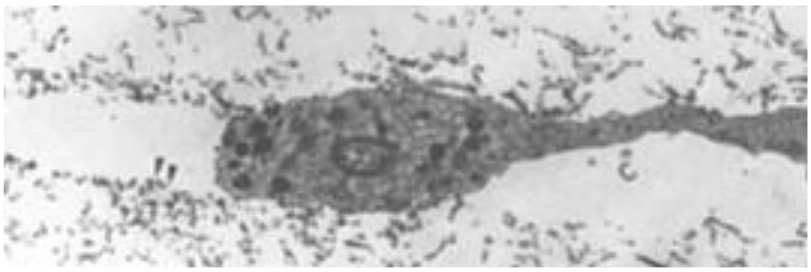


A fibroblast within a tethered lattice, after 13 days, with a cavity surrounding the cell and areas of packed collagen fibrils *(Porter et al. 1998 Wound Rep. Reg. 6: 157-166)*

ISMB NEWSLETTER 40 January 2022 Editor: Sylvie Ricard-Blum

FROM THE PRESIDENT'S DESK

Dear Fellow Matrix Biologists:

Happy New Year! Contrary to our hopes, Covid-19 continues to have a say in our lives. Like most people today, my major reactions to the pandemic are still broadly the same, i.e., a resigned acceptance of that fact coupled with guarded optimism.

It has been quite fascinating to read about the chain of research findings, some going back 50 years that led to development of the current Covid vaccines and treatments, and to listen to interviews with some of the people behind them. At the time, some of the fundamental discoveries were driven simply by curiosity and personal conviction; there was no inkling whatsoever that seemingly obscure enzymes and processes might one day offer the gift of vaccines to the world. This history emphasizes the eventual long-term value of incremental gains in knowledge and the need for a strong base of fundamental science alongside translational research. Perhaps each of us, working on specific aspects of ECM, will contribute, if even in very small ways, to future developments in medicine that will benefit many. So, let's keep at it, despite the myriad ways in which the pandemic restrains us. The work is rewarding in itself and there is also the satisfaction of knowing that we are each placing another brick in the lasting edifice of knowledge that we are building as a community.

In the context of knowledge and community, you will see on the following page a message from John Whitelock, Editor-in-Chief of the Matrix Biology journals encouraging us to submit our manuscripts to Matrix Biology and Matrix Biology Plus, and I add my voice to that call. In the past year, my group has published a research paper in each journal. We were pleased with the ease of submission and expertise of the reviews, which is not a given if a matrix-focused paper is submitted to journals with a broader mission and many competing disciplines.

With all best wishes for good health and research success in 2022,
Yours sincerely,
Suneel

Suneel Apte, President of the ISMB (aptes@ccf.org)

Content

News from Matrix Biology & Matrix Biology Plus

Dear Fellow Matrix Biologists,

Welcome to 2022, I hope that you were able to enjoy some relaxing time with families and friends over the holidays. In reflection, 2021 was another challenging year for all of us particularly students, new investigators and early to mid-career researchers due to restricted access to laboratories impacting progression of research projects.

I would like to extend a warm welcome to Hiromi Yanagisawa, Karl Kadler and Roy Zent on their recent appointments as Editors of both Matrix Biology and Matrix Biology Plus. They join Sylvie Ricard-Blum, Joanne Murphy-Ullrich and Suneel Apte who were appointed at the end of 2021. I would like to thank the Editors for their enthusiasm and commitment guiding the strategic direction of the journals.

In 2021, 319 manuscripts were submitted to Matrix Biology, of which 46 were accepted for publication. The number of submissions in 2021 was similar to that received in 2020, there was a decrease in the number of accepted publications, down from 62 in 2020. For Matrix Biology Plus, there were 54 manuscripts submitted in 2021 with 36 accepted, this represents an increase in the number of submissions, up from 29 in 2020 with 27 published.

For both journals, our aim is to increase the number of high-quality submissions received and published. To support this, we plan to grow the number of editorial board members with expertise across the fields of research and discipline areas relevant to matrix biology research. One of our focus areas in 2022 is the growth of Matrix Biology Plus, and we are aiming to generate an impact factor, which will support the future increase of submissions and growth of this journal. Therefore, we would like to encourage everybody, particularly our senior matrix biology colleagues and mentors to support this aim for Matrix Biology Plus by submitting high-quality papers that may not necessarily fit the scope for Matrix Biology.

As we embark on this new year, I would like to encourage everybody to continue sending your manuscripts to Matrix Biology and Matrix Biology Plus as well as encouraging your colleagues and collaborators to submit their work for review. Keep an eye out for our 2022 Special Issues, focusing on the Glycocalyx, the Supramolecular Structure of the ECM, and the Matrisome. We encourage ideas for future Special Issues by sending your suggestions to the Editors for consideration. Finally, I would like to extend my best wishes to you all for your on-going good health and productive research activities, hoping to see you all in person at a Matrix conference in 2022.

Best of regards,

John Whitelock
Editor-in-Chief
Matrix Biology and Matrix Biology Plus

Awards

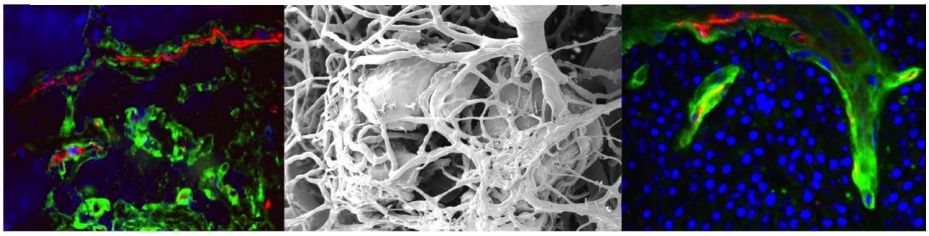
Professor Tony Weiss was awarded the Prime Minister's Prize for Innovation. The Prime Minister's Prizes for Science are Australia's most prestigious awards for outstanding achievements in scientific research, research-based innovation, and excellence in science teaching.

The University of Sydney's Professor Anthony (Tony) Weiss AM is recognised for his pioneering research and commercialisation of synthetic tropoelastin-based biomaterials, which can accelerate and improve the repair of human tissue. For the past two decades, he has pioneered global research into tropoelastin and elastic fibres, which are found in human tissue ranging from the skin to the lungs and arteries.

In 2008, he founded the company Elastagen to commercialise his research and inventions. The company raised $35 million in venture capital and grant funding, completed clinical trials and scaled-up production. Ten years later, Elastagen was sold to one of the world's biggest biopharmaceutical companies for $334 million, one of the largest transactions ever completed in Australia's life science sector.

https://www.industry.gov.au/data-and-publications/prime-ministers-prizes-for-science-2021/2021-prime-ministers-prize-for-innovation

Post-doctoral positions



The Roles of Radiotherapy on the Tumor Microenvironment

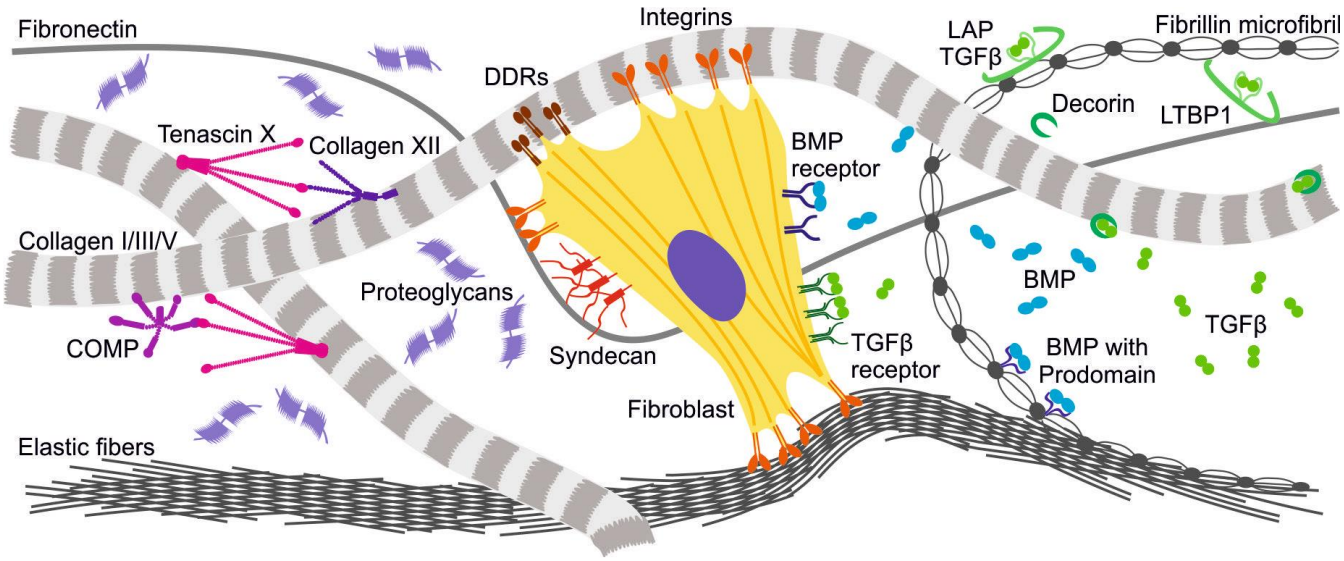
In the **Aviesan ITMO Cancer** funded project "**RADIO-3R: Understanding and REFINING the influence of RADIOtherapy on the tumor microenvironment, by applying novel models to REDUCE and REPLACE animal models"** two research laboratories in Strasbourg are collaborating in developing and applying photon 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. A major goal is to enhance on-target effects of radiotherapy with the future aim to improve immune checkpoint therapy.

A 24 months postdoc position 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*). We have demonstrated pivotal roles of tenascin-C 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, Spenle et al., 2021, Front Immunol*). We showed that tenascin-C orchestrates an immune suppressive microenvironment and established a novel concept that could explain how matrix counteracts immune checkpoint therapy by demonstrating that tenascin-C immobilizes CD8 TIL thus physically separating them from the tumor cells (*Spenlé et al., 2020, Cancer Immun Res, Murdamoothoo et al., 2021 EMBO Mol Med*). 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 **Gertraud Orend** (gertraud.orend@inserm.fr).



Postdoc position (E13) available immediately
for 3 years in the research group
Translational Matrix Biology
University of Cologne, Medical Faculty (Germany)

This position is funded within a DFG research grant focusing on the **regulation of collagen secretion and its modulation by inhibitory peptides**. The aim of the project is the development of a novel therapeutic approach to target fibrotic diseases.

We are looking for a highly motivated candidate with a solid background in molecular & cell biology and/or protein chemistry.

Interested candidates are asked to send their CV and contacts of 3 references to:

Prof. Dr. Thomas Krieg
thomas.krieg@uni-koeln.de

Spotlights on methods that other ISMB members may find useful

If you would like to feature in the next newsletter, please email Communication Group Coordinator Julia Etich (Julia.Etich@kgu.de)

In Focus

ECM PROTEOMICS

Comparison of extracellular matrix enrichment protocols for the improved characterization of the skin matrisome by mass spectrometry.

Dussoyer M, Page A, Delolme F, Rousselle P, Nyström A, Moali C. J Proteomics. 2022 Jan 16;251:104397. doi: 10.1016/j.jprot.2021.104397.

Corresponding author: catherine.moali@ibcp.fr

Abstract: *A striking feature of skin organization is that the extracellular matrix (ECM) occupies a larger volume than the cells. Skin ECM also directly contributes to aging and most cutaneous diseases. In recent years, specific ECM enrichment protocols combined with in silico approaches allowed the proteomic description of the matrisome of various organs and tumor samples. Nevertheless, the skin matrisome remains under-studied and protocols allowing the efficient recovery of the diverse ECM found in skin are still to be described. Here, we compared four protocols allowing the enrichment of ECM proteins from adult mouse back skin and found that all protocols led to a significant enrichment (up to 65%) of matrisome proteins when compared to total skin lysates. The protocols based on decellularization and solubility profiling gave the best results in terms of numbers of proteins identified and confirmed that skin matrisome proteins exhibit very diverse solubility and abundance profiles. We also report the first description of the skin matrisome of healthy adult mice that includes 236 proteins comprising 95 core matrisome proteins and 141 associated matrisome proteins. These results provide a reliable basis for future characterizations of skin ECM proteins and their dysregulations in disease-specific contexts. SIGNIFICANCE: Extracellular matrix proteins are key players in skin physiopathology and have been involved in several diseases such as genetic disorders, wound healing defects, scleroderma and skin carcinoma. However, skin ECM proteins are numerous, diverse and challenging to analyze by mass spectrometry due to the multiplicity of their post-translational modifications and to the heterogeneity of their solubility profiles. Here, we performed the thorough evaluation of four ECM enrichment protocols compatible with the proteomic analysis of mouse back skin and provide the first description of the adult mouse skin matrisome in homeostasis conditions. Our work will greatly facilitate the future characterization of skin ECM alterations in preclinical mouse models and will inspire new optimizations to analyze the skin matrisome of other species and of human clinical samples.*

Evaluation and Refinement of Sample Preparation Methods for Extracellular Matrix Proteome Coverage.

McCabe MC, Schmitt LR, Hill RC, Dzieciatkowska M, Maslanka M, Daamen WF, van Kuppevelt TH, Hof DJ, Hansen KC. Mol Cell Proteomics. 2021;20:100079. doi: 10.1016/j.mcpro.2021.100079.

Corresponding author: kirk.hansen@cuanschutz.edu

Abstract: *The extracellular matrix is a key component of tissues, yet it is underrepresented in proteomic datasets. Identification and evaluation of proteins in the extracellular matrix (ECM) has proved challenging due to the insolubility of many ECM proteins in traditional protein extraction buffers. Here we separate the decellularization and ECM extraction steps of several prominent methods for evaluation under real-world conditions. The results are used to optimize a two-fraction ECM extraction method. Approximately one dozen additional parameters are tested, and recommendations for analysis based on overall ECM coverage or specific ECM classes are given. Compared with a standard in-solution digest, the optimized method yielded a fourfold improvement in unique ECM peptide identifications.*

MODELING METASTATIC COLONIZATION IN A DECELLULARIZED ORGAN SCAFFOLD-BASED PERFUSION BIOREACTOR

Rafaeva M, Horton ER, Jensen ARD, Madsen CD, Reuten R, Willacy O, Brøchner CB, Jensen TH, Zornhagen KW, Crespo M, Grønseth DS, Nielsen SR, Idorn M, Straten PT, Rohrberg K, Spanggaard I, Højgaard M, Lassen U, Erler JT, Mayorca-Guiliani AE. Adv Healthc Mater. 2022 Jan;11(1):e2100684. doi: 10.1002/adhm.202100684.

Corresponding author: janine.erler@bric.ku.dk and alejandro.mayorca@bric.ku.dk

Abstract: *Metastatic cancer spread is responsible for most cancer-related deaths. To colonize a new organ, invading cells adapt to, and remodel, the local extracellular matrix (ECM), a network of proteins and proteoglycans underpinning all tissues, and a critical regulator of homeostasis and disease. However, there is a major lack in tools to study cancer cell behavior within native 3D ECM. Here, an in-house designed bioreactor, where mouse organ ECM scaffolds are perfused and populated with cells that are challenged to colonize it, is presented. Using a specialized bioreactor chamber, it is possible to monitor cell behavior microscopically (e.g., proliferation, migration) within the organ scaffold. Cancer cells in this system recapitulate cell signaling observed in vivo and remodel complex native ECM. Moreover, the bioreactors are compatible with co-culturing cell types of different genetic origin comprising the normal and tumor microenvironment. This degree of experimental flexibility in an organ-specific and 3D context, opens new possibilities to study cell-cell and cell-ECM interplay and to model diseases in a controllable organ-specific system ex vivo.*

DEVELOPMENT OF A BI-LAYERED CRYOGENIC ELECTROSPUN POLYLACTIC ACID SCAFFOLD TO STUDY CALCIFIC AORTIC VALVE DISEASE IN A 3D CO-CULTURE MODEL

Stadelmann K, Weghofer A, Urbanczyk M, Maulana TI, Loskill P, Jones PD, Schenke-Layland K. Acta Biomater. 2021 Nov 25:S1742-7061(21)00780-7. doi: 10.1016/j.actbio.2021.11.030.

Corresponding author: katja.schenke-layland@uni-tuebingen.de

Abstract: *Calcified aortic valve disease (CAVD) is the most prevalent valve disease in the elderly. Targeted pharmacological therapies are limited since the underlying mechanisms of CAVD are not well understood. Appropriate 3D in vitro models could potentially improve our knowledge of the disease. Here, we developed a 3D in vitro aortic heart valve model that resembles the morphology of the valvular extracellular matrix and mimics the mechanical and physiological behavior of the native aortic valve fibrosa and spongiosa. We employed cryogenic electrospinning to engineer a bi-layered cryogenic electrospun scaffold (BCES) with defined morphologies that allowed valvular endothelial cell (VEC) adherence and valvular interstitial cell (VIC) ingrowth into the scaffold. Using a self-designed cell culture insert allowed us to establish the valvular co-culture simultaneously by seeding VICs on one side and VECs on the other side of the electrospun scaffold. Proof-of-principle calcification studies were successfully performed using an established osteogenic culture protocol and the here designed 3D in vitro aortic*

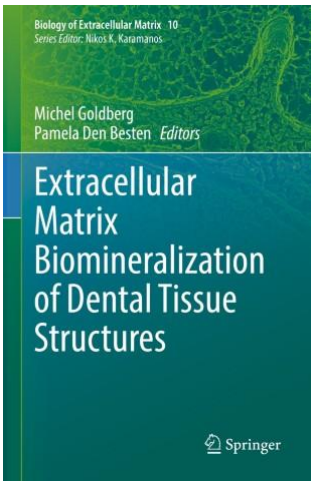
*heart valve model. STATEMENT OF SIGNIFICANCE: Three-dimensional (3D) electrospun scaffolds are widely used for soft tissue engineering since they mimic the morphology of the native extracellular matrix. Several studies have shown that cells behave more naturally on 3D materials than on the commonly used stiff two-dimensional (2D) cell culture substrates, which have no biological properties. As appropriate 3D models for the study of aortic valve diseases are limited, we developed a novel bi-layered 3D in vitro test system by using the versatile technique of cryogenic electrospinning in combination with the influence of different solvents to mimic the morphology, mechanical, and cellular distribution of a native aortic heart valve leaflet. This 3D in vitro model can be used to study valve biology and heart valve-impacting diseases such as calcification to elucidate therapeutic targets***.***

Books & Special Issues on the Extracellular Matrix

PUBLISHED

The "Biology of Extracellular Matrix" book series "**Extracellular Matrix Biomineralization of Dental Tissue Structures**", edited by Michel Goldberg and Pamela Den Besten, Springer

- Explores the structural and biological properties of dental and peridental tissue structures
- Presents the molecular mechanisms of dental tissue biomineralization and tissue turnover
- Elaborates on environmental factors causing enamel defects



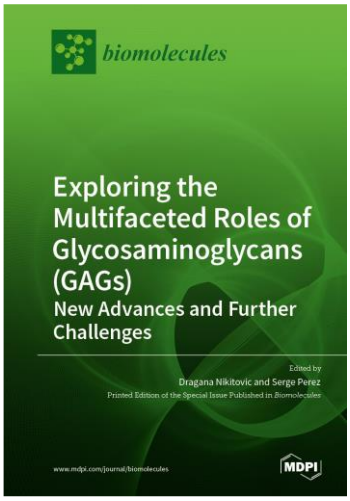
DOI https://doi.org/10.1007/978-3-030-76283-4

Both the electronic version and the hardcover edition are now available. **The coupon code "ISMB40" for ISMB members is already valid for both versions as well.**

Exploring the Multifaceted Roles of Glycosaminoglycans (GAGs) - New Advances and Further Challenges

Edited By: Dragana Nikitovic & Serge Perez

mdpi.com/books/pdfview/book/4762
ISBN 978-3-0365-2677-5 (Hbk)
ISBN 978-3-0365-2676-8 (PDF)

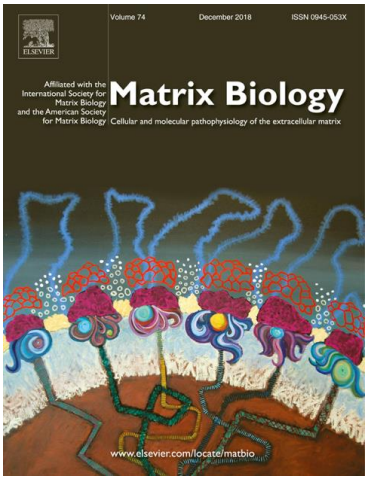


Glycosaminoglycans are linear, anionic polysaccharides (GAGs) consisting of repeating disaccharides. GAGs are ubiquitously localized throughout the extracellular matrix (ECM) and to the cell membranes of cells in all tissues. They are either conjugated to protein cores in the form of proteoglycans, e.g., chondroitin/dermatan sulfate (CS/DS), heparin/heparan sulfate (Hep/HS) and keratan sulfate (KS), as well as non-sulfated hyaluronan (HA). By modulating biological signaling GAGs participate in the regulation of homeostasis and also participate in disease progression. The book, entitled "Exploring the multifaceted roles of glycosaminoglycans (GAGs)—new advances and further challenges", features original research and review articles. These articles cover several GAG-related timely topics in structural biology and imaging; morphogenesis, cancer, and other disease therapy and drug developments; tissue engineering; and metabolic engineering. This book also includes an article illustrating how metabolic engineering can be used to create the novel chondroitin-like polysaccharide. A prerequisite for communicating in any discipline and across disciplines is familiarity with the appropriate terminology. Several nomenclature rules exist in the field of biochemistry. The historical description of GAGs follows IUPAC and IUB nomenclature. New structural depictions such as the structural nomenclature for glycan and their translation into machine-readable formats have opened the route for cross-references with popular bioinformatics resources and further connections with other exciting "omics" fields.

ON GOING

Beyond the Matrisome: New Frontiers in ECM Research A Special Issue of *Matrix Biology*

Edited by Alexandra Naba & Suneel Apte



2021 marks a decade since conception and delineation of the matrisome, which provided a road map for extracellular matrix research. To start the next decade, Matrix Biology will host a Special Issue titled "Beyond the Matrisome: New Frontiers in ECM Research" guest-edited by Alexandra Naba and Suneel Apte.
The overall goal of the Special Issue is a forward-looking view of the matrisome illustrated by state-of-the-art invited reviews and conceptually novel and preferably mechanistic research articles.

Research articles submitted for consideration for the Special Issue can span the full band-width of -omic applications for mechanistic ECM research, new developments in understanding molecular networks within the ECM, or mechanistic studies on ECM molecules and complexes, covering the breadth of the field from fundamental molecular sciences to applications to development, diseases and tissue engineering. Matrix Biology invites you to contribute a research article for this upcoming Special Issue, offering the quality, visibility and impact that you would expect from the flagship journal in ECM research, combined with the convenience and reach of open access. Articles are published online, quickly after acceptance, and constantly so there are no print delays or long waits for publication. The deadline for manuscript submission for consideration for the Special Issue is January 31, 2022.

Manuscripts judged on initial review by the special issue co-editors to not fit well with the intended scope of the issue will be redirected into the regular manuscript stream of Matrix Biology.

Please remember the following items:

- Please make sure that you select the name of the Special Issue when you upload your manuscript: Please, mention this on the top of your cover letter as well:
- Include the names and emails of four potential expert reviewers. All the manuscripts will be peer-reviewed.
- Please follow the recommended Matrix Biology style.
- Include the mandatory Highlights, in bullet form with 87 characters maximum.

Thank you very much in advance for your contribution to this special issue of Matrix Biology.

Best wishes.

Alexandra Naba, PhD, University of Illinois-Chicago, USA
Suneel S. Apte, MBBS, DPhil, Cleveland Clinic Lerner Research Institute., Cleveland, USA

Deciphering the role of proteoglycans and glycosaminoglycans in health and disease

American Journal of Physiology-Cell Physiology - Special Collection Coming June 2022

Guest Editor: Liliana Schaefer, MD, AJP-Cell Physiology Editor-in-Chief

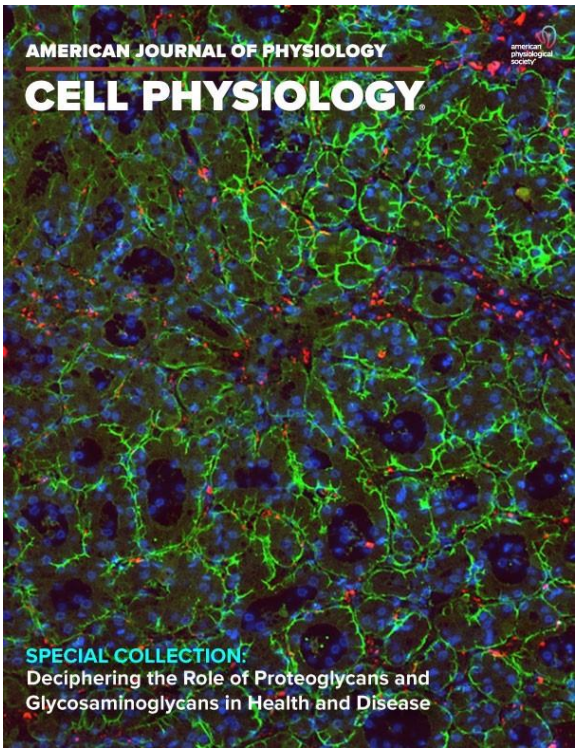
This upcoming *AJP-Cell Physiology* special collection will feature a series of invited reviews discussing recent advances in proteoglycans and glycosaminoglycans.

Proteoglycans are biologically active components of the extracellular matrix. They consist of a specific protein core that is post-translationally modified and covalently linked with linear glycosaminoglycans. These glycosaminoglycans consist of repeating disaccharides.

An emerging body of evidence indicates that secreted proteoglycans act as signaling molecules in addition to their canonical function in maintaining and regulating the architecture of various extracellular matrices.

See the full description and learn how to submit your review proposal today: bit.ly/AJPCellProteoglycans

@AJPCellPhys



The winning image that will serve as the cover for the proteoglycans special collection later this year in AJP-Cell Physiology (https://bit.ly/AJPCellProteoglycans). **The image was created by Ilona Kovalszky, Professor of Pathology, Semmelweis University (Budapest, Hungary).** The fluorescent immunohistochemical picture depicts a hepatocellular carcinoma, with syndecan-1 positivity on the surface of tumor cells (green) and macrophages in the tumor stroma (red). Nuclei are shown by DAPI (blue).

Extracellular matrix the dynamic structural & functional network in health and disease
IUBMB Life Special issue

Guest editors: Nikos Karamanos (University of Patras, Greece), Sylvie Ricard-Blum (University of Lyon, France), and Dimitris Kletsas (National Center for Scientific Research Demokritos, Athens, Greece)

Scope of the issue: Extracellular matrices (ECMs), as dynamic 3 -dimensional networks of macromolecules, play key roles in structural organization, cell-cell and cell-matrix interactions affecting cell properties, gene expression, tissue remodeling and cell signaling and therefore are implicated in several pathophysiological processes. Cell prolife ration, differentiation, migration, angiogenesis and autophagy are among cell processes regulated by ECM macromolecules. Better knowledge on how ECM modulates cell functions could be used for pharmacologically targeting ECMin diseases including cancer, cardiovascular disease and immune-related disorders.

We invite investigators to contribute original research articles that address the ECM as a key player in health and disease, in cell functional properties and behavior, in disease diagnosis and pharmacological targeting/treatment approaches, as well as in bioengineering and biotechnology. Themes related to development, evolution, tumor biology, therapeutics, -omics and aging are also welcomed. Research approaches could address either ECM networks or macromo lecules such as collagens, proteoglycans, glycosaminoglycans, integrins, cell-matrix receptors, matrix-degrading and modifying enzymes and matrix-related proteins/glycoproteins. Critical reviews in areas not recently covered are also welcomed upon invitation or approval of proposals by the guest editors.

Topics: Suggested potential topics include but are not limited to the following:
1. ECM composition and structural organization in health and disease
2. Cell communication approaches: cell-cell and cell-matrix interactions
3. Regulatory role of ECM in various pathological conditions
4. Tumor microenvironment, stromal cells and ECM in cancer
5. The role of ECM in cell signaling and functional properties
6. Therapeutic strategies based on pharmaceuticaltargeting
7. ECM-based biotechnological approaches in disease treatment

The issue is scheduled for publication in summer 2022. Manuscripts should be submitted by 28 February 2022. Upon acceptance, the manuscripts will appear online and be citable within 3-4 days. Expected issue publication will be September, 2022

Submit your manuscript through the IUBMB Life ScholarOne site at https://mc.manuscriptcentral.com/tbmb During the submission process you will be asked if your manuscript is for a special issue. From the dropdown menu, please select “Extracellular matrix”. If you have questions about topic suitability, please contact Guest Editor Nikos Karamanos (n.k.karamanos@upatras.gr). For questions about manuscript submission, contact the IUBMB Life Special Issues Editor, Gwen Taylor (gtaylor@wiley.com)
https://iubmb.onlinelibrary.wiley.com/journal/15216551

International travel grants

ISMB provides international travel grants (on average 500 € for young scientists (graduate students or postdocs up to 5 years after Ph.D.) to allow them to attend major meetings in matrix biology anywhere in the world. While priority will be given to meetings directly supported by ISMB (including Matrix Biology Europe, the American Society for Matrix Biology and the Pan Pacific Connective Tissue Societies Symposium), applications are accepted for any meeting, provided that the scope of the meeting agrees with the aims of the Society.

In the current context of the COVID-19 pandemic, applications for on-line, hybrid and in-person meetings will all be considered.

To apply for a travel grant, please send your application to the ISMB secretary, in the form of a single pdf file containing: (1) a letter giving information about the meeting, the amount requested and a detailed justification for support, (2) the abstract of your poster/short talk, (3) your curriculum vitae and list of publications.

Please apply several months in advance of the meeting, before one of the following deadlines: January 1, April 1, July 1, October 1.

Candidates should be members of the ISMB (see membership page for details), and a graduate student or postdoc. up to 5 years after Ph.D., (with extensions for maternity leave, military service, etc). Grants are for international travel only and will be awarded on the basis of scientific excellence and relevance to matrix biology. Successful candidates will be notified no more than one month after each deadline. Following the meeting, awardees will be expected to send to the ISMB a certificate of attendance as well as a short report (to appear on the ISMB web site with some selected for the ISMB newsletter) in the form of a personal perspective on their experience at the meeting. All reimbursement claims and reports must be received within 3 months after the end of the conference.

Recent publications

Multi-modal Profiling of the Extracellular Matrix of Human Fallopian Tubes and Serous Tubal Intraepithelial Carcinomas. Renner C, Gomez C, Visetsouk MR, Taha I, Khan A, McGregor SM, Weisman P, Naba A, Masters KS, Kreeger PK. J Histochem Cytochem. 2021 Dec 5:221554211061359. https://doi.org/10.1369/00221554211061359

Corresponding authors: : kreeger@wisc.edu, kmasters@wisc.edu, anaba@uic.edu

Abstract: *Recent evidence supports the fimbriae of the fallopian tube as one origin site for high-grade serous ovarian cancer (HGSOC). The progression of many solid tumors is accompanied by changes in the microenvironment, including alterations of the extracellular matrix (ECM). Therefore, we sought to determine the ECM composition of the benign fallopian tube and changes associated with serous tubal intraepithelial carcinomas (STICs), precursors of HGSOC. The ECM composition of benign human fallopian tube was first defined from a meta-analysis of published proteomic datasets that identified 190 ECM proteins. We then conducted de novo proteomics using ECM enrichment and identified 88 proteins, 7 of which were not identified in prior studies (COL2A1, COL4A5, COL16A1, elastin, LAMA5, annexin A2, and PAI1). To enable future in vitro studies, we investigated the levels and localization of ECM components included in tissue-engineered models (type I, III, and IV collagens, fibronectin, laminin, versican, perlecan, and hyaluronic acid) using multispectral immunohistochemical staining of fimbriae from patients with benign conditions or STICs. Quantification revealed an increase in stromal fibronectin and a decrease in epithelial versican in STICs. Our results provide an in-depth picture of the ECM in the benign fallopian tube and identified ECM changes that accompany STIC format.*

Serglycin Is Involved in Adipose Tissue Inflammation in Obesity. Doncheva AI, Norheim FA, Hjorth M, Grujic M, Paivandy A, Dankel SN, Hertel JK, Valderhaug TG, Böttcher Y, Fernø J, Mellgren G, Dalen KT, Pejler G, Kolset SO. J. Immunol. 2022, 208121-132. doi: 10.4049/jimmunol.2100231.

Corresponding authors: s.o.kolset@medisin.uio.no

Abstract: *Chronic local inflammation of adipose tissue is an important feature of obesity. Serglycin is a proteoglycan highly expressed by various immune cell types known to infiltrate adipose tissue under obese*

conditions. To investigate if serglycin expression has an impact on diet-induced adipose tissue inflammation, we subjected Srgn +/+ and Srgn -/- mice (C57BL/6J genetic background) to an 8-wk high-fat and high-sucrose diet. The total body weight was the same in Srgn +/+ and Srgn -/- mice after diet treatment. Expression of white adipose tissue genes linked to inflammatory pathways were lower in Srgn -/- mice. We also noted reduced total macrophage abundance, a reduced proportion of proinflammatory M1 macrophages, and reduced formation of crown-like structures in adipose tissue of Srgn -/- compared with Srgn +/+ mice. Further, Srgn -/- mice had more medium-sized adipocytes and fewer large adipocytes. Differentiation of preadipocytes into adipocytes (3T3-L1) was accompanied by reduced Srgn mRNA expression. In line with this, analysis of single-cell RNA sequencing data from mouse and human adipose tissue supports that Srgn mRNA is predominantly expressed by various immune cells, with low expression in adipocytes. Srgn mRNA expression was higher in obese compared with lean humans and mice, accompanied by an increased expression of immune cell gene markers. SRGN and inflammatory marker mRNA expression was reduced upon substantial weight loss in patients after bariatric surgery. Taken together, this study introduces a role for serglycin in the regulation of obesity-induced adipose inflammation.

Multiscale modelling of the extracellular matrix

Wong H, Crowet JM, Dauchez M, Ricard-Blum S, Baud S, Belloy N. Matrix Biology Plus volume 13, February 2022 doi: 10.1016/j.mbplus.2021.100096

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Abstract: *The extracellular matrix is a complex three-dimensional network of molecules that provides cells with a complex microenvironment. The major constituents of the extracellular matrix such as collagen, elastin and associated proteins form supramolecular assemblies contributing to its physicochemical properties and organization. The structure of proteins and their supramolecular assemblies such as fibrils have been studied at the atomic level (e.g., by X-ray crystallography, Nuclear Magnetic Resonance and cryo-Electron Microscopy) or at the microscopic scale. However, many protein complexes are too large to be studied at the atomic level and too small to be studied by microscopy. Most extracellular matrix components fall into this intermediate scale, so-called the mesoscopic scale, preventing their detailed characterization. Simulation and modelling are some of the few powerful and promising approaches that can deepen our understanding of mesoscale systems. We have developed a set of modelling tools to study the self-organization of the extracellular matrix and large motion of macromolecules at the mesoscale level by taking advantage of the dynamics of articulated rigid bodies as a mean to study a larger range of motions at the cost of atomic resolution.*

Raman Imaging and Fluorescence Lifetime Imaging Microscopy for Diagnosis of Cancer State and Metabolic Monitoring.

Becker L, Janssen N, Layland SL, Mürdter TE, Nies AT, Schenke-Layland K, Marzi J. Cancers (Basel). 2021 Nov 13;13(22):5682. doi: 10.3390/cancers13225682.

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Abstract: *Hurdles for effective tumor therapy are delayed detection and limited effectiveness of systemic drug therapies by patient-specific multidrug resistance. Non-invasive bioimaging tools such as fluorescence lifetime imaging microscopy (FLIM) and Raman-microspectroscopy have evolved over the last decade, providing the potential to be translated into clinics for early-stage disease detection, in vitro drug screening, and drug efficacy studies in personalized medicine. Accessing tissue- and cell-specific spectral signatures, Raman microspectroscopy has emerged as a diagnostic tool to identify precancerous lesions, cancer stages, or cell malignancy. In vivo Raman measurements have been enabled by recent technological advances in Raman endoscopy and signal-enhancing*

setups such as coherent anti-stokes Raman spectroscopy or surface-enhanced Raman spectroscopy. FLIM enables in situ investigations of metabolic processes such as glycolysis, oxidative stress, or mitochondrial activity by using the autofluorescence of co-enzymes NADH and FAD, which are associated with intrinsic proteins as a direct measure of tumor metabolism, cell death stages and drug efficacy. The combination of non-invasive and molecular-sensitive in situ techniques and advanced 3D tumor models such as patient-derived organoids or microtumors allows the recapitulation of tumor physiology and metabolism in vitro and facilitates the screening for patient-individualized drug treatment options.

New insights into the phosphorylation of the threonine motif of the β1 integrin cytoplasmic domain.
Böttcher RT, Strohmeyer N, Aretz J, Fässler R. Life Sci Alliance. 2022 Jan 7;5(4):e202101301. doi: 10.26508/lsa.202101301.
Corresponding author: faessler@biochem.mpg.de
Abstract: *Integrins require an activation step before ligand binding and signaling that is mediated by talin and kindlin binding to the β integrin cytosolic domain (β-tail). Conflicting reports exist about the contribution of phosphorylation of a conserved threonine motif in the β1-tail (β1-pT788/pT789) to integrin activation. We show that widely used and commercially available antibodies against β1-pT788/pT789 integrin do not detect specific β1-pT788/pT789 integrin signals in immunoblots of several human and mouse cell lysates but bind bi-phosphorylated threonine residues in numerous proteins, which were identified by mass spectrometry experiments. Furthermore, we found that fibroblasts and epithelial cells expressing the phospho-mimicking β1-TT788/789DD integrin failed to activate β1 integrins and displayed reduced integrin ligand binding, adhesion initiation and cell spreading. These cellular defects are specifically caused by the inability of kindlin to bind β1-tail polypeptides carrying a phosphorylated threonine motif or phospho-mimicking TT788/789DD substitutions. Our findings indicate that the double-threonine motif in β1-class integrins is not a major phosphorylation site but if phosphorylated would curb integrin function.*

The Role of Decorin and Biglycan Signaling in Tumorigenesis.
Diehl V, Huber LS, Trebicka J, Wygrecka M, Iozzo RV, Schaefer L. Front Oncol. 2021 Nov 30;11:801801. doi: 10.3389/fonc.2021.801801.
Corresponding author: schaefer@med.uni-frankfurt.de
Abstract: *The complex and adaptive nature of malignant neoplasm constitute a major challenge for the development of effective anti-oncogenic therapies. Emerging evidence has uncovered the pivotal functions exerted by the small leucine-rich proteoglycans, decorin and biglycan, in affecting tumor growth and progression. In their soluble forms, decorin and biglycan act as powerful signaling molecules. By receptor-mediated signal transduction, both proteoglycans modulate key processes vital for tumor initiation and progression, such as autophagy, inflammation, cell-cycle, apoptosis, and angiogenesis. Despite of their structural homology, these two proteoglycans interact with distinct cell surface receptors and thus modulate distinct signaling pathways that ultimately affect cancer development. In this review, we summarize growing evidence for the complex roles of decorin and biglycan signaling in tumor biology and address potential novel therapeutic implications.*

Lipidome profiling with Raman microspectroscopy identifies macrophage response to surface topographies of implant materials.

Feuerer N, Marzi J, Brauchle EM, Carvajal Berrio DA, Billing F, Weiss M, Jakobi M, Schneiderhan-Marra N, Shipp C, Schenke-Layland K. Proc Natl Acad Sci U S A. 2021 Dec 28;118(52):e2113694118. doi: 10.1073/pnas.2113694118.

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Abstract: *Biomaterial characteristics such as surface topographies have been shown to modulate macrophage phenotypes. The standard methodologies to measure macrophage response to biomaterials are marker-based and invasive. Raman microspectroscopy (RM) is a marker-independent, noninvasive technology that allows the analysis of living cells without the need for staining or processing. In the present study, we analyzed human monocyte-derived macrophages (MDMs) using RM, revealing that macrophage activation by lipopolysaccharides (LPS), interferons (IFN), or cytokines can be identified by lipid composition, which significantly differs in M0 (resting), M1 (IFN-γ/LPS), M2a (IL-4/IL-13), and M2c (IL-10) MDMs. To identify the impact of a biomaterial on MDM phenotype and polarization, we cultured macrophages on titanium disks with varying surface topographies and analyzed the adherent MDMs with RM. We detected surface topography-induced changes in MDM biochemistry and lipid composition that were not shown by less sensitive standard methods such as cytokine expression or surface antigen analysis. Our data suggest that RM may enable a more precise classification of macrophage activation and biomaterial-macrophage interaction.*

Dystrophic Epidermolysis Bullosa: Secondary Disease Mechanisms and Disease Modifiers.

Nyström A, Bruckner-Tuderman L, Kiritsi D. Front Genet. 2021 Sep 28;12:737272. doi: 10.3389/fgene.2021.737272.

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Abstract: *The phenotypic presentation of monogenetic diseases is determined not only by the nature of the causative mutations but also is influenced by manifold cellular, microenvironmental, and external factors. Here, heritable extracellular matrix diseases, including dystrophic epidermolysis bullosa (DEB), are no exceptions. Dystrophic epidermolysis bullosa is caused by mutations in the COL7A1 gene encoding collagen VII. Deficiency of collagen VII leads to skin and mucosal fragility, which progresses from skin blistering to severe fibrosis and cancer. Clinical and pre-clinical studies suggest that targeting of secondary disease mechanisms or employment of natural disease modifiers can alleviate DEB severity and progression. However, since many of these mechanisms are needed for tissue homeostasis, informed, selective targeting is essential for safe and efficacious treatment. Here, we discuss a selection of key disease modifiers and modifying processes active in DEB, summarize the still scattered knowledge of them, and reflect on ways forward toward their utilization for symptom-relief or enhancement of curative therapies.*

Systemic Collagen VII Replacement Therapy for Advanced Recessive Dystrophic Epidermolysis Bullosa.

Gretzmeier C, Pin D, Kern JS, Chen M, Woodley DT, Bruckner-Tuderman L, de Souza MP, Nyström A. J Invest Dermatol. 2021 Oct 2:S0022-202X(21)02273-9. doi: 10.1016/j.jid.2021.09.008.

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Abstract: *Recessive dystrophic epidermolysis bullosa (RDEB) is a genetic skin blistering disease associated with progressive multiorgan fibrosis. RDEB is caused by biallelic mutations in COL7A1 encoding the extracellular matrix protein collagen VII (C7), which is necessary for epidermal–dermal adherence. C7 is not simply a structural protein but also has multiple functions, including the regulation of TGFβ bioavailability and the inhibition of skin scarring. Intravenous (IV) administration of recombinant C7 (rC7) rescues C7-deficient mice from neonatal lethality. However, the effect on established RDEB has not been determined. In this study, we used small and large adult*

RDEB animal models to investigate the disease-modulating abilities of IV rC7 on established RDEB. In adult RDEB mice, rC7 accumulated at the basement membrane zone in multiple organs after a single infusion. Fortnightly IV injections of rC7 for 7 weeks in adult RDEB mice reduced fibrosis of skin and eye. The fibrosis-delaying effect was associated with a reduction of TGFβ signaling. IV rC7 in adult RDEB dogs incorporated in the dermal–epidermal junction of skin and improved disease by promoting wound healing and reducing dermal–epidermal separation. In both species, IV C7 was well-tolerated. These preclinical studies suggest that repeated IV administration of rC7 is an option for systemic treatment of established adult RDEB.

The cell cycle-related genes RHAMM, AURKA, TPX2, PLK1, and PLK4 are associated with the poor prognosis of breast cancer patients.

Kahl I, Mense J, Finke C, Boller AL, Lorber C, Győrffy B, Greve B, Götte M, Espinoza-Sánchez NA. J Cell Biochem. 2022 Jan 10. doi: 10.1002/jcb.30205.

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Abstract: *Breast cancer is the third most common type of cancer diagnosed. Cell cycle is a complex but highly organized and controlled process, in which normal cells sense mitogenic growth signals that instruct them to enter and progress through their cell cycle. This process culminates in cell division generating two daughter cells with identical amounts of genetic material. Uncontrolled proliferation is one of the hallmarks of cancer. In this study, we analyzed the expression of the cell cycle-related genes receptor for hyaluronan (HA)-mediated motility (RHAMM), AURKA, TPX2, PLK1, and PLK4 and correlated them with the prognosis in a collective of 3952 breast cancer patients. A high messenger RNA expression of all studied genes correlated with a poor prognosis. Stratifying the patients according to the expression of hormonal receptors, we found that in patients with estrogen and progesterone receptor-positive and human epithelial growth factor receptor 2-negative tumors, and Luminal A and Luminal B tumors, the expression of the five analyzed genes correlates with worse survival. qPCR analysis of a panel of breast cancer cell lines representative of major molecular subtypes indicated a predominant expression in the luminal subtype. In vitro experiments showed that radiation influences the expression of the five analyzed genes both in luminal and triple-negative model cell lines. Functional analysis of MDA-MB-231 cells showed that small interfering RNA knockdown of PLK4 and TPX2 and pharmacological inhibition of PLK1 had an impact on the cell cycle and colony formation. Looking for a potential upstream regulation by microRNAs, we observed a differential expression of RHAMM, AURKA, TPX2, PLK1, and PLK4 after transfecting the MDA-MB-231 cells with three different microRNAs. Survival analysis of miR-34c-5p, miR-375, and miR-142-3p showed a different impact on the prognosis of breast cancer patients. Our study suggests that RHAMM, AURKA, TPX2, PLK1, and PLK4 can be used as potential targets for treatment or as a prognostic value in breast cancer patients.*

Loss of endothelial cell MMP14 reduces melanoma growth and metastasis by increasing tumor vessel stability.

Kümper M, Hessenthaler S, Zamek J, Niland S, Pach E, Mauch C, Zigrino P. J Invest Dermatol. 2021 Dec 27:S0022-202X(21)02633-6. doi: 10.1016/j.jid.2021.12.016.

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Abstract: *MMMP14 belongs to a large family of zinc-dependent endopeptidases and plays a critical role in skin physiological and pathological processes. Complete loss of the protease resulted in severe developmental defects leading to early death. However, because of the premature death of the mice, the functional significance for endothelial cell expression of MMP14 in skin physiology and pathology in vivo postnatal is yet unknown. Using a mouse model with constitutive endothelial cell-specific deletion of MMP14 ($MMP14^{EC-/-}$), we demonstrated that*

mice developed and bred normal, but melanoma growth and metastasis were reduced. While vascularity was unaltered, vessel permeability was decreased. Deletion of MMP14 in ECs led to increased vessel coverage by pericytes and VE-cadherin expression in mice in vivo and in vitro, but not human ECs. eNOS expression and nitric oxide production were significantly reduced in MMP14$^{EC-/-}$ ECs and MMP14-silenced HUVECs. A direct correlation between eNOS and MMP14 expression was detected in intratumoral vessels of human malignant melanomas. Altogether, we show that endothelial MMP14 controls tumor vessel function during melanoma growth. These data suggest that EC-MMP14 direct targeting alone or with vascular stabilizing agents may be therapeutically crucial in inhibiting melanoma growth and metastasis.

Matrix Metalloproteinases Shape the Tumor Microenvironment in Cancer Progression.
Niland S, Riscanevo AX, Eble JA. Int J Mol Sci. 2021 Dec 23;23(1):146. doi: 10.3390/ijms23010146.
Corresponding author: nilands@uni-muenster.de
Abstract: *Cancer progression with uncontrolled tumor growth, local invasion, and metastasis depends largely on the proteolytic activity of numerous matrix metalloproteinases (MMPs), which affect tissue integrity, immune cell recruitment, and tissue turnover by degrading extracellular matrix (ECM) components and by releasing matrikines, cell surface-bound cytokines, growth factors, or their receptors. Among the MMPs, MMP-14 is the driving force behind extracellular matrix and tissue destruction during cancer invasion and metastasis. MMP-14 also influences both intercellular as well as cell-matrix communication by regulating the activity of many plasma membrane-anchored and extracellular proteins. Cancer cells and other cells of the tumor stroma, embedded in a common extracellular matrix, interact with their matrix by means of various adhesive structures, of which particularly invadopodia are capable to remodel the matrix through spatially and temporally finely tuned proteolysis. As a deeper understanding of the underlying functional mechanisms is beneficial for the development of new prognostic and predictive markers and for targeted therapies, this review examined the current knowledge of the interplay of the various MMPs in the cancer context on the protein, subcellular, and cellular level with a focus on MMP14*.

Extracellular Matrix Remodeling by Fibroblast-MMP14 Regulates Melanoma Growth.
Pach E, Kümper M, Fromme JE, Zamek J, Metzen F, Koch M, Mauch C, Zigrino P. Int J Mol Sci. 2021 Nov 12;22(22):12276. doi: 10.3390/ijms222212276.
Corresponding author: paola.zigrino@uni-koeln.de
Abstract: *Maintaining a balanced state in remodeling the extracellular matrix is crucial for tissue homeostasis, and this process is altered during skin cancer progression. In melanoma, several proteolytic enzymes are expressed in a time and compartmentalized manner to support tumor progression by generating a permissive environment. One of these proteases is the matrix metalloproteinase 14 (MMP14). We could previously show that deletion of MMP14 in dermal fibroblasts results in the generation of a fibrotic-like skin in which melanoma growth is impaired. That was primarily due to collagen I accumulation due to lack of the collagenolytic activity of MMP14. However, as well as collagen I processing, MMP14 can also process several extracellular matrices. We investigated extracellular matrix alterations occurring in the MMP14-deleted fibroblasts that can contribute to the modulation of melanoma growth. The matrix deposited by cultured MMP14-deleted fibroblast displayed an antiproliferative and anti-migratory effect on melanoma cells in vitro. Analysis of the secreted and deposited-decellularized fibroblast's matrix identified a few altered proteins, among which the most significantly changed was collagen*

XIV. This collagen was increased because of post-translational events, while de novo synthesis was unchanged. Collagen XIV as a substrate was not pro-proliferative, pro-migratory, or adhesive, suggesting a negative regulatory role on melanoma cells. Consistent with that, increasing collagen XIV concentration in wild-type fibroblast-matrix led to reduced melanoma proliferation, migration, and adhesion. In support of its anti-tumor activity, enhanced accumulation of collagen XIV was detected in peritumoral areas of melanoma grown in mice with the fibroblast's deletion of MMP14. In advanced human melanoma samples, we detected reduced expression of collagen XIV compared to benign nevi, which showed a robust expression of this molecule around melanocytic nests. This study shows that loss of fibroblast-MMP14 affects melanoma growth through altering the peritumoral extracellular matrix (ECM) composition, with collagen XIV being a modulator of melanoma progression and a new proteolytic substrate to MMP14.

Hedgehog lipids: Promotors of alternative morphogen release and signaling?: Conflicting findings on lipidated Hedgehog transport and signaling can be explained by alternative regulated mechanisms to release the morphogen.

Manikowski D, Ehring K, Gude F, Jakobs P, Froese J, Grobe K. Bioessays. 2021 Nov;43(11):e2100133. doi: 10.1002/bies.202100133.

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Abstract: *Two posttranslational lipid modifications present on all Hedgehog (Hh) morphogens-an N-terminal palmitate and a C-terminal cholesterol-are established and essential regulators of Hh biofunction. Yet, for several decades, the question of exactly how both lipids contribute to Hh signaling remained obscure. Recently, cryogenic electron microscopy revealed different modes by which one or both lipids may contribute directly to Hh binding and signaling to its receptor Patched1 (Ptc). Some of these modes demand that the established release factor Dispatched1 (Disp) extracts dual-lipidated Hh from the cell surface, and that another known upstream signaling modulator called Scube2 chaperones the dual-lipidated morphogen to Ptc. By mechanistically and biochemically aligning this concept with established in vivo and recent in vitro findings, this reflection identifies remaining questions in lipidated Hh transport and evaluates additional mechanisms of Disp- and Scube2-regulated release of a second bioactive Hh fraction that has one or both lipids removed.*

MiR-181a Targets RSPO2 and Regulates Bone Morphogenetic Protein - WNT Signaling Crosstalk During Chondrogenic Differentiation of Mesenchymal Stromal Cells.

Melnik S, Hofmann N, Gabler J, Hecht N, Richter W. Front Cell Dev Biol. 2021 Oct 29;9:747057. doi: 10.3389/fcell.2021.747057.

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Abstract: *Mechanisms of WNT and bone morphogenetic protein (BMP) signaling crosstalk is in the focus of multiple biological studies, and it also has been discovered to play important roles in human mesenchymal stromal cells (MSC) that are of great interest for neocartilage engineering due to their high chondrogenic differentiation potential. However, MSC-derived chondrocytes undergo hypertrophic degeneration that impedes their clinical application for cartilage regeneration. In our previous study, we established that several microRNAs (miRs) are differentially expressed between articular chondrocytes (AC) - and MSC-derived neocartilage, with miR-181a being the most prominent candidate as key microRNA involved in the regulation of a balance between chondral and endochondral differentiation. The aim of this study was the identification of precise mRNA targets and signaling pathways regulated by miR-181a in MSC during chondrogenesis. MiR-181a was upregulated during chondrogenesis of MSC, along with an increase of the hypertrophic phenotype in resulting cartilaginous tissue. By*

in silico analysis combined with miR reporter assay, the WNT signaling activator and BMP signaling repressor RSPO2 was suggested as a target of miR-181a. Further validation experiments confirmed that miR-181a targets RSPO2 mRNA in MSC. It was found that in human MSC miR-181a activated BMP signaling manifested by the accumulation of SOX9 protein and increased phosphorylation of SMAD1/5/9. These effects, together with the concomitant reduction of canonical WNT signaling induced by miR-181a mimic, were in accordance with the effects expected by the loss of RSPO2, thus indicating the causative link between miR-181a and RSPO2. Moreover, we observed that a tight correlation between miR-181a and miR-218 expression levels in healthy human cartilage tissue was disrupted in osteoarthritis (OA) highlighting the importance of the WNT-BMP signaling crosstalk for preventing OA.

Hyaluronic Acid-Functionalized Hybrid Gelatin-Poly-L-Lactide Scaffolds with Tunable Hydrophilicity.
Piccirillo G, Feuerer N, Carvajal Berrio DA, Layland SL, Reimer Hinderer S, Bochicchio B, Schenke-Layland K. Tissue Eng Part C Methods. 2021 Nov;27(11):589-604. doi: 10.1089/ten.TEC.2021.0178.
Corresponding author: katja.schenke-layland@uni-tuebingen.de
Abstract: *In this study, we describe the production of hybrid gelatin-poly-L-lactide electrospun scaffolds whose hydrophilicity was controlled by binding increasing concentrations of hyaluronic acid (HA). We show that cross-linking has advantages over coating when aiming to functionalize the scaffolds with HA. The here described scaffolds structurely mimicked the complexity of the extracellular matrix, and when excited by second harmonic generation, they produced a signal that is typical of collagen-containing biological fibers. Fluorescence lifetime imaging microscopy (FLIM) was used to marker-independently monitor the growth of human dermal fibroblasts on the electrospun scaffolds using reduced (phosphorylated) nicotinamide adenine dinucleotide as target. Benefitting from the different fluorescence lifetimes of the polymer and the endogenous cellular fluorophore, we were able to distinguish and separate the signals produced by the cells from the signals generated by the electrospun scaffolds. FLIM further allowed the detection of metabolic differences in the cells seeded on the HA-functionalized scaffolds compared with cells that were cultured on nonfunctionalized control scaffolds.*

ER Stress in ERp57 Knockout Knee Joint Chondrocytes Induces Osteoarthritic Cartilage Degradation and Osteophyte Formation.
Rellmann Y, Eidhof E, Hansen U, Fleischhauer L, Vogel J, Clausen-Schaumann H, Aszodi A, Dreier R. Int J Mol Sci. 2021 Dec 24;23(1):182. doi: 10.3390/ijms23010182.
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Abstract: *Ageing or obesity are risk factors for protein aggregation in the endoplasmic reticulum (ER) of chondrocytes. This condition is called ER stress and leads to induction of the unfolded protein response (UPR), which, depending on the stress level, restores normal cell function or initiates apoptotic cell death. Here the role of ER stress in knee osteoarthritis (OA) was evaluated. It was first tested in vitro and in vivo whether a knockout (KO) of the protein disulfide isomerase ERp57 in chondrocytes induces sufficient ER stress for such analyses. ER stress in ERp57 KO chondrocytes was confirmed by immunofluorescence, immunohistochemistry, and transmission electron microscopy. Knee joints of wildtype (WT) and cartilage-specific ERp57 KO mice (ERp57 cKO) were analyzed by indentation-type atomic force microscopy (IT-AFM), toluidine blue, and immunofluorescence/-histochemical staining. Apoptotic cell death was investigated by a TUNEL assay. Additionally, OA was induced via forced exercise on a treadmill. ER stress in chondrocytes resulted in a reduced compressive stiffness of knee cartilage. With ER stress, 18-month-old mice developed osteoarthritic cartilage degeneration with osteophyte formation in knee joints. These degenerative changes were preceded by apoptotic death in articular chondrocytes.*

Young mice were not susceptible to OA, even when subjected to forced exercise. This study demonstrates that ER stress induces the development of age-related knee osteoarthritis owing to a decreased protective function of the UPR in chondrocytes with increasing age, while apoptosis increases. Therefore, inhibition of ER stress appears to be an attractive therapeutic target for OA.

Sympathectomy aggravates subchondral bone changes during osteoarthritis progression in mice without affecting cartilage degeneration or synovial inflammation.

Rösch G, El Bagdadi K, Muschter D, Taheri S, Dorn C, Meurer A, Straub RH, Zaucke F, Schilling AF, Grässel S, Jenei-Lanzl Z. Osteoarthritis Cartilage. 2021 Dec 2:S1063-4584(21)00979-1.

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Abstract: *Objective: Osteoarthritis (OA) pathogenesis involves the interaction of articular cartilage with surrounding tissues, which are innervated by tyrosine hydroxylase-positive (TH+) sympathetic nerve fibers suggesting a role of the sympathetic nervous system (SNS) during OA progression. We analyzed the effects of sympathectomy (Syx) in a murine OA model. Methods: Peripheral Syx was generated by 6-hydroxydopamine (6-OHDA) injections in male C57BL/6 mice. OA was induced in wild-type (WT) and Syx mice by destabilization of the medial meniscus (DMM). TH+ fibers and splenic NE were analyzed to evaluate Syx efficiency. OA progression was examined by OARSI and synovitis scores and micro-CT. Expression of TH, α2A- and ß2-adrenergic receptors (AR), and activity of osteoblasts (ALP) and osteoclasts (TRAP) was investigated by stainings. Results: Syx resulted in synovial TH+ fiber elimination and splenic NE decrease. Cartilage degradation and synovitis after DMM were comparably progressive in both WT and Syx mice. Calcified cartilage (CC) and subchondral bone plate (SCBP) thickness and bone volume fraction (BV/TV) increased in Syx mice due to increased ALP and decreased TRAP activities compared to WT 8 weeks after DMMWT and Syx mice developed osteophytes and meniscal ossicles without any differences between the groups. AR numbers decreased in cartilage but increased in synovium and osteophyte regions after DMM in both WT and Syx mice. Conclusion: Peripheral dampening of SNS activity aggravated OA-specific cartilage calcification and subchondral bone thickening but did not influence cartilage degradation and synovitis. Therefore, SNS might be an attractive target for the development of novel therapeutic strategies for pathologies of the subchondral bone.*

Mitochondrial metabolism coordinates stage-specific repair processes in macrophages during wound healing.

Willenborg S, Sanin DE, Jais A, Ding X, Ulas T, Nüchel J, Popović M, MacVicar T, Langer T, Schultze JL, Gerbaulet A, Roers A, Pearce EJ, Brüning JC, Trifunovic A, Eming SA. Cell Metab. 2021 Dec 7;33(12):2398-2414.e9. doi: 10.1016/j.cmet.2021.10.004.

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Abstract: W*ound healing is a coordinated process that initially relies on pro-inflammatory macrophages, followed by a pro-resolution function of these cells. Changes in cellular metabolism likely dictate these distinct activities, but the nature of these changes has been unclear. Here, we profiled early- versus late-stage skin wound macrophages in mice at both the transcriptional and functional levels. We found that glycolytic metabolism in the early phase is not sufficient to ensure productive repair. Instead, by combining conditional disruption of the electron transport chain with deletion of mitochondrial aspartyl-tRNA synthetase, followed by single-cell sequencing analysis, we found that a subpopulation of early-stage wound macrophages are marked by mitochondrial ROS (mtROS) production and HIF1α stabilization, which ultimately drives a pro-angiogenic program essential for timely healing. In contrast, late-phase, pro-resolving wound macrophages are marked by IL-4Rα-*

mediated mitochondrial respiration and mitohormesis. Collectively, we identify changes in mitochondrial metabolism as a critical control mechanism for macrophage effector functions during wound healing.

Meeting announcements

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List of invited speakers and more detailed information will follow soon!

Contact : antje.steidl@kgu.de; frank.zaucke@kgu.de; www.matrixbiologie.de

British Society for Matrix Biology

The next Spring Meeting of the British Society for Matrix Biology will be hosted virtually by the University of Surrey on the 12th and 13th of April 2022.

Organized by: Dr Giovanna Nalesso

The theme of the meeting is "Interactions between Lipids/Derivatives and the ECM: pre-clinical and clinical relevance".

The conference will include 5 plenary sessions covering different aspects of the interactions between lipids and lipid-derivatives such as hormones and pro-inflammatory molecules with the ECM, in different areas of research. The speakers we have invited to present their work are internationally renowned scientists in different fields of research, spanning from respiratory diseases and embryology to regenerative medicine and cell to cell communication: Robert Snelgrove (Imperial College, UK), Sirio Dupont (University of Padua, Italy), Giampietro Schiavo (UCL, UK), Rami Hannoush (Genentech, USA), Stephen Badylacks (University of Pittsburgh Medical Centre, USA), Nicholas Davidson (Washington University, USA), Dawei Zhang (University of Alberta, Canada).

The meeting will also host a BSMB Medal Award presentation, which will be given by Prof Kathy Cheah, from the University of Hong Kong.

We have also invited a special guest, Dr Steve Cross, a public engagement and communication consultant (https://drstevecross.wordpress.com/), who will deliver an entertaining science communication session entitled "Communicating Science and being silly", at the end of day one. To encourage networking, attendees will also be invited to a "speed networking" session.

Registration is open.

For further information please visit: https://bsmb.ac.uk/meetings/fatty-matrix-biochemistry-and-clinical-relevance-lipidmatrix-interactions/

FEBS Advanced Lecture Course Matrix Pathobiology, Signaling and Molecular Targets - The Island of Crete - Greece, 5-10 May 2022

https://mpst2022.febsevents.org

Deadlines

- **Applications Opening** now open
- **Youth Travel Fund Grants** Deadline January 21, 2022
- **Applications Closing** February 4, 2022

Dear Colleagues and Friends,

On behalf of the Organizing Committee, it is a pleasure to invite you to the 8th FEBS Advanced Lecture Course on Matrix Pathobiology, Signaling and Molecular Targets, to be held in Aldemar Knossos Royal's conference center (https://www.aldemarknossosroyal.gr/events/conferences/) on 5th to 10th May 2022.

Cell biology and biochemistry have recently increasingly turned their attention to the space between cells and revealed an elaborate network of macromolecules essential for structural support, cell migration, adhesion and signaling. The 6-days meeting will offer oral sessions with invited plenary lectures, talks by confirmed speakers, general lectures and tutorials, selected talks related to the topics of the presented abstracts, poster and flash presentations, panel discussions and speakers' corner/meet the experts. These sessions will address both basic and applied science topics that appeal to the range of participants working in the fields of matrix organization and assembly, cell adhesion, matrix-mediated signaling, as well as the matrix macromolecular effectors, namely proteoglycans and glycans, integrins, novel collagen types, growth factors and matrix metalloproteinases and other matrix degrading enzymes that affect the cell behavior.

The Organizing Committee has put together an outstanding group of internationally recognized experts as invited speakers. Open slots for talks will include selected short talks, flash poster presentations, and confirmed registered speakers as well. The lectures and tutorials will provide you with an update of important new knowledge covering key areas of the field. Young Travel Fellowships and Young Investigator Awards will also be available upon application/selection procedure for graduates and fellows up to 5-years after their PhD.

The most important goal of this meeting is to bring together scientists from biochemistry, life sciences, molecular cell biology and bioinformatics on an important and fast growing scientific field and to create the environment for a superb science, warm collegiality, an all-around rewarding experience and social events during this special time of the year.

We are looking forward to welcome you in Greece for an exciting and memorable scientific meeting.

Nikos Karamanos, Chairman of the Organizing Committee

The Extracellular Matrix Pharmacology Congress (ECM2022)

Join us at ECM2022 23-25 June 2022, in Copenhagen Denmark. Alterations to the extracellular matrix are a common denominator in most chronic diseases. ECM2022 aims to unlock the potential of the extracellular matrix. The congress will focus on development of new drugs and improve our understanding of the extracellular matrix across chronic diseases. It is time to create a forum for experts to discuss, share and learn from other disease fields!

Session highlights will include:

- The essential components of the ECM
- The importance of ECM in cancer: Barrier for entry or exit?
- Should we treat the ECM or cells in fibrotic diseases?
- The importance of ECM in lung diseases
- The importance of ECM in liver diseases
- Cardiorenal axis and the ECM
- Tissue destruction in inflammatory diseases
- Pharmacological targets of the ECM
- ECM signaling

Speaker highlights:

- Valerie Weaver, University of California, USA
- Raghu Kalluri, University of Texas MD Anderson Cancer Center, USA
- Sylvie Ricard-Blum, University of Lyon, France.
- Mina Bissell, Lawrence Berkeley National Laboratory, USA
- Richard O. Hynes, Massachusetts Institute of Technology, US

Abstract submission is now open.
Register now to get the early bird discount: www.ecm-congress.org

Abstract deadline: 15 March 2022
Registration early bird: 15 April 2022
Late breaking abstract: 16 May 2022

Proteoglycans GRS (July 9-10, 2022) & GRC (July 10-15, 2022)

Proctor Academy, Andover, NH, USA

https://www.grc.org/proteoglycans-conference/2022/

ETRS 2022

EUROPEAN TISSUE REPAIR SOCIETY ANNUAL MEETING 2022

September 15th - 17th, 2022
Lyon - FRANCE

EARLY-CARRER PRE-CONFERENCE

September 14th, 2022

NEW PERSPECTIVES FOR TRANSLATIONAL MEDICINE

Topics

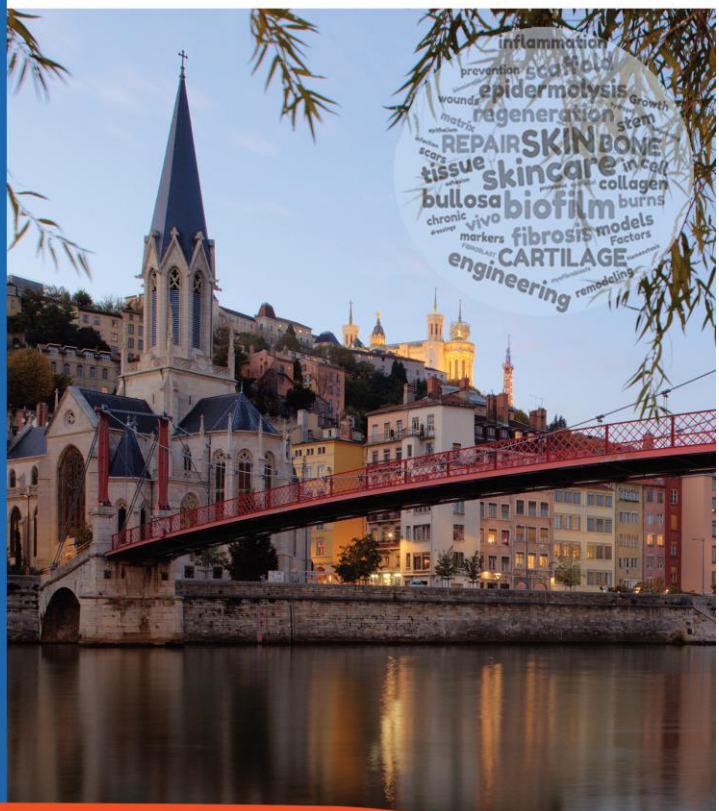
1. Tissue regeneration lessons from organisms' diversity
2. Epithelial insults and innovative therapies
3. Tissue engineering and 3D printing
4. Bone and cartilage repair
5. Cell dynamics in tissue remodeling
6. Chronic, infected wounds and biomarkers
7. Dermo-cosmetic approaches of skin regeneration

Invited Speakers

Leena Bruckner-Tuderman, Germany
Céline Colnot, France
Jeffrey M. Davidson, USA
Patrizia Ferretti, UK
Nadira Frescaline, France
Boris Hinz, Canada
Jean Philippe Lavigne, France
Colin McGuckin, France
Christophe Marquette, France
Nadia Mercader Huber, Switzeland
Graziella Pellegrini, Italy
Ernst Reichmann, Switzeland
Eric Röttinger, France
Marjana Tomic-Canic, USA
Dimitrios Zeugolis, Ireland
Marcy Zenobi-Wong, Switzeland

Organising Committee

Fabienne Braye, MD/PhD, Lyon
Alexis Desmoulière, PharmD/PhD, Limoges
Christophe Egles, PhD, Compiègne
Jean Jacques Lataillade, MD/PhD, Paris
Frédéric Mallein-Gerin, PhD, Lyon
Catherine Moali, PhD, Lyon
Patricia Rousselle, PharmD/PhD, Lyon
Florence Ruggiero, PhD, Lyon
Dominique Sigaudo-Roussel, PhD, Lyon



Includes a joint session with the Cosmet'In Lyon

http:// etrs2022.univ-lyon1.fr
etrs2022@univ-lyon1.fr

Matrix Biology Europe meeting
September 28-30, 2022, Florence (Italy)

Dear Colleagues,

The Matrix Biology Europe (MBE) conference is one of the most important congresses in the world addressing extracellular biological polymers, which represent key molecules in several pathophysiological processes.

This international event is held every two years and gives the opportunity to hundreds of senior and young researchers to present their research and to interact with outstanding experts in the field.

Beside the basic science presentations, several sessions are focused on the clinical and biotechnological applications of proteoglycans, which represent very promising targets in human pathology. The program will cover all aspects of the extracellular matrix biology in health and disease, the cell-matrix interactions and signalling, the pathology and tumor environment as well as the advances in matrix disease mechanisms and pharmacological targeting.

The Organizing and Scientific Committees have put together internationally recognized experts as well as younger group leaders as invited speakers. The scientific program will involve several Plenary Lectures and short talks selected from the submitted abstracts.

We really hope to see you again in presence in Florence for a great Congress and it will be a great opportunity to share our experiences after the COVID-19.

We look forward to welcoming you in Florence from 28 to 30 September 2022!

With our best regards,
Alberto G. Passi

Local Organizing Committee

Alberto Passi (President)

Federica Boraldi
Angela D'Ascola
Antonella Forlino
Marilena Formato
Marco Franchi
Evgenia Karousou
Maurizio Onisto
Arianna Parnigoni
Davide Vigetti
Manuela Viola

Scientific board

Stephan Brezillon
University of Reims (France)

Renato Iozzo
Thomas Jefferson University Philadelfia (USA)

Paraskevi Heldin
University of Uppsala (Sweden)

Nikolaos Karamanos
University of Patras (Greece)

Sylvie Ricard-Blum
University of Lyon (France)

Irit Sagi
Weizmann Institute (Israel)

Liliana Schaefer
University of Frankfurt (Germany)

Tom Van Agtmael
University of Glasgow (UK)

2023 Collagen Gordon Research Seminar

Colby Sawyer College, NH (USA)
Chairs: Delfien Syx & Jonathan A. Roth
https://www.grc.org/collagen-grs-conference/2021/

2023 Collagen Gordon Research Conference

July 9-14, 2023
Colby Sawyer College, NH (USA)
Chair: Taina Pihlajaniemi
Vice Chair: Douglas B. Gould
https://www.grc.org/collagen-conference/2021/

Gordon Research Conferences
Frontiers of Science

Physiological and Disease Relevance and the Underlaying Molecular Properties of Collagens

- Keynote Session: From 4-Hydroxyproline in Collagen to Hypoxia Control
- Functional Effects and Translational Potential of Mutations in Collagens
- Collagen Transport, Turnover and Homeostasis
- Collagens and Related Molecules in Stem Cell Regulation
- Musculoskeletal Development and Pathology
- Tumor Growth and Metastasis
- Collagens: Systems Approaches, Networks and Interactomes
- Fibrosis and Tissue Repair
- Bioengineering and Materials Design

2023 Elastin, Elastic Fibers & Microfibrils Gordon Research Seminar

Southern New Hampshire University, NH (USA)
Chairs: Muthu Lakshmi Muthu & Kirklann N. Lau
https://www.grc.org/elastin-elastic-fibers-and-microfibrils-grs-conference/2021/

2023 Elastin, Elastic Fibers & Microfibrils Gordon Research Conference

Chair: Dianna Milewicz
Vice Chair: Beth A. Kozel
Southern New Hampshire University, NH (USA)
https://www.grc.org/elastin-elastic-fibers-and-microfibrils-conference/2021/

Gordon Research Conferences
Frontiers of Science

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.

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, University of Freiburg (Germany) pauline.nauroy@uniklinik-freiburg.de, @PaulineNauroy)
Chloé Yeung (Institute of Sports Medicine Copenhagen Denmark, chloe.yeung@gmail.com, @ccstorytime)
The ISMB correspondents of National Societies for Matrix Biology for Facebook & Twitter

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

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** (see below). We would be happy to share your announcements with the #MatrixBiology world!

The International Society for Matrix Biology (ISMB) Twitter @IntSocMatBio
Julia Etich, Goethe University Frankfurt (Germany) julia.etich@kgu.de
Valerio Izzi, University of Oulu (Finland) valerio.Izzi@oulu.fi

The American Society for Matrix Biology (ASMB) Twitter @amsocmatbio
Alexandra Naba, University of Illinois, Chicago (USA) anaba@uic.edu

The British Society for Matrix Biology (BSMB) Twitter @BSMB1
Michal Dudek, University of Manchester (UK) michal.dudek@manchester.ac.uk

The Danish Society for Matrix Biology (DSMB) Twitter @DSMB_dk
Christine Chuang, University of Copenhagen (Denmark) cchuang@sund.ku.dk

The Finnish Connective Tissue Society (FSMB)
Valerio Izzi, University of Oulu (Finland) Valerio.izzi@oulu.fi
Piia Takabe, University of Eastern Finland, Kuopio (Finland) piia.takabe@uef.fi

The French Society for Matrix Biology (SFBMec) Twitter @SFBMEc
Patricia Rousselle, University of Lyon (France) Patricia.rousselle@ibcp.fr

The German Society for Matrix Biology (DGMB) Twitter @Matrixbiologie
Julian Nüchel, Max Planck Institute for Biology of Ageing, Cologne (Germany) jnuechel@age.mpg.de

Matrix Biology Ireland (MBI) Twitter @MBIreland
Alexandre Trotier, National University of Ireland, Galway (Ireland) A.TROTIER1@nuigalway.ie

Matrix Biology Society of Australia and New Zealand (MBSANZ) Twitter @MatrixBioANZ
Luise Kung, Murdoch Childrens Research Institute, Melbourne (Australia) louise.kung@mcri.edu.au

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