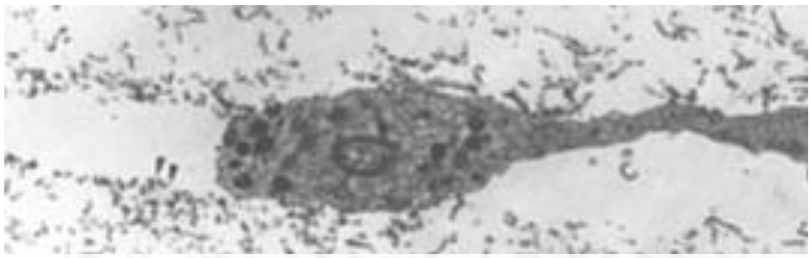

A fibroblast within a tethered lattice, after 13 days, with a cavity surrounding the cell and areas of packed collagen fibrils *(Porter et al. 1998 Wound Rep. Reg. 6: 157-166)*

ISMB NEWSLETTER 35 May 2020
Editor: Sylvie Ricard-Blum

FROM THE PRESIDENT'S DESK

Dear ISMB members,

I hope you are all keeping well in the context of the COVID-19 pandemic. Numerous research institutes and universities were closed, and many meetings were canceled or postponed including Matrix Biology Europe 2020, which should now be held in October in Florence (Italy), and the Gordon Research Conference on Proteoglycans, which will be held in 2022 as detailed on pages 27 and 28. Alternatives were also developed in these challenging times, and ASMB has embarked on a series of online "e-Symposia", advertised on page 5.

Two members of the Council left last December, and I warmly thank them for all the work they did for the ISMB. Anthony Day was a member of the Council and of the Travel subcommittee for several years, and is now the President of the President of the International Society for Hyaluronan Sciences (ISHAS). Our warmest congratulations to him. Chloé Yeung was very active in promoting the activities of our Society, and created the "In Focus" section of the newsletter. Julia Etich is now in charge of this section, so please do not hesitate to contact her (Julia.Etich@kgu.de) if you want to share a method with ISMB members.

Further to the voting for candidates for the 2020 ISMB Council vacancies, I am very pleased to let you know that Gertraud Orend (France) has been elected to the regular Council member post, and Valerio Izzi (Finland) has been elected to the Early career council post. We thank all the ISMB members who stood for election and we congratulate Gertraud and Valerio on starting their service on Council.

Last, the next International travel bursary application deadline is July 1, 2020, and we will continue to consider applications.

Take care and keep well,
Best wishes.

Sylvie Ricard-Blum, President of the International Society for Matrix Biology (sylvie.ricard-blum@univ-lyon1.fr)

COMPOSITION OF ISMB COUNCIL SUBCOMMITTEES

Meetings and travel grants
Ruud Bank (The Netherlands, chair)
Gerhard Sengle (Germany)
Hide Watanabe (Japan)

Membership
Hide Watanabe (Japan)
Suneel Apte (USA)

Like ISMB on Facebook
https://www.facebook.com/IntSocMatBio/

and follow the ISMB on Twitter
ISMB@IntSocMatBio https://twitter.com/intsocmatbio

Communication group coordinated by Julia Etich (Germany, Julia.Etich@kgu.de)
Valerio Izzi (Finland, Valerio.Izzi@oulu.fi)
Pauline Nauroy (Germany, pauline.nauroy@uniklinik-freiburg.de)
Chloé Yeung (Denmark, chloe.yeung@gmail.com)
The ISMB correspondents of National Societies for Matrix Biology for Facebook & Twitter

ISMB correspondents of National Societies for Matrix Biology for Facebook & Twitter

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Matrix Biology Ireland.
Alexandre Trotier, National University of Ireland, Galway (Ireland)
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Matrix Biology Society of Australia and New Zealand (MBSANZ)
Luise Kung, Murdoch Childrens Research Institute, Melbourne (Australia)
louise.kung@mcri.edu.au

The Swiss Society for Matrix Biology (SSMB)
Collin Ewald, ETH Zurich (Switzerland)
collin-ewald@ethz.ch
Twitter of SSMB: @SwissMatrixBio

Matrix Biology World on Twitter
We are delighted to announce that the ISMB together with National Societies for Matrix Biology continues to strengthen the visibility of Matrix Biology Research on social media. **Please include @IntSocMatBio on your tweets or contact the representatives of the Societies**. We would be happy to share your announcements with the #MatrixBiology world!

MEETING REPORTS

The annual meeting of the Finnish Society for Matrix Biology, February 13, 2020, Helsinki (Finland)

The annual meeting of the Finnish Connective Tissue Society was held at Biomedicum in the heart of Helsinki.
On this day, our society underwent a major evolution by changing its name to the Finnish Society for Matrix Biology. After official meeting of the society, we had a great scientific symposium organized together with the Finnish Society for Cell Biology. One-day meeting was free of charge and open for everyone. Almost one hundred participants were listening to wonderful presentations by the ISMB president, Professor Sylvie Ricard-Blum from Lyon and Professor Janine Erler from Copenhagen. Presenters from Finland included Johanna Ivaska (Turku), Sara Wickström (Helsinki), Eija Jokitalo (Helsinki), Sanna Pasonen-Seppänen (Kuopio), Diana Toivola (Turku), and Valerio Izzi (Oulu). We also had short talks by Aleksi Isomursu (Turku) and Artemis Filippou (Helsinki) chosen from submitted abstracts. The seminar covered various themes from areas of matrix biology, cancer, mechanotransduction and cell biology. In addition to high quality talks, the meeting provided plenty of opportunities for informal discussions and networking.
The Finnish Society for Matrix Biology wants to thank all the speakers, participants, and organizers for an amazing day!

On behalf of FSMB,
Jarkko Koivunen, Chair
jarkko.koivunen@oulu.fi

Elina Siljamäki and Jarkko Koivunen are opening the seminar

The ISMB president, Sylvie Ricard-Blum

Janine Erler giving a presentation

The annual meeting of the Finnish Society for Matrix Biology, February 13, 2020, Helsinki (Finland)

The annual meeting of the Finnish Society for Matrix Biology, February 13, 2020, Helsinki, Finland

Like everyone, ASMB is dealing with the challenges of COVID-19 and social distancing. In an effort to maintain our community and to give members an opportunity to share their work, ASMB has embarked on a series of on-line "e-Symposia". The first event was held on April 23, 2020 and drew an international audience of over 250 participants, with lively scientific discussions between the speakers and audience members. Maybe you were there? Featured talks were:

Pan-Cancer analysis of the expression and regulation of matrisome genes across 32 tumor types, Speaker: Valerio Izzi, University of Oulu, Oulu, Finland

Targeting Fibro-adipogenic progenitor differentiation in myocardial pathologies involving fibrosis and fibrofatty degeneration, Speaker: Hesham Soliman, University of British Columbia, Vancouver, BC, Canada

Plectin linkages help move the nucleus during cell migration through 3D matrices, Speaker: Pragati Chengappa, Drexel University, Philadelphia, PA

ASMB will be continuing this online symposium series which is open to everyone. Check the website and twitter feed for information about upcoming events. We hope to see you there! @amsocmatbio

ASMB
American Society for Matrix Biology

ASMB e-Symposium 2 - The Extracellular Matrix Reloaded

Join us on Thursday, May 14, 11:00am - 12:30 pm US EDT.
Invited speakers will present for 15 minutes with an additional 5 minutes for questions.

Age related differences in fibrin properties, *ASMB 2020 Junior Investigator Awardee,* **Ashley Brown**, *North Carolina State University & UNC-Chapel Hill*

Investigating the extracellular matrix during kidney development, **Mychel Raony P.T. Morais**, *Wellcome Centre for Cell-Matrix Research, Faculty of Biology, Medicine and Health, University of Manchester (UK)*

Organization of lamellae in the corneal stroma: New insights in the pathomechanism of keratoconus, Uwe Hansen, *Institute for Musculoskeletal Medicine, University Hospital Münster, Germany*

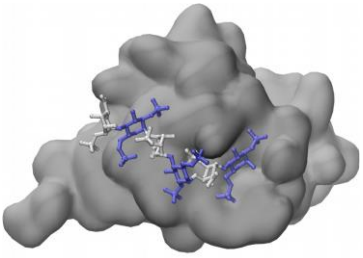
Fibrosis in PDA Initiation and Progression - Collagen Activation of DDRs as a Driver of Fibrosis and Cancer Progression, **Huocong Huang**, *University of Texas Southwestern*

POSITIONS AVAILABLE

See also on ISMB website (http://ismb.org/career/)

PhD student and Postdoctoral Researcher positions
Sergey Samsonov's group, Faculty of Chemistry, University of Gdańsk, Gdańsk (Poland)

• Project title: Mechanistic insights into the specificity of glycosaminoglycan interactions with regulatory proteins



• The goal is to understand molecular basis of the specificity in protein-glycosaminoglycan interactions by means of molecular modeling approaches, some of which will be developed in this study. The work will be carried out within intensive collaborations with NMR experiments performed on same molecular systems at the University of Leipzig. The result of this research will serve to guide the design of new methods for tissue regeneration and healing.
• Collaboration: University of Leipzig (Research Group of Prof. Daniel Huster)
• Funding: BEETHOVEN CLASSIC Grant from The National Science Centre of Poland
- PhD student: fellowship of 54 000 PLN/year (brutto brutto) for 3 years
- Postdoctoral Researcher: full time employment for up to 36 months, contract renewed each year, salary: 120 000 PLN/year (brutto brutto).
• CV and contact data of two referees should be provided to Dr Hab. Sergey Samsonov via e-mail sergey.samsonov@ug.edu.pl with the topic "PhD Student, BEETHOVEN CLASSIC" **or "**Postdoctoral Researcher, BEETHOVEN CLASSIC"
• Application deadline: 30 June 2020, Starting date: 31 August 2020.

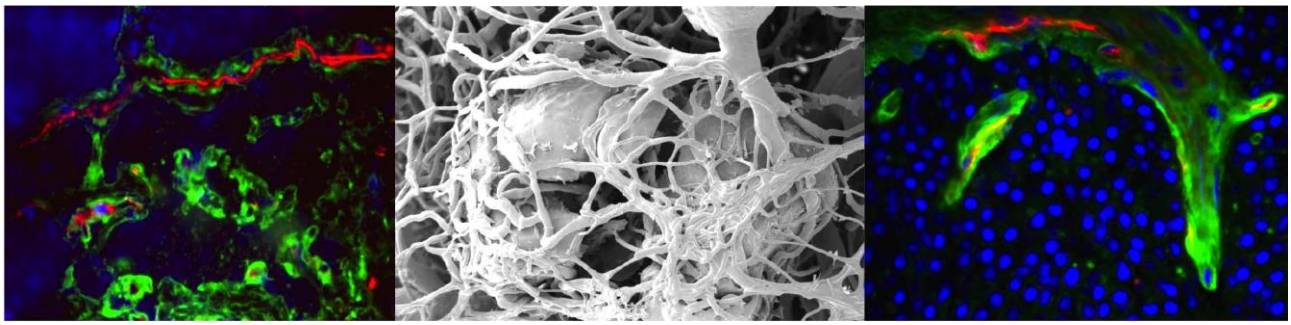
Requirements for the PhD position
- Master in Physics/Chemistry/Biology/Computer Sciences or related areas
- Experience with modeling techniques, Linux environment and scripting are advantages
- Interest in the interdisciplinary aspect of the project, motivation, creativity, liability, ability to work both independently and as a part of the team, good command of English
Research tasks:
- Molecular docking of glycosaminoglycans and their mimetics
- Molecular dynamics-based analysis of protein-glycosaminoglycan, protein-small molecules, protein-DNA/RNA systems;
- Participation in writing publications and presentation of the results at scientific meetings

Requirements for the Postdoctoral Researcher position
- PhD in Physics/Chemistry/Biology/Computer Sciences
- Solid experience with modeling techniques as molecular docking, molecular dynamics of biomolecular systems; experience with protein-carbohydrate systems is an advantage
- Solid experience with Linux environment; experience with scripting (python, bash, awk, R)
- Interest in the interdisciplinary aspect of the project
- Proficiency in written and spoken English
- Excellent presenting and communication skills

Research tasks:
- Molecular docking of glycosaminoglycans and their mimetics;
- Molecular dynamics-based analysis of protein-glycosaminoglycan, protein-small molecules, protein-DNA/RNA systems;
- Participation in writing publications and presentation of the results at scientific meetings

Two Postdoctoral Research Positions available

To study the Roles of Radiotherapy on the Tumor Microenvironment



In the INCa (Institut National contre le Cancer)-funded project **"RADIO-3R: Understanding and REFINING the influence of RADIOtherapy on the tumor microenvironment, by applying novel models to REDUCE and REPLACE animal models"** two research laboratories in Strasbourg will collaborate in developing and applying photon and proton irradiation protocols in 3D cell cultures and in tumor mice with the goal to understand the impact of radiotherapy on the tumor microenvironment and to develop surrogates for tumor mouse models. In this project the impact of proton and photon therapy on the tumor microenvironment in breast cancer and oral squamous cell carcinoma (OSCC) models will be determined. A major goal is to enhance on-target effects of radiotherapy with the future aim to improve immune checkpoint therapy.

One postdoc position (36 months) is available in the **Radiobioloy laboratory of the Institut de Cancérologie Strasbourg Europe, Paul Strauss Comprehensive Center** of **Pr Georges Noël** (UMR 7178, Strasbourg). The Radiobiology laboratory is an expert in radiobiology and is specialized in the establishment and application of radiotherapy protocols (photon and proton irradiations) in cultured cells and tumor mice (*Waissi et al., submitted; Beddok et al., 2019, Acta Oncol, Ohnleiter et al., 2017, Cancer Radiother, Bibault et al., 2017, Int J Radiat Oncol Biol Phys*). In frame of this project proton and photon irradiation protocols will be established and applied to autochthonous tumor mice and to novel to-be-established tumor spheroid cultures of murine breast and tongue tumor models. Mechanistic studies will follow by applying gene expression analysis and proteomics to fully understand responses to the radiotherapy protocols.

We offer: access to irradiation production facilities and expertise in radiobiology, support by a group of radiobiologist expert scientists, technical personal and a biostatistician and a high-level interdisciplinary platform

of radiation treatment with highly engaged physicians, physicists and technical personnel. The salary remuneration follows UNICANCER guidelines.
We search: a highly motivated scientist with background in radiobiology, cell biology and cell culture and mouse tumor models, high team spirit and good English communication skills.

One postdoc position (36 months) is available in the **Tumor Microenvironment group** of **Gertraud Orend** (INSERM U1109, Strasbourg). This laboratory (https://orend-tme-group.com) is specialized in the analysis of the tumor microenvironment with particular emphasis on the extracellular matrix molecule tenascin-C (*Midwood et al., 2016, J Cell Sci*) in tumor angiogenesis (*Saupe et al., 2013, Cell Reports, Rupp et al., 2016, Cell Reports*), metastasis (*Sun et al., 2018, Cancer Res, Sun et al., 2019, Mat Bio*) and tumor immunity (*Deligne 2020, Cancer Immun Res*). In frame of this project the candidate will investigate irradiated tumor mice and tumor organoids in a comprehensive manner by using flow cytometry, tissue staining, gene expression analysis, proteomics and gain and loss of function approaches.
We offer: a highly dynamic and supportive group of colleagues including researchers, postdocs, PhD and master students and technical personnel with expertise in extracellular matrix research, murine tumor models and tumor immunity. The salary remuneration follows INSERM guidelines taking into account previous experience.
We search: a highly motivated scientist with background in tumor biology, mouse tumor models, immunology and cell culture, high team spirit and good English communication skills.

Interested candidates are invited to send their CV together with a motivation letter and the names of three referees to **Georges Noël** (g.noel@icans.eu) and **Gertraud Orend** (gertraud.orend@inserm.fr).

One PhD student position available

medizinische fakultät
Westfälische
Wilhelms-Universität Münster

At the **Institute of Physiological Chemistry and Pathobiochemistry** we are looking as of July 1, 2020 until June 30, 2024 for a **PhD student**
Area of expertise: Biochemistry, Biology, Chemistry, Pharmacy
Reference number 04827
Part-time employed with 50% of the weekly working time
Remuneration depending on qualification & assignment of tasks according to TV-L E 13

Institute of
Physiological
Chemistry &
Pathobiochemistry

We investigate the regulation of the membrane-bound matrix metalloproteinase MMP14, which is essential for the metastasis of breast cancer cells. The focus will be on cell contacts mediated by integrins with collagen and other extracellular matrix proteins.
We offer an excellent biochemical, molecular and cell biological research environment with international employees.
We expect a highly motivated and willing to learn employee with outstanding skills in the field of protein chemistry and cell biology.
The collagen-dependent regulation of MMP14 on the cell surface and during its intracellular vesicle transport at the transcriptional and translational level is to be investigated. For this purpose, molecular biological, protein chemical and cell biological methods are to be used. These include the following

Tasks:

- Molecular biological cloning, analysis and intervention methods, such as qRT-PCR and CRISPR/Cas9;

- Protein chemical work on integrins and collagens, such as immunoblots and detection of enzymatic activity of MMP14 in vitro and in vivo;
- Various modalities of microscopy, such as immunofluorescence and confocal laser scanning microscopy, and cell biological methods, such as cell adhesion and migration tests as well as zymographic assays.

If you have any questions, please contact Professor Dr. Johannes Eble
Email: johannes.eble@uni-muenster.de.

We look forward to your application with (1) cover letter/motivation letter, in which you state your research interests with reference to the specified requirements on a maximum of 2 pages; (2) curriculum vitae with academic and extracurricular achievements as well as all research experience; (3) short summary of both the Bachelor and Master thesis and (4) contact details of at least two references; summarized in a single pdf file. Please send this, specifying the reference number above, to the Human Resources Department of the University Hospital of Münster, applicant management, Albert-Schweitzer-Campus 1, building D5, 48149 Münster or by email to bewerbung@ukmuenster.de by May 26, 2020. The University Hospital Münster is an equal opportunity-employer.

ISMB MEMBERSHIP: BECOME A MEMBER OF ISMB!

ISMB is dedicated to promoting matrix biology research on a global scale and to facilitating communication among matrix-related organizations and researchers from different countries. Junior members are eligible for discounted registration fees at matrix biology meetings supported by ISMB. The Society sends out newsletters highlighting recent research advances, descriptions of matrix biology resources, new appointments and awards, together with announcements of relevant meetings.

Every two years, the Society presents the Rupert Timpl Award to a young scientist (<40 years old), who is starting on their independent career, for the best paper related to matrix biology published in the previous two years and gives the Distinguished Investigator Award for lifetime achievement in the field of matrix biology. ISMB sponsors travel grants for young scientists to attend international matrix meetings. If you work in the matrix biology area, consider becoming a member of ISMB to support the international matrix community and give your input on ways to improve interactions and communication. See the website www.ismb.org to join, for recent job postings and newsletters.

WELCOME TO NEW MEMBERS

Anna Gatseva	PhD student	University of Glasgow (UK)
John Couchman	Senior scientist	BRIC, University of Copenhagen (Denmark)

TRAVEL AWARDS

For Matrix Biology Europe meeting October 4th to 8th 2020 in Florence (Italy).

• Kristina Bubb, Department of Pediatrics and Adolescent Medicine, Medical Faculty, University of Cologne (Germany)
• Anna Gatseva, Institute of Cardiovascular & Medical Sciences, Glascow (UK)

• Shouyuan Jiang, University of New South Wales, Sydney (Australia)

RECENT PAPERS

miR-200b restrains EMT and aggressiveness and regulates matrix composition depending on ER status and signaling in mammary cancer. Piperigkou Z, Franchi M, Riethmüller C, Götte M, Karamanos NK. **Matrix Biology Plus (in press) 2020**
Corresponding author: martingotte@uni-muenster.de and n.k.karamanos@upatras.gr
Abstract: *Secreted microRNAs (miRNAs) reside in a complex regulatory network with extracellular matrix (ECM) macromolecules, which affect cell-cell communication, therefore miRNA expression highlights its significance in several aspects of human diseases, including cancer. miRNA-mediated regulation of breast cancer has received considerable attention due to evidence that shows miRNAs to mediate estrogen receptor (ER) status, metastasis, chemoresistance and epithelial-to-mesenchymal transition (EMT). miR-200b is a pluripotent miRNA, which is inversely regulated by ERα and ERβ in mammary cancer. It has been identified as tumor suppressor and EMT inhibitor serving as a critical biomarker, as its expression in breast tumor determines the disease-free survival, thus highlighting its roles in breast cancer invasion and metastasis. The main goal of this study was to investigate the role of miR-200b in modulating the behavior of breast cancer cells with different ER status. We demonstrate that estrogen signaling through ERs reduces miR-200b expression levels in ERα-positive breast cancer cells. Moreover, miR-200b upregulation reduces the aggressive phenotype of ERβ-positive breast cancer cells by inhibiting cell invasiveness and motility, followed by ECM reorganization as well as cytoskeletal and morphological changes concluded from deep inspection of cell topography. Future investigation towards the mechanistic perspective of miR-200b effects in the behavior of aggressive mammary cancer cells appears rewarding in order to expand our understanding of miR-200b as a novel mediator beyond breast cancer diagnosis and pharmaceutical targeting.*

A paracrine activin A-mDia2 axis promotes squamous carcinogenesis via fibroblast reprogramming. Cangkrama M, Wietecha M, Mathis N, Okumura R, Ferrarese L, Al-Nuaimi D, Antsiferova M, Dummer R, Innocenti M, Werner S. EMBO Mol Med. 2020 Mar 9:e11466. doi: 10.15252/emmm.201911466. [Epub ahead of print]
Corresponding author: sabine.werner@biol.ethz.ch
Abstract: *Cancer-associated fibroblasts (CAFs) are key regulators of tumorigenesis and promising targets for next-generation therapies. We discovered that cancer cell-derived activin A reprograms fibroblasts into pro-tumorigenic CAFs. Mechanistically, this occurs via Smad2-mediated transcriptional regulation of the formin mDia2, which directly promotes filopodia formation and cell migration. mDia2 also induces expression of CAF marker genes through prevention of p53 nuclear accumulation, resulting in the production of a pro-tumorigenic matrisome and secretome. The translational relevance of this finding is reflected by activin A overexpression in tumor cells and of mDia2 in the stroma of skin cancer and other malignancies and the correlation of high activin A/mDia2 levels with poor patient survival. Blockade of this signaling axis using inhibitors of activin, activin receptors, or mDia2 suppressed cancer cell malignancy and squamous carcinogenesis in 3D organotypic cultures, ex vivo, and in vivo, providing a rationale for pharmacological inhibition of activin A-mDia2 signaling in stratified cancer patients.*

Role of Glycosaminoglycans in Procathepsin B Maturation: Molecular Mechanism Elucidated by a Computational Study. Bojarski KK, Karczyńska AS, Samsonov SA. J Chem Inf Model. 2020 Apr 1. doi: 10.1021/acs.jcim.0c00023. [Epub ahead of print]

Corresponding author: sergery.samsonov@ug.edu.pl
Abstract: *Procathepsins are an inactive, immature form of cathepsins, predominantly cysteine proteases present in the extracellular matrix (ECM) and in lysosomes that play a key role in various biological processes such as bone resorption or intracellular proteolysis. The enzymatic activity of cathepsins can be mediated by glycosaminoglycans (GAGs), long unbranched periodic negatively charged polysaccharides found in ECM that take part in many biological processes such as anticoagulation, angiogenesis, and tissue regeneration. In addition to the known effects on mature cathepsins, GAGs can mediate the maturation process of procathepsins, in particular, procathepsin B. However, the detailed mechanism of this mediation at the molecular level is still unknown. In this study, for the first time, we aimed to unravel the role of GAGs in this process using computational approaches. We rigorously analyzed procathepsin B-GAG complexes in terms of their dynamics, energetics, and potential allosteric regulation. We revealed that GAGs can stabilize the conformation of the procathepsin B structure with the active site accessible for the substrate and concluded that GAGs most probably bind to procathepsin B once the zymogen adopts the enzymatically active conformation. Our data provided a novel mechanistic view of the maturation process of procathepsin B, while the approaches elaborated here might be useful to study other procathepsins. Furthermore, our data can serve as a rational guide for experimental work on procathepsin-GAG systems that are not characterized in vivo and in vitro yet.*

The liver matrisome, looking beyond collagens Gavin E. Arteel and Alexandra Naba, JHEP Reports https://www.jhep-reports.eu/article/S2589-5559(20)30049-5/fulltext

Corresponding authors: Gavin Arteel (gearteel@pitt.edu) and Alexandra Naba (anaba@uic.edu)
Abstract: *The extracellular matrix (ECM) is a diverse microenvironment that maintains bi-directional communication with surrounding cells to regulate cell and tissue homeostasis. The classical definition of the ECM has more recently been extended to include non-fibrillar proteins that either interact or are structurally affiliated with the ECM and has been coined the 'matrisome.' In addition to providing the structure and architectural support for cells and tissue, the matrisome serves as a reservoir for growth factors and cytokines, as well as a signaling hub via which cells can communicate with their environment and vice-versa. The matrisome is a master regulator of tissue homeostasis and organ function and dynamically and appropriately respond to any stress or injury. Failure to properly regulate these responses can lead to changes in the matrisome that are maladaptive. Hepatic fibrosis is a canonical example of ECM dyshomeostasis, leading to accumulation of predominantly collagenous ECM; indeed, hepatic fibrosis is considered almost synonymous with collagen accumulation. However, the qualitative and quantitative alterations of the hepatic matrisome during fibrosis are much more diverse than simple accumulation of collagens and occur long before fibrosis is histologically detected. A deeper understanding of the hepatic matrisome and its response to injury could yield new mechanistic insights into disease progression and regression, as well as potentially identify new biomarkers for both. This review discusses the current state of knowledge of the hepatic ECM in liver diseases, and new "omic" approaches to study this compartment.*

Pigmentation chemistry and radical-based collagen degradation in alkaptonuria and osteoarthritic cartilage.
Chow WY, Norman BP, Roberts NB, Ranganath LR, Teutloff C, Bittl R, Duer MJ, Gallagher JA, Oschkinat H.
Angew. Chem. Int. Ed. (2020) doi: 10.1002/anie.202000618. [Epub ahead of print]
https://onlinelibrary.wiley.com/doi/abs/10.1002/anie.202000618

Corresponding authors: wingying.chow@gmail.com, oschkinat@fmp-berlin.de, J.A.Gallagher@liverpool.ac.uk
Abstract: *Alkaptonuria (AKU) is a rare disease characterized by high levels of homogentisic acid (HGA); patients suffer from tissue ochronosis: dark brown pigmentation, especially of joint cartilage, leading to severe early osteoarthropathy. No molecular mechanism links elevated HGA to ochronosis; the pigment's chemical identity is still not known, nor how it induces joint cartilage degradation. Here we give key insight on HGA-derived pigment composition and collagen disruption in AKU cartilage. Synthetic pigment and pigmented human cartilage tissue*

both showed hydroquinone-resembling NMR signals. EPR spectroscopy showed that the synthetic pigment contains radicals. Moreover, we observed intrastrand disruption of collagen triple helix in pigmented AKU human cartilage, and in cartilage from patients with osteoarthritis. We propose that collagen degradation can occur via transient glycyl radicals, the formation of which is enhanced in AKU due to the redox environment generated by pigmentation.

Omic approaches to decipher the molecular mechanisms of fibrosis, and design new anti-fibrotic strategies.
Ricard-Blum S, Miele AE. Semin Cell Dev Biol. 2020 May;101:161-169.
Corresponding author: sylvie.ricard-blum@univ-lyon1.fr
Abstract: We review here omics approaches including transcriptomics, proteomics, glycomics, metabolomics and interactomics, databases and computational tools for omic and multi-omic investigations of fibrosis to understand the molecular mechanisms underlying fibrogenesis and fibrosis, to identify biomarkers of diagnosis, prognosis or disease progression, and new therapeutic targets and to design new anti-fibrotic drugs. We also provide perspectives for future studies including lipid and glycosaminoglycan profiling, and the design of virtual patient models as a basis for personalised medicine and virtualisation of drug development.

Extracellular Redox Regulation of α7β Integrin-Mediated Cell Migration Is Signaled via a Dominant Thiol-Switch.
Bergerhausen L, Grosche J, Meißner J, Hecker C, Caliandro MF, Westerhausen C, Kamenac A, Rezaei M, Mörgelin M, Poschmann G, Vestweber D, Hanschmann EM, Eble JA. Antioxidants (Basel). 2020 Mar 10;9(3):227.
Corresponding author: johannes.eble@uni-muenster.de
Abstract: *While adhering to extracellular matrix (ECM) proteins, such as laminin-111, cells temporarily produce hydrogen peroxide at adhesion sites. To study the redox regulation of α7β1 integrin-mediated cell adhesion to laminin-111, a conserved cysteine pair within the α-subunit hinge region was replaced for alanines. The molecular and cellular effects were analyzed by electron and atomic force microscopy, impedance-based migration assays, flow cytometry and live cell imaging. This cysteine pair constitutes a thiol-switch, which redox-dependently governs the equilibrium between an extended and a bent integrin conformation with high and low ligand binding activity, respectively. Hydrogen peroxide oxidizes the cysteines to a disulfide bond, increases ligand binding and promotes cell migration toward laminin-111. Inversely, extracellular thioredoxin-1 reduces the disulfide, thereby decreasing laminin binding. Mutation of this cysteine pair into the non-oxidizable hinge-mutant shows molecular and cellular effects similar to the reduced wild-type integrin, but lacks redox regulation. This proves the existence of a dominant thiol-switch within the α subunit hinge of α7β1 integrin, which is sufficient to implement activity regulation by extracellular redox agents in a redox-regulatory circuit. Our data reveal a novel and physiologically relevant thiol-based regulatory mechanism of integrin-mediated cell-ECM interactions, which employs short-lived hydrogen peroxide and extracellular thioredoxin-1 as signaling mediators.*

Skin Fragility: Perspectives on Evidence-based Therapies. Bruckner-Tuderman L. Acta Derm Venereol. 2020 Feb 12;100(5):adv00053.
Corresponding author: bruckner-tuderman@uniklinik-freiburg.de
Abstract: *The term skin fragility disorders describes a group of conditions in which the structural integrity of the skin is compromised and its resistance to external shear forces diminished. Skin fragility can have different causes, ranging from genetic variations to inflammatory or physical phenomena. The genetic skin fragility disorders, collectively called epidermolysis bullosa, serve as a paradigm for the study of causes and mechanisms of skin fragility. Recent biomedical research has revealed substantial genetic heterogeneity of the epidermolysis bullosa group, delivered ample new knowledge on its pathophysiology, and facilitated the design of evidence-based therapeutic strategies. The therapy development process extends from in vitro testing to preclinical validation in animal models, and clinical trials. This article reviews different approaches to curative and symptom-relief therapies, and appraises their status and perspectives for clinical implementation.*

Fibronectin Adsorption on Electrospun Synthetic Vascular Grafts Attracts Endothelial Progenitor Cells and Promotes Endothelialization in Dynamic In Vitro Culture. Daum R, Visser D, Wild C, Kutuzova L, Schneider M, Lorenz G, Weiss M, Hinderer S, Stock UA, Seifert M, Schenke-Layland K. Cells. 2020 Mar 23;9(3):778.
Corresponding author: katja.schenke-layland@med.uni-tuebingen.de
Abstract: *Appropriate mechanical properties and fast endothelialization of synthetic grafts are key to ensure long-term functionality of implants. We used a newly developed biostable polyurethane elastomer (TPCU) to engineer electrospun vascular scaffolds with promising mechanical properties (E-modulus: 4.8 ± 0.6 MPa, burst pressure: 3326 ± 78 mmHg), which were biofunctionalized with fibronectin (FN) and decorin (DCN). Neither uncoated nor biofunctionalized TPCU scaffolds induced major adverse immune responses except for minor signs of polymorph nuclear cell activation. The in vivo endothelial progenitor cell homing potential of the biofunctionalized scaffolds was simulated in vitro by attracting endothelial colony-forming cells (ECFCs). Although DCN coating did attract ECFCs in combination with FN (FN + DCN), DCN-coated TPCU scaffolds showed a cell-repellent effect in the absence of FN. In a tissue-engineering approach, the electrospun and biofunctionalized tubular grafts were cultured with primary-isolated vascular endothelial cells in a custom-made bioreactor under dynamic conditions with the aim to engineer an advanced therapy medicinal product. Both FN and FN + DCN functionalization supported the formation of a confluent and functional endothelial layer.*

Significance of MEF2C and RUNX3 Regulation for Endochondral Differentiation of Human Mesenchymal Progenitor Cells. Dreher SI, Fischer J, Walker T, Diederichs S, Richter W. Front Cell Dev Biol. 2020 Mar 4;8:81.
Corresponding author: wiltrud.richter@med.uni-heidelberg.de
Abstract: *Guiding progenitor cell development between chondral versus endochondral pathways is still an unachieved task of cartilage neogenesis, and human mesenchymal progenitor cell (MPC) chondrogenesis is considered as a valuable model to better understand hypertrophic development of chondrocytes. Transcription factors Runx2, Runx3, and Mef2c play prominent roles for chondrocyte hypertrophy during mouse development, but little is known on the importance of these key fate-determining factors for endochondral development of human MPCs. The aim of this study was to unravel the regulation of RUNX2, RUNX3, and MEF2C during MPC chondrogenesis, the pathways driving their expression, and the downstream hypertrophic targets affected by their regulation. RUNX2, RUNX3, and MEF2C gene expression was differentially regulated during chondrogenesis of MPCs, but remained low and unregulated when non-hypertrophic articular chondrocytes were differentiated under the same conditions. RUNX3 and MEF2C mRNA and protein levels rose in parallel to hypertrophic marker upregulation, but surprisingly, RUNX2 gene expression changed only by trend and RUNX2 protein remained undetectable. While RUNX3 expression was driven by TGF-β and BMP signaling, MEF2C responded to WNT-, BMP-, and Hedgehog-pathway inhibition. MEF2C but not RUNX3 levels correlated significantly with COL10A1, IHH, and IBSP gene expression when hypertrophy was attenuated. IBSP was a downstream target of RUNX3 and MEF2C but not RUNX2 in SAOS-2 cells, underlining the capacity of RUNX3 and MEF2C to stimulate osteogenic marker expression in human cells. Conclusively, RUNX3 and MEF2C appeared more important than RUNX2 for human endochondral MPC chondrogenesis. Pathways altering the speed of chondrogenesis (FGF, TGF-β, BMP) affected RUNX2 or RUNX3, while pathways changing hypertrophy (WNT, PTHrP/HH) regulated mainly MEF2C. Taken together, reduction of MEF2C levels is a new goal to shift human cartilage neogenesis toward the chondral pathway.*

Induction of heparanase via IL-10 correlates with a high infiltration of CD163+ M2-type tumor-associated macrophages in inflammatory breast carcinomas. El-Nadia M, Hassan H, Saleh ME, Nassar E, Ismael YM, Amer M, Greve B, Götte M, El-Shinawi M, Ibrahim SA. Matrix Biology Plus (in press) 2020
Corresponding author: martingotte@uni-muenster.de and isherif@sci.cu.edu.eg

Abstract: *Inflammatory breast cancer (IBC) is the most aggressive and lethal form of breast cancer, characterized by a high infiltration of tumor-associated macrophages and poor prognosis. To identify new biomarkers and to elucidate the molecular mechanisms underlying IBC pathogenesis, we investigated the expression pattern of heparanase (HPSE) and its activator cathepsin L (CTSL). First, we quantitated the HPSE and CTSL mRNA levels in a cohort of breast cancer patients after curative surgery (20 IBC and 20-non-IBC). We discovered that both HPSE and CTSL mRNA levels were significantly induced in IBC tissue vis-à-vis non-IBC patients (p <0 .05 and p <0 .001, respectively). According to the molecular subtypes, HPSE mRNA levels were significantly higher in carcinoma tissues of triple negative (TN)-IBC as compared to TN-non-IBC (p <0 .05). Mechanistically, we discovered that pharmacological inhibition of HPSE activity resulted in a significant reduction of invasiveness in the IBC SUM149 cell line. Moreover, siRNA-mediated HPSE knockdown significantly downregulated the expression of the metastasis-related gene MMP2 and the cancer stem cell marker CD44. We also found that IBC tumors revealed robust heparanase immune-reactivity and CD163+ M2-type tumor-associated macrophages, with a positive correlation of both markers. Moreover, the secretome of axillary tributaries blood IBC CD14+ monocytes and the cytokine IL-10 significantly upregulated HPSE mRNA and protein expression in SUM149 cells. Intriguingly, massively elevated IL-10 mRNA expression with a trend of positive correlation with HPSE mRNA expression was detected in carcinoma tissue of IBC. Our findings highlight a possible role played by CD14+ monocytes and CD163+ M2-type tumor-associated macrophages in regulating HPSE expression possibly via IL-10. Overall, we suggest that heparanase, cathepsin L and CD14+ monocytes-derived IL-10 may play an important role in the pathogenesis of IBC and their targeting could have therapeutic implications.*

Impact of knee joint loading on fragmentation of serum cartilage oligomeric matrix protein. Firner S, Zaucke F, Heilig J, de Marées M, Willwacher S, Brüggemann GP, Niehoff A. J Orthop Res. 2020 Jan 14. doi: 10.1002/jor.24586.

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Abstract: *The aim of the study was to examine the effect of mechanical knee joint loading on the fragmentation pattern of serum cartilage oligomeric matrix protein (COMP). Ten healthy men ran with knee orthoses that were passive or active (+30.9 N·m external flexion moments) on a treadmill (30 minute; v = 2.2 m/s). Lower-limb mechanics, serum COMP levels, and fragmentation patterns (baseline; 0, 0.5, 1, 2 hours postrunning) were analyzed. Running with active orthoses enhanced knee flexion moments, ankle dorsiflexion, and knee flexion angles (P < .05). There was an increase in serum COMP (+25%; pre: 8.9 ± 2.4 U/l; post: 10.7 ± 1.9 U/l, P = .001), COMP pentamer/tetramer (+88%; 1.88 ± 0.81, P = .007), trimer (+209%; 3.09 ± 2.65, P = .005), and monomer (+78%; 1.78 ± 0.85, P = .007) after running with passive orthoses and in serum COMP (+41%; pre: 8.5 ± 2.7 U/l; post: 11.3 ± 2.1 U/l, P < .001), COMP pentamer/tetramer (+57%; 1.57 ± 0.39, P = .007), trimer (+86%; 1.86 ± 0.47, P = .005), and monomer (+19%; 1.19 ± 0.34, P = .114) after running with active orthoses. Increased fragmentation might indicate COMP release from cartilage while running. Interestingly, 0.5 h up to 2 hours after running with passive orthoses, trimer (0.5 hour: 2.73 ± 3.40, P = .029; 2 hours: 2.33 ± 2.88, P = .037), and monomer (0.5 hour: 2.23 ± 2.33, P = .007; 1 hour: 2.55 ± 1.96, P = .012; 2 hours: 2.65 ± 2.50, P = .009) increased while after running with active orthoses, pentamer/tetramer (1 hour: 0.79 ± 0.28, P = .029), and trimer (1 hour: 0.63 ± 0.14, P = .005; 2 hours: 0.68 ± 0.34, P = .047) decreased. It seems that COMP degradation and clearance vary depending on joint loading characteristics.*

Antibody-mediated inhibition of syndecan-4 dimerisation reduces interleukin (IL)-1 receptor trafficking and signalling. Godmann L, Bollmann M, Korb-Pap A, König U, Sherwood J, Beckmann D, Mühlenberg K, Echtermeyer F, Whiteford J, De Rossi G, Pap T, Bertrand J. Ann Rheum Dis. 2020 Apr;79(4):481-489.

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Abstract: *Objective: Syndecan-4 (sdc4) is a cell-anchored proteoglycan that consists of a transmembrane core protein and glucosaminoglycan (GAG) side chains. Binding of soluble factors to the GAG chains of sdc4 may result in the dimerisation of sdc4 and the initiation of downstream signalling cascades. However, the question of how sdc4 dimerisation and signalling affects the response of cells to inflammatory stimuli is unknown. Methods: Sdc4 immunostaining was performed on rheumatoid arthritis (RA) tissue sections. Interleukin (IL)-1 induced extracellular signal-regulated kinases (ERK) phosphorylation and matrix metalloproteinase-3 production was investigated. Il-1 binding to sdc4 was investigated using immunoprecipitation. IL-1 receptor (IL1R1) staining on wild-type, sdc4 and IL1R1 knockout fibroblasts was performed in fluorescence-activated cell sorting analyses. A blocking sdc4 antibody was used to investigate sdc4 dimerisation, IL1R1 expression and the histological paw destruction in the human tumour necrosis factor-alpha transgenic mouse. Results: We show that in fibroblasts, the loss of sdc4 or the antibody-mediated inhibition of sdc4 dimerisation reduces the cell surface expression of the IL-1R and regulates the sensitivity of fibroblasts to IL-1. We demonstrate that IL-1 directly binds to sdc4 and in an IL-1R-independent manner leads to its dimerisation. IL-1-induced dimerisation of sdc4 regulates caveolin vesicle-mediated trafficking of the IL1R1, which in turn determines the responsiveness to IL-1. Administration of antibodies (Ab) against the dimerisation domain of sdc4, thus, strongly reduces the expression IL1R1 on arthritic fibroblasts both in vitro and an animal model of human RA. Conclusion: Collectively, our data suggest that Ab that specifically inhibit sdc4 dimerisation may support anti-IL-1 strategies in diseases such as inflammatory arthritis.*

SETD3 acts as a prognostic marker in breast cancer patients and modulates the viability and invasion of breast cancer cells. Hassan N, Rutsch N, Győrffy B, Espinoza-Sánchez NA, Götte M. Sci Rep. 2020 Feb 10;10(1):2262.
Corresponding author: martin.goette@ukmuenster.de
Abstract: *In several carcinomas, the SET Domain Containing 3, Actin Histidine Methyltransferase (SETD3) is associated with oncogenesis. However, there is little knowledge about the role of SETD3 in the progression and prognosis of breast cancer. In this study, we first analyzed the prognostic value of SETD3 in breast cancer patients using the database of the public Kaplan-Meier plotter. Moreover, in vitro assays were performed to assess the role of SETD3 in the viability and capacity of invasion of human breast cancer cell lines. We observed that the high expression of SETD3 was associated with better relapse-free survival (RFS) of the whole collective of 3,951 patients, of Estrogen Receptor-positive, and of Luminal A-type breast cancer patients. However, in patients lacking expression of estrogen-, progesterone- and HER2-receptor, and those affected by a p53-mutation, SETD3 was associated with poor RFS. In vitro analysis showed that SETD3 siRNA depletion affects the viability of triple-negative cells as well as the cytoskeletal function and capacity of invasion of highly invasive MDA-MB-231 cells. Interestingly, SETD3 regulates the expression of other genes associated with cancer such as β-actin, FOXM1, FBXW7, Fascin, eNOS, and MMP-2. Our study suggests that SETD3 expression can act as a subtype-specific biomarker for breast cancer progression and prognosis.*

Collagen IX deficiency leads to premature vascularization and ossification of murine femoral heads through an imbalance of pro- and antiangiogenic factors. Heilig J, Dietmar HF, Brachvogel B, Paulsson M, Zaucke F, Niehoff A. Osteoarthritis Cartilage. 2020 Apr 10:S1063-4584(20)30977-8.
Corresponding author: niehoff@dshs-koeln.de
Abstract: *Objective: The vascular invasion of cartilage is an essential process in the endochondral ossification of long bones. In contrast, vascularization of articular cartilage constitutes a pathological mechanism in the development of osteoarthritis. Polymorphisms of Col9a1 have been described as risk factors for hip osteoarthritis (OA) and the loss of collagen IX is known to lead to premature OA of the hip joint in mice but the underlying mechanism is so far unknown. Design: To understand the contribution of collagen IX to OA development in the hip joint, we analyzed the early development of murine Col9a1-/- femoral heads between newborn stage and 16 weeks of age. Results: We found significantly accelerated ossification of the femoral heads in the absence of*

collagen IX as well as premature vascular and osteoclast invasion, even though hypertrophic differentiation was delayed. The loss of collagen IX led to anatomically altered femoral heads lacking the epiphyseal tubercle. Interestingly, this region was found to contain highest levels of the antiangiogenic protein thrombospondin-1 (TSP-1). Hence, TSP-1 levels were strongly reduced in the Col9a1-/- femoral heads. In addition, antiangiogenic matrilin-1 was found to be decreased, while proangiogenic active MMP-9 levels were increased in the collagen IX deficient mice compared to wildtype controls. Conclusion: We conclude that collagen IX protects against premature vascularization and cartilage to bone transition in femoral heads by increasing the levels of antiangiogenic TSP-1 and matrilin-1 and decreasing the levels of proangiogenic active MMP-9.

Adrenoceptor Expression during Intervertebral Disc Degeneration. Kupka J, Kohler A, El Bagdadi K, Bostelmann R, Brenneis M, Fleege C, Chan D, Zaucke F, Meurer A, Rickert M, Jenei-Lanzl Z. Int J Mol Sci. 2020 Mar 18;21(6):2085.
Corresponding author: zsuzsa.jenei-lanzl@friedrichsheim.de
Abstract: *Healthy and degenerating intervertebral discs (IVDs) are innervated by sympathetic nerves, however, adrenoceptor (AR) expression and functionality have never been investigated systematically. Therefore, AR gene expression was analyzed in both tissue and isolated cells from degenerated human IVDs. Furthermore, human IVD samples and spine sections of wildtype mice (WT) and of a mouse line that develops spontaneous IVD degeneration (IVDD, in SM/J mice) were stained for ARs and extracellular matrix (ECM) components. In IVD homogenates and cells α1a-, α1b-, α2a-, α2b-, α2c-, β1-, and β2-AR genes were expressed. In human sections, β2-AR was detectable, and its localization parallels with ECM alterations. Similarly, in IVDs of WT mice, only β2-AR was expressed, and in IVDs of SM/J mice, β2AR expression was stronger accompanied by increased collagen II, collagen XII, decorin as well as decreased cartilage oligomeric matrix protein expression. In addition, norepinephrine stimulation of isolated human IVD cells induced intracellular signaling via ERK1/2 and PKA. For the first time, the existence and functionality of ARs were demonstrated in IVD tissue samples, suggesting that the sympathicus might play a role in IVDD. Further studies will address relevant cellular mechanisms and thereby help to develop novel therapeutic options for IVDD*.

Mice Lacking the Matrilin Family of Extracellular Matrix Proteins Develop Mild Skeletal Abnormalities and Are Susceptible to Age-Associated Osteoarthritis. Li P, Fleischhauer L, Nicolae C, Prein C, Farkas Z, Saller MM, Prall WC, Wagener R, Heilig J, Niehoff A, Clausen-Schaumann H, Alberton P, Aszodi A Int J Mol Sci. 2020 Jan 19;21(2):666.
Corresponding author: attila.Aszodi@med.uni-muenchen.de
Abstract: *Matrilins (MATN1, MATN2, MATN3 and MATN4) are adaptor proteins of the cartilage extracellular matrix (ECM), which bridge the collagen II and proteoglycan networks. In humans, dominant-negative mutations in MATN3 lead to various forms of mild chondrodysplasias. However, single or double matrilin knockout mice generated previously in our laboratory do not show an overt skeletal phenotype, suggesting compensation among the matrilin family members. The aim of our study was to establish a mouse line, which lacks all four matrilins and analyze the consequence of matrilin deficiency on endochondral bone formation and cartilage function. Matn1-4-/- mice were viable and fertile, and showed a lumbosacral transition phenotype characterized by the sacralization of the sixth lumbar vertebra. The development of the appendicular skeleton, the structure of the growth plate, chondrocyte differentiation, proliferation, and survival were normal in mutant mice. Biochemical analysis of knee cartilage demonstrated moderate alterations in the extractability of the binding partners of matrilins in Matn1-4-/- mice. Atomic force microscopy (AFM) revealed comparable compressive stiffness but higher collagen fiber diameters in the growth plate cartilage of quadruple mutant compared to wild-type mice. Importantly, Matn1-4-/- mice developed more severe spontaneous osteoarthritis at the age of 18 months, which was accompanied by changes in the biomechanical properties of the articular cartilage. Interestingly, Matn4-/- mice also developed*

age-associated osteoarthritis suggesting a crucial role of MATN4 in maintaining the stability of the articular cartilage. Collectively, our data provide evidence that matrilins are important to protect articular cartilage from deterioration and are involved in the specification of the vertebral column.

Decellularization and antibody staining of mouse tissues to map native extracellular matrix structures in 3D. **Nat Protoc. 2020 Mar 16.** Mayorca-Guiliani AE, Willacy O, Madsen CD, Rafaeva M, Elisabeth Heumüller S, Bock F, Sengle G, Koch M, Imhof T, Zaucke F, Wagener R, Sasaki T, Erler JT, Reuten R
Corresponding author: alejandro.mayorca@bric.ku.dk, janine.erler@bric.ku.dk and raphael.reuten@bric.ku.dk
Correction to: *Nature Protocols https://doi.org/10.1038/s41596-019-0225-8, published online 8 November 2019. In the version of this article initially published, the immunofluorescence staining images for TGFBI in Fig. 7 and Supplementary Fig. 7 inadvertently displayed the same image. This error does not affect the conclusions for either figure (the staining pattern is identical). Fig. 7 has been replaced with the correct image in the HTML and PDF versions of the article.*

Impact of the Sensory and Sympathetic Nervous System on Fracture Healing in Ovariectomized Mice. Niedermair T, Straub RH, Brochhausen C, Grässel S. Int J Mol Sci. 2020 Jan 8;21(2):405.
Corresponding author: susanne.graessel@ukr.de
Abstract: *The peripheral nervous system modulates bone repair under physiological and pathophysiological conditions. Previously, we reported an essential role for sensory neuropeptide substance P (SP) and sympathetic nerve fibers (SNF) for proper fracture healing and bone structure in a murine tibial fracture model. A similar distortion of bone microarchitecture has been described for mice lacking the sensory neuropeptide α-calcitonin gene-related peptide (α-CGRP). Here, we hypothesize that loss of SP, α-CGRP, and SNF modulates inflammatory and pain-related processes and also affects bone regeneration during fracture healing under postmenopausal conditions. Intramedullary fixed femoral fractures were set to 28 days after bilateral ovariectomy (OVX) in female wild type (WT), SP-, α-CGRP-deficient, and sympathectomized (SYX) mice. Locomotion, paw withdrawal threshold, fracture callus maturation and numbers of TRAP-, CD4-, CD8-, F4/80-, iNos-, and Arg1-positive cells within the callus were analyzed. Nightly locomotion was reduced in unfractured SP-deficient and SYX mice after fracture. Resistance to pressure was increased for the fractured leg in SP-deficient mice during the later stages of fracture healing, but was decreased in α-CGRP-deficient mice. Hypertrophic cartilage area was increased nine* days after *fracture in SP-deficient mice. Bony callus maturation was delayed in SYX mice during the later healing stages. In addition, the number of CD 4-positive cells was reduced after five days and the number of CD 8-positive cells was additionally reduced after 21 days in SYX mice. The number of Arg1-positive M2 macrophages was higher in α-CGRP-deficient mice five days after fracture. The alkaline phosphatase level was increased in SYX mice 16 days after fracture. Absence of α-CGRP appears to promote M2 macrophage polarization and reduces the pain threshold, but has no effect on callus tissue maturation. Absence of SP reduces locomotion, increases the pain-threshold, and accelerates hypertrophic callus tissue remodeling. Destruction of SNF reduces locomotion after fracture and influences bony callus tissue remodeling during the later stages of fracture repair, whereas pain-related processes are not affected.*

Neuropilin: Handyman and Power Broker in the Tumor Microenvironment. Niland S, Eble JA. Adv Exp Med Biol. 2020;1223:31-67.
Corresponding author: nilands@uni-muenster.de
Abstract: *Neuropilin-1 and neuropilin-2 form a small family of transmembrane receptors, which, due to the lack of a cytosolic protein kinase domain, act primarily as co-receptors for various ligands. Performing at the molecular level both the executive and organizing functions of a handyman as well as of a power broker, they are instrumental in controlling the signaling of various receptor tyrosine kinases, integrins, and other molecules*

involved in the regulation of physiological and pathological angiogenic processes. In this setting, the various neuropilin ligands and interaction partners on various cells of the tumor microenvironment, such as cancer cells, endothelial cells, cancer-associated fibroblasts, and immune cells, are surveyed. The suitability of various neuropilin-targeting substances and the intervention in neuropilin-mediated interactions is considered as a possible building block of tumor therapy.

Synovial fibroblasts and articular tissue remodelling: Role and mechanisms. Pap T, Dankbar B, Wehmeyer C, Korb-Pap A, Sherwood J. Semin Cell Dev Biol. 2020 Jan 16:S1084-9521(19)30300-3.
Corresponding author: thomas.pap@uni-muenster.de
Abstract: *Synovial joints are unique functional elements of the body and provide the ability for locomotion and for physical interaction with the environment. They are composed of different connective tissue structures, of which the synovial membrane is one central component. It shows a number of peculiarities that makes it different from other membranes in our body, while several lines of evidence suggest that synovial fibroblasts, also termed fibroblast-like synoviocytes (FLS) critically contribute to these peculiarities. This becomes evident particularly under disease conditions such as in rheumatoid arthritis and osteoarthritis, where the synovium is a key pathophysiological component. Therefore, an in-depth knowledge of FLS biology is not only important for understanding key features of articular function but also provides explanations for important characteristics of both degenerative and inflammatory joint diseases. This article reviews the structure, biochemical composition and functions of the synovial membrane and by focusing on the role of synovial fibroblasts explains key features of articular tissue remodelling particularly under disease conditions.*

Pathomechanisms of Posttraumatic Osteoarthritis: Chondrocyte Behavior and Fate in a Precarious Environment. Riegger J, Brenner RE. Int J Mol Sci. 2020 Feb 25;21(5):1560.
Corresponding author: rolf.brenner@uni-ulm.de
Abstract: *Traumatic injuries of the knee joint result in a wide variety of pathomechanisms, which contribute to the development of so-called posttraumatic osteoarthritis (PTOA). These pathogenetic processes include oxidative stress, excessive expression of catabolic enzymes, release of damage-associated molecular patterns (DAMPs), and synovial inflammation. The present review focuses on the underlying pathomechanisms of PTOA and in particular the behavior and fate of the surviving chondrocytes, comprising chondrocyte metabolism, regulated cell death, and phenotypical changes comprising hypertrophy and senescence. Moreover, possible therapeutic strategies, such as chondroanabolic stimulation, anti-oxidative and anti-inflammatory treatment, as well as novel therapeutic targets are discussed.*

Serum Cartilage Oligomeric Matrix Protein in Late-Stage Osteoarthritis: Association with Clinical Features, Renal Function, and Cardiovascular Biomarkers. Riegger J, Rehm M, Büchele G, Brenner H, Günther KP, Rothenbacher D, Brenner RE. J Clin Med. 2020 Jan 18;9(1):268**.**
Corresponding author: rolf.brenner@uni-ulm.de
Abstract: *This study aimed to assess associations between serum cartilage oligomeric matrix protein (sCOMP) and phenotypic characteristics in late-stage hip and knee Osteoarthritis (OA) as well as its correlation with further serum markers of possible comorbidities in the Ulm Osteoarthritis Study. Moreover, the prognostic relevance of preoperative sCOMP concentrations for short-term functionality and pain outcomes after hip or knee joint replacement was explored. Preoperative serum samples and detailed information about the health status (i.e., WOMAC scores, Hannover Functionality Status (FFbH)) of 754 OA patients undergoing total joint replacement were included. Spearman rank-correlation coefficients and multiple linear regression models were used to evaluate the relationships between sCOMP, other serum markers, and health outcomes. There was a significant positive association between sCOMP and markers of renal (cystatin C, creatinine, and eGFR) and cardiac (e.g., NT-*

proBNP) impairment. Since renal failure might cause accumulation of sCOMP, additional adjustment with eGFR was performed. Preoperative sCOMP levels in knee OA but not hip OA patients were positively associated with FFbH, WOMAC function sub-scale and total WOMAC scale as well as the post-operative WOMAC stiffness sub-scale six months after surgery. Our data clearly demonstrate an association between sCOMP and renal function as well as other confounding factors, which should be considered in future biomarker studies.

Involvement of Syndecan-1 and Heparanase in Cancer and Inflammation. Teixeira FCOB, Götte M. Adv Exp Med Biol. 2020;1221:97-135.
Corresponding author: martin.goette@ukmuenster.de
Abstract: *The cell surface heparan sulfate proteoglycan Syndecan-1 acts as an important co-receptor for receptor tyrosine kinases and chemokine receptors, and as an adhesion receptor for structural glycoproteins of the extracellular matrix. It serves as a substrate for heparanase, an endo-β-glucuronidase that degrades specific domains of heparan sulfate carbohydrate chains and thereby alters the functional status of the proteoglycan and of Syndecan-1-bound ligands. Syndecan-1 and heparanase show multiple levels of functional interactions, resulting in mutual regulation of their expression, processing, and activity. These interactions are of particular relevance in the context of inflammation and malignant disease. Studies in animal models have revealed a mechanistic role of Syndecan-1 and heparanase in the regulation of contact allergies, kidney inflammation, multiple sclerosis, inflammatory bowel disease, and inflammation-associated tumorigenesis. Moreover, functional interactions between Syndecan-1 and heparanase modulate virtually all steps of tumor progression as defined in the Hallmarks of Cancer. Due to their prognostic value in cancer, and their mechanistic involvement in tumor progression, Syndecan-1 and heparanase have emerged as important drug targets. Data in preclinical models and preclinical phase I/II studies have already yielded promising results that provide a translational perspective*.

Knockdown of Musashi RNA Binding Proteins Decreases Radioresistance but Enhances Cell Motility and Invasion in Triple-Negative Breast Cancer. Troschel FM, Minte A, Ismail YM, Kamal A, Abdullah MS, Ahmed SH, Deffner M, Kemper B, Kiesel L, Eich HT, Ibrahim SA, Götte M, Greve B. Int J Mol Sci. 2020 Mar 21;21(6):2169**.**
Corresponding author: martin.goette@ukmuenster.de and burkhard.greve@ukmuenster.de
Abstract: *The therapeutic potential of Musashi (MSI) RNA-binding proteins, important stemness-associated gene expression regulators, remains insufficiently understood in breast cancer. This study identifies the interplay between MSI protein expression, stem cell characteristics, radioresistance, cell invasiveness and migration. MSI-1, MSI-2 and Notch pathway elements were investigated via quantitative polymerase chain reaction (qPCR) in 19 triple-negative breast cancer samples. Measurements were repeated in MDA-MB-231 cells after MSI-1 and -2 siRNA-mediated double knockdown, with further experiments performed after MSI silencing. Flow cytometry helped quantify expression of CD44 and leukemia inhibitory factor receptor (LIFR), changes in apoptosis and cell cycle progression. Proliferation and irradiation-induced effects were assessed using colony formation assays. Radiation-related proteins were investigated via Western blots. Finally, cell invasion assays and digital holographic microscopy for cell migration were performed. MSI proteins showed strong correlations with Notch pathway elements. MSI knockdown resulted in reduction of stem cell marker expression, cell cycle progression and proliferation, while increasing apoptosis. Cells were radiosensitized as radioresistance-conferring proteins were downregulated. However, MSI-silencing-mediated LIFR downregulation resulted in enhanced cell invasion and migration. We conclude that, while MSI knockdown results in several therapeutically desirable consequences, enhanced invasion and migration need to be counteracted before knockdown advantages can be fully exploited.*

The role of extracellular matrix in biomechanics and its impact on bioengineering of cells and 3D tissues. Urbanczyk M, Layland SL, Schenke-Layland K. Matrix Biol. 2020 Jan;85-86:1-14.
Corresponding author: katja.schenke-layland@med.uni-tuebingen.de

Abstract: *The cells and tissues of the human body are constantly exposed to exogenous and endogenous forces that are referred to as biomechanical cues. They guide and impact cellular processes and cell fate decisions on the nano-, micro- and macro-scale, and are therefore critical for normal tissue development and maintaining tissue homeostasis. Alterations in the extracellular matrix composition of a tissue combined with abnormal mechanosensing and mechanotransduction can aberrantly activate signaling pathways that promote disease development. Such processes are therefore highly relevant for disease modelling or when aiming for the development of novel therapies. In this mini review, we describe the main biomechanical cues that impact cellular fates. We highlight their role during development, homeostasis and in disease. We also discuss current techniques and tools that allow us to study the impact of biomechanical cues on cell and tissue development under physiological conditions, and we point out directions, in which in vitro biomechanics can be of use in the future.*

Spatial-omics: Novel Approaches to Probe Cell Heterogeneity and Extracellular Matrix Biology
Grace C. Bingham, Fred Lee, Alexandra Naba, Thomas H.Barker. Matrix Biol. Available online 19 May 2020
https://doi.org/10.1016/j.matbio.2020.04.004
Corresponding author: thomas.barker@virginia.edu
Abstract: *Complex intercellular interactions as well as biomolecular and biomechanical cues from the extracellular matrix (ECM) profoundly affect cellular functions. Traditional transcriptomic and proteomic approaches have provided insight into disease progression by identifying discrete cellular subpopulations or microenvironmental signatures characteristic of normal or pathological tissues, however these techniques do not examine how a given cellular state relates to its interactions with neighboring cells or its surrounding ECM with multiparametric characterization (i.e. ECM alignment, mechanical forces, crosslinking, etc.). Emerging spatial-omic techniques can provide high-resolution mapping of expression profiles similar to scRNA-seq and mass spectroscopy directly within tissues. The ability to preserve the spatial context of cells within samples, their cellular geometry, as well as their surrounding ECM gives spatial-omics the opportunity to interrogate previously unexplored signaling modalities, which has the potential to revolutionize ECM research and our understanding of fibrotic diseases. In this review, we present current spatial transcriptomic and proteomic techniques and discuss how they may be applied to investigate cell-ECM interactions.*

SPECIAL ISSUES ON THE EXTRACELLULAR MATRIX

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Special issue Translating Extracellular Matrix: from cancer progression to therapeutics
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Role of heparanase in tumor progression: Molecular aspects and therapeutic options
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The pleiotropic role of proteoglycans in extracellular vesicle mediated communication in the tumor microenvironment
M. Cerezo-Magaña, A. Bång-Rudenstam, M. Belting Pages 99-107

Tumorigenic functions of serglycin: Regulatory roles in epithelial to mesenchymal transition and oncogenic signaling
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Estrogen receptor-mediated targeting of the extracellular matrix network in cancer
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Epithelial-to-mesenchymal transition and invadopodia markers in breast cancer: Lumican a key regulator
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Exploring the roles of MACIT and multiplexin collagens in stem cells and cancer
Valerio Izzi, Ritva Heljasvaara, Anne Heikkinen, Sanna-Maria Karppinen, ... Taina Pihlajaniemi Pages 134-148

Laminin 332 in cancer: When the extracellular matrix turns signals from cell anchorage to cell movement
Patricia Rousselle, Jean Yves Scoazec Pages 149-165

Cancer-associated fibroblasts in desmoplastic tumors: emerging role of integrins
Cédric Zeltz, Irina Primac, Pugazendhi Erusappan, Jahedul Alam, ... Donald Gullberg Pages 166-181

The role of senescence in cancer development
Eleni Mavrogonatou, Harris Pratsinis, Dimitris Kletsas Pages 182-191

Emerging roles of ECM remodeling processes in cancer
Vishnu Mohan, Alakesh Das, Irit Sagi Pages 192-200

Authors who would be interested in providing a manuscript either as a discovery paper or as a review may contact Kim Midwood (kim.midwood@kennedy.ox.ac.uk), Gertraud Orend (gertraud.orend@inserm.fr) or Kyoko Imanaka-Yoshida (imanaka@doc.medic.mie-u.ac.jp).

MATRIX MEETING ANNOUNCEMENTS

Matrix Biology Europe meeting, May 24th-28th, 2020, Florence (Italy)
Postponed to October,4th-8th, 2020, Florence (Italy)

Conference chair: Professor Alberto Passi (http://www.mbe2020.org/)

The 4th International Keloid Symposium - Jefferson Matrix Biology and Pathology Symposium June 12-14, 2020, Thomas Jefferson University, Philadelphia (USA)

https://keloidsymposium.com/4th-international-keloid-symposium-focus-on-keloid-disorder/

4th International Keloid Symposium

Dear Friends and Colleagues,

In light of COVID-19 pandemic, we are planning to hold our 4th International Keloid Symposium virtually, and via **video-conferencing**. Over the next several weeks, we will share more information with you. For the time being, we will refund all the registrations and will invite attendees to sign up for our virtual meeting instead.

Please take note of the following:

1. All the registration fees are will be refunded.
2. Those who wish to participate in a virtual meeting shall register again.
3. Please do NOT make any travel arrangements as the meeting will be held virtually.

Yours sincerely,

The Organizing Committee
Michael H. Tirgan, MD, Jouni Uitto, MD, PhD, Reza Ghonestani, MD, PhD, Renato V. Iozzo, MD, PhD
Joel Rosenbloom PhD

ASMB 2020 Biennial meeting, November 8-11, 2020, St Louis, MO (USA)

The American Society for Matrix Biology will hold its biennial meeting from November 8-11, 2020 in St. Louis, Missouri at the Hyatt Regency St. Louis at the Arch. The overall theme of the meeting is “Matrix, Cells, and Interactions in Health, Disease, Aging, and Regeneration”. Please contact Meeting Chair Jeff Miner (jeffminer@wustl.edu) or ASMB Executive Director Kendra LaDuca (kladuca@asmb.net) for further information. Travel Awards for trainees will be available.
Hyatt Regency at the Arch, St. Louis, MO (USA) https://www.asmb.net/biennial-meeting

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ASMB Biennial Meeting News – SPECIAL INTEREST SESSIONS

As you know, ASMB is planning a biennial meeting for November 8-11, 2020. The program is set, speakers are confirmed, and fun social activities are planned. Like all of you, ASMB recognizes the significant challenges COVID-19 has placed on the scientific and medical communities and we are working to make necessary adjustments to accommodate attendance at the meeting this fall. As of today, the meeting is on! This is a fluid situation however, and we will continue to update you as

additional information becomes available. Meanwhile, we are pleased to share more of the scientific program with you. ASMB will host three Special Interest Sessions organized by trainees. These sessions will take place at the Biennial Meeting. We hope to see you there!

SIS 1: Not Just Tissue Inhibitors of Metalloproteinases (TIMPs)
David Peeney, *National Cancer Institute*
Tissue inhibitors of metalloproteinases (TIMPs) are a family of endogenous proteins that were initially defined by their ability to inhibit the enzymatic activity of matrix metalloproteinases (MMPs), the major mediators of extracellular matrix (ECM) breakdown and turnover. In turn, this function of TIMPs makes them important regulators of ECM structure. However, since their original discovery additional MMP-independent functions have been attributed to TIMP family members leading to their designation as multifunctional proteins, with discrete functional domains. However, despite their multi-functional abilities, TIMPs are routinely confined to the ontology of metalloproteinase inhibition by researchers. The aim of this Special Interest Session is to provide a deeper insight into the biological activities of TIMP family members, and how their regulation and therapeutic targeting can modulate ECM structure and function.
Sunday, November 8, 2:45pm

SIS 2: Novel Regulators of Vascular Remodeling and Matrix Assembly
Matthew Scott, LSU Shreveport
Extracellular matrix structure and composition regulates multiple aspects of cardiovascular function, including vascular development, tissue remodeling, and pathogenic changes in cell phenotype. For instance, fibronectin deposition has been observed in atherosclerosis-prone regions of the aorta and carotid arteries, where it is involved in the inflammatory response. Fibronectin has also been detected within atherosclerotic plaques, where it is deposited by vascular smooth muscle cells in a manner regulated by EphA2, a receptor tyrosine kinase. Matrix assembly/disassembly is a complex process involving a variety of proteins, including matricellular proteins (i.e. thrombospondins) and metalloproteases (i.e. ADAMTS family). This special interest session will explore some of the novel regulators of vascular ECM remodeling and matrix assembly.
Monday, November 9, 2:30pm

SIS 3: ECM Characterization Modalities
Lauren Schmitt and Maxwell McCabe, *University of Colorado Anschutz Medical Campus*
The extracellular matrix (ECM) governs a wide range of biological processes including cell differentiation, wound healing, and fibrosis. Knowledge of ECM composition and architecture is critical to fields ranging from biomedical to biomaterials science. However, due to the high degree of modification and insolubility of most ECM proteins, data regarding the ECM proteome is sparse. This session will address new techniques and tools that have been developed to provide improved analysis of the ECM. Several speakers will focus on mass spectrometry-based analysis of the ECM while others will focus on IHC and bioengineering approaches.
Wednesday, November 11, 11:30 am

The full ASMB Biennial Meeting Program can be found online at: https://asmb.memberclicks.net/2020-biennial-meeting

The PAN PACIFIC CONNECTIVE TISSUE SOCIETIES SYMPOSIUM 2020

It will be held in conjunction with the scientific meetings of the Australasian Wound & Tissue Repair Society (AWTRS) and the Matrix Biology Society of Australia and New Zealand (MBSANZ). It will take place on 22nd to 26th November, 2020, in Melbourne, Australia. For the latest information see: https://ppctss2020.smalltalkevents.com.au

The Australasian Wound & Tissue Repair Society (AWTRS) and the Matrix Biology Society of Australia and New Zealand (MBSANZ) are two leading scientific societies focused on the fundamental biological and biochemical mechanisms involved in wound healing and tissue repair and their application in the clinic, as well as the roles of the extracellular matrix in biology and pathology.

It is with great pleasure that we announce that the 12th Pan Pacific Connective Tissue Societies Symposium in conjunction with the scientific meetings of the AWTRS and MBSANZ will be held in Melbourne in November 2020. The meeting will be at the University of Melbourne, which is in the heart of the prestigious and internationally renowned Biomedical Precinct that delivers outstanding patient care, cutting edge research and fundamental discoveries and training of some of the country's brightest minds, leading to significant economic value to Victoria and Australia.

This website will be kept up to date with all the latest news about the symposium program, speakers, registration, abstract submission and much more, so please bookmark this page for future reference. We very much look forward to welcoming you to Melbourne in November 2020.

Thematic Sessions on Glycosylation and Extracellular Matrix in Development, Repair, and Disease at American Society for Biochemistry and Molecular Biology (ASBMB) 2020 Meeting

Plans are to hold these sessions at the EB2021 meeting in Indianapolis, IN (USA) May 1-4, 2021.

The ASBMB 2020 Meeting should have been held April 4-7 at the San Diego convention center (USA) Along with outstanding award lectures, poster sessions, and workshops, this year six thematic sessions covering foundational areas of biochemistry and molecular biology will meet each of the three mornings of the conference.
One of the themes is entitled, Glycosylation and Extracellular Matrix in Development, Repair, and Disease, co-chaired by Drs. Jamey Marth and Joanne Murphy-Ullrich. They have invited 12 world-class scientists to speak in this three-day theme. Speakers from the ECM community include Lynn Sakai, Joanne Murphy-Ullrich, Kim Midwood, Jeff Esko, Fernando Gomez-Pinilla, and Fei-Fei Liu.

We hope to have many abstracts submitted relevant to glycosylation and extracellular matrix. Additional Spotlight sessions will be added to the program drawn from the submitted abstracts, allowing students, postdoctoral scholars, and other young scientists to present their work orally. Additional abstracts will be chosen for 1 min flash talks, giving the presenter an opportunity to advertise their poster during the morning

sessions. Don't miss this opportunity to have your work on the matrix highlighted for the broader ASBMB community! For more details about the conference, see https://www.asbmb.org/meeting2020/

2021 Collagen Gordon Research Seminar
July 10-11, 2021
Colby Sawyer College, NH (USA)
Chairs: Delfien Syx & Jonathan A. Roth

2021 Collagen Gordon Research Conference
July 11-16, 2021
Colby Sawyer College, NH (USA)
Chair: Taina Pihlajaniemi
Vice Chair: Douglas B. Gould
The conference chair is currently developing a list of session titles. This information will be available by September 11, 2020.

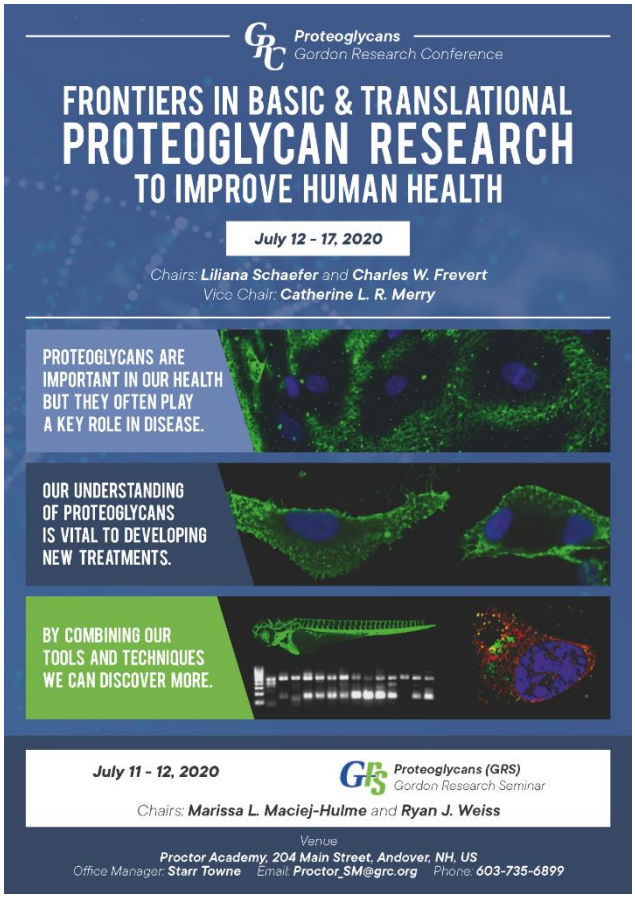
Proteoglycans GRS and GRC, July 2020, Proctor Academy, Andover, NH (USA)
Postponed to July 2022

Proteoglycans Research Seminar, July 11-12, 2020
Chairs: Marissa L. Maciej-Hulme and Ryan J. Weiss

Proteoglycans Research Conference, July 12-17, 2020
Chairs: Liliana Schaefer and Charles W. Frevert
Vice-chair: Catherine L. Merry

https://www.grc.org/proteoglycans-conference/2020/

https://www.journals.elsevier.com/matrix-biology/news/liliana-schaefer-editor-of-matrix-biology



Gordon Research Conference on Proteoglycans 2020: Cancelled… but we are frontiers in proteoglycan research in 2022 again!

Dear Matrix Biology Community,

I would like to kindly inform you due to the global coronavirus pandemic the GRC Board of Trustees has decided to officially close the 2020 Conference on Proteoglycans. This conference is rescheduled for July 2022 in Proctor Academy, NH, USA.

The 2022 conference schedule will be posted by the end of December of this year.
The current chair(s) and vice-chair(s) will remain in place and run the conference in 2022. Applications for 2022 meetings will open at the end of December of this year and you can reapply to the conference at that time.

We will write a new NIH grant to support young investigators in our field.
I would like to take the opportunity to thank all organization and companies to support our meeting. Our budget will be rescheduled for 2022.

I am very grateful to my Co-Chair Charles Frevert for his constant support. I would like to thank all formal GRC Chairs, the Advisory Committee, Chair persons, Speakers, and Participants for their advice, enthusiasm and friendship.
Anyhow this is an honor to be a Chair of the GRC twice!
With your help we will organize the 2022 GRC on Proteoglycans!

Please stay well!!

I am looking forward to give a big hug to all of you in 2022 in Proctor Academy, Andover, NH.

Best wishes,
Liliana Schaefer
Chair of the 2020 & 2022 GRC on Proteoglycans