmacie.univ-mrs.fr) and Sylvie Ricard-Blum (s.ricard-blum@ibcp.fr). Further information can obtained at the meeting web site:
www.fects2008.pharmacie.univ-mrs.fr.

Gordon Conference on Proteoglycans

July 6-11, 2008 Proctor Academy, Andover, NY

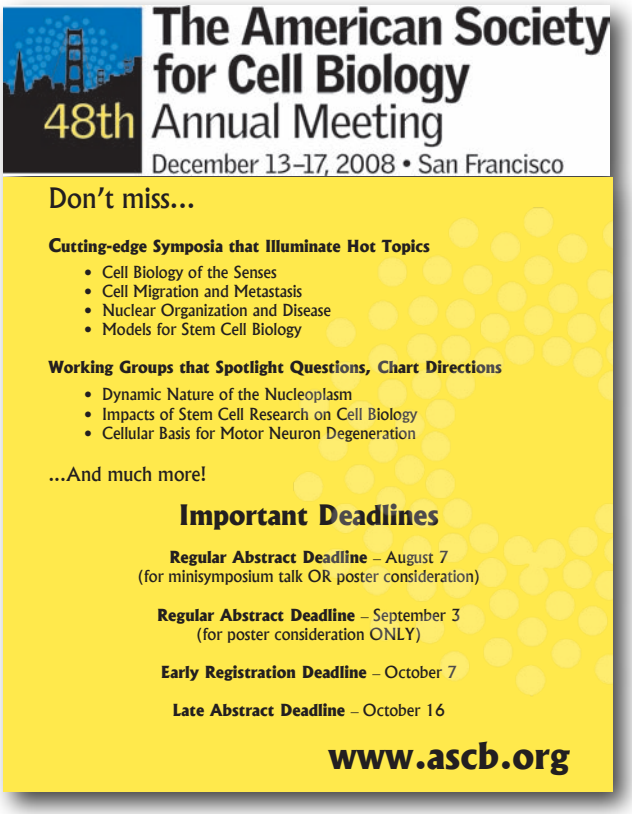
http://www.grc.org/programs.aspx?year=2008&program=proteoglyc

Things to Do in San Diego at ASMB

While in San Diego December 7-10, 2008 for the ASMB meeting, consider some of these sight seeing options while you're in town. The hotel and its location offer the best that the city has to offer. Ideally situated on the waterfront, you can walk out your door to Seaport Village for lunch, take a short walk to the Gaslamp Quarter, hopand hop on the trolley which offers a convenient way to see many local sights or even take a 5 minute walk from the hotel to tour the USS Midway Aircraft Carrier. Some other local attractions include:

Birch Aquarium at Scripps
Botanical Building and Lily Pond
Cabrillo National Monument
Heritage Park
Hotel del Coronado
Japanese Friendship Garden
San Diego Aerospace Museum
San Diego Automotive Museum

For more touring ideas, please visit
http://manchestergrand.hyatt.com/hyatt/hotels/services/local/attractions/listings.jsp?destinationId=&categoryType=&start=5&pageIndex=1




2008 MEETING
AMERICAN SOCIETY FOR MATRIX BIOLOGY
SAN DIEGO
December 7-10
San Diego
AMERICAN SOCIETY FOR MATRIX BIOLOGY
December 7 – 10, 2008
Manchester Grand Hyatt
Registration, Abstract, and Special Interest Group Submissions Now Being Accepted At:
www.asmb.net/2008meeting/
Join us in San Diego to:
• Learn new technologies for advancing the field of Matrix Biology
• Maximize exposure to new ideas and young scientists
• Focus on new extracellular matrix research directions
Meeting Chair:
Renato Iozzo, Thomas Jefferson University
Program Committee Chair:
Bill Parks, University of Washington
Special Interest Group Submissions Deadline ..... July 1, 2008
Abstract Submission Deadline ..... July 15, 2008
Early Registration Deadline ..... September 15, 2008
Hotel Registration Deadline ..... November 14, 2008
We would like to thank our 2008 sponsors:
Elsevier
FibroGen
Genentech
Life Cell
Thomas Jefferson University
Shriners Hospitals for Children
New England Biolabs
In association with the International Society for Matrix Biology (ISMB)
For Additional Information:
Jennifer Holland • Meeting Coordinator
Phone: 301-634-7814 • Fax: 301-634-7455 • jholland@faseb.org

Schedule

www.asmb.net/2008meeting/

Sunday, December 7

1:00-3:00 pm **Special Interest Groups Session I**

3:30-5:30 pm **Special Interest Groups Session II**

6:30-7:45 pm **President's Welcome Reception**
Renato Iozzo

7:45-8:30 pm **Keynote Lecture**
Carlo Croce

Monday, December 8

8:30-10:00 am **Plenary I**
ECM in Stem Cell Niches
Marian Young, Robert Linhardt, and *Susan Bellis*

10:30-noon **Plenary II**
Matrix Structure
Senior Investigator Awardee TBA
William Horton, and Hiromi Yanagisawa
Sponsored by: Shriners Hospitals for Children

1:30-3:00 pm **Concurrent Sessions**

Concurrent A - Angiogenesis
Moderator/Speaker: *James Quigley*

Concurrent B - Proteoglycans
Moderator/Speaker: *Jeff Esko*

Concurrent C - ECM Turnover
Moderator/Speaker: *Kenn Holmbeck*

3:30-5:00 pm **Concurrent Sessions**

Concurrent D - Matricellular Proteins
Moderator/Speaker: *Josephine Adams*

Concurrent E - Molecular & Computational Modeling
Moderator/Speaker: *Arthur Lander*

Concurrent F - Inflammation
Moderator/Speaker: TBA

5:00-7:00 pm **Poster Session I and Exhibitor Reception**

Tuesday, December 9

8:30-10:00 am **Plenary III**
ECM Influences in Disease Pathogenesis
Paul Noble, Yves DeClerck, and Junior Investigator Awardee TBA

10:30 am-noon **Plenary IV**
International Society for Matrix Biology Guest Symposium
Moderator/Speaker: *Reinhard Fässler*

1:30-3:00 pm **Concurrent Sessions**

Concurrent G - Proteolytic Pathways
Moderator/Speaker: *Rama Khokha*

Concurrent H - Development
Moderator/Speaker: *Ray Keller*

Concurrent I - Glycosaminoglycans
Moderator/Speaker: *Gordon Laurie*

3:30-5:00 pm **Concurrent Sessions**

Concurrent J - Integrins
Moderator/Speaker: *Dean Sheppard*

Concurrent K - Basement Membrane
Moderator/Speaker: *Matthew Hoffman*

Concurrent L - Vascular Biology
Moderator/Speaker: TBA

5:00-7:00 pm **Poster Session II and Exhibitor Reception**

7:30-10:00 pm **Gala Reception**

Wednesday, December 10

8:30-10:00 am **Plenary V**
Mechanical Influences
Dennis Discher, Clare Waterman-Storer, and *Valerie Weaver*

10:30-noon **Concurrent Sessions**

Concurrent M - Invasion/Migration
Moderator/Speaker: TBA

Concurrent N - Control of Gene Expression
Moderator/Speaker: TBA

Concurrent O - ECM–Cytokines Interactions
Moderator/Speaker: *Sarah Dallas*

Use The ASMB Web Site www.asmb.net

Website Features

- Information about the organization, including bylaws, officers, membership, etc.
- Announcements--items of interest to matrix biologists
- Information about the ASMB National Meeting
- Employment & Funding Opportunities
- ASMB Newsletter archive
- Directory of members
- Links to members' web sites

ASMB business

- When you log onto the "Members Only" page (login using your email address and password. If you have forgotten your password, contact the ASMB office at **asmb@asmb.net**), you will immediately see your dues payment status and a listing of your journal subscriptions.
- You can pay your dues and subscribe to journals by selecting the "Membership Dues" button.
- The "Update" and "Search" buttons allow you to review and update your own contact information as well as search our member database.

To post information about a job opening or job wanted, send detailed information to our Administrative Assistant: **asmb@asmb.net**

Job opportunities and announcements will also be printed in our Society newsletter.

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 2008 Annual 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:

- Membership and recognition in an emerging, important scientific discipline.
- A two-year membership rate that is significantly less expensive per year than the one-year rate.
- For two-year renewals, a significant discount on the registration fee for the 2008 ASMB National Meeting in San Diego.
- Access to the "Members only" web material where you can search the membership list, the meeting abstracts published in Matrix Biology and other interesting information relating to matrix biology
- A Newsletter containing information about Society activities.

Job Position Openings

East Carolina University - Assistant Professor of Anatomy and Cell Biology

The Department of Anatomy and Cell Biology of the Brody School of Medicine at East Carolina University (ECU) is seeking a full-time faculty member at the Assistant Professor level. A tenure track, open rank or fixed term appointment is available. The Ph.D. degree in Anatomy or Cell Biology (or related discipline) and two years of postdoctoral research experience in cell and molecular biology are required. The applicant should demonstrate the potential for research, publication and extramural funding. The new faculty member will contribute to the departmental research missions in cell biology with an expectation to compliment the strength of ongoing research [http://www.ecu.edu/anatomy] and participate in the training of graduate students. Preference will be given to applicants having basic research experience and interest in the extracellular matrix, cell-matrix interactions, signal transduction and cell-cell interactions. Medical student education in the anatomical sciences is another educational mission of the department, with additional teaching responsibilities to a variety of professional students. The applicant must demonstrate potential for excellent teaching in these disciplines. Appropriate professional service will also be expected. East Carolina University is a AA/EOE institution.

ECU is a constituent institution of the University of North Carolina located in Greenville, NC, a city of ~70,000. The Brody School of Medicine is affiliated with the Pitt County Memorial Hospital, the Leo W. Jenkins Cancer Center and the new East Carolina Heart Institute. ECU is the educational centerpiece of eastern North Carolina and the Brody School of Medicine is one component of the rapidly growing Health Sciences campus that also includes the Schools of Allied Health and Nursing; plans for a new dental school are progressing. Greenville itself is about a one-hour drive east of Raleigh-Durham, UNC-Chapel Hill and Research Triangle Park. The central eastern seaboard, with the famous Outer Banks, is a two hour drive.

Applicants need to apply on line at: http://www.ecu.edu. Click to select "Jobs at ECU" on the menu on the left side. Screening begins on December 1, 2007 and continues until the position is filled. Applicants should also send a CV and a cover letter that includes a statement of teaching experience, research interests and proposed NIH specific aims to: Cheryl B. Knudson, Ph.D., Professor and Chair, Department of Anatomy and Cell Biology, The Brody School of Medicine at East Carolina University, 600 Moye Blvd, 7N-100 Brody Bldg, Greenville, NC, 27834; or via e-mail to: knudsonc@ecu.edu.

The Division of Rheumatology of the Department of Medicine of the Medical College of Wisconsin

The Division of Rheumatology of the Department of Medicine of the Medical College of Wisconsin invites applications from qualified individuals with a PhD degree and appropriate postdoctoral and professional experience for the appointment to a tenured track position at a rank commensurate with their academic experience. The successful applicant will have interest or experience in extracellular matrix, matrix mineralization, or connective tissue biology with some preference for those who have worked with cartilage or tendon. Laboratory space will be available. Appointees will be expected to develop an externally funded research program, and to participate in the educational and academic activities of the Division of Rheumatology.

Applications including curriculum vitae, description of current/planned activities, and letters from three references should be submitted online to: Dr. Ann Rosenthal, MD, Professor of Medicine at akrose@mcw.edu.

Postdoctoral Position - Johns Hopkins University School of Medicine

A Post-doctoral position is available immediately to study the role of extracellular matrix in modulating inflammation and immune functions using the mouse as a model system. More about our lab interests are at http://www.jhu.edu/~schakravarti/. The applicant must be self-motivated, hard working with a Ph. D. degree, have a strong background in cell biology and immunology and able to work with mouse models. Apply to Dr. Shukti Chakravarti, Department of Medicine, Johns Hopkins University School of Medicine, email: schakra1@jhmi.edu.

Interesting Science

New Study Links Hensin Function to Integrins in the Kidney

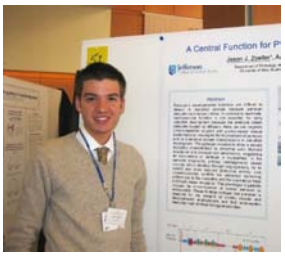
The recent article entitled "Role of Integrins in the Assembly and Function of Hensin in Intercalated Cells" by Vijayakumar et al, which was recently published in "JASN" and, proposed that hensin, an ECM that forms 50-100 nm long fibers composed of several fibrils, plays an important role in the terminal differentiation of intercalated cells of the renal collecting duct.

Hensin is produced by the collecting duct cells and its synthesis is regulated by integrin αvβ1. Following polymerization and deposition into the ECM, hensin binds to α6 containing integrins, and this interaction plays a critical role in converting epithelial cells to a cuboidal-like phenotype capable of apical endocytosis. The likely integrin that mediates not only cell-hensin interactions but also changes in epithelial cell phenotype is αvβ1. Although it is not clear how hensin might promote integrin α6β4 activation, one could postulate that this ECM component might directly bind and activate integrin alpha α6β4; it may change the expression of the natural ligand for integrin α6β4, namely laminin-332; or it might enhance the interaction of laminin-332 with integrin α6β4.

These studies demonstrate that there is a critical role for the spatial/temporal expression of ECM proteins and their receptors in renal epithelial cell terminal differentiation. It is highly likely that similar cell-ECM interactions play an important role in the terminal differentiation of cells in all organs during development and repair process following injury, making this observation important for the field of matrix biology in general.

Contributed by: Roy Zent

Today's Catch: Zebrafish Perlecan



The research by Jason Zoeller et al. (a graduate students in Renato Iozzo's laboratory, see picture on the right), recently published in The Journal of Cell Biology, applied the zebrafish as a model system combined with a morpholino knockdown approach to examine the developmental function of perlecan. Zoeller and colleagues identified a central role for perlecan in skeletal muscle and cardiovascular development (Zoeller JJ, McQuillan A, Whitelock J, Ho S-Y and Iozzo RV. A central function for perlecan in skeletal muscle and cardiovascular development.
J Cell Biol. 181:381-394, 2008). This paper was selected by the Faculty-of-1000 in 2008.
http://www.f1000biology.com/article/id/1109031/evaluation.

Embryonic lethality by targeted gene knockout hinders a complete examination of gene function during in utero development of higher organisms. The zebrafish *Danio rerio*, coupled with morpholino antisense knockdown technology offers a unique alternative for new and improved developmental analysis of gene function. The zebrafish embryo exhibits external development and a transparent nature, permitting real-time *in vivo* analysis of early embryogenesis and the developmental consequences of morpholino-mediated gene knockdown. Perlecan knockdown disrupts muscle fiber actin filament orientation and organization of the sarcomere, and inhibits angiogenic blood vessel development of the intersegmental and sub-intestinal vessels. Human perlecan or domain V/endorepellin was capable of rescuing the perlecan knockdown phenotype, suggesting domain V/endorepellin mediates most of perlecan's biological activity. The study serves as an excellent example for future investigation of other matrix components from a developmental perspective.

Contributed by:Renato Iozzo

New Techniques Developed to Examine Haptotaxis and ECM Function

Generation of controlled, reproducible surface-immobilized protein gradients is important for the study of haptotaxis. In our article, (*Georgescu W, Jourquin J, Estrada L et al. Model-controlled hydrodynamic focusing to generate multiple overlapping gradients of surface-immobilized proteins in microfluidic devices. Lab on a Chip 2008:238-244.*) we describe a new method that allows surface deposition of any one-dimensional protein gradient profile in a simple microfluidic device. The gradients are generated by controlling the position and dwell time of a protein stream inside a channel. We use computer-driven pumps to create a thin protein stream inside the device by hydrodynamically focusing a protein solution in between two laminar flows containing buffer. This way, any surface density profile can be deposited and later recalled as a series of times and flow rates in a software control file. Because the complexity of gradient generation is moved to dynamic computer control, a simple microfluidic device can be used to deposit overlapping non-monotonic gradients consisting of one or multiple proteins. Due to their relevance in haptotaxis, we used the ECM proteins fibronectin and type IV collagen to generate our gradient profiles. The profiles depend crucially on the adsorption kinetics of the protein. To extract the kinetics we calculate the protein surface concentrations for different stream dwell times and fit them to existing deposition models.

The research team headed by JP Wikswo at Vanderbilt University in Nashville showed that different models fit the observed adsorption data depending on the protein type and bulk fluid concentration.
Contributed by Ambra Pozzi

Type-I Collagen Structure-Function Modeling Implicates Novel Functional Domains

Jim San Antonio of Thomas Jefferson University and his collaborators have published the first structure-function model of the type I collagen fibril, the predominant protein and extracellular matrix molecule of humans and all other vertebrates (Sweeney, S.M., et al., "Candidate cell and matrix interaction domains on the collagen fibril, the predominant protein of vertebrates". J. Biol. Chem., In Press). Type I collagen is a major component of skin, bones, tendons, large blood vessels, and many other tissues. Their research team analyzed the distribution of functional sites and mutations on a two-dimensional model of the type I collagen fibril they constructed, and on an X-ray diffraction structure of collagen in vertebrate tissues. The study suggests the hypothesis that the collagen fibril is made up of two domains- one governing dynamic cell-collagen interactions and collagen remodeling, and other assuming a structural role, where proteoglycans bind, and intermolecular cross-linking and mineralization occur. It was also reported that these same domain features are also found in other fibrillar collagens, such as type II collagen, a major component of cartilage in joints. This work may open new avenues for the therapeutic modulation of collagen function and metabolism in diseases including fibrosis, atherosclerosis, and osteogenesis imperfecta, where the protein plays a prominent role, and for the engineering of fibrillar collagens and synthetic polymers for numerous applications in human medicine.
Contributed by Jim San Antoinio

Site-1 Protease: A New Player for Building Matrix

Site-1 protease (S1P), also known as the membrane-bound transcription factor protease, site-1 (MBTPS1), is a golgi-resident, proprotein convertase that processes endoplasmic reticulum (ER) membrane-bound, latent transcription factors (TFs) to their free and active form. The most studied of these TFs include the SREBPs that play a role in fatty acid and cholesterol homeostasis and ATF6 which plays a role in ER stress signaling (ERSS) to alleviate ER stress. The translocation of SREBPs (during low fatty acid and cholesterol levels) and ATF6 (on onset of ER stress) from the ER to the golgi is a regulated event and the processing of these TFs take place when they are brought to the proximity of S1P in the golgi complex, the liberated TFs translocating to the nucleus to activate the necessary transcription program. The notion that S1P may influence cartilage development was seen by the study of the Zebra fish gonzo phenotype which demonstrated both lipid and cartilage defects. The role of S1P in skeletal development however remained elusive. To understand how S1P affects skeletal development, the authors created a cartilage-specific S1P knockout mouse ($S1P^{cko}$) by combining Col2-Cre with S1P floxed mice. (Site-1 protease is essential for endochondral bone formation in mice.D. Patra, X. Xing, S. Davies, J. Bryan, C. Franz, E. B. Hunziker, L. J. SandellJournal of Cell Biology 2007 Nov 19;179(4):687-700.) The resulting $S1P^{cko}$ mice exhibited severe chondrodysplasia due to the lack of endochondral bone development even though the molecular program required for bone formation appears intact in these mice. Interestingly, the phenotype in these mice can could be traced to a defective cartilage ECM. The properties of the $S1P^{cko}$ matrix are reminiscent of that seen in the Col2a1 knockout mice. Indeed, despite adequate expression of the Col2a1 gene, the authors were unable to extract collagen type IIB (Col IIB) from the $S1P^{cko}$ matrix after pepsin digestion of 4M Gu-HCl extracted cartilage. Double immunofluorescence demonstrated that the $S1P^{cko}$ matrix has drastically reduced Col IIB; most of the Col IIB appears trapped inside the cell. Deposition of Col IIA is not affected. Ultrastructural analysis demonstrated that the ER in $S1P^{cko}$ mice is fragmented and engorged with crystalline material, characteristic of ER stress. These findings draw attention to the secretory nature of the chondrocyte and its role in complex cartilage matrix protein synthesis. Like other secretory cells such as the differentiating plasma cells which resort to switching on the ERSS to respond to increased protein synthesis in the ER, chondrocytes may go through a similar phase on differentiating from chondroprogenitor cells to the secretory chondrocytes. However in the absence of S1P, the $S1P^{cko}$ chondrocytes are presumably unable to turn on ERSS and therefore unable to cope with ER stress and the demands for high volume protein production. This results in poor Col IIB deposition into the matrix resulting in an alien matrix which is recalcitrant to vascular invasion and consequent endochondral bone deposition. As other TFs besides ATF6, namely OASIS and CREBH, are also processed by S1P and play a role in ERSS, it remains to be seen which of these TFs if at all may play a role in chondrocytes. This leaves open the possibility that chondrocytes may have a unique secretory pathway or a unique ERSS pathway. The authors are currently exploring these issues and the nature of ER stress and ERSS in chondrocytes through the use of $S1P^{cko}$ mice.
Contributed by Linda Sandell