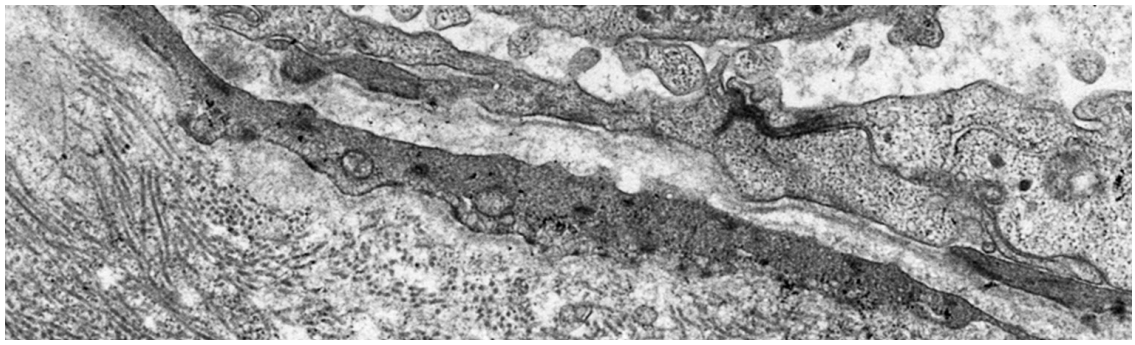


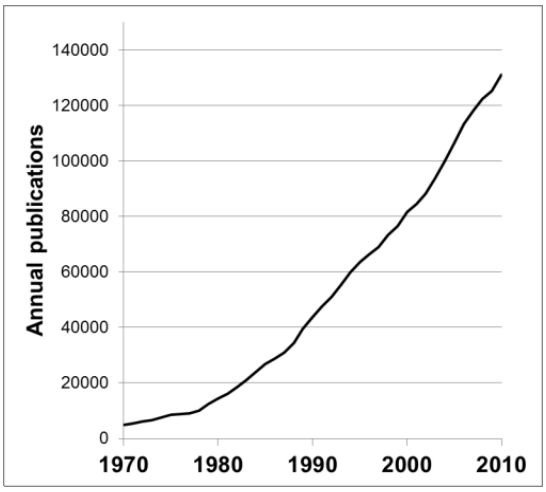
ISMB NEWSLETTER

February 2012

Matrix Biology 2012

This year the ISMB is proudly supporting two major international meetings in matrix biology: the FECTS meeting in Poland in August (www.fects.pl) and the ASMB/SFG meeting in San Diego in November (http://www.asmbsfg2012.org). The programs for both meetings look really exciting and we look forward to strong participation from the matrix biology community. In addition to the Rupert Timpl award to an outstanding young scientist and the distinguished investigator award, ISMB will be funding a number of travel grants for students and postdocs to attend these meetings. Watch the ISMB web site for further information (www.ismb.org)!

There seems to be a rumor going around that matrix biology research has somehow passed its peak. I don't know where this rumor came from, but let me assure you that it is entirely unfounded! The graph below shows the total number of publications per year in the field over the past 40 years. As you see, matrix biology is very much alive and well!



It looks like we still have some work to do in trying to explain to people just exactly what matrix biology is all about. The graph includes all publications in PubMed using the following search terms: extracellular matrix, extracellular/membrane glycoproteins/proteoglycans, integrins and other receptors, growth factors, chemokines, cytokines, extracellular/cell surface proteases and other enzymes, tissue engineering, mechanotransduction and intercellular signaling. Though no doubt the search could be further refined, it seems to me that it covers most of what we understand as matrix biology. And the numbers are impressive, over 130,000 publications in 2010, accounting for 14% of all publications in PubMed! You might want to pass on the message to your funding bodies!

David Hulmes
President ISMB

From the Secretary's/treasurer's desk

Dear ISMB-member,
It is the time, again, to select new members of the ISMB Council. Our constitution stipulates a maximum of 18 members, including the president, the vice-president, and the secretary / treasurer. We currently have 13 members. The terms last three years and elections/re-elections should be carried out every year with the three senior-most members to be replaced. The constitution says that the Council proposes candidates for the new or to be re-elected members of Council and the membership then elects from these candidates. So much for the rules.

I, personally, would be in favour of a change, here. My suggestion is as follows: If we replace three Council members every year and the number in Council (other than the president, the vice-president, and the secretary / treasurer) is 10, the term for each member would be about 3 years. I propose to increase the number of Council members to 12 (15) for the following reasons:

1. The number of 12 can be divided by 3 (10 does not).
2. 12 members, with three being replaced/re-elected) each year, would mean a term of 4 years per member.
3. The term extension to 4 years does not mean an inappropriately excessive work load.
4. The continuity of office would be improved.
5. The constitution allows this enlargement of Council.
6. Affairs would only imperceptibly be complicated by a larger Council

In conclusion, I propose only one Council member to step down in 2012 and to elect/re-elect three new members. This proposal has been discussed in the Council and everybody actually agreed with me.

But this was not the end of my proposals. I also suggested to extend the tenure of the presidents and vice-presidents to three years, for reasons similar to those mentionned above, My experience tells me that this would be advantageous. This requires a change of constitution, though. If a majority of Council is in favour, which was the case, I was meant to present this change of the constitution to the next general assembly of ISMB. Changes of the bylaws require a two-third-majority. But I am looking forward already now to your opinions about this. Please, send me an e-mail and - from time to time - I shall communicate these opinions to the membership. This could actually lead up to a thread that we may set up on the ISMB web page.

But we already can proceed with the elections to the Council. According to my records, the most senior member is Jamie Fitzgerald, our out-going editor of this Newsletter. Although he was proposed for re-election, he prefers not to stand any more. So, we thank Jamie not only for his services as the Newsletter editor but also for his contributions to the affairs of Council.

So, we have now the following candidates to propose to you (in alphabetical order, they all have agreed to stand):
Billy Hudson, Francesco (Checco) Ramirez, Liliana Schaefer, Collin Stultz, Sara Wickström, and Roy Zent.

I shall soon set up a Doodle ballot using pseudonyms, as we have done in past elections. The procedure will keep your identity confidential. Strictly speaking, your identity could be known to me if I bother to look up more than just your pseudonym. However, no one else has this option. If you don't vote by the pseudonym which you are given in your e-mail, for example by stating your name rather than the pseudonym, your vote will be void. If you make up your own code your vote will be anonymous and, hence, also void.

You will receive an e-mail, soon, with all the information needed. If you don't receive it you have not yet settled your 2012 membership. If that should be the case, you will receive the e-mail later after your obolus has fallen into the treasury with a loud noise....

Peter Bruckner
ISMB Treasurer/Secretary

Meeting Announcements

Joint meeting of the British Society for Matrix Biology and the German Connective Tissue Society

"Matrix Molecular Biology: Integrator of Tissue Function and Disease"
Organizers: Philippa Hulley, Mandy Plumb, John Couchman and Liliana Schaefer (DGBF)

Matrix biology is a dynamically growing field with equal relevance to normal tissue function and disease pathogenesis. This open-themed meeting celebrates the breadth and depth of matrix molecular biology in areas as diverse as nano-technology and cancer. It is also an extended, joint meeting of the BSMB and the DGBF, marking the occasion of the 25th anniversary of the German Connective Tissue Society. Confirmed international speakers include Clare Waterman, Joachim Spatz, Matthew Paszek, Liliana Schaefer, Dietmar Vestweber, John Couchman, Reinhard Faessler, Oliver Eickelberg, Paddy Prendergast, Yoshifumi Itoh, Kairbaan Hodivala-Dilke, Cathy Merry, Francesco dell'Accio, George Bou-Gharios and Paul Martin.

There will be slots in every session for short oral presentations selected from the abstracts as well as interactive poster sessions. A highlight will be the BSMB Fell Muir lecture, this year presented by Prof Roger Mason (London) and there will be a presentation by the 2012 DGBF Young Investigator Awardee.

St Catherine's College, Oxford, with its beautiful gardens and Arne Jacobsen designed buildings provides the venue for this residential conference, including the social events http://www.stcatz.ox.ac.uk/

Key dates:
Early Bird Registration closes 2 March 2012
Abstracts close 16 March 2012

Registration is now open at www.bsmb.ac.uk

The XXIIIrd FECTS meeting will take place in Katowice, Poland from August 25th to 29th, 2012
Chaired by Aleksander Sieroń (alsieron@sum.edu.pl).

The 7th European Elastin Meeting will be held in Ghent, Belgium from September 1st to September 4th 2012.
Chaired by Anne De Paepe & Olivier Vanakker.

Joint meeting of the American Society for Matrix Biology and the Society for Glycobiology.
November 11-14th, 2012
Sheraton San Diego Hotel and Marina, San Diego, CA, USA
Meeting Chairs: Jeffrey Davidson and Hudson Freeze

Matrix Research Update

Processing of CXCL12 by Different Osteoblast-Secreted Cathepsins.
Staudt ND, Maurer A, Spring B, Kalbacher H, Aicher WK, Klein G.
Stem Cells Dev. 2012 Jan 4. [Epub ahead of print]

Hematopoietic stem and progenitor cells (HSPCs) are known to reside in specialized niches at the endosteum in the trabecular bone. Osteoblasts are the major cell type of the endosteal niche. It is well established that secreted proteases are involved in cytokine-induced mobilization processes that release stem cell from their niches. However, migratory processes such as the regular trafficking of HSPCs between their niches and the periphery are not fully understood. In the current study we analyzed whether osteoblast-secreted cysteine cathepsins are able to reduce the direct interaction of HSPCs with bone-forming osteoblasts. Isolated human osteoblasts were shown to secrete proteolytically active cysteine cathepsins, such as cathepsins B, K, L, and X. All of these cathepsins were able to digest, although with different efficacy, the chemokine CXCL12, which is known to be important for retaining HSPCs in their niches. Of the 4 identified cathepsins, only cathepsin X was able to reduce binding of HSPCs to osteoblasts. Interestingly, nonactivated pro-cathepsin X and mature cathepsin X did not interfere with HSPC-osteoblast interactions. Only pro-cathepsin X treated with dithiothreitol, which unfolds but does not lead to full maturation of cathepsin X, significantly reduced HSPC adhesion to osteoblasts. These observations argue for a role of the accessible cathepsin X prodomain in diminishing cell binding. Our findings strongly suggest that the cysteine cathepsins B, K, and L constitutively secreted by osteoblasts are part of the fine-tuned regulation of CXCL12 in the bone marrow, whereas pro-cathepsin X with its prodomain can affect HSPC trafficking in the niche.

TopFIND, a knowledgebase linking protein termini with function.
Lange, P.F. and Overall, C.M.
Nat. Methods, 8, 703-4, 2011

TopFIND 2.0--linking protein termini with proteolytic processing and modifications altering protein function.
Lange, P.F., Huesgen, P.F. and Overall, C.M.
Nucleic Acids Research, 40, D351-D361,2012

Limited proteolysis is among the most important post-translational modifications in the extracellular matrix post secretion. To understand the functional properties of the ECM it is critical to know the amounts of intact versus cleaved ECM proteins and growth factors. Thus, the identification of the original protein mature termini and protease generated neo-N-termini provide critical insights into the functional state of individual proteins and of the proteome. With recent advances in specific proteomics approaches to enrich for N- and C-terminomes, the global analysis of whole terminomes at a proteome-wide scale is now possible. Information on the actual N- and C-termini of proteins in vivo and any post-translational modifications, including their generation by proteolytic processing, is rapidly accumulating including annotation of the N-terminomes of fibroblast secretomes and other connective tissues in inflammation. To access this information Overall and Lange present the 'Termini-Oriented Protein Function Inferred Database' TopFIND (http://clipserve.clip.ubc.ca/topfind), a knowledgebase for protein termini, terminus modifications and underlying proteolytic processing. Built on a protein-centric framework TopFIND covers five species: Homo sapiens, Mus musculus, Arabidopsis thaliana, Saccharomyces cerevisiae and Escherichia coli and incorporates information from curated community submissions, publications, UniProtKB and MEROPS. A dynamic network representation of the relationship between proteases, their substrates and inhibitors as well as visualization of protease cleavage site specificities complements the information displayed. TopFIND supports matrix research by in depth investigation of protein termini information to spark new hypotheses on protein function by correlating cleavage events and termini with protein domains and mutations.

Fibronectin is essential for hepatocyte survival but is not indispensable for hepatocyte proliferation following liver injury
Moriya K, Sakai K, Yan, MH, Sakai T
Hepatology (Accepted on January 18, 2012)

Acute liver injury causes massive hepatocyte apoptosis and/or fatal liver damage. Fibronectin, an extracellular matrix glycoprotein, is prominently expressed during adult tissue repair. However, the extent of fibronectin dependence on the hepatocyte response to acute liver damage remains to be defined. As identification of hepatic survival factors is critical for successful therapeutic intervention in liver failure, this relationship has been investigated using a fibronectin-deficient mouse model of acute liver injury. Here we show that the lack of fibronectin induces significantly increased hepatocyte

apoptosis, which is accompanied by significant downregulation of the anti-apoptotic protein Bcl-xL. Furthermore, fibronectin deficiency leads to a significantly elevated production of hepatocyte growth factor in hepatic stellate cells post injury, which in turn results in an earlier onset and acceleration of hepatocyte regeneration. Primary hepatocytes on fibronectin are protected from reactive oxygen species (ROS)-induced cellular damage, retaining expression of Bcl-xL, whereas those on type I collagen are not. This retained expression of Bcl-xL is inhibited by PI3-kinase inhibitor LY294002. Conclusion: We provide evidence that the fibronectin-mediated matrix survival signals for hepatocytes are transduced through the PI3-kinase-Bcl-xL signaling axis in response to injury. This work defines fibronectin as a novel anti-apoptotic factor for hepatocytes following acute liver injury but demonstrates that fibronectin is not
essential for subsequent hepatocyte proliferation.

Thrombospondin-1 is a novel negative regulator of liver regeneration after partial hepatectomy via TGF-β1 activation in mice.
Hayashi H, Sakai K, Baba H, Sakai T.
Hepatology. 2011 Nov 22. [Epub ahead of print].

The matricellular protein thrombospondin-1 (TSP-1) is prominently expressed during tissue repair. TSP-1 binds to matrix components, proteases, cytokines, and growth factors and activates intracellular signals via its multiple domains. TSP-1 converts latent transforming growth factor-β1 (TGF-β1) complexes into biologically active form. TGF-β plays significant roles in cell-cycle regulation, modulation of differentiation, and induction of apoptosis. Although TGF-β1 is a major inhibitor of proliferation in cultured hepatocytes, the functional requirement of TGF-β1 during liver regeneration remains to be defined in vivo. We generated a TSP-1- deficient mouse model of a partial hepatectomy and explored TSP-1 induction, progression of liver regeneration, and TGF-β-mediated signaling during repair process following hepatectomy. We show here that TSP-1-mediated TGF-β1 activation plays an important role in suppressing hepatocyte proliferation. TSP-1 expression was induced in endothelial cells as an immediate early gene in response to partial hepatectomy. TSP-1 deficiency resulted in significantly reduced TGF-β/Smad signaling and accelerated hepatocyte proliferation via downregulation of p21 protein expression. TSP-1 expression in endothelial cells was induced by reactive oxygen species (ROS) and modulated TGF-β/Smad signaling and proliferation in hepatocytes in vitro, suggesting that the immediately and transiently produced ROS in the regenerating liver were the responsible factor for TSP-1 induction. Conclusion: We have identified TSP-1 as an inhibitory element in regulating liver regeneration via TGF-β1 activation. Our work defines TSP-1 as a novel immediate early gene that could be a potential therapeutic target to accelerate liver regeneration

Heritability of articular cartilage regeneration and its association with ear-wound healing.
Rai MF, Hashimoto S, Johnson EE, Janiszak KL, Fitzgerald J, Heber-Katz E, Cheverud JM, Sandell LJ.
Arthritis Rheum. 2012 Jan 24. [Epub ahead of print]

OBJECTIVE.: Emerging evidence suggests that genetic components contribute significantly to cartilage degeneration in osteoarthritis pathophysiology but little evidence is available on genetics of cartilage regeneration. Therefore, we investigated cartilage regeneration in genetic murine models using common inbred strains and a set of recombinant inbred lines generated from LG/J (healer of ear-wounds) and SM/J (non-healer) inbred strains.
METHODS.: An acute full-thickness cartilage injury was introduced through microsurgery in the trochlear groove of 8-weeks old mice (N=265). Knee joints were sagittally sectioned and stained with toluidine blue to evaluate regeneration. For ear-wound phenotype, a bilateral 2-mm through-and-through puncture was made (N=229) at 6-weeks and healing outcomes measured after 30-days. Broad-sense heritability and genetic correlations were calculated for both phenotypes.
RESULTS.: Time-course studies from recombinant inbred lines show no significant regeneration until 16-weeks post-surgery; at that time, the strains can be segregated into three categories: good, intermediate and poor healers. Heritability (H(2)) showed that both cartilage regeneration (H(2) =26%; p=0.006) and ear-wound closure (H(2) =53%; p<0.00001) are significantly heritable. The genetic correlations between the two healing phenotypes for common inbred strains (r=0.92) and recombinant inbred lines (r=0.86) were found to be extremely high.
CONCLUSION.: We report that i) articular cartilage regeneration is heritable, ii) the differences between the lines being due to genetic differences and iii) a strong genetic correlation between the two phenotypes exists indicating that they plausibly share a common genetic basis. We, therefore, surmise that LG/J by SM/J intercross can be used to dissect the genetic basis of variation in cartilage regeneration.

Cartilage and Bone Changes during Development of Post-Traumatic Osteoarthritis in Selected LGXSM Recombinant Inbred Mice
Hashimoto S, Rai MF, Janiszak KL, Cheverud JM, Sandell LJ
Osteoarthritis and Cartilage. Accepted Jan 31, 2012

Little evidence is available on the natural course of osteoarthritis development and the genes that protect and predispose individuals to it. This study was designed to compare strain-dependent development of osteoarthritis and its association with tissue regeneration in mice. Two recombinant inbred lines LGXSM-6 and LGXSM-33 generated from LG/J and SM/J intercross were used. Previous studies have indicated that LGXSM-6 can regenerate both articular cartilage and ear hole punch while LGXSM-33 cannot.
Methods: Transection of the medial meniscotibial ligament was performed on 10-week-old male mice to induce osteoarthritis. Cartilage damage was analyzed by histology and bone morphology was evaluated using micro-CT. Ear punches were performed and evaluated by measurement of residual hole diameter.
Results: Cartilage analysis showed that LGXSM-33 developed a significantly higher grade of osteoarthritis than LGXSM-6. Bone analysis showed that LGXSM-33 had substantial subchondral bone and trabecular bone thickening 8 weeks post-surgery, while LGXSM-6 showed bone loss over time. We also confirmed that LGXSM-6 can heal ear tissues significantly better than LGXSM-33.
Conclusions: Osteoarthritis was found to be negatively correlated with the degree of tissue regeneration. LGXSM-33, a poor healer of ear tissues (and articular cartilage), developed more osteoarthritis compared to LGXSM-6, which had better regenerative ability for ear tissues and articular cartilage. While these lines have different distribution of the alleles, we assume that the phenotypic differences observed here are due to genetic differences further suggesting that similar sets of physiological processes and gene variants may mediate variation in human osteoarthritis development and tissue regeneration.

Tropoelastin bridge region positions the cell-interactive C terminus and contributes to elastic fiber assembly.
Yeo GC, Baldock C, Tuukkanen A, Roessle M, Dyksterhuis LB, Wise SG, Matthews J, Mithieux SM, Weiss AS.
Proc Natl Acad Sci U S A. 2012 Feb 10. [Epub ahead of print]

The tropoelastin monomer undergoes stages of association by coacervation, deposition onto microfibrils, and cross-linking to form elastic fibers. Tropoelastin consists of an elastic N-terminal coil region and a cell-interactive C-terminal foot region linked together by a highly exposed bridge region. The bridge region is conveniently positioned to modulate elastic fiber assembly through association by coacervation and its proximity to dominant cross-linking domains. Tropoelastin constructs that either modify or remove the entire bridge and downstream regions were assessed for elastogenesis. These constructs focused on a single alanine substitution (R515A) and a truncation (M155n) at the highly conserved arginine 515 site that borders the bridge. Each form displayed less efficient coacervation, impaired hydrogel formation, and decreased dermal fibroblast attachment compared to wild-type tropoelastin. The R515A mutant protein additionally showed reduced elastic fiber formation upon addition to human retinal pigmented epithelium cells and dermal fibroblasts. The small-angle X-ray scattering nanostructure of the R515A mutant protein revealed greater conformational flexibility around the bridge and C-terminal regions. This increased flexibility of the R515A mutant suggests that the tropoelastin R515 residue stabilizes the structure of the bridge region, which is critical for elastic fiber assembly.

Jobs

Postdoctoral Research Associate
Abnormal Collagen in Age-Related Fibroses and Tissue Degeneration: Evaluation as a Stem Cell Biomarker
University of Liverpool (Leahurst Campus), UK
Closing date: 14th March 2012
Informal enquiries to: Dr Liz Laird (elizabeth.laird@liv.ac.uk)

Applications are invited for a PDRA position to determine how normal and abnormal collagen synthesis is regulated in stem cells and in fibrotic/degenerative disease. You should have a PhD in a relevant area (Cell/Molecular/Matrix Biology) together with an interest in stem cell research and age-related musculoskeletal disease. Experience of stem cell culture, quantitative RT-PCR, protein labeling and epigenetic analyses would be an advantage. This post is funded by the Medical Research Council (MRC) for 3 years.

For full details and to apply please visit:
http://www.liv.ac.uk/working/job_vacancies/research/R-578027.htm

Postdoctoral position in organ development and stem cell biology

A postdoctoral position is available to study the role of the peripheral nervous system in organ development, repair and regeneration. Our work integrates mouse embryonic ex vivo culture systems with molecular genetic and imaging approaches to study epithelial-neuronal-stem cell communication, and how these signaling pathways regulate epithelial organ development and regeneration (e.g. Science 2010;329(5999):1645-7). Ongoing projects include: 1) defining the signal transduction pathways mediated by the nerves in maintaining epithelial stem cells and 2) determining the influence of epithelial-neuronal signaling during organ regeneration after injury.

The position is in the laboratory of Dr. Sarah Knox in the UCSF Department of Cell and Tissue Biology (http://ctb.ucsf.edu/; School of Dentistry) and Program in Craniofacial and Mesenchymal Biology (http://cmb.ucsf.edu/). The laboratory is located at the UCSF Parnassus Heights campus, in the center of San Francisco. UCSF offers an outstanding developmental biology and stem cell community and a supportive working environment.

Candidates with a Ph.D. degree in a biological science and research experience in stem cell biology, neuroscience, molecular biology, genetics, or biochemistry should submit a C.V. and names of at least 2 references via email to: sarah.knox@ucsf.edu

Matrix Biology 31 (2012) 79–80

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Matrix Biology

journal homepage: www.elsevier.com/locate/matbio

From the editor's desk

Dear readers of Matrix Biology,

Genetic studies of rare human inherited disorders have two major goals. One goal is to obtain insights into normal physiological processes via the elucidation of abnormalities caused by disease. A second goal is to identify targets for development of therapies to prevent or ameliorate the consequences of specific gene mutations in patients. The recognition that studies of rare conditions provide a productive strategy for gaining insight into normal body function is not new and is not limited to genetic studies. At the end of his life as a physician-scientist (1657) William Harvey stated in a letter to John Vlackveld that "Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows tracings of her workings apart from the beaten paths; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature, by careful investigation, of rarer forms of disease." However, with modern genetic tools, identification of disease-linked mutations opens the door to molecular pathogenetic processes, and thus also the second goal, in ways that Harvey had no basis for anticipating.

In the context of current technology that makes it possible to manipulate genes almost at will in mice and other organisms it is important to keep in mind that human inherited disorders are "experiments" of nature. As a result, genetic studies of human disease can lead to unique insights that are not easily obtained from planned genetic experiments carried out in laboratory animals. A most exciting example is provided by recent studies of the disorder named cherubism (Berendsen and Olsen, 2011).

Cherubism, initially described as a dominantly inherited disorder in a Canadian family by Jones (1933), is characterized by excessive bone resorption and remodeling in the jaws with accumulation of inflammatory/fibrous tissue in the lower face. Curiously, the progressive pathological changes first appear 2–4 years after birth and can regress after puberty. Following mapping of the cherubism gene to chromosome 4 (Mangion et al., 1999; Tiziani et al., 1999), causative mutations were found in the c-Abl-binding protein SH3BP2 in several families (Ueki et al., 2001). All the mutations were missense mutations within a hexapeptide sequence located upstream of a carboxy-terminal SH2-domain in SH3BP2. Since the SH3BP2 gene is located within a region that is frequently deleted in Wolf-Hirschhorn syndrome and individuals with this syndrome do not exhibit cherubism traits, it was concluded that cherubism mutations were unlikely to represent loss-of-function mutations. This was confirmed when the most common mutation, a proline-to-arginine substitution, was knocked into the mouse SH3BP2 locus (Ueki et al., 2007).

Homozygous mutant mice developed major hallmarks of cherubism after birth, mutant macrophages had increased levels of TNF-α expression and mutant osteoclasts were unusually large and highly active. Overexpression of wild-type SH3BP2 in macrophages and osteoclasts had the same effects, indicating that the cherubism mutations result in gain of SH3BP2 function. When the cherubism mice were crossed with TNF-α knock-out mice, the inflammatory component and a substantial portion of the bone loss phenotype in the cherubism mice were eliminated, suggesting that increased TNF-α expression, as a consequence of gain of SH3BP2 function, is a major mediator of the tissue abnormalities seen in cherubism. This raises the possibility that the anti-TNF-α therapies may ameliorate the phenotypic consequences of cherubism.

These studies of cherubism mice did not identify the mechanism by which the cherubism mutations result in gain of SH3BP2 function. The surprising answer to that question is to be found in two elegant studies recently published in Cell (Guettler et al., 2011; Levaot et al., 2011). The two papers demonstrate that the oligopeptide sequence region with mutations in SH3BP2 is the recognition site for binding of SH3BP2 to the enzymes Tankyrase-1 and -2. The two enzymes are members of the poly (ADP-ribose) polymerase family. Tankyrase PARsylates wild-type SH3BP2 and this tagging is followed by ubiquitylation (by the E3-ubiquitin ligase RNF146 in osteoclasts) and proteasome mediated destruction. In a sense, cherubism is therefore a site-specific mutagenesis experiment by nature, mapping out the Tankyrase binding site in SH3BP2. In the study by Guettler et al., the authors used the SH3BP2 wild-type and mutant binding site sequences as a starting point to determine the sequence rules that govern substrate recognition by Tankyrase. Through analyzing the crystal structure of a substrate binding domain of the enzyme bound to the wild-type SH3BP2 recognition peptide they provide an explanation for how mutations in this sequence result in loss of SH3BP2 binding to Tankyrase. Finally, they used the recognition rules to scan the human proteome for potential Tankyrase binding sites.

Based on this analysis it appears that a large number of proteins, perhaps in the hundreds, may be Tankyrase targets. The enzyme has already been found to be involved in processes that require regulation of protein levels/activities, including control of telomerase activity (Smith et al., 1998), translocation of the glucose transporter Glut4 and insulin-regulated aminopeptidase (Chi and Lodish, 2000; Yeh et al., 2007), and regulation of Wnt signaling (Huang et al., 2009). With the large number of potential targets now identified, one can look forward to a rapid expansion of the validated Tankyrase "targetome". Cherubism is so far the only human genetic disorder that has been linked to mutations in a Tankyrase recognition sequence, but given the large number of potential targets it would not be surprising to find that mutations in such target sequences may be associated with other dominantly inherited human disorders.

0945-053X/$ – see front matter
doi:10.1016/j.matbio.2012.01.008

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SGBM
SPEMANN GRADUATE SCHOOL
OF BIOLOGY AND MEDICINE

UNI FREIBURG

University of Freiburg (Germany)

INTERNATIONAL PhD PROGRAM

The Spemann Graduate School of Biology and Medicine (SGBM),

an interdisciplinary international graduate school funded by the German Excellence Initiative of the German Research Foundation is recruiting students in the following research fields:

- Protein Structure and Function
- Signaling and Synthetic Biology
- Developmental Biology
- Neurosciences
- Immunology/Virology
- Molecular Medicine
- Molecular Plant Sciences

SGBM relies on the expertise provided by the Excellence Cluster bioss (Center for Biological Signalling Studies), several outstanding collaborative research centers as well as the Max Planck Institute of Immunobiology and Epigenetics and the Bernstein Center for Computational Neuroscience. SGBM also offers an MD/PhD program. At present, the school counts 79 PhD students. The program runs exclusively in English, and knowledge of German is not necessary.

What we offer:

- a doctoral fellowship or salary
- a high-profile research environment
- an exchange program with universities and industry around the world
- an efficient supervision and mentoring program
- courses in novel technologies and soft skills
- an interdisciplinary teaching program
- campus in the center of the city with lecture hall, social & guest rooms

What we expect:

- an excellent recent university degree: M.Sc. or German diploma (Candidates about to obtain such a degree are welcome to apply.)
- Motivation & interest to join one of the interdisciplinary research areas of the Graduate School
- good communication skills in English
- interest and creativity to shape your own project and select your thesis committee

Freiburg is one of the most attractive cities in Germany, close to the trinational border to France and Switzerland.

Are you interested?
Then use our online application system at:

www.sgbm.uni-freiburg.de

Deadline for application: April 1, 2012.

Interviews will take place from July 3-5, 2012.

Decisions will be communicated by mid July, 2012.

Selected students will start in September, 2012.

Oxford 2012 Joint Meeting

British Society for Matrix Biology

And

German Connective Tissue Society (25th Anniversary)

"Matrix Molecular Biology: Integrator of Tissue Function and Disease"

2nd-4th April, St Catherine's College, University of Oxford

Local Organisers: Mandy Plumb and Philippa Hulley

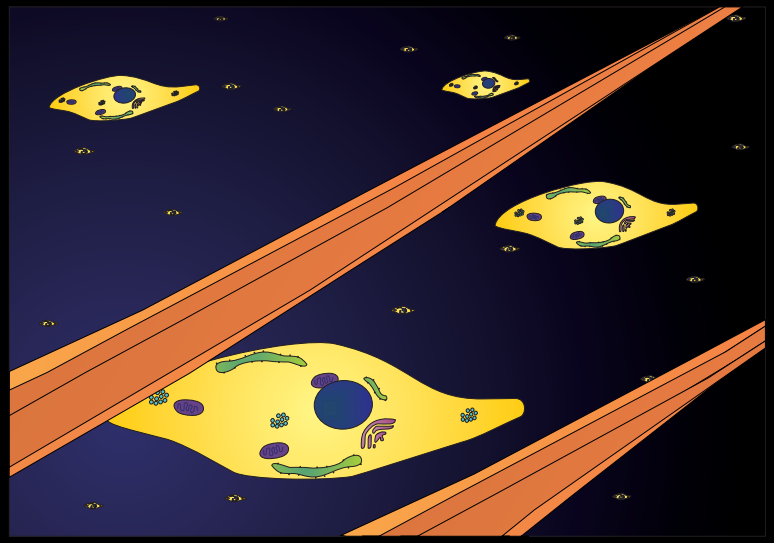
International Chairs: John Couchman and Liliana Schaefer

Fell Muir award Lecture: **Roger Mason**

Confirmed speakers:

Reinhard Fässler, Clare Waterman, Matthew Paszek, Joachim Spatz, Liliana Schaefer, Dietmar Vestweber, John Couchman, Oliver Eickelberg, Paddy Prendergast, Yoshifumi Itoh, Kebs Hodivala-Dilke, Cathy Merry, Francesco dell'Accio, George Bou-Gharios, Paul Martin

For more information visit www.bsmb.ac.uk



7TH EUROPEAN ELASTIN MEETING

SEPTEMBER 1ST - 4TH 2012

Het Pand, Ghent, Belgium

TOPICS

- Microfibrils and elastic fibres: structure, assembly and function
- Elastogenic engineering and biomaterials
- Animal models
- Elastic fibre-associated cell signaling
- Heritable and acquired elastic fibre diseases
- Therapeutic advances in elastinopathies

MORE INFORMATION

Scientific information:
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Ghent (CMGG)
Faculty of Medicine
Ghent University Hospital
Prof. Dr. A. De Paepe
C/o Mrs. I. Andries
De Pintelaan 185
B-9000 Ghent, Belgium
E-mail:
elastin.2012@medgen.ugent.be
Telephone: +32 (0)9 332 56 46

Logistic & administrative information:
Semico n.v.
Korte Meer 16
B-9000 Ghent, Belgium
E-mail: elastin2012@semico.be
Telephone: +32 (0)9 233 86 60

WEBSITE

www.Elastin2012.be

August 25th to 29th, 2012
KATOWICE "Center City", Poland


"Pejzaż Śląski" Paweł Wróbel (1913-1984), Muzeum Śląskie Katowice

FEDERATION OF EUROPEAN CONNECTIVE TISSUE SOCIETIES
POLISH BIOCHEMICAL SOCIETY
SECTION OF CONNECTIVE TISSUE

INTERNATIONAL SOCIETY FOR MATRIX BIOLOGY

1st Announcement

XXIIIrd FECTS and ISMB Joint Meeting

Please mark your 2012 calendar in order to join researchers in the ECM field from Europe and around the world

On behalf of the organizing committee Aleksander L. Sieron

www.fects.pl

Joint Meeting of the American Society for Matrix Biology and the Society for Glycobiology

November 11-14, 2012
Sheraton San Diego Hotel & Marina
San Diego, CA, USA

Meeting Chairs:

Jeffrey Davidson,
Vanderbilt University

Hudson Freeze,
Sanford Burnham Medical Research Institute

San Diego

ASMB
American Society *for* Matrix Biology

SFG
Society *for* Glycobiology

Plenary Session Topics:

Immunology and Inflammation
Biomaterials and Matrix Engineering
Biosynthesis, Secretion, and Assembly
Stem and Progenitor Cells, Genetic Therapy, and Regenerative Medicine
Rare Glycosylation and Matrix Diseases
Development and Morphogenesis

Concurrent Session Topics Including:

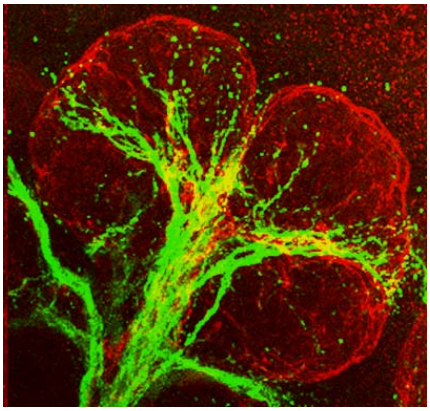
Development
Chemical Glycobiology/Glycomics
Cancer Microenvironment
Receptors, Signaling, and Cytoplasmic Glycosylation
Stem/Progenitor Cells and Their Environment
Mechanobiology & Biomedical Engineering
Protein Folding, Secretion, and Matrix Assembly
Matrix and Carbohydrate Immunology
Basement Membranes
Genetics and Gene Expression
Matricellular Proteins
And a few surprises…

www.asmbsfg2012.org
asmbsfg2012@faseb.org

San Diego

Postdoctoral position in organ development and stem cell biology

A postdoctoral position is available to study the role of the peripheral nervous system in organ development, repair and regeneration. Our work integrates mouse embryonic ex vivo culture systems with molecular genetic and imaging approaches to study epithelial-neuronal-stem cell communication, and how these signaling pathways regulate epithelial organ development and regeneration (e.g. Science 2010;329(5999):1645-7). Ongoing projects include: 1) defining the signal transduction pathways mediated by the nerves in maintaining epithelial stem cells and 2) determining the influence of epithelial-neuronal signaling during organ regeneration after injury.



The position is in the laboratory of Dr. Sarah Knox in the UCSF Department of Cell and Tissue Biology (http://ctb.ucsf.edu/; School of Dentistry) and Program in Craniofacial and Mesenchymal Biology (http://cmb.ucsf.edu/). The laboratory is located at the UCSF Parnassus Heights campus, in the center of San Francisco. UCSF offers an outstanding developmental biology and stem cell community and a supportive working environment.

Candidates with a Ph.D. degree in a biological science and research experience in stem cell biology, neuroscience, molecular biology, genetics, or biochemistry should submit a C.V. and names of at least 2 references via email to: sarah.knox@ucsf.edu

University of California
San Francisco