International Society for Matrix Biology Newsletter

No. 7 - October 2007

Contents

From the President's Desk

Dear ISMB members,

Greetings! I hope this finds you all suitably refreshed after the summer break.

New Council Members elected

In the last ISMB Newsletter we asked ISMB members to vote for two new Council members. The response of our members was great – 97 members cast their votes and it was a really close election. The enthusiastic response of the membership is a really healthy sign for the ISMB. I am happy to announce that our new Council members are: David Hulmes and Yasunori Okada. Many congratulations to our new Council members.

ISMB Awards Session at Pan Pacific Connective Tissues Societies Symposium (PPCTS)

In the last issue we announced some new ISMB awards at the upcoming PPCTS symposium in association with ISMB, to be held in Cairns, Australia, from October 28 to November 1, 2007. These awards will be presented in a special ISMB Awards session at the PPCTS. Although it was not intentional, it turns out that the awardees are from diverse geographical locations.

Dr. Tony Poole of the University of Otago, New Zealand, has won the ISMB-*Matrix Biology* 2006/2007 Best Paper Award. The article: *Articular cartilage and growth plate defects are associated with chondrocyte cytoskeletal abnormalities in Tg737orpk mice lacking the primary cilia protein polaris* (volume 26/4) was selected as the winner of the award by the editorial board of *Matrix Biology.* The award will be officially presented at the ISMB/7th Pan Pacific Connective Tissue Societies Symposium 28 October to 1 November, 2007. Dr Poole receives US$1000 in award money as well as an announcement of the award in the journal. He will give a talk entitled *"The primary cilium and mechanosensation: a cellular cybernetic probe for connective tissue cells"* at the ISMB/Pan Pacific Connective Tissues Societies Symposium where he will also receive the award. The ISMB is affiliated with *Matrix Biology,* and we are very grateful to the publishers for agreeing to sponsor this ISMB award.

The winners of the ISMB- *Matrix Biology* Best Poster Awards will be announced in the next newsletter, and many thanks to those ISMB members who will be judging the posters. Watch this space in the next newsletter!

ISMB also sponsored an ISMB lecture at 7th PPCTS Symposium. After many nominations, vigorous discussion and voting at Council, the ISMB speaker will be Dr. Zhongjun Zhou of the University of Hong Kong who will give a talk entitled *"Lamin A in genome maintenance and premature ageing".* We also will give a new award at the PPCTS - the ISMB New Investigator Award, to an investigator within 5 years of PhD. This award will go to Dr. Takashi Ogawa of Kihara Institute for Biological Research, Yokohama City University who will give a talk entitled "*Biological activity of laminin*

γ2chain monomer and its roles in tumor growth and invasion".

Those of us who will be attending the PPCTS meeting look forward to seeing the ISMB flag flying high!

Looking forward
In July 2008, seven of the Council members who were attending the Collagen Gordon Conference were able to meet to reflect on recent initiatives and plan future activities of ISMB. Arising from very useful discussion then, and subsequently with the full Council, a number of new initiatives are planned.

Partnership with the American Society of Matrix Biology 2008 meeting
In 2008 we expect ISMB to continue to reach out and link matrix biologists world-wide by facilitating international participation at the meetings of national matrix biology societies. Once again we are very fortunate that the publishers of *Matrix Biology* will make a significant contribution to help ISMB with this partnership with ASMB at their 2008 meeting. ISMB-*Matrix Biology* will be sponsoring poster prizes and travel awards for PhD students and junior investigators (up to 10 years postdoc experience, but not yet an independent group leader). There will be an ISMB special session in which the recipient of the ISMB Distinguished Investigator Prize (see below) will give a special plenary lecture and short presentations will be made by the winners of the poster prizes.

ISMB Distinguished Investigator Prize
We also plan to launch a new award at the ASMB meeting – the ISMB Distinguished Investigator Prize - to recognize excellence in matrix biology in 2005-2007. There will be no age limit for eligibility for this award. Members will be asked to nominate a worthy recipient of this award. We will be shortly circulating a form for nominations.

ISMB Logo Competition
Members may have noticed that we don't really have an official logo! After discussion, Council felt that a logo for ISMB would help highlight our identity. So we have decided to launch a competition for a design of a new logo for ISMB. We hope that members will contribute to the society by participating in this Logo competition. Please send in your entry to Jamie (fitzgerj@ohsu.edu) or Kathy (hrmbdkc@hkusua.hku.hk) – you may win one year ISMB membership and US$100!

Hopefully the response to these new initiatives will be as enthusiastic as it was for the election of Council members.

Membership recruitment drive and fund raising

In the last year I have been very encouraged at the increasing enthusiasm and participation of the membership in the ISMB affairs. Due to some sterling effort by our Council members and especially Peter Bruckner who undertook to send by "old fashioned" (but effective!) post, a personal letter from himself and myself, to "lapsed" members, we have now have managed to reactivate members and recruit new ones, so that the membership now stands at 250 (although only 199 of these are fully paid-up for 2007). Another piece of good news is that the publishers of *Matrix Biology* have generously agreed to help us to support some of our awards on an annual basis.

Council feels that to achieve ISMB's goals of linking the matrix biology community and to sustain our initiatives, we need to further increase our membership. In 2008 the FECTS meeting will be held and ISMB hopes to be also affiliated with the symposium so as to complete a circle which embraces Australia, Asia, North America and Europe. And then there are the other initiatives on the wish-list, such as travel fellowships to facilitate collaborative research across continents, training courses etc. All of these need injection of new funds – by additional sponsorship and of course increased membership numbers. So please help us recruit new members and send us suggestions to help promote the society!

Until the next newsletter, all good wishes for success in your research.

Kathy Cheah
President, ISMB

Notice from the Treasurer

Dear ISMB-member,

You may have noticed that there are several new activities of ISMB. There is support for international meetings in the form of various new awards. Some of them are intended for our junior members. Others, such as the Distinguished Matrix Biologist award, are issued competitively for everybody, junior members included.

Also, Jamie Fitzgerald and Dieter Reinhardt merit our applause for reviving the Newsletter. And, so far, they have been successful in recruiting contributions by ISMB-members. I am certain that this upward trend will continue.

But, what is the cause that ISMB is trying to further? It is actually very simple. We want matrix biology to succeed in becoming a prime field of biology and we would like to see our concepts accepted by the rest of the community active in life sciences. ISMB advances this cause on an international level, with the national societies as partners. Although I admit to my past scepticism that ISMB has a place in the scientific world I now believe that this is the case.

Which brings up my next thought. There have been several Presidents and Councils of ISMB since the

society was started in 1994 (incidentally, only two members have served as secretary/treasurer). This is because our society guidelines stipulate a change of president after two years. This has been a clear disadvantage because it was very hard to maintain continuity and speed. I understand that the American Society for Matrix Biology has gone through a similar round of discussions.

I think we need to prolong the tenure of the president and the vice-president. My preference would be for the president and vice-president to serve four years instead of two. And we should be allowed to re-elect a successful president. It is already difficult to find a "good citizen" who is willing to invest a significant fraction of her/his time into a service for the common good. And it is simply foolish to let an active president slip away after two years. This will just put the society to sleep.

I propose to hold an e-mail referendum to change the bylaws. I suggest to partially change Article IX from "*The president will serve for a term of 2 years, non renewable. It is expected that the vice-president will assume the duties of president 2 years after his election as a vice-president. Candidates for vice-president will be nominated by the members of the Council and elected by all members of the Society through a mail ballot.*" to read "*The president and the vice-president will serve for a term of 4 years, renewable by re-election. Candidates for president and vice-president will be nominated by the members of the Council and elected by all members of the Society through a mail ballot.*"

Please forward your opinion on this matter, either by writing a contribution for the next Newsletter, or in an e-mail to myself to be distributed among the members.

I have another request for you, dear reader. Are you by any chance among those many who still have not yet renewed their memberships for 2007? Better late than never. Just take out your VISA- or Master/Euro-Card and go to http://www.ismb.org. You will find directions under "Membership" on how to proceed. It is simple. If you are the proud owner of a credit card and also have access to the internet there is simply no excuse for you. It is as safe as any other SSL-encoded transaction that you may conduct over the internet.

One further request: would you support Kathy Cheah and myself in our effort to recruit new members? Give your colleagues our internet-address and help them to find, download, and process the application form. All of the new members we signed up of last summer at the 2007 Gordon Conference on Collagen were actually surprised by the low membership fee they were expected to pay. I wish you all the luck you need from this world!

Peter Bruckner
ISMB Treasurer
peter.bruckner@uni-muenster.de

Meeting Announcements

7th Pan Pacific Connective Tissue Societies Symposium

Shangri-La Resort, Cairns, Australia
October 28 – November 1, 2007
Conference convener: Shireen Lamande
E-mail: connective@asnevents.net.au
www.connectivetissue2007.org/

OARSI World Congress on Osteoarthritis

Ft Lauderdale, Florida, USA
December 6-9, 2007
http://www.oarsi.org/meetings/07Congress/index.cfm

Gordon Research Conference Fibroblast Growth Factors in Development and Disease

Il Ciocco Lucca (Barga), Italy
March 2-7, 2008
Chairs: Dave Fernig & Gail Martin
Vice Chair: Sabine Werner
Additional information is available at http://www.grc.org/programs.aspx?year=2008&program=fibro

Fibrous Proteins: transforming structural knowledge into new materials

Mount Eliza, Melbourne, Australia
March 31st – April 3rd, 2008
This meeting will discuss the latest knowledge on the structures of fibrous proteins and their hierarchical organisation into higher order structures and into tissues. It will cover a wide range of fibre forming proteins, including collagens, elastin, keratins, silks, muscle proteins and amyloid structures. These data will also be examined for how the structural insights are providing opportunities to design new materials for various medical and technical applications.
Organiser: John Ramshaw
fibrousproteins@csiro.au

Annual Meeting of the German Connective Tissue Society

Freiburg, Germany
April 3 – 5, 2008
Chair: Leena Bruckner Tuderman
E-mail: bruckner-tuderman@uniklinik-freiburg.de

Experimental Biology 2008

San Diego, CA
April 5-9, 2008
The Histochemical Society will be meeting with the American Society for Biochemistry and Molecular Biology at Experimental Biology 2008, April 5-9, at the San Diego Convention Center. HCS and ASBMB are co-sponsoring two symposia on Sunday, April 6: "Live Imaging of Developmental Processes" and "Laser Capture Microdissection for Molecular Analysis". The organizers of each symposium will select several short

presentations from submitted abstracts. The abstract deadline is November 7, 2007. If you would like to be considered as a speaker for the above symposia, please submit your abstract to Experimental Biology, http://www.eb2008.org/ and to the Histochemical Society, mail@histochemicalsociety.org. Organizers will contact those chosen for oral presentations.

Canadian Connective Tissue Conference 2008

Montreal, Canada
June 5 – 7, 2008
Chairs: Dieter Reinhardt and Mari Kaartinen
E-mail: dieter.reinhardt@mcgill.ca; mari.kaartinen@mcgill.ca

Basement Membranes Gordon Research Conference

University of New England, Maine (near Boston)
June 22-27th, 2008
Chair: Jeffrey Miner
Vice-chair: Monique Aumailley
This will be the fourteenth in a highly successful series of biannual meetings that have been major international forums for dissemination of new concepts regarding the structure and function of basement membranes. The 2008 Conference will present a diverse mixture of sessions on basement membrane protein structure, biosynthesis, assembly, and function during development and in disease. In addition to invited speakers, **there will be numerous opportunities for oral presentations by graduate students, postdocs, and junior faculty based on submitted abstracts**. Additional information is available at www.grc.org.

Gordon Research Conference Proteoglycans

Andover, NH, Proctor Academy
July 6-11, 2008
Chair: Thomas N. Wight
Vice Chair: Marian F. Young
Additional information is available at http://www.grc.org/programs.aspx?year=2008&program=proteoglyc

XXI meeting of the Federation of European Connective Tissue Societies

Marseille, France
July 9-13, 2008
Chair: Phillippe Charpiot
philippe.charpiot@pharmacie.univ-mrs.fr
Vice-chair: Sylvie Ricard-Blum
s.ricard-blum@ibcp.fr

Invited speakers
Sunneel APTE (Cleveland, USA)
Yann BARRANDON (Lausanne (Suisse)
Antony DAY (Manchester, UK)
Holger GERHARDT (London, UK)
Marie-Madeleine GIRAUD-GUILLE (Paris, France)
Eckhard LAMMERT (Dresden, Germany)
Birgit LEITINGER (London, UK)
Robert MECHAM (St Louis, USA)
Stefan MUNDLOS (Berlin, Germany)
Johanna MYLLYHARJU (Oulu, Finland)
Tomoyuki NAKAMURA (Kyoto, Japan)
Chris OVERALL (Vancouver, Canada)
Mario RASPANTI (Varese, Italy)
Florence RUGGIERO (Lyon, France)

Workshop topics:
Cell-matrix interactions and signalling, Dynamic aspects of the ECM, ECM and cancer, ECM and development, ECM diseases and therapies, ECM: from inside the cell to the matrix, ECM: from molecules to extracellular machines, ECM maturation and aging, ECM: source and reservoir of bioactive molecules, Metalloproteinases: remodelling of the extracellular matrix and cell surface, Stem cells, Systems biology, Tissue engineering: from the lab to the patient, Vascular Biology and angiogenesis

5th European Elastin Meeting 2008

Alcala de Henares, Spain
July 16-19, 2008
Chair: Julia Bujan

The 16th Biennial National Conference on Osteogenesis Imperfecta

Crystal City, VA, USA
August 1-3, 2008
www.oif.org/site/PageServer?pagename=06conf_splash&JServSessionIdr006=ccdbf0x1f2.app1a

Gordon Research Conference Biomineralization

New London, NH, Colby-Sawyer College
August 10-15, 2008
Chair: James J. De Yoreo
Vice Chair: Lia Addadi
Additional information is available at http://www.grc.org/programs.aspx?year=2008&program=biomin

American Society for Matrix Biology 2008 meeting

San Diego, CA, USA
December 7-11, 2008
Chair: Bill Parks
Detail information on registration and call for abstracts will be announced in the next ASMB newsletter and on the ASMB website at www.asmb.net.

Short Course Announcement

Principles & Applications of Immunocytochemistry A Short Course at Experimental Biology 2008
8 AM-4:30 PM, April 5, 2008, San Diego Marriott & Marina

Organizers: Denis G. Baskin and William L. Stahl

The Histochemical Society is offering a course in the techniques of immunocytochemistry that is aimed at

investigators and students who are new to the field but may also be useful for experienced investigators. The course provides an understanding of the basic principles and applications of immunocytochemistry for research in biochemistry, molecular biology, cell biology, and pathology. Topics include fixation, antigen retrieval, double labeling, and controls.

Space is limited and advance registration is required by February 15, 2008. There will be no on-site registration. Registration is $250 for graduate students and $300 for all other attendee. Registration includes all course materials, refreshment breaks and lunch. For further information, please visit:
http://immunocytochem.wordpress.com
http://www.histochemicalsociety.org

Matrix Research Update

Site-1 Protease is Essential for Endochondral Bone Formation in Mice

Debabrata Patra, Xiaoyun Xing, Sherri Davies, Jennifer Bryan, Carl Franz, Ernst B. Hunziker, Linda J. Sandell

Journal of Cell Biology (in press)

Site-1 protease (S1P) has an essential function in the conversion of latent, membrane-bound transcription factors to their free, active form. In mammals, abundant expression of S1P in chondrocytes suggests an involvement in chondrocyte function. To determine the requirement of S1P in cartilage and bone development, we have created cartilage-specific S1P knockout mice ($S1P^{cko}$). $S1P^{cko}$ mice exhibit chondrodysplasia and a complete lack of endochondral ossification even though Runx2 expression, Ihh signaling, and osteoblastogenesis is intact. However, there is a significant increase in chondrocyte apoptosis in the cartilage of $S1P^{cko}$ mice. Extraction of type II collagen is significantly lower from $S1P^{cko}$ cartilage. In $S1P^{cko}$ mice the collagen network is disorganized and collagen becomes entrapped in chondrocytes. Ultrastructural analysis reveals that the endoplasmic reticulum (ER) in $S1P^{cko}$ chondrocytes is engorged and fragmented in a manner characteristic of severe ER stress. These data suggest that S1P is essential to the secretion and organization of type II collagen necessary for genesis of a normal cartilage and thus endochondral ossification. The mechanism is likely through the release of a membrane-bound transcription factor(s) in the ER/Golgi by Site-1 protease that initiates a specific cascade of events that enable proper protein secretion by chondrocytes.

Job Advertisements

Postdoctoral position in Lyon, France

Towards scar-free wound healing: The project is funded by the French National Research Agency. It involves 3 research groups, two based in Lyon (Hulmes, Damour) and the third in Toulouse (Malecaze). The idea is to use a mouse model of corneal scarring to study the role of tolloid proteinases and associated proteins in the process of wound healing, and to develop novel anti-scarring strategies. Scarring frequently accompanies wound repair following events such as surgery, burns and infections. Several structural proteins, enzymes and growth factors are involved in wound repair. It has recently become apparent that members of the tolloid family of metallo-proteinases play several important roles in wound healing and development (Ge and Greenspan, 2006), either by processing structural proteins or by activating enzymes and growth factors in the extracellular matrix (ECM). The activities of tolloid proteinases can be stimulated several fold by other ECM proteins, called PCPEs. We have recently shown that PCPE-1 can stimulate the activity of one of the tolloid proteinase BMP-1, in a substrate specific manner, to selectively accelerate procollagen processing (Moali et al., 2005) and we have identified structural features in PCPE-1 required for stimulating activity (Blanc et al., 2007). The aims of the project are to identify new substrates for tolloid proteinases using proteomic approaches, to understand the molecular mechanisms of action of tolloid proteinases and PCPEs and to find novel inhibitors to be tested in both an animal model and using reconstructed corneas.

Blanc G, Font B, Eichenberger D, Moreau C, Ricard-Blum S, Hulmes DJ, Moali C (2007) J Biol Chem 282, 16924-16933.

Ge G, Greenspan DS (2006) Birth Defects Res C Embryo Today 78: 47-68.

Moali C, Font B, Ruggiero F, Eichenberger D, Rousselle P, Francois V, Oldberg A, Bruckner-Tuderman L, Hulmes DJS (2005) J Biol Chem 280: 24188-24194.

Working environment - The research will be carried out in the group of David Hulmes (currently 3 permanent staff, one postdoc, one PhD student and a Masters student) at the Institut de Biologie et Chimie des Protéines (IBCP), which is a joint CNRS/ University of Lyon institute located in the Gerland region of Lyon. The institute (www.ibcp.fr) consists of 160 staff (including postdocs and students), organised in three scientific departments and 14 research groups as well as common facilities for protein production and characterisation. The department of matrix biology and tissue engineering consists of 6 research groups, with interests ranging from structural biochemistry, cell biology, development and tissue repair. Structural biology and bioinformatics are also major areas of expertise. The IBCP is part of a grouping of local institutes in the Gerland area, the IFR 128 Biosciences Lyon-Gerland (www.ifr128.prd.fr).

Lyon is one of the major cities in France (www.lyon.fr/vdl/sections/en) and is ideally located in the centre of Europe within two hours of Paris, the Alps and the Mediterranean. It has a strong cultural and intellectual tradition, is widely known as the gastronomic centre of France, and the old town is a UNESCO World Heritage site.

Candidates should have a strong background in biochemistry. Experience in structural biology or proteomics would also be an advantage. Knowledge of the French language would be helpful but not essential. There are no restrictions on nationality. *Net salary* - 2039 euros/month.

Applications should be sent to David Hulmes at the following address. Send full CV, list of publications and names and contact details of at least two scientific referees. **Deadline 1 November 2007.**

David Hulmes
Institut de Biologie et Chimie des Protéines
7 passage du Vercors
69367 Lyon cedex 7
Tel : +33 (0)472722667
Fax : +33 (0)472722604
e-mail : d.hulmes@ibcp.fr

Postdoctoral Fellowship in New Zealand

We seek a talented new PhD graduate with extensive experience in mechanobiology, including cell signalling pathways, to undertake biomechanical studies on the role of primary cilia in the development of fibrosis during polycystic kidney disease. The applicant must have skills in cell and tissue culture, Western blotting, real-time calcium imaging and analysis, and some familiarity with dynamic loading systems such as the Flexercell system would be an advantage. A strong understanding of connective tissue biology and the role of primary cilia in cellular mechanosensation will also be essential. This is a new position funded by the Royal Society of New Zealand for 3 years in the first instance, and the successful candidate will join Dr Tony Poole's laboratory in the Section of Orthopaedic Surgery, Department of Medical and Surgical Sciences, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand. The University of Otago is New Zealand's top ranked university for Research. Please send expressions of interest and Curriculum Vitae to Associate Professor Tony Poole at <tony.poole@stonebow.otago.ac.nz> in the first instance.

Postdoctoral Research Position

Laboratory for Glycobiology & Developmental Genetics
Department of Human Genetics, VIB & University of Leuven (Belgium)

The position (immediately available) is initially for two years, with possible renewal up to a period of three years. The position is funded by a grant from the Interuniversity Attraction Poles (IUAP) Program of the Belgian Government. This program grant supports a network of Belgian research laboratories with a strong, shared interest in unravelling the molecular and cellular mechanisms that steer animal development. Approaches are multidisciplinary, using cellular and animal models, in particular zebrafish. Prior research expertise with zebrafish, and expertise in developmental signaling and molecular cell biology represent strong assets. Interested candidates should send their application (CV, bibliography, specific research interests, motivation, references) to Mrs Marie-Anne Everaerts, Centre for Human Genetics, Herestraat 49, PBox 602, Leuven (Belgium) (Marie-Anne.Everaerts@med.kuleuven.be), for the attention of Professor Guido David, Department of Human Genetics, Kuleuven (Guido.David@med.kuleuven.be).

Project description: *Glypican-controls on developmental signaling*

Glypicans are required for the robustness of the (Wnt, Bmp and Hh) signaling pathways that determine the proliferation, differentiation and migration of the cells during embryogenesis. How glypicans participate in the regulation of the dispersal and reception of developmental signals, and of their well documented dose-dependent effects, remains unknown. The glypicans are cell surface heparan sulfate proteoglycans which are linked to the plasma membrane by a GPI-anchor. The general objectives are (i) to clarify by what precise cellular and molecular mechanisms glypicans influence morphogen signaling, and (ii) to identify the specific contributions of the glypican core proteins to glypican function. This includes addressing questions such as: with what signaling components or signal-modulators do these proteins interact? How do these interactions influence the association of ligand-receptor complexes with distinctive membrane compartments in the endocytic pathway, with signal-transduction components and with effectors? Does this contribute to the sometimes cell-specific effect of growth factors? Are sequence variants or inappropriate expressions of these 'co-receptors' relevant for the pathogenesis of complex disease? Can such knowledge be translated in tools and approaches to modulate signaling pathways in embryogenesis, tissue regeneration, and cancer?

The laboratory of GB&DG has extensive expertise in the (cell and developmental) biology of the glypicans. Collaborating laboratories have strong expertise in developmental signaling, in particular Bmp/Smad-signaling. The candidate should have a keen interest in the endocytotic controls of developmental signaling, the unifying theme and core subject of this project, and in the validation of cell biological findings in vertebrate models (zebrafish), and vice-versa. Keywords: Cell biology / developmental biology: endocytosis, vesicular trafficking, receptor recycling, signal transduction, proteomics, RNAi, morpholino's, live imaging, zebrafish.

Further information at http://med.kuleuven.be/cme-mg/LabIntro/GuidoDavid_en.html

Postdoctoral Research Position

Laboratory for Glycobiology & Developmental Genetics
Department of Human Genetics, VIB & University of Leuven (Belgium)

The position (immediately available) is initially for two years, with possible extension up to a period of three years, and is funded by a grant from the Belgian Cancer Fund (BFK). Prior research expertise that is directly relevant to the project is not an absolute requirement, but represents a strong asset. Interested candidates should send their application (CV, bibliography, specific research interests, motivation, references) to Mrs Marie-Anne Everaerts, Centre for Human Genetics, Herestraat 49, PBox, Leuven (Belgium)(MarieAnne. Everaerts@med.kuleuven.be), to the attention of Professor Guido David, Department of Human Genetics, KULeuven (Guido.David@med.kuleuven.be).

Project situation and description: *Mammalian heparanase, a target for the control of tumour-angiogenesis.*

Heparanase-1 (an endo-glycosidase that cleaves heparan sulfate) is strongly implicated in the growth and invasiveness of tumor cells, and in the development of the vasculature that supports tumor growth. Heparanase-1 is synthesized (i.e. by tumor cells and inflammatory cells) as a larger, enzymatically-inactive precursor protein (pro-heparanase-1). The enzymatically-active form of the protein is derived from the precursor by proteolytic processing, and is mainly localized in intracellular endosomal / lysosomal compartments. Both the pro-form and the mature form of heparanase-1 influence cell behaviour. Importantly, some of the biological effects of (pro)heparanase appear to be independent of the known enzymatic potential/activity of the protein. Cells (e.g. vascular endothelial cells) rapidly bind and internalize any (e.g. tumour) secreted pro-heparanase-1, transferring the internalized precursor to late endosomes/lysosomes, where it is processed into the mature active form of the enzyme and stays localized. As we have demonstrated, the binding and (re-)uptake of secreted heparanase-1 precursor are mediated by cell surface heparan sulfate proteoglycans (HSPGs), by low density lipoprotein receptor-related proteins (LRP) and by mannose-6-phosphate (M-6-P) receptors [Vreys et al., 2005]. Cells also rapidly bind and internalize the active form of the enzyme. In that case uptake appears to be strictly LRP-dependent. Furthermore, our data suggest that endosomal heparanase may play an important and specific role in FGF-receptor activation (and thus in angiogenesis). Altogether, effects of (pro)heparanase-1 on cells likely result from the engagement of specific cell surface receptors, leading to internalization and gain in enzymatic activity, and direct and indirect effects on receptor-mediated signalling processes.

The aim of the project is to substantiate the hypothesis that heparanase-1 represents a physiologically relevant mode of 'paracrine' signalling, supporting tumor-angiogenesis, and that heparanase-1 can be usefully targeted, preventing tumour progression.

The approach will consist in developing and optimizing recombinant camel single chain antibodies (nanobodies) that block the interaction of heparanase-1 with cell surfaces, signalling and endocytic receptors and that interfere with the activation and activity of heparanase under in vitro and in vivo situations, suppressing or slowing down tumour-angiogenesis and tumour progression. Techniques: recombinant DNA, protein, imaging, cellular and animal modelling.

Reference: Vreys, V. et al (2005) Cellular uptake of mammalian heparanase precursor involves low density lipoprotein receptor-related proteins, mannose 6-phosphate receptors, and heparan sulfate proteoglycans. J Biol Chem. 280:33141-8.

Further information at http://med.kuleuven.be/cme-mg/LabIntro/GuidoDavid_en.html

Postdoctoral position in tumor biology

Department of Biomedicine, University of Bergen, Norway

A postdoctoral research fellow position is available at the Department of Biomedicine (laboratory of Dr. Donald Gullberg) to study different aspects of the tumor stroma (3-year project). The research is focused on studying the role of integrin-related mechanisms in the tumor stroma. Experimental approaches in the laboratory make use of fibroblast spheroid cultures, xenograft tumor models in mice, co-cultures in 3-D collagen gels, matrix metalloproteinase analysis and microarray analysis.

The successful applicant must hold a Ph.D. *in cell biology, molecular biology, tumor biology* or a related discipline, be proficient in spoken and written English and have a strong background in the methods used in the laboratory, in particular cell biology methods. Experience with animal work, mammalian cell transfections, generation of stable overexpressing cell lines and siRNA knockdown technology, are considered a merit.

A completed Ph.D. or foreign education at Ph.D. level is a minimal requirement for the postdoctoral position. The term of employment for this position is 3 years. It is not possible for any person to work under more than one temporary appointment at the same institution. The position is funded by the Research Council of Norway.

More information on this advertised position is available from Professor Donald Gullberg (Donald.gullberg@biomed.uib.no; tel: +47-55586332).

A postdoctoral position is a temporary appointment. The objective of postdoctoral positions is to qualify the selected candidates for work in senior positions in their disciplines.

The salary will be paid in accordance with level 54 on the government salary scale (code 1352).

It is a goal that the period of appointment is to be carried out as a continuous research program. Leave of absence will normally not be given, within the period of appointment as a postdoctoral fellow, for other purposes than those which are regulated by law.

The government workforce shall to the largest possible extent reflect the diversity of the population. The University of Bergen has therefore adopted a personnel policy objective to ensure that a balanced age and sex composition and the recruitment of persons of various ethnic backgrounds is achieved. Candidates of different ethnic backgrounds are therefore encouraged to apply for the position.

The successful applicant must comply with the guidelines that at any given time apply to the position.

The University of Bergen applies the principles of public access to information in connection with appointments to academic positions.

The application should include a statement of motivation and the names and contact details of 2-3 senior scientists for further reference. Enclosed with the application shall be a complete overview of previous education and relevant experience, copies of examination certificates, testimonies, a list of all scientific publications and reprints of selected scientific publications (all in 4 copies).

The application shall be sent to Donald Gullberg, Department of Biomedicine, Jonas Lies vei 91, NO-500 Bergen, Norway. The **application deadline is November 15th 2007.**

Postdoctoral Position in Proteoglycan Research, Cancer and Angiogenesis

Thomas Jefferson University, Philadelphia, PA

A postdoctoral position is available to investigate the biology of perlecan and endorepellin in vertebrate vascular development and tumor angiogenesis. The candidate will join a multi-disciplinary team of researchers involved in investigating the molecular mechanisms through which perlecan and its angiostatic, C-terminal fragment endorepellin affect the development of new blood vessels both in vitro and in vivo (J. Cell Biol. 166:97-109, 2004; J. Biol. Chem. 280:32468-32479, 2005; Nature Rev. Mol. Cell. Biol. 6:646-656, 2005; J. Natl. Cancer Inst. 15: 1634-1646, 2006; Blood 109: 3745-3749, 2007).

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

Renato V. Iozzo, M.D.
Department of Pathology, Anatomy & Cell Biology
Thomas Jefferson University
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Thomas Jefferson University is an equal opportunity employer.

TWO OPEN POSITIONS FOR PhD STUDENTS

Project 1. *Importance and treatment of viral cardiomyopathy.*

Cardiotrophic viruses are found in 70 % of patients with heart failure of unknown origin. However, it remains unknown whether these viruses really cause heart failure or just mark hearts that are destined to succumb to some sort of dysfunction anyway? The main objectives of this project are therefore to:
1. Definitively demonstrate the causal role of virus persistence in heart failure.
2. Identify the mRNA and microRNA (miRNA) mechanisms that cause the persistence of the virus in the heart, and the development of cardiac failure in the presence of a virus.
3. Elaborate the therapeutic possibilities of two specific targets: inhibition of matrix metalloproteinases and administration of thrombospondin-2 (TSP-2), for viral cardiomyopathy.

This work is embedded in the Cardiovascular Research Institute of Maastricht, University of Maastricht, in close collaboration with the Center of Transgene Technology and Gene Therapy. The project leader is Stephane Heymans. The grant is for 4 years, including salary and bench fee

Project 2. *Proteases and matrix proteins as novel targets for the diagnosis and treatment after cardiac transplantation.*

Rejection after cardiac transplantation (HTx) causes myocyte injury and allograft vasculopathy. Matrix metalloproteinases (MMPs) play a central role in cardiac inflammation and remodeling during heart falure. Exciting preliminary data revealed that intragraft transcript and plasma levels of MMPs and TIMPs positively correlated with cardiac rejection. This project aims to study the mechanisms by which MMPs/TIMPs may affect cardiac rejection and transplant vasculopathy,

and determine their predictive value for these complications. In addition, the role of matricellular proteins (thrombospondins, SPARC, osteopontin) that protect against exaggerated inflammation and cardiac failure in ischemic heart disease will be addressed in regard to transplant rejection and vasculopathy.

This work is embedded in the Department of Cardiology, transplant center, University of Leuven, in close collaboration with the Center of Transgene Technology and Gene Therapy, University of Leuven. The grant is for 1 year. During this year, a new grant will be looked for.

For both positions please send detailed CV and motivation letter to S.Heymans@cardio.unimaas.nl

PhD position in tumor biology

Department of Biomedicine, University of Bergen, Norway

At the Department of Biomedicine a position as research fellow within the field of tumor biology is open for 3 years.

The candidates' project is aiming at dissecting tumor-host interactions during cancer progression. This includes experiments to investigate modulations of the stromal tissue and fibroblasts in tumours, and how these alterations influence the malignant cell compartment. A main objective will be to identify tumor-specific alterations in the stromal tissue that can be targeted therapeutically. The work will involve cell culture and *in vitro* studies as well as *in vivo* studies and include techniques such as immunohistochemistry, western-blot, PCR, cloning, *in vivo* experiments and MRI imaging. The candidate will join a multi-diciplinary team with a broad scientific expertise spanning from basic science to clinical translation. The project leader is professor Donald Gullberg and the supervisor is Per Øyvind Enger, The Department of Biomedicine.

Additional information on the position is obtainable from professor Donald Gullberg (donald.gullberg@biomed.uib.no; tel:+47-55586332) or associate professor Per Øyvind Enger (per.enger@biomed.uib.no, tel:+47-55586347), The Department of Biomedicine, University of Bergen, Jonas Lies vei 91, 5009 Bergen, Norway.

Applicants must hold a master's degree in molecular cell biology, or equivalent. The master's degree must be completed by the application deadline. The candidate must be able to communicate on English.

The research fellow must take part in the University's approved PhD programme leading to the degree within a time limit of 3 years. Hence, applicants must meet the formal admission requirements for the PhD programme.

In total, the fellowship period is 3 years. The length of the fellowship period may be reduced if the successful applicant has held previous employment as a research fellow.

Starting salaries at salary level 39 (code 1017) on the government salary scale (corresponding to NOK 287,500 per year), following ordinary meriting regulations. (Wage levels 39/46).

The application should include CV, University diplomas/certificates, minimum 2 references from previous collegues/supervisors (4 exampoles in total).

ISMB Membership news

We have a new member: Alfonso Aviano, Italy. Congratulations!

However, this is all the information we have on this new member. Can anybody help in getting the address and/or e-mail of this person?

To best serve the matrix biology community it is important to keep our membership details up-to-date. Please let us know if you change email address or regular mailing address. Please email Jamie Fitzgerald (fitzgerj@ohsu.edu) and Peter Bruckner (peter.bruckner@uni-muenster.de) with any address changes so we can update our records.

In Memoriam

JARO SODEK

It is with enormous sadness that we record the recent death of our colleague Jaroslav Sodek. Jaro's initial degree was from the University of Sheffield, England in 1964 which he followed with a Ph.D. from the University of Toronto awarded in 1970. After a post-doctoral fellowship at the University of Alberta he returned to Toronto, where he was an inaugurating member of the Medical Research Council Group in Periodontal Physiology at the Faculty of Dentistry commencing in 1973 and was the Director of the Group from 1983 until 2000. He has been a principal investigator in the CIHR Group in Matrix Dynamics and a Professor in the Department of Biochemistry, Faculty of Medicine.

Jaro characterized the first active site of aspartyl proteinases and first demonstrated the heptad repeat structure of coiled-coil proteins, such as tropomyosin. He developed novel approaches to analyze collagen remodeling and the processing of collagen precursors *in vivo*. He showed rapid turnover of collagen in periodontal tissues, a process that is important for tooth eruption and orthodontic tooth movement.

Furthermore, Jaro devised extraction procedures to selectively isolate and characterize mineral associated proteins in bone and dentine and showed the temporal-spatial correlation between the expression of bone sialoprotein and mineral crystal formation *in vitro* and *in vivo*. In recent studies, he used a combination of biochemistry, molecular biology and cell biology to study the intricate regulation of bone sialoprotein and osteopontin expression and determined the functions of these proteins. Of particular interest is the characterization of an intracellular form of osteopontin, which was first identified in migrating cells in his laboratory, and its role in the metastasis of cancer cells.

His work on connective tissue biology was continuously funded from 1973 onwards by Canadian and other agencies. Jaro was academically 'hyperactive' with over 200 refereed publications to his credit and with a very strong citation record. His research was characterized by perception, care, industry and articulate reporting. He produced a body of work second to none which is, and will continue to be, heavily cited.

Jaro supervised 18 Ph.D. students many of whom have gone on to be outstanding researchers and academics in their own right. He is properly famous for his collegial and cooperative interactions with colleagues or whoever would benefit from his sage and friendly advice. He has been an ideal mentor for many junior Faculty members at the University of Toronto.

All of those who have been associated with Jaro have benefited from his dedicated work. He leaves behind an enormous scientific legacy and a pattern of conduct that many might aspire to but few achieve. It is such a pity he has left us. He will be more than missed.

GR Holland (University of Michigan, USA)
WF Vogel (University of Toronto, Canada)

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From the Editor's Desk

Dear readers of Matrix Biology,

In this issue of the journal, enjoy a guest editorial from D. Gullberg on recent exciting work on α8β1 integrin.

Neuronal pathways leading to the kidney

Ever since the finding that a specific cell surface receptor (integrin α8β1) was not required in the brain as expected, but rather in the kidney, the quest has been to find out why this molecule is so crucial for kidney development. A new paper solves the mystery and suggests a new mechanism whereby integrins might regulate organ morphogenesis.

Integrins are heterodimeric αβ cell surface receptors which in addition to acting as extracellular matrix receptors also engage in some types of transient cell–cell interactions. The largest subfamily of integrins all contains the β1 subunit. Inactivation (knockout) of the gene encoding the β1 integrin protein in mice causes embryonic lethality at the time of blastocyst implantation (Fassler and Meyer, 1995). More recently, tissue specific knockouts have shown the importance of β1-containing integrins in neuronal tissue, neural crest cells, skin, muscle and cartilage. However, with few exceptions, the specific integrin αβ heterodimers involved in the respective tissues are not known. In cartilage for example, conditional inactivation of β1 integrin leads to defects in cartilage matrix organization, but no individual integrin α-chain knockout with this phenotype has been described. Skeletal muscle offers another example. In the absence of integrin β1 in the muscle lineage, a severe myoblast fusion defect not observed in individual integrin α-chain mutants results, indicating that certain combinations of integrin heterodimers are required to regulate myoblast fusion and differentiation (Schwander et al., 2003). In a recent paper by Linton et al. (2007), many years of systematic work trying to understand the importance of cell adhesion in kidney development, now takes a big step forward. The publication presents what might be a new paradigm for how integrins regulate organogenesis. Similar mechanisms might also be at play in different pathological conditions involving integrin interactions (for example inflammation and tumor–stroma interactions in cancer).

The journey of trying to figure out the role of integrins in kidney development has indeed been a long one. Initial work using antibodies and organ cultures, indicated the importance of basement membrane assembly, and a role for α6β1 integrin. Intriguingly, mice lacking α6 integrin did not show an obvious kidney phenotype. Instead, genetic data indicated an important role for the α8β1 integrin, since mice deficient in α8 integrin lacked one or both kidneys (Muller et al., 1997). This finding was unexpected since initial work on α8 integrin, based on tissue distribution and in vitro data, suggested a role in neuronal outgrowth and pathfinding, and it raised two major questions: One question concerned the identity of the ligand for α8β1 integrin in the kidney; a second question concerned the nature of the mechanism underlying the dramatic effect that lack of α8 integrin had on kidney development. Using an innovative approach based on an overlay assay, it was established that the crucial ligand for α8β1 in the kidney was a protein named nephronectin (Brandenberger et al., 2001). In their recent work, Linton et al. (2007) demonstrate that nephronectin is indeed a ligand for α8β1 in vivo. Mice deficient in nephronectin phenocopy the α8 integrin mutant phenotype. The authors also elucidate part of the molecular mechanism whereby defects in this integrin–ligand pair impair kidney development. Using microarray technology they establish that one effect of disturbed α8β1–nephronectin interaction is deficient glial cell derived neurotrophic factor (GDNF) synthesis, implying that the integrin–ligand interaction regulates a paracrine cytokine axis. It is also postulated that GDNF-mediated signalling might explain variable penetrance of the α8-deficient mouse phenotype and this can be proven by different mouse breedings.

In summary, the work by Linton et al. (2007) shows that integrins can work in mysterious ways and that α8β1 is a molecule full of surprises. First identified in neuronal tissues, it turns out to have a unique role in kidney development. The latest twist in this story reveals that its mode of action on adjacent cells is via regulating the release of a soluble morphogen. It is not the first time that integrins have been shown to regulate growth factor release. In mice lacking another integrin, the integrin β3 chain, a complex regulation of the fibrotic cytokine TGF-β has been reported. The discovery of this mode of integrin action, where integrins not only integrate the connection between two molecular networks, the ECM and the cytoskeleton, but also integrate paracrine signalling, warrants re-examination of integrin action in different systems. It is likely that we are in for more surprises from the integrin family.

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