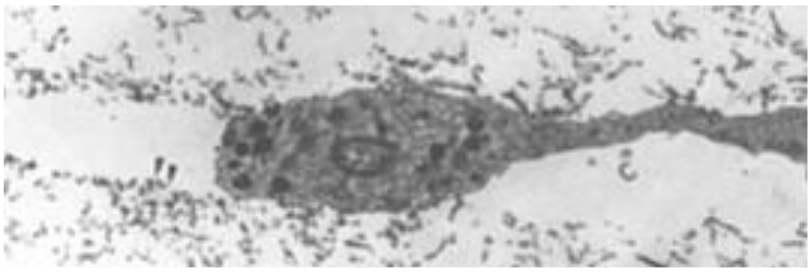


A fibroblast within a tethered lattice, after 13 days, with a cavity surrounding the cell and areas of packed collagen fibrils *(Porter et al. 1998 Wound Rep. Reg. 6: 157-166)*

ISMB NEWSLETTER 43 January 2023 Editor: Sylvie Ricard-Blum

FROM THE PRESIDENT'S DESK

Dear ISMB members, friends, and colleagues,

With the first issue of the ISMB Newsletter in 2023, I would like to wish you all a new year full of health, happiness, inspirations, and scientific achievements.

It is a great honor to serve as the President of the ISMB with colleagues supporting the Executive committee: Suneel Apte as Past President, Julia Etich as Secretary, Ruud Bank as Treasurer. I would like to welcome Valerio Izzi elected as the new Vice-President, Zoi Piperigkou as the new elected ECR member. Together with the experienced ISMB council members, we will drive the ISMB to new venues for the benefit of the Society and the field of Matrix Biology.

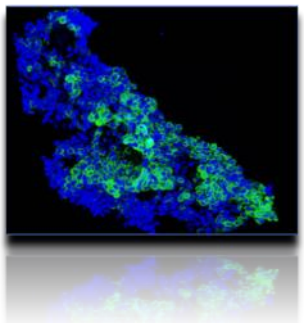
Here, I would extent my great thanks to the past president Suneel Apte, the driving force of the society for the last two years, during the very difficult period due to SARS-CoV-2 pandemic as well as to Sylvie Ricard Blum for editing the Newsletter but also supporting the very demanding administration issues of the ISMB.

The fresh looking and more user-friendly website, thanks to Valerio Izzi, offers several new options and even an easy way for new applications and members' area.

Research in the field of Extracellular Matrix has been expanded the last years, actually there is an exposure in the area, and searching in Pubmed, and the various publishers' websites, one can easily see that there are hundred thousand of peer-review publications as well as patents published every year. It is, therefore, a great challenge that the Society will attract and bring new members and incorporate innovative and important for the future directions in the area.

The ISMB will do its best to continue supporting the travel fellowships for young fellows and to sponsor well-established scientific meetings including ASMB, MBE, FEBS Matrix Pathobiology Courses and Pan-Pacific meetings.

With this, I wish you all a prosperous New Year. **Nikos Karamanos, *ISMB President*** (n.k.karamanos@upatras.gr)



Prof. N. Karamanos is the team leader of a research focus is based on matrix pathobiology, cell signaling, molecular targeting, pre-clinical evaluation of drugs at cell level and cytotoxicity of novel compounds synthesized, including biopolymers, nanomaterials, and nanocomposites. Current research activities in collaboration with elected *As. Prof. Z. Piperigkou* focus on advanced *in vitro* models for the formation of cancer-derived 3D spheroids. The dynamic interplay between microRNAs and the extracellular matrix as well as the matrix-mediated miRNAs in cancer progression are also studied. Nikos Karamanos was selected as a Highly Cited Researcher by WoS, for the year 2022. He has been named as one of the most cited researchers worldwide, according to this year's "Highly Cited Researchers" list from Clarivate, based on the widely recognized Web of Science database

Content

Awards

The 2022 ISMB Distinguished Investigator Award

Professor Taina Pihlajaniemi, University of Oulu, Finland

Professor Taina Pihlajaniemi (MD, PhD, University of Oulu, Finland) has been selected as the recipient of the 2022 ISMB Distinguished Investigator Award for lifetime achievements in the field of extracellular matrix. The award will be presented in a plenary session of the 2023 meeting of the American Society for Matrix Biology, which will be held in Salt Lake City (UT, USA) in October 2023 where she will deliver her award lecture.
In the meatime she is very busy chairing the Gordon Research Conference to be held on July 9 - 14, 2023 in New London (NH, USA, see page 35 of this newsletter).

Our warmest congratulations to Taina for this very well-deserved recognition of her lifetime research and her oustanding contributions to the field of extracellular matrix with a focus on collagens XIII, XV and XVIII.

Obituaries

Benoit de Crombrugghe (1935-2022)

"Consider well, he is a Prince!
More! he is a man!"
The Magic Flute

The passing of Benoit de Crombrugghe, Benoit for all of us, struck me to my inner core for many reasons that I need to put aside to present him. But how can one present the scientist and more importantly give at least a glimpse of the richness of this exceptional man? Thirty-three years after leaving his lab, 24 years after leaving the department he headed what remains are the many lessons as a scientist and as a person, I learned sometimes unbeknownst to him from Benoit. What I would like to convey here is less a litany of his many accomplishments that what I see as the essence of Benoit, gathered through an encounter that lasted 12 years, a type of encounter one is happy if it happens once in one's lifetime.

Benoit was a private, guarded, closed, and closeted as he was rich, complex, courageous, supremely intelligent of an intelligence all in nuances and that needed not to brag; intellectually elegant, and the definition of class. I do not want to be contradictory for the sake of being catchy, but Benoit was a living contradiction. He was in the

best sense of the word remarkably conventional in his social life and extraordinarily unconventional and free in his professional life. The contradiction resides in the fact that I think, Benoit loved both aspects of his life.

Benoit was born in 1935 in Bruges, Belgium, a beautiful city his family contributed to found, many centuries ago. One of seven children in one of the oldest noble family of Belgium. As a son of a noble, wealthy rooted in Bruges since immemorial times, family of bankers and lawyers, nothing was more distant to his cultural environment than medicine not to mention science. Yet in the first of many ruptures in what should have been a predictable life, Benoit chose medicine as a professional path at the end of high school. He always viewed medicine less as a craft that one learns to practice than as a door that open to his own secret garden: the world of intellectual curiosity, of exploration of the unknown, of inebriating escape of the daily routine.
Benoit was exposed to medical research early on during his training and was sufficiently intelligent to say the least, to foresee at a young age the repetitive nature of clinical medicine. When he saw it, he decided in another rupture with his background to go to the NIH to become a post-doc in the prestigious Clinical Endocrinology Branch (CEB) in 1963. There he was just another anonymous post-doc, but he encountered what he was looking, what fits its nature: the free, the wild nature of basic science. Although he was working with Harold Edelhoch, a brilliant thyroidologist, it is at the CEB that Benoit met the man who would shape his professional life as much as one can shape the life of such an intelligent man. Ira Pastan, another intellectual maverick. It is also during this first stay at NIH that Benoit met the love of his life, his wife Emma. These two encounters fortified in Benoit his quest for a life somewhat different than the one promised to him.

Yet Benoit had to go back to Belgium to do his mandatory military service and possibly start his professional life. But for him like for anyone the stay at NIH had not been neutral. It had strengthened and legitimized the intellectual tastes of his blossoming love of basic science. One can imagine how altogether dearly familiar and oddly foreign, the family of bankers and lawyers may have appeared to him coming back from Bethesda. How sleepy the beautiful old city he was literally part of the fabric, must have felt for this young man who had experienced the camaraderie of the American way of life and the intoxicating power of the exploration of the unknown. Eventually, the last rupture occurred, as close to his heart as Belgium was (and it will always remain that way), it also felt too small, maybe too conventional for Benoit and Emma. They returned to the NIH and Benoit joined Ira Pastan's laboratory in 1967.

This is in Ira's lab that Benoit started to study what he never stopped studying: the regulation of gene expression first in bacteria and, starting in the mid '70s, in fibroblasts. I do not want to take space in this by definition too short a tribute to an extraordinary man to present every one of his many scientific accomplishments. Sufficed to say that his lifelong study of the regulation of gene expression culminated at the end of his career in the elucidation of the transcriptional program of chondrocyte differentiation. Not a small feat. For the rest, the cloning of the collagen genes when cloning was truly heroic, the study of their regulation, the CCAAT binding factor, Osterix, etc…. all that can be found elsewhere.
Instead, I would like to speak of Benoit. And René Magritte. And their double life.

It is no secret that Benoit loved Magritte, the paintings of Magritte. More importantly, Benoit was drawn to what he saw in Magritte's personal life which is nothing else than what his own life was. Benoit often spoke of how Magritte raised in the world of bourgeoise escaped its intellectual constraints through art and imagination as a painter. The similarities are obvious. Yes, Benoit was an aristocrat, he like and never renounced this part of himself but at the same time he had a passion, and this passion took over him: biological research as an art of improvisation. In the lab, and Benoit was there every day, Benoit was looking for the new, the unknown, the frontier, the unheard of. At the same time, he approached science with the caution of a banker, the merciless rigor of an exigent, exceptional scientist who knew too well the slings and arrows that come with the job when it

is not well done. Benoit was warm with his post-docs and yet ever so slightly distant but always stimulating. He taught me that if there are hundreds of ways to show, to say the same thing, only one is by far more convincing than the others and as an artist who knew his craft as well as his public, he was the best at finding it. He was merciless with the data but always fair with the experimentalist. In short, he was exemplary.
There was always a peaceful and fascinating contradiction between the acceptance of the rules of life and the courage to sidestep them through was not a hobby but a profession: the austere but boundless joys of basic research. To me, Benoit was, like Rene Magritte, an artist who touched the life and mind of whoever worked with him. I consider myself fortunate to have been one of them. The legacy of Benoit, the importance of his contributions to the field, and of his influence to his trainees will continue to grow.

Gerard Karsenty
The Paul A. Marks M.D., Professor and Chair of the Department of Genetics and Development? Columbia University Medical center, New York City (USA)

In Memoriam: Jouni Uitto, MD PhD
Passing a giant of matrix biology research (1943 - 2022)

We are deeply saddened by the sudden and unexpected passing of Jouni Uitto, well known to all of us in the field of "Connective tissue research". Jouni was the Chair of the Department of Dermatology and Cutaneous Biology at Thomas Jefferson University in Philadelphia. He was the longest-lived Chair of any Department of Dermatology in USA since he held this position for over 36 years. Jouni was an incredibly productive scientist having authored ~1,000 scientific papers and reviews, with nearly 70,000 citations and an astronomical *h*-index of 133. Just in 2022, Jouni had 43 scientific contributions to our research field.

Jouni Uitto, Philadelphia 2022

Jouni´s lab has made remarkable contributions to discovery of the genetic background of heritable skin diseases, in particular epidermolysis bullosa and pseudoxanthoma elasticum, by cloning genes for several basement membrane and other proteins and disclosing pathogenic variants in them. In collaboration with patient advocacy organizations, his lab also launched diagnostic services to provide accurate diagnosis for many individuals and families living with these disorders.

Jouni graduated from the University of Helsinki in 1970. After finishing his MD/PhD in Kari Kivirikko´s lab, he planned a postdoctoral fellowship in Darwin Prockop´s lab in Philadephia – and ended up staying in the US for more than 50 years! After a 5-year postdoc in biochemistry, he undertook clinical residency in dermatology at Washington University School of Medicine in St. Louis and moved then as a faculty member to the University of California, Los Angeles. From there he was recruited in 1986 to Thomas Jefferson University in Philadelphia as a Chair of the Department of Dermatology and Cutaneous Biology, a position he held to the end.

Jouni was the recipient of numerous national and international awards over the course of his career. His most prestigious research awards include: the Alfred Marchionini Gold Medal from the International League of Dermatological Societies; the Society for Investigative Dermatology's most prestigious awards, the Montagna Lecture and Rothman award; and the American Academy of Dermatology's Marion B. Sulzberger Memorial Award and Lectureship, and the Eugene J. Van Scott Award for Innovative Therapy of the Skin.

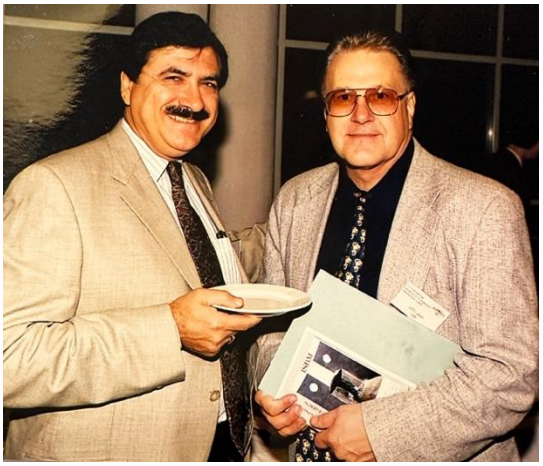
A native of Finland, Jouni always had very good relationships with the Finnish scientific community. He trained numerous Finnish scientists and clinician-scientists with whom he continued to collaborate after they returned home. For his contributions to science and medicine Jouni was awarded the prestigious Matti Äyräpää Lectureship of the Finnish Medical Society and the "*Knight of the White Rose, First Order*" award of the Republic of Finland. Further, he received Honorary Doctorates from the Universities of Kuopio, Oulu, and Turku.

Jouni at a Christmas party, circa 1993

Jouni has affected and touched so many lives. He trained over 140 scholars, students, visiting scientists, and residents. At least 19 of his trainees are chairs of departments in their respective fields, and Jouni has been a great friend of both of us.

On a personal level, Jouni was instrumental in my (RVI) early career move from the University of Pennsylvania, a big Ivy league school in Philadelphia, to Thomas Jefferson University which at that time, 1988, did not have a great reputation as a research institution. When I called Jouni, who was already there together with Darwin Prockop, the Chair of Biochemistry, he said " Come Renato , it's a great place to work". So, I moved to Thomas Jefferson University and never left.

Jouni and I have organized several meetings, including the well-attended meetings of the East Coast Connective Tissue Society, the precursor of the current ASMB, which represents the fusion of the various regional meetings in USA. We always met at the Holidays parties of our department and his as well as in official festivities and committees at our university. Jouni was a real "frequent flier". In October 2022, we were both involved in an interdepartmental committee, and I was asked by the Chair about the number of my airline miles. Instead of answering I asked Jouni how many airline miles he accumulated. His answer was 3.3 million miles!!



Jouni in Salzburg, Austria, 2002

To me (LBT), Jouni was a fellow countryman, friend, colleague, and collaborator for decades. We were both first trained in Kari Kivirikko´s lab in Finland and then Darwin Prockop´s lab in the US. Later, both of us became dermatologists and continued our careers abroad, Jouni in the US and I in Switzerland and Germany, both becoming Chairs of Dermatology Departments, positions that allowed us to emphasize the importance of and implement experimental translational research in clinical medicine. Jouni was an External Senior Fellow at the Freiburg Institute of Advanced Studies (FRIAS), and he spent "mini-sabbaticals"

in Freiburg collaborating with us and mentoring young researchers in my lab, who profited from Jouni´s scientific excellence, international experience, and vibrant personality.

Jouni was world leader and a great friend, so full of life and joy. He was always positive and inspirational to the point that we (Carlo Croce, Maurizio Pacifici, Checco Ramirez, and me) made him an "Honorary Italian". (See figure)

Jouni Uitto, Carlo Croce, Renato Iozzo, Maurizio Pacifici, and Checco Ramirez. ASMB biennial meeting, San Diego, California 2010

We will remember Jouni as an eminent scientist committed to extracellular matrix research and cutaneous biology, a mentor of young researchers, a supporter of international collaboration and a great friend. We will miss him.

Renato V. Iozzo, MD PhD
Thomas Jefferson University, Philadelphia, USA

Leena Bruckner-Tuderman, MD PhD
University of Freiburg, Freiburg, Germany

In Memoriam: Jouni Uitto, MD PhD

It is with great sadness that we learned about the passing of Pr. Jouni Uitto.

Professor Uitto received his MD and PhD degrees in 1970 from the University of Helsinki, Finland, and completed his residency training in dermatology at Washington University School of Medicine, St. Louis, Missouri. After a few years in California, he became Chair of the Department of Dermatology and Cutaneous Biology at Jefferson Medical College, in Philadelphia, Pennsylvania, in 1986. He was also Director of the Jefferson Institute of Molecular Medicine at Thomas Jefferson University.
Jouni was a World expert and renown scientist in the biology of collagen and elastic tissue, He was a pioneer in the genetic analysis of genodermatoses and elucidated the origin of a number of including epidermolysis bullosa or pseudoxanthoma elasticum among many other skin diseases.

While his list of achievements is almost endless, one should cite that Dr Uitto has been the recipient of numerous national and international awards, professorships and honorary doctorates from prestigious universities in Finland, his native country, England, Japan, South Korea, the United Kingdom, the USA and many other countries. Among those are a Research Career Development Award from the National Institutes of Health, the Distinguished Service Award from the Dystrophic Epidermolysis Bullosa Research Association of America, the William Montagna Lectureship Award from the Society for Investigative Dermatology, the Earl of Litchfield Lectureship Award of Oxford University, The Dohi Memorial Lectureship Award from the Japanese Dermatological Society, the Kung-Sun Oh Memorial Lectureship from Yonsei University, Seoul, Korea, the prestigious Matti Äyräpää Lectureship, the highest physician-scientist award in Finland. In 1993, he was designated as the "Professor of the Year" by the American Academy of Dermatology. In 1996, Dr Uitto was appointed as Anglo-American Visiting Professor of the Royal Society of Medicine, London, United Kingdom. He has received an Honorary Doctorate in Medicine from the Universities of Kuopio, Turku and the University of Oulu, Finland, as well as the Honorary Professor title from China Medical University.

In addition to his scientific excellence, Jouni has been a wonderful teacher and mentor to many young dermatologists and skin biologists from all over the World. His lab was a melting pot that allowed for great interactions and networking.

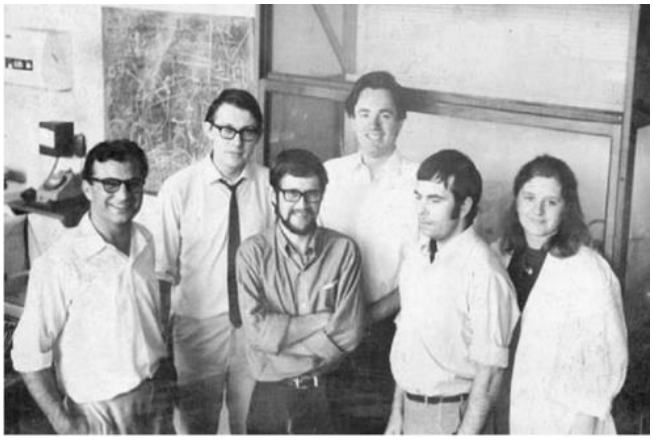
On a personal note, I spent 10 years in Pr Uitto's lab during the 90s and maintained a close relationship with him over the years. Most recently, Jouni was the guest of honor of the Keloid Symposium organized by the Keloid Foundation (NY, USA) in Montpellier, France in October 2022, where I was given the privilege to be the recipient of the Annual Jouni Uitto MD, PhD International Visiting Professorship and Lecture in Molecular Dermatology. Jouni was the same very enthusiastic scientist I had always known, eager to learn and ready to have fun after working sessions were over. Jouni had this extraordinary charisma and ability that made everyone feel comfortable approaching him despite this enormous aura and CV. His enthusiasm, his collegiality and his inimitable sociability remained at the highest level through the years and he will be missed dearly. No scientific meeting will ever be the same without him.

Our sincerest condolences go to his family.

Dr Alain Mauviel, PhD, Inserm Research Director, Curie Institute, Orsay, France

In memory of Professor Emeritus Constantinos P. Tsiganos

We are saddened to learn of the loss of Professor Emeritus, Constantinos P. Tsiganos, who passed away in December 2022. His loss is significant, both for his family and the members of the Biochemistry Laboratory since Con. Tsiganos served in the Department of Chemistry at the University of Patras from 1973 to 2004 as Professor of Biochemistry and he was one of the pioneers of Biochemistry in Greece, a founding member of the Hellenic Society of Biochemistry and Molecular Biology, and the former Hellenic Society of Connective Tissue Research, now known as Hellenic Matrix Biology Section of HSMB (http://eebmb.gr/index.php/en/), with many activities in the scientific, professional and social sphere. Many of the PhDs he supervised and inspired served or are still serving in top University positions, and in high positions in the Public or Private Sector. He introduced Matrix Biology in the Laboratory of Biochemistry, and he was the first to organize the *XVIIth meeting of the Federation of the European Connective Tissue Societies (FECTS, later named Matrix Biology Europe)* in the University of Patras (see the attached poster of the meeting). He collaborated with distinguished scientists, including among others Helen Muir, Tim Hardingham and Dick Heinegard (see attached photo), and he edited *the first Special Issue of Matrix Biology in 2000* "On the occasion of the XVII Meeting of the FECTS (XVIIth FECTS S.I.)". He will be remembered by his immense scientific contributions to the scientific community. His teaching and training of thousands of young minds in the fields of Biochemistry and Matrix Biology will help to continue the legacy of this exceptional scientist and honorable person.



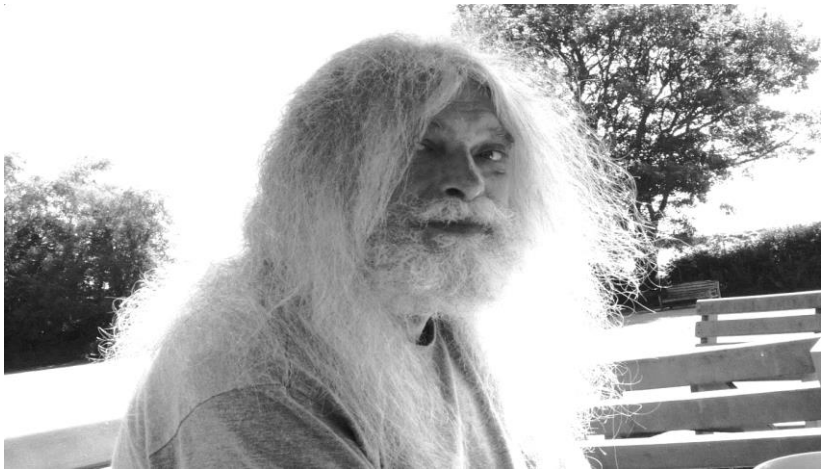
In memoriam Konrad Beck, PhD


Patricia Rousselle & Konrad Beck, 2004

It is with great sadness that we learned of Konrad Beck's untimely passing in November 2022. After obtaining his Ph.D in Biophysics at the Max Planck Institute of Biophysics in 1984, he traveled the world making major contributions in the field of the extracellular matrix, in particular by elucidating the structure of various conserved motifs of matrix proteins such as supercoiled helical motifs and revealing their structure/function relationship. He then moved to Cardiff (UK) as Professor of Protein Biophysics, Cardiff University, College of Biomedical and Life Sciences. At a time when work on basement membranes was just starting, he significantly contributed to the understanding of laminin diversity, multifunctionality and chain assembly. His works remain important references to this day. I had the privilege of welcoming Konrad to my laboratory in Lyon, as a guest researcher (2002-2004), a period during which he interacted extensively with all the members of our Extracellular Matrix department at the Institute of Biology and Chemistry of Proteins. Konrad's rigor, availability and kindness will be deeply missed by all those who knew and worked with him.

Patricia Rousselle, PhD, CNRS Research Director, Tissue Biology and Therapeutic Engineering Laboratory, Lyon, France

Born 10th April, 1956 in Vreden, Germany who passed away on 5th November, 2022 in Cardiff

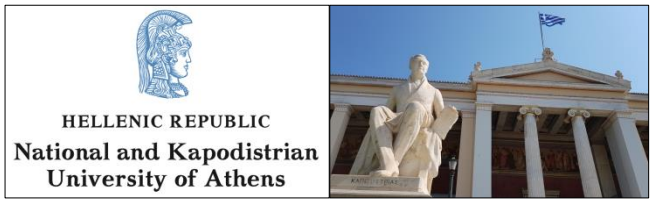


You were taken out of our lives, unexpectedly and much too soon.

New laboratories

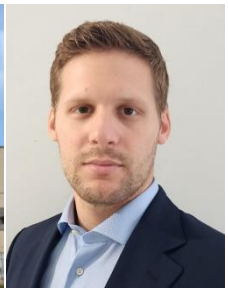
Afratis Lab (P.I: Assistant Professor Nikolaos Afratis), University of Athens (Greece)

Afratis' lab was recently established at National and Kapodistrian University of Athens in Greece and it is embedded in Department of Agricultural Development, Agrofood & Management of Natural Resources. The lab is localized in Evripos Campus. Afratis' lab focuses its scientific efforts on defining the role of nutrition in modulation of microbe-mediated extracellular matrix in health and disease. In detail, due to the fact that microbiome orchestrates metabolic processes of the host through various mechanisms, including digestion of nutrients, regulation of energy harvest from diet, and production of metabolites, Afratis' lab analyses the role of metabolites input on ECM enzyme activity mediated by microbes, as well as the impact of microbe-modified ECM matrix homeostasis in physiological and pathological conditions and the interplay with the immune system.



Microbiome contains 100-fold more genes than the human genome, and is considered to have fundamental roles in pathological situations including obesity, non-alcoholic fatty liver disease, inflammatory diseases, cancer, autoimmune diseases, metabolic diseases, cardiovascular disease, aging and neurodegenerative disorders. Expression of those genes modulates the ECM microenvironment during pathological situations and minimizes the efficiency of therapeutic approaches and can even lead to resistance to treatments. For this reason, the lab examines the impact of microbiome in ECM composition during diseases and engineers novel microbes in order to be used as a payload vesicle using highly-specific inhibitors for modulation of ECM composition, which can be used as food complements either for prophylactic actions or for increasing drugs efficiency.

The transition to an independent group leader position for Prof. Afratis was greatly facilitated by the outstanding mentorship received over the years by Prof. Irit Sagi (Weizmann Institute of Science), Prof. Nikos Karamanos (University of Patras) and Prof. John Couchman (University of Copenhagen). During this time, he worked on the development of rational design of endogenous-like inhibitors and modulators targeting specific matrix remodeling enzymes. In addition, he investigated the role of syndecans during disease progression as well as their signaling in metastatic breast cancer. More information you can find on lab's website http://scholar.uoa.gr/nafratis. The lab will fully operate during the second half of this year and information about job offers will be announced soon via lab's website and ISMB newsletter.



News from national societies

New board of the German Society for Matrix Biology

Dr. Julia Etich, Chairwoman
Prof. Dr. Frank Zaucke, Vice-chairman
Prof. Dr. Gerhard Sengle, Treasurer
Prof. Dr. Martin Götte, Secretary
Prof. Dr. Katja Schenke-Layland, Elected Committee
Dr. Alexander Nyström, Elected Committee
Dr. Julia Marzi, Early Career Researcher Representative

he American and the International Society for Matrix Biology are offering a joint e-Symposium on January 26, 2023

09:00 AM in Eastern Time (US and Canada)

It is FREE and open to all.

Register at https://us02web.zoom.us/webinar/register/WN_XC-GTAAFQyKRB23lx7gE5g

MAKE IT OR BREAK IT: How ECM production and degradation fuels disease

A collaborative event with ISMB, Organized by: Valerio Izzi (Finland) and Raphael Reuten (Germany)

Roles of fibroblast/ECM functional units in pancreatic cancer, Edna Cukierman, *Fox Chase Cancer Center (USA)*

CAF metabolism coordinates tumour ECM production, Sara Zanivan, *University of Glasgow (UK)*

Dysregulated matrix remodeling emerges as important pathophysiological disease biomarker, Irit Sagi, *Weizmann Institute of Science (Israel)*

ASMB Image contest opens January 16, 2023

ISMB members may apply. This is a fun contest that highlights beautiful and interesting matrix images. See ASMB website for details (https://www.asmb.net/).

Last day to submit is February 14. Send some matrix love on Valentine's Day and submit your image to the contest!

PhD and post-doctoral positions

Post-doctoral fellowship in protease and arthritis research

Cleveland Clinic
Lerner Research Institute

A post-doctoral fellowship is available for a recent PhD graduate at the The project will utilize degradomics to identify protease substrates in the extracellular matrix and will undertake development of new protease inhibitors for arthritis therapy.
Please visit the Apte laboratory website for details of our interests and activities: https://www.lerner.ccf.org/bme/apte/lab/. If interested, please contact Suneel Apte with your CV at aptes@ccf.org and include full contact details for 3 references.

PhD student positions in the German Research Foundation (DFG) funded Research Unit FOR2722
"ECM biology and musculoskeletal diseases"

The Research Unit has an open call for **17 PhD student positions** to join our network of excellent and passionate scientists located in one of the most vibrant cities in the center of Europe - Cologne.

We work on the **extracellular matrix** (ECM), the complex and highly information-containing molecular network that surrounds cells. The ECM influences most aspects of cellular function by binding to cell surface receptors or modulating growth factor signalling. It is thereby intimately involved in many forms of inherited or acquired disease.

Join our vivid network on extracellular matrix biology & musculoskeletal diseases and make a difference!
- Work with leading experts on connective tissue diseases, uncover novel molecular pathomechanisms and develop tailored therapies.
- Enjoy a highly interdisciplinary research environment with 18 internationally recognized group leaders from basic science to translational medicine with focus on mechanobiology, systems biology, biochemistry, molecular and developmental biology, human genetics and diseases, clinical translation.
- Interact with groups of our collaborative research network at renowned institutions:
The Childrens Hospital & research institutes of the University of Cologne - the German Sport University Cologne - the Max Planck Institute for the Biology of Aging - the Cluster of Excellence CECAD – the Institute for Musculoskeletal Medicine (Münster) - the Dr. Rolf M. Schwiete Research Unit (Frankfurt)

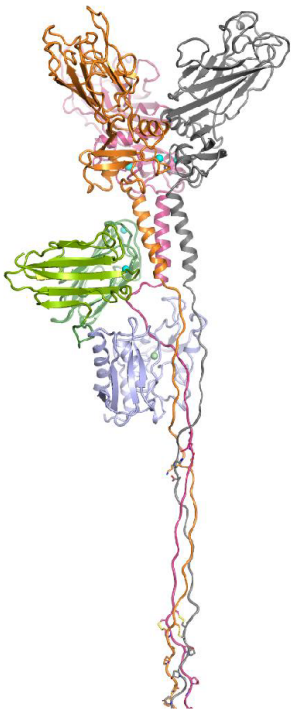
You will benefit from

- Excellent projects that address basic and translational questions in extracellular matrix biology and connective tissue diseases
- Access to advanced imaging/mass spectrometry/genomic & gene editing technologies, disease models (mouse, fish, organoids) and translational approaches (protein targeting & therapeutic antibody development)
- Advanced training, mentoring and networking in a cohort of PhD students entirely dedicated to the extracellular matrix and connective tissue diseases
- Training workshops in extracellular matrix biology and musculoskeletal diseases, high throughput data analysis and clinical aspects of connective tissue diseases
- Soft skills courses (presentation & scientific writing, good scientific conduct)
- Structured PhD programme and thesis advisory committees
- Participation and organization of summer schools, seminar series, annual retreats and international symposia
- Mobility grants for national and international short term lab visits
- Full funding for international and German students, no tuition costs

We invite highly motivated applicants with an MSc (or equivalent) degree and a strong background in life sciences e.g. biochemistry, molecular medicine, pharmacy, veterinary medicine, medicine and bioengineering. Apply now and send your application including a letter of motivation, copy of certificates, a CV and names of two references to trine.riemer@uni-koeln.de
For further information visit us on Twitter @DFG_FOR2722 or https://for2722.uni-koeln.de

Post-doc position LBTI, Lyon
Group Metalloproteinases and Tissue Remodeling (C. Moali)

Structure-function analysis of a prominent target in fibrosis: the proteolytic maturation complex of fibrillar collagens



The biosynthesis of fibrillar collagens is severely dysregulated in fibrosis, the common and deleterious outcome of a great diversity of tissue injuries. A better understanding of the various steps leading from the synthesis of individual procollagen chains to collagen fibrils would greatly benefit the development of new therapeutic tools. In the *P³-complex* project, we focus on the C-terminal proteolytic maturation of fibrillar procollagens in order to :

- better understand, at the molecular level, how the various components of the maturation complex (substrate, protease, regulatory proteins) associate and work together. This is done mainly by cryo-electron microscopy and through a combination of biochemical/biophysical approaches.

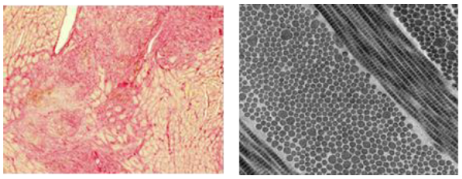
- learn more about how this complex affects tissue biology and extracellular matrix remodelling using transcriptomics, targeted mass spectrometry and biochemical assays.

This project is funded by the French Research Agency (ANR) and is performed in collaboration with the OPIC (Oxford Particle Imaging Center) facility in Oxford for cryo-EM and with the University Hospital of Dijon for fibrosis samples. It will contribute to optimize innovative tools, currently under development in the group, to diagnose and treat fibrosis.

Skills :
- Excellent theoritical and practical knowledge of molecular biology and protein biochemistry
- Experience in running protein-protein interaction analyses (ideally SPR) and biochemical assays to measure protein concentrations (ELISA, mass spectrometry)
- Knowledge in structural biology; previous experience in cryo-EM would be an advantage
- Knowledge in extracellular matrix biology

More information and applications here :
https://emploi.cnrs.fr/Offres/CDD/UMR5305-CATMOA-007/Default.aspx?lang=EN

We invite highly motivated candidates to apply directly on the above website (detailed CV with publication list and names of 2 references, cover letter) or by sending their documents to catherine.moali@ibcp.fr before **February 20, 2023**. The position is already open and can start immediately.



Laboratoire de Biologie Tissulaire et Ingénierie thérapeutique
Institut de Biologie et Chimie des Protéines
Unité Mixte de Recherche 5305 - CNRS / Université Lyon 1
https://lbti.ibcp.fr/

Spotlights on methods that other ISMB members may find useful

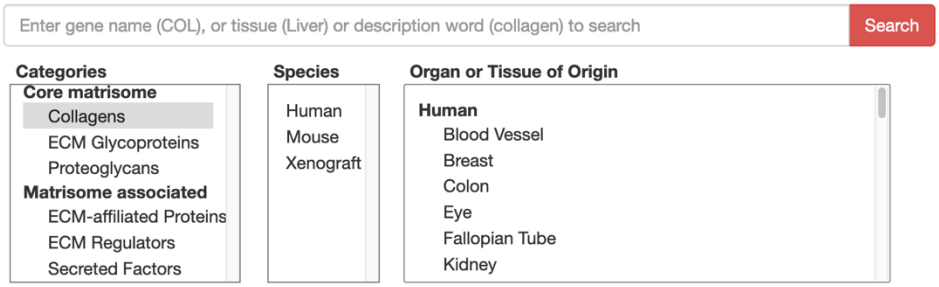
If you would like to feature in the next newsletter, please email Communication Group Coordinator Julia Etich (julia.etich@uni-koeln.de)

In Focus

MatrisomeDB 2.0: 2023 updates to the ECM-protein knowledge database

Shao X, Gomez CD, Kapoor N, Considine JM, Grams C, Gao YT, **Naba A***.
Nucleic Acids Research (2022) gkac1009. https://doi.org/10.1093/nar/gkac1009
MatrisomeDB is accessible at: https://matrisomedb.org, *Correspondence: Alexandra Naba, anaba@uic.edu

Mass-spectrometry (MS)-based proteomics has become a method of choice to characterize the protein composition of the ECM of tissues. To facilitate the re-use and re-interpretation of MS datasets by non-specialists, we have developed MatrisomeDB, a searchable collection of curated proteomic datasets focused on the analysis of the extracellular matrix (ECM) of healthy and diseased tissues.
In brief ECM proteomics datasets are retrieved from public repositories, including the ProteomeXchange, PRIDE, and MassIVE, and are reprocessed using unified search parameters and criteria to allow inter-study comparison. Taxonomies included in the current database comprise *Homo sapien*s and *Mus Musculus*. The new release of MatrisomeDB includes data on over 2,000 human and 949 mouse matrisome proteoforms from 42 studies and over 80 different tissue types.
Users can query MatrisomeDB by entering gene symbol(s), protein name(s), and/or tissue type(s) in the "Search" box, or by selecting different inputs (matrisome categories, species, and/or organ or tissue of origin).



The output from the data reprocessing workflow is displayed in the form of a downloadable table and different hierarchically-clustered distribution heatmaps computing confidence scores and protein abundance. Additional features include peptide mapping on primary amino-acid sequences, SMART-domain-based representation of proteins, and 3D protein structures retrieved from AlphaFold, power by the Sequence Cover Visualizer. These features are provided at the sample level and the database level. The knowledgebase component of MatrisomeDB provides links to external databases including GeneCards, UniProt, the CPTAC (Clinical Proteomic Tumor Analysis Consortium) assay portal, and the Peptide Atlas, and with link to original publications and raw mass spectrometry data files. For more information, we invite prospective users to review our tutorial: https://matrisomedb.org/tutorial/.
We hope that MatrisomeDB contributes to advance our knowledge of ECM and accelerates the discovery of prognostic ECM biomarkers and treatment targets.
If you are a MatrisomeDB user and wish to provide feedback, please email Dr. Naba!

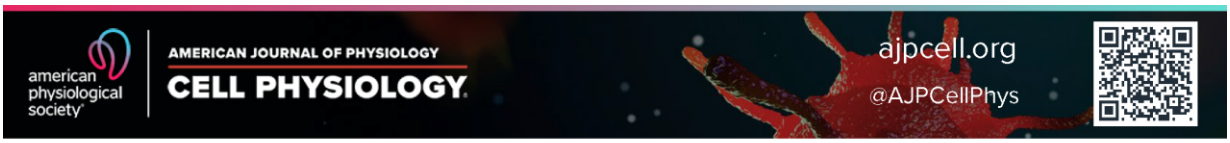
Adipose-Derived Stromal Cells: Isolation, Expansion, and Differentiation

Buchert JM, Lotz B, Diederichs S, Richter W. Methods Mol Biol. 2023;2598:75-85. doi: 10.1007/978-1-0716-2839-3_7.
Corresponding author: Wiltrud.Richter@med.uni-heidelberg.de
Abstract: Adipose-derived stromal cells (ASC) are a promising alternative cell source to chondrocytes as well as to bone marrow-derived mesenchymal stromal cells (BMSC) in cartilage tissue engineering and repair. Here we describe ASC isolation from liposuction by-products by collagenase-based tissue digestion combined with cell filtration and followed by monolayer attachment and expansion culture. Quality control requires confirmation of correct surface marker expression and multilineage differentiation potential by a trilineage differentiation assay.

Establishment of a 3D co-culture model to investigate the role of primary fibroblasts in ductal carcinoma in situ of the breast.

Sourouni M, Opitz C, Radke I, Kiesel L, Tio J, Götte M, von Wahlde MK.
Cancer Rep (Hoboken). 2022 Dec 19:e1771. doi: 10.1002/cnr2.1771.
Corresponding author: msourouni@gmail.com
Abstract: Background: Ductal carcinoma in situ (DCIS) is a precursor form of breast cancer. 13%-50% of these lesions will progress to invasive breast cancer, but the individual progression risk cannot be estimated. Therefore, all patients receive the same therapy, resulting in potential overtreatment of a large proportion of patients. Aims: The role of the tumor microenvironment (TME) and especially of fibroblasts appears to be critical in DCIS development and a better understanding of their role may aid individualized treatment. Methods and results: Primary fibroblasts isolated from benign or malignant punch biopsies of the breast and MCF10DCIS.com cells were seeded in a 3D cell culture system. The fibroblasts were cultured in a type I collagen layer beneath a Matrigel layer with MCF10DCIS.com cells. Dye-quenched (DQ) fluorescent collagen I and IV were used in collagen and Matrigel layer respectively to demonstrate proteolysis. Confocal microscopy was performed on day 2, 7, and 14 to reveal morphological changes, which could indicate the transition to an invasive phenotype. MCF10DCIS.com cells form smooth, round spheroids in co-culture with non-cancer associated fibroblasts (NAFs). Spheroids in co-culture with tumor-associated fibroblasts (TAFs) appear irregularly shaped and with an uneven surface; similar to spheroids formed from invasive cells. Therefore, these morphological changes represent the progression of an in situ to an invasive phenotype. In addition, TAFs show a higher proteolytic activity compared to NAFs. The distance between DCIS cells and fibroblasts decreases over time. Conclusion: The TAFs seem to play an important role in the progression of DCIS to invasive breast cancer. The better characterization of the TME could lead to the identification of DCIS lesions with high or low risk of progression. This could enable personalized oncological therapy, prevention of overtreatment and individualized hormone replacement therapy after DCIS.

Extracellular Matrix special Issues & journals



CALL FOR PAPERS

Decoding Fibrosis

Fibrotic disorders are a major societal concern. We seek research on novel cellular and extracellular mechanisms of fibrosis, new fibrogenic factors and biomarkers, and diagnostic methods and drug delivery systems for the management of fibrosis.

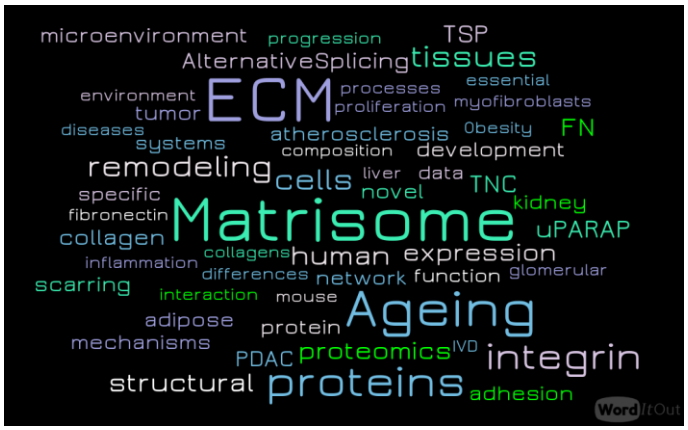
SUBMIT YOUR RESEARCH TODAY

Deadline: May 1, 2023

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

Beyond the Matrisome: New Frontiers in Extracellular Matrix Research

Special Issue of Matrix Biology edited by Suneel Apte and Alexandra Naba



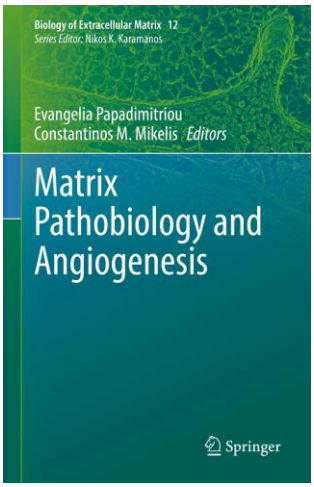
2022 marks a decade since conceptualization and delineation of the modern “matrisome”, a term which is now readily accepted within the ECM community, and has better defined the field for access by scientists who are focused on the interior of the cell. To jump-start the next decade of matrisome research, and with an intent to capture the current state of the field, this Special Issue of Matrix Biology includes reviews and primary research papers spanning the full range of -omic applications to provide a forward-looking view of matrisome research. The editors hope that this Special Issue will stimulate readers to ask: What have we learnt to date and what are the major gaps in knowledge? What are the big questions that can be addressed with existing technologies? What technological developments will be needed to make a leap forward to 10 years hence?

https://www.sciencedirect.com/journal/matrix-biology/special-issue/10R66KP1L4T

Matrix Pathobiology and Angiogenesis

Editors: Evangelia Papadimitriou, Constantinos M. Mikelis

- Provides an overview of the various roles of the ECM during angiogenesis
- Discusses regulatory aspects of endothelial cells by the ECM
- Discusses the exploitation of ECM molecules for designing therapeutic approaches



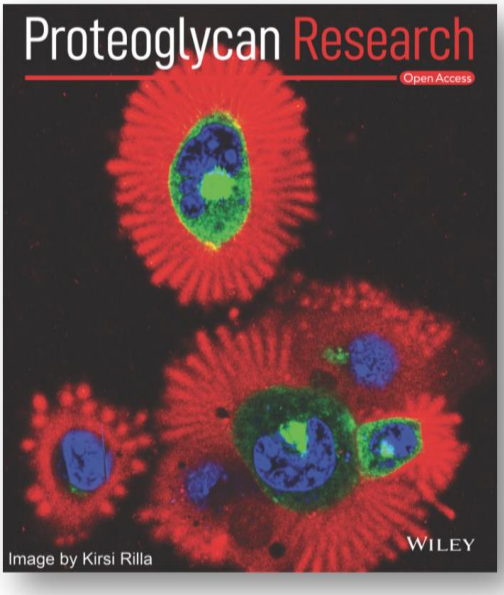
Part of the book series: Biology of Extracellular Matrix (BEM, volume 12)
Series Editor Nikos K. Karamanos
https://link.springer.com/book/10.1007/978-3-031-19616-4

Proteoglycan Research

Dear Proteoglycan Researchers,
I hope this finds you well. The journal is now a reality.
Please go to the developing home page:
https://onlinelibrary.wiley.com/journal/28323556

Proteoglycan Research will consider both mechanistic and correlative papers including research articles, brief reports, full-length and mini-reviews, perspectives, method papers and technical advances. Please view our Guide to Authors for additional information.

I have written an editorial introducing the new journal which will appear in near future after we have at least four or five papers to be published together. I already received several papers from our community, and all are under review; however, none has been accepted yet at the time of this writing. Likely, we will have the first papers in the next month or so.



It would be great if you could submit research papers from your lab and co-workers. If you are interested in writing a minireview or a perspective focused on emerging fields of research in proteoglycans, please, contact me directly with your idea/proposal via e-mail to renato.iozzo@jefferson.edu.

The publisher, Wiley, gave us 20 waivers and if you are early, there will be no fee for the open access.
I wish you a peaceful, healthy, and very productive 2023.

Renato V. Iozzo, MD PhD
Editor-In-Chief
Proteoglycan Research

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.

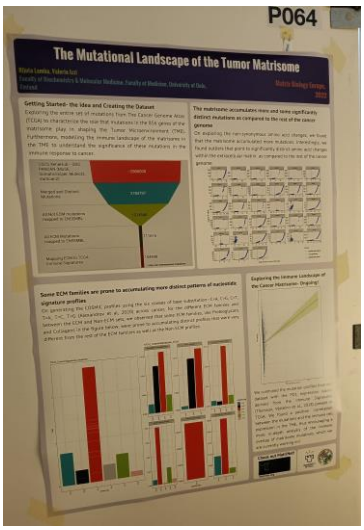
To apply for a travel grant, please send your application to the ISMB secretary, in the form of a single pdf file containing: (1) a letter giving information about the meeting, the amount requested and a detailed justification for support, (2) the abstract of your poster/short talk, (3) your curriculum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

Meeting reports

From a young scientist awarded ISMB travel fellowship

I 

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am Rijuta, I am a Doctoral Researcher in the Izzi Group, at the University of Oulu. I'd like to begin by thanking ISMB for the travel grant, it made my travel to the conference possible and for that I am grateful! As a bioinformatician working on cancer mutations in the matrisome, I really look forward these meetings with the matrix community as it provides me an opportunity to keep myself up to date with various wet lab procedures and the world matrix research in general and the MBE was no different. The talks were absolutely enriching, and I was particularly intrigued by the immune-matrisome research, and I really carried home patient derived auto antibody and matrix remodelling enzymes in the cancer microenvironment work presented by Dr. Irit Sagi and the immune suppressive regulatory model of Tenascin-C in the Tumor

Microenvironment presented by Dr. Gertraud Orend. As an early career researcher, what I found exceptionally illuminating was exchanging ideas with my fellow doctoral researchers during the Poster sessions where I was presenting our work on the Mutational Landscape of the Matrisome in Cancer. I was very happy to learn about a multitude of things starting from mechano-fluidics of matrix molecules to several in-vivo models that were presented to understand a wide range of clinically important questions! It was heartening and humbling to talk about the ins-and-outs of research and academia and to exchange ideas with so many brilliant minds!
To summarize, the conference delivered and went beyond on the most important aspects of academia- good research, an opportunity to learn from some of the best matrix researchers and an honest exchange of ideas with my peers and this was what made it an extraordinary experience!
Rijuta Lamba, University of Oulu (Finland)

Report of the 6th National Matrix Biology Academic Conference 2022 Chinese society of Matrix Biology

On November 3 to November 5, 2022, sponsored by **Chinese society of matrix biology (CSMB) of the Chinese Association for Physiological Sciences (CAPS),** and undertaken by **the School of Life Sciences of Xiamen University, the School of Medicine of Xiamen University, the National Key Laboratory of Cell Stress Biology (Xiamen University), and the Xiang'an Innovation Laboratory**, the "Sixth National Matrix Biology Academic Conference in 2022" was successfully held in **Xiamen Haiyue Villa Hotel, No. 3999, Huandao South Road, Siming District, Xiamen, Fujian Province, China**. A total of more than 100 scholars participated in the academic event offline. Affected by the epidemic, many other experts and scholars participated in the conference through video conference and live broadcast. The opening ceremony was presided over by Professor Zhi-gang Zhang, current chairman of the Chinese Society of Matrix Biology and chairman of the conference.

The academic exchange of the conference includes special invitation report, youth report and poster exchange. The topics cover several aspects of matrix biology: **1. ECM in Immunity and Cancer; 2. ECM and Mechanizing; 3. Signing from the Matrix; 4. Novel Conceptual and Technical Advances in Matrix**. The wonderful display of the Youth Forum and poster exchange also left a deep impression on the participants, allowing them to witness the dynamic development trend and bright prospects in this field.

Recent publications

Targeting Aggrecanases for Osteoarthritis Therapy: From Zinc Chelation to Exosite Inhibition
Cuffaro D, Ciccone L, Rossello A , Nuti E, Santamaria S. J Med Chem 2022 65:13505-13532.
Corresponding authors: elisa.nuti@unipi.it, s.santamaria@imperial.ac.uk, s.santamaria@surrey.ac.uk
Abstract: Osteoarthritis (OA) is the most common degenerative joint disease. In 1999, two members of the A Disintegrin and Metalloproteinase with Thrombospondin Motifs (ADAMTS) family of metalloproteinases, ADAMTS4 and ADAMTS5, or aggrecanases, were identified as the enzymes responsible for aggrecan degradation in cartilage. The first aggrecanase inhibitors targeted the active site by chelation of the catalytic zinc ion. Due to the generally disappointing performance of zinc-chelating inhibitors in preclinical and clinical studies, inhibition strategies tried to move away from the active-site zinc in order to improve selectivity. Exosite inhibitors bind to proteoglycan-binding residues present on the aggrecanase ancillary domains (called exosites). While exosite inhibitors are generally more selective than zinc-chelating inhibitors, they are still far from fulfilling their potential, partly due to a lack of structural and functional data on aggrecanase exosites. Filling this gap will inform the design of novel potent, selective aggrecanase inhibitors.

Tropoelastin improves post-infarct cardiac function by increasing scar elastin.
Hume, R.D., Kanagalingam, S., Deshmukh, T., Chen, S., Mithieux, S.M., Rashid, F., Roohani, I., Lu, J., Doan, T., Graham, D., Clayton, Z.E., Slaughter, E., Kizana, E., Stempien-Otero, A.S., Brown, P., Thomas, L., Weiss, A.S. and Chong, J.J.H. Circ Res 2022 Dec 1. doi: 10.1161/CIRCRESAHA.122.321123. Online ahead of print
Corresponding author: james.chong@sydney.edu.au
Abstract *Background*: Myocardial infarction (MI) is among the leading causes of death worldwide. Following MI, necrotic cardiomyocytes are replaced by a stiff collagen-rich scar. Compared to collagen, the extracellular matrix protein elastin has high elasticity and may have more favorable properties within the cardiac scar. We sought to improve post-MI healing by introducing tropoelastin, the soluble subunit of elastin, to alter scar mechanics early after MI. *Methods and results*: We developed an ultrasound-guided direct intramyocardial injection method to administer tropoelastin directly into the left ventricular anterior wall of rats subjected to induced MI. Experimental groups included shams and infarcted rats injected with either PBS vehicle control or tropoelastin. Compared to vehicle treated controls, echocardiography assessments showed tropoelastin significantly improved left ventricular ejection fraction (64.7±4.4% versus 46.0±3.1% control) and reduced left ventricular dyssynchrony (11.4±3.5 ms versus 31.1±5.8 ms control) 28 days post-MI. Additionally, tropoelastin reduced post-MI scar size (8.9±1.5% versus 20.9±2.7% control) and increased scar elastin (22±5.8% versus 6.2±1.5% control) as determined by histological assessments. Ribonucleic acid sequencing analyses of rat infarcts showed that tropoelastin injection increased genes associated with elastic fiber formation 7 days post-MI and reduced genes associated with immune response 11 days post-MI. To show translational relevance, we performed immunohistochemical analyses on human ischemic heart disease cardiac samples and showed an increase in tropoelastin within fibrotic areas. Using ribonucleic acid sequencing we also demonstrated the tropoelastin gene ELN is upregulated in human ischemic heart disease and during human cardiac fibroblast-myofibroblast differentiation. Furthermore, we showed by immunocytochemistry that human cardiac fibroblast synthesize increased elastin in direct response to tropoelastin treatment. *Conclusions*: We demonstrate for the first time that purified human tropoelastin can significantly repair the infarcted heart in a rodent model of MI and that human cardiac fibroblast synthesize elastin. Since human cardiac fibroblasts are primarily responsible for post-MI scar synthesis, our findings suggest exciting future clinical translation options designed to therapeutically manipulate this synthesis.

Rapid regeneration of a neoartery with elastic lamellae.
Wang, Z., Mithieux, S.M., Vindin, H., Wang, Y., Zhang, M., Liu, L., Zbinden, J., Blum, K.M., Yi, T., Matsuzaki, Y., Oveissi, F., Akdemir, R., Lockley, K.M., Zhang, L., Ma, K., Guan, J., Waterhouse, A., Pham, N.T.H., Hawkett, B.S., Shinoka, T., Breuer, C.K. and Weiss, A.S. Adv Mater 2022 Nov;34(47):e2205614. doi: 10.1002/adma.202205614
Corresponding author: tony.weiss@sydney.edu.au
Abstract: Native arteries contain a distinctive intima-media composed of organized elastin and an adventitia containing mature collagen fibrils. In contrast, implanted biodegradable small-diameter vascular grafts do not present spatially regenerated, organized elastin. The elastin-containing structures within the intima-media region encompass the elastic lamellae (EL) and internal elastic lamina (IEL) and are crucial for normal arterial function. Here, the development of a novel electrospun small-diameter vascular graft that facilitates de novo formation of a structurally appropriate elastin-containing intima-media region following implantation is described. The graft comprises a non-porous microstructure characterized by tropoelastin fibers that are embedded in a PGS matrix. After implantation in mouse abdominal aorta, the graft develops distinct cell and extracellular matrix profiles that approximate the native adventitia and intima-media by 8 weeks. Within the newly formed intima-media region there are circumferentially aligned smooth muscle cell layers that alternate with multiple EL similar to that found in the arterial wall. By 8 months, the developed adventitia region contains mature collagen fibrils and the neoartery presents a distinct IEL with thickness comparable to that in mouse abdominal aorta. It is proposed that this new class of material can generate the critically required, organized elastin needed for arterial regeneration.

Changes in elastin structure and extensibility induced by hypercalcemia and hyperglycemia.
Yang, C., Weiss, A.S. and Tarakanova, A. Acta Biomater 2022 Mar 30;S1742-7061(22)00180-5.
doi: 10.1016/j.actbio.2022.03.041.
Corresponding author: anna.tarakanova@uconn.edu
Abstract: Elastin is a key elastomeric protein responsible for the elasticity of many organs, including heart, skin, and blood vessels. Due to its intrinsic long life and low turnover rate, damage in elastin induced by pathophysiological conditions, such as hypercalcemia and hyperglycemia, accumulates during biological aging and in aging-associated diseases, such as diabetes mellitus and atherosclerosis. Prior studies have shown that calcification induced by hypercalcemia deteriorates the function of aortic tissues. Glycation of elastin is triggered by hyperglycemia and associated with elastic tissue damage and loss of mechanical functions via the accumulation of advanced glycation end products. To evaluate the effects on elastin's structural conformations and elasticity by hypercalcemia and hyperglycemia at the molecular scale, we perform classical atomistic and steered molecular dynamics simulations on tropoelastin, the soluble precursor of elastin, under different conditions. We characterize the interaction sites of glucose and calcium and associated structural conformational changes. Additionally, we find that elevated levels of calcium ions and glucose hinder the extensibility of tropoelastin by rearranging structural domains and altering hydrogen bonding patterns, respectively. Overall, our investigation helps to reveal the behavior of tropoelastin and the biomechanics of elastin biomaterials in these physiological environments. STATEMENT OF SIGNIFICANCE: Elastin is a key component of elastic fibers which endow many important tissues and organs, from arteries and veins, to skin and heart, with strength and elasticity. During aging and aging-associated diseases, such as diabetes mellitus and atherosclerosis, physicochemical stressors, including hypercalcemia and hyperglycemia, induce accumulated irreversible damage in elastin, and consequently alter mechanical function. Yet, molecular mechanisms associated with these processes are still poorly understood. Here, we present the first study on how these changes in elastin structure and extensibility are induced by hypercalcemia and hyperglycemia at the molecular scale, revealing the essential roles that calcium and glucose play in triggering structural alterations and mechanical stiffness. Our findings yield critical insights into the first steps of hypercalcemia- and hyperglycemia-mediated aging.

Differential MMP-14 Targeting by Biglycan, Decorin, Fibromodulin and Lumican Unraveled by *In Silico* Approach.

Rivet R, Rao RM, Nizet P, Belloy N, Huber L, Dauchez M, Ramont L, Baud S, Brézillon S. Am J Physiol Cell Physiol. 2022 Dec 19. doi: 10.1152/ajpcell.00429.2022. PMID: 36534501

Corresponding author: stephane.brezillon@univ-reims.fr

Abstract: *Small leucine-rich proteoglycans (SLRPs) are major regulators of extracellular matrix assembly and cell signaling. Lumican, a member of the SLRPs family, and its derived peptides possess anti-tumor activity by interacting directly with the catalytic domain of MMP-14 leading to the inhibition of its activity. The aim of this report was to characterize by in silico 3D modeling the structure and the dynamics of four SLRPs including their core protein and their specific polysaccharide chains to assess their capacity to bind to MMP-14 and to regulate its activity. Molecular docking experiments were performed to identify the specific amino acids of MMP-14 interacting with each of the four SLRPs. The inhibition of each SLRP (100nM) on MMP-14 activity and the constants of inhibition (Ki) were evaluated. The impact of the number of glycan chains, structures and dynamics of lumican on the interaction with MMP-14 was assessed by molecular dynamics simulations. Molecular docking analysis showed that all SLRPs bind to MMP-14 through their concave face, but in different regions of the catalytic domain of MMP-14. Each SLRPs inhibited significantly the MMP-14 activity. Finally, molecular dynamics showed the role of glycan chains in interaction with MMP-14 and shielding effect of SLRPs. Altogether, the results demonstrated that each SLRP exhibited inhibition of MMP-14 activity. However, the differential targeting of MMP-14 by the SLRPs was shown to be related not only to the core protein conformation but also to the glycan chain structures and dynamics.*

Regulation of stem cell fate by HSPGs: implication in hair follicle cycling.

Colin-Pierre C, El Baraka O, Danoux L, Bardey V, André V, Ramont L, Brézillon S. NPJ Regen Med. 2022 Dec 28;7(1):77. doi: 10.1038/s41536-022-00267-y. Review.

Corresponding author: charlie.pierre@basf.com

Abstract: *Heparan sulfate proteoglycans (HSPGs) are part of proteoglycan family. They are composed of heparan sulfate (HS)-type glycosaminoglycan (GAG) chains covalently linked to a core protein. By interacting with growth factors and/or receptors, they regulate numerous pathways including Wnt, hedgehog (Hh), bone morphogenic protein (BMP) and fibroblast growth factor (FGF) pathways. They act as inhibitor or activator of these pathways to modulate embryonic and adult stem cell fate during organ morphogenesis, regeneration and homeostasis. This review summarizes the knowledge on HSPG structure and classification and explores several signaling pathways regulated by HSPGs in stem cell fate. A specific focus on hair follicle stem cell fate and the possibility to target HSPGs in order to tackle hair loss are discussed in more dermatological and cosmeceutical perspectives.*

Rapamycin- induced autophagy in osteosarcoma cells is mediated via the biglycan/Wnt/β-catenin signaling axis

Giatagana E-M., Berdiaki A., Gaardløs M., Tsatsakis A., Samsonov S.A., Nikitovic D. American Journal of Physiology-Cell Physiology. 2022 323:C1740-C1756. https://doi.org/10.1152/ajpcell.00368.2022

Corresponding author: nikitovic@uoc.gr

Abstract: *Biglycan is a class I secreted small leucine-rich proteoglycan (SLRP), which regulates signaling pathways connected to bone pathologies. Autophagy is a vital catabolic process with a dual role in cancer progression. Here, we show that biglycan inhibits autophagy in two osteosarcoma cell lines ($P \leq 0.001$), while rapamycin-induced autophagy decreases biglycan expression in MG63 osteosarcoma cells and abrogates the biglycan-induced cell growth increase ($P \leq 0.001$). Rapamycin also inhibits β-catenin translocation to the nucleus, inhibiting the Wnt*

pathway (P ≤ 0.001) and reducing biglycan's colocalization with the Wnt coreceptor LRP6 (P ≤ 0.05). Furthermore, biglycan exhibits protective effects against the chemotherapeutic drug doxorubicin in MG63 OS cells through an autophagy-dependent manner (P ≤ 0.05). Cotreatment of these cells with rapamycin and doxorubicin enhances cells response to doxorubicin by decreasing biglycan (P ≤ 0.001) and β-catenin (P ≤ 0.05) expression. Biglycan deficiency leads to increased caspase-3 activation (P ≤ 0.05), suggesting increased apoptosis of biglycan-deficient cells treated with doxorubicin. Computational models of LRP6 and biglycan complexes suggest that biglycan changes the receptor's ability to interact with other signaling molecules by affecting the interdomain bending angles in the receptor structure. Biglycan binding to LRP6 activates the Wnt pathway and β-catenin nuclear translocation by disrupting β-catenin degradation complex (P ≤ 0.01 and P ≤ 0.05). Interestingly, this mechanism is not followed in moderately differentiated, biglycan-nonexpressing U-2OS OS cells. To sum up, biglycan exhibits protective effects against the doxorubicin in MG63 OS cells by activating the Wnt signaling pathway and inhibiting autophagy.

ESR2 Drives Mesenchymal-to-Epithelial Transition in Triple-Negative Breast Cancer and Tumorigenesis In Vivo

Front Oncol 2022 3;12:917633.
Corresponding author:
Abstract: *Estrogen receptors (ERs) have pivotal roles in the development and progression of triple-negative breast cancer (TNBC). Interactions among cancer cells and tumor microenvironment are orchestrated by the extracellular matrix that is rapidly emerging as prominent contributor of fundamental processes of breast cancer progression. Early studies have correlated ERβ expression in tumor sites with a more aggressive clinical outcome, however ERβ exact role in the progression of TNBC remains to be elucidated. Herein, we introduce the functional role of ERβ suppression following isolation of monoclonal cell populations of MDA-MB-231 breast cancer cells transfected with shRNA against human ESR2 that permanently resulted in 90% reduction of ERβ mRNA and protein levels. Further, we demonstrate that clone selection results in strongly reduced levels of the aggressive functional properties of MDA-MB-231 cells, by transforming their morphological characteristics, eliminating the mesenchymal-like traits of triple-negative breast cancer cells. Monoclonal populations of shERβ MDA-MB-231 cells undergo universal matrix reorganization and pass on a mesenchymal-to-epithelial transition state. These striking changes are encompassed by the total prevention of tumorigenesis in vivo following ERβ maximum suppression and isolation of monoclonal cell populations in TNBC cells. We propose that these novel findings highlight the promising role of ERβ targeting in future pharmaceutical approaches for managing the metastatic dynamics of TNBC breast cancer.*

EMILIN1 deficiency causes arterial tortuosity with osteopenia and connects impaired elastogenesis with defective collagen fibrillogenesis.
Adamo CS, Beyens A, Schiavinato A, Keene DR, Tufa SF, Mörgelin M, Brinckmann J, Sasaki T, Niehoff A, Dreiner M, Pottie L, Muiño-Mosquera L, Gulec EY, Gezdirici A, Braghetta P, Bonaldo P, Wagener R, Paulsson M, Bornaun H, De Rycke R, De Bruyne M, Baeke F, Devine WP, Gangaram B, Tam A, Balasubramanian M, Ellard S, Moore S, Symoens S, Shen J, Cole S, Schwarze U, Holmes KW, Hayflick SJ, Wiszniewski W, Nampoothiri S, Davis EC, Sakai LY, Sengle G, Callewaert B. Am J Hum Genet. 2022 Dec 1;109(12):2230-2252. doi: 10.1016/j.ajhg.2022.10.010.
Corresponding author: gsengle@uni-koeln.de and bert.callewaert@ugent.be
Abstract: *EMILIN1 (elastin-microfibril-interface-located-protein-1) is a structural component of the elastic fiber network and localizes to the interface between the fibrillin microfibril scaffold and the elastin core. How EMILIN1 contributes to connective tissue integrity is not fully understood. Here, we report bi-allelic EMILIN1 loss-of-function*

variants causative for an entity combining cutis laxa, arterial tortuosity, aneurysm formation, and bone fragility, resembling autosomal-recessive cutis laxa type 1B, due to EFEMP2 (FBLN4) deficiency. In both humans and mice, absence of EMILIN1 impairs EFEMP2 extracellular matrix deposition and LOX activity resulting in impaired elastogenesis, reduced collagen crosslinking, and aberrant growth factor signaling. Collagen fiber ultrastructure and histopathology in EMILIN1- or EFEMP2-deficient skin and aorta corroborate these findings and murine Emilin1-/- femora show abnormal trabecular bone formation and strength. Altogether, EMILIN1 connects elastic fiber network with collagen fibril formation, relevant for both bone and vascular tissue homeostasis.

Structure, evolution and expression of zebrafish cartilage oligomeric matrix protein (COMP, TSP5). CRISPR-Cas mutants show a dominant phenotype in myosepta.

Forte-Gomez HF, Gioia R, Tonelli F, Kobbe B, Koch P, Bloch W, Paulsson M, Zaucke F, Forlino A, Wagener R. Front Endocrinol (Lausanne). 2022 Nov 14;13:1000662. doi: 10.3389/fendo.2022.1000662.

Corresponding author: raimund.wagener@uni-koeln.de

Abstract: *COMP (Cartilage Oligomeric Matrix Protein), also named thrombospondin-5, is a member of the thrombospondin family of extracellular matrix proteins. It is of clinical relevance, as in humans mutations in COMP lead to chondrodysplasias. The gene encoding zebrafish Comp is located on chromosome 11 in synteny with its mammalian orthologs. Zebrafish Comp has a domain structure identical to that of tetrapod COMP and shares 74% sequence similarity with murine COMP. Zebrafish comp is expressed from 5 hours post fertilization (hpf) on, while the protein is first detectable in somites of 11 hpf embryos. During development and in adults comp is strongly expressed in myosepta, craniofacial tendon and ligaments, around ribs and vertebra, but not in its name-giving tissue cartilage. As in mammals, zebrafish Comp forms pentamers. It is easily extracted from 5 days post fertilization (dpf) whole zebrafish. The lack of Comp expression in zebrafish cartilage implies that its cartilage function evolved recently in tetrapods. The expression in tendon and myosepta may indicate a more fundamental function, as in evolutionary distant Drosophila muscle-specific adhesion to tendon cells requires thrombospondin. A sequence encoding a calcium binding motif within the first TSP type-3 repeat of zebrafish Comp was targeted by CRISPR-Cas. The heterozygous and homozygous mutant Comp zebrafish displayed a patchy irregular Comp staining in 3 dpf myosepta, indicating a dominant phenotype. Electron microscopy revealed that the endoplasmic reticulum of myosepta fibroblasts is not affected in homozygous fish. The disorganized extracellular matrix may indicate that this mutation rather interferes with extracellular matrix assembly, similar to what is seen in a subgroup of chondrodysplasia patients. The early expression and easy detection of mutant Comp in zebrafish points to the potential of using the zebrafish model for large scale screening of small molecules that can improve secretion or function of disease-associated COMP mutants.*

Tenascin C is a valuable marker for melanoma progression independent of mutational status and MAPK inhibitor therapy.

Fromme JE, Dummer R, Mauch C, Zigrino P. Exp Dermatol. 2022 Nov 27. doi: 10.1111/exd.14717.

Corresponding author: paola.zigrino@uni-koeln.de

Research Letter, no abstract available

A20 binding and inhibitor of nuclear factor kappa B (NF-κB)-1 (ABIN-1) - a novel modulator of mitochondrial autophagy.

Merline R, Rödig H, Zeng-Brouwers J, Poluzzi C, Tascher G, Michaelis J, Lopez-Mosqueda J, Rhiner A, Huber LS, Diehl V, Dikic I, Kögel D, Münch C, Wygrecka M, Schaefer L. Am J Physiol Cell Physiol. 2022 Nov 28. doi: 10.1152/ajpcell.00493.2022.

Corresponding author: LSchaefer@physiology.org and rmerline@med.uni-frankfurt.de

Abstract: *A20 binding inhibitor of nuclear factor kappa B (NF-κB)-1 (ABIN-1), a polyubiquitin-binding protein, is a signal-induced autophagy receptor that attenuates NF-κB-mediated inflammation and cell death. The present study aimed to elucidate the potential role of ABIN-1 in mitophagy, a biological process whose outcome is decisive in diverse physiological and pathological settings. Microtubule-associated proteins 1A/1B light chain 3B-II (LC3B-II) was found to be in complex with ectopically expressed hemagglutinin (HA)-tagged-full length (FL)-ABIN-1. Bacterial expression of ABIN-1 and LC3A and LC3B showed direct binding of ABIN-1 to LC3 proteins, while mutations in the LC3-interacting region (LIR) 1 and 2 motifs of ABIN-1 abrogated ABIN-1/LC3B-II complex formation. Importantly, induction of autophagy in HeLa cells resulted in co-localization of ABIN-1 with LC3B-II in autophagosomes and with lysosomal associated membrane protein 1 (LAMP-1) in autophagolysosomes, leading to co-degradation of ABIN-1 with p62. Interestingly, ABIN-1 was found to translocate to damaged mitochondria in HeLa-mCherry-Parkin cells. In line with this observation, CRISPR/Cas9-mediated deletion of ABIN-1 significantly inhibited the degradation of the mitochondrial outer membrane proteins voltage-dependent anion-selective channel 1 (VDAC-1), mitofusin-2 (MFN2), and translocase of outer mitochondrial membrane (TOM)20. Additionally, siRNA-mediated knockdown of ABIN-1 significantly decreased lysosomal uptake of mitochondria in HeLa cells expressing mCherry-Parkin and the fluorescence reporter mt-mKEIMA. Collectively, our results identify ABIN-1 as a novel and selective mitochondrial autophagy regulator that promotes mitophagy, thereby adding a new player to the complex cellular machinery regulating mitochondrial homeostasis.*

Lack of evidence for a role of anthrax toxin receptors as surface receptors for collagen VI and for its cleaved-off C5 domain/endotrophin.

Przyklenk M, Heumüller SE, Freiburg C, Lütke S, Sengle G, Koch M, Paulsson M, Schiavinato A, Wagener R. iScience. 2022 Sep 12;25(10):105116. doi: 10.1016/j.isci.2022.105116.

Corresponding author: aschiav1@uni-koeln.de and raimund.wagener@uni-koeln.de

Abstract: *The microfibril-forming collagen VI is proteolytically cleaved and it was proposed that the released C-terminal Kunitz domain (C5) of the α3 chain is an adipokine important for tumor progression and fibrosis. Designated "endotrophin," C5 is a potent biomarker for fibroinflammatory diseases. However, the biochemical mechanisms behind endotrophin activity were not investigated. Earlier, anthrax toxin receptor 1 was found to bind C5, but this potential interaction was not further studied. Given the proposed physiological role of endotrophin, we aimed to determine how the signal is transmitted. Surprisingly, we could not detect any interaction between endotrophin and anthrax toxin receptor 1 or its close relative, anthrax toxin receptor 2. Moreover, we detect no binding of fully assembled collagen VI to either receptor. We also studied the collagen VI receptor NG2 (CSPG4) and confirmed that NG2 binds assembled collagen VI, but not cleaved C5/endotrophin. A cellular receptor for C5/endotrophin, therefore, still remains elusive.*

Cartilage Extracellular Matrix-derived Matrikines in Osteoarthritis.

Rapp AE, Zaucke F. Am J Physiol Cell Physiol. 2022 Dec 26. doi: 10.1152/ajpcell.00464.2022.

Corresponding author: frank.zaucke@kgu.de

Abstract: *Osteoarthritis (OA) is among the most frequent diseases of the musculoskeletal system. Degradation of cartilage extracellular matrix (ECM) is a hallmark of OA. During the degradation process intact/full-length proteins as well as proteolytic fragments are released which then might induce different downstream responses via diverse receptors, therefore leading to different biological consequences. Collagen type II and the proteoglycan aggrecan are the most abundant components of the cartilage ECM. However, over the last decades, a large number of minor components have been identified and for some of those a role in the manifold processes associated with OA has already been demonstrated. To date, there is still no therapy able to halt or cure OA. A better understanding of the matrikine landscape occurring with or even preceding obvious degenerative changes in joint tissues is needed*

and might help to identify molecules that could serve as biomarkers, druggable targets, or even be blueprints for DMOADs. For this narrative review, we screened PubMed for relevant literature in English language and summarized the current knowledge regarding the function of selected ECM molecules and the derived matrikines in the context of cartilage and OA.

New refinements aim to optimize articular cartilage tissue engineering.
Schäfer N, Grässel S. Nat Rev Rheumatol. 2023 Jan 5. doi: 10.1038/s41584-022-00889-y.
Corresponding author: susanne.graessel@klinik.uni-regensburg.de
Year in Review, no abstract available

Targeted therapy for osteoarthritis: progress and pitfalls.
Schäfer N, Grässel S. Nat Med. 2022 Dec;28(12):2473-2475. doi: 10.1038/s41591-022-02057-x.
Corresponding author: susanne.graessel@klinik.uni-regensburg.de
Comment, no abstract available

Targeting of bone morphogenetic protein complexes to heparin/heparan sulfate glycosaminoglycans in bioactive conformation.
Spanou CES, Wohl AP, Doherr S, Correns A, Sonntag N, Lütke S, Mörgelin M, Imhof T, Gebauer JM, Baumann U, Grobe K, Koch M, Sengle G. FASEB J. 2023 Jan;37(1):e22717. doi: 10.1096/fj.202200904R.
Corresponding author: gsengle@uni-koeln.de
Abstract: *Bone morphogenetic proteins (BMP) are powerful regulators of cellular processes such as proliferation, differentiation, and apoptosis. However, the specific molecular requirements controlling the bioavailability of BMPs in the extracellular matrix (ECM) are not yet fully understood. Our previous work showed that BMPs are targeted to the ECM as growth factor-prodomain (GF-PD) complexes (CPLXs) via specific interactions of their PDs. We showed that BMP-7 PD binding to the extracellular microfibril component fibrillin-1 renders the CPLXs from an open, bioactive V-shape into a closed, latent ring shape. Here, we show that specific PD interactions with heparin/heparan sulfate glycosaminoglycans (GAGs) allow to target and spatially concentrate BMP-7 and BMP-9 CPLXs in bioactive V-shape conformation. However, targeting to GAGs may be BMP specific, since BMP-10 GF and CPLX do not interact with heparin. Bioactivity assays on solid phase in combination with interaction studies showed that the BMP-7 PD protects the BMP-7 GF from inactivation by heparin. By using transmission electron microscopy, molecular docking, and site-directed mutagenesis, we determined the BMP-7 PD-binding site for heparin. Further, fine-mapping of the fibrillin-1-binding site within the BMP-7 PD and molecular modeling showed that both binding sites are mutually exclusive in the open V- versus closed ring-shape conformation. Together, our data suggest that targeting exquisite BMP PD-binding sites by extracellular protein and GAG scaffolds integrates BMP GF bioavailability in a contextual manner in development, postnatal life, and connective tissue disease.*

Semaphorin 3A-Neuropilin-1 Signaling Modulates MMP13 Expression in Human Osteoarthritic Chondrocytes.
Stöckl S, Reichart J, Zborilova M, Johnstone B, Grässel S. Int J Mol Sci. 2022 Nov 16;23(22):14180. doi: 10.3390/ijms232214180.
Corresponding author: susanne.graessel@ukr.de
Abstract: *Osteoarthritis (OA) is a complex disorder of diarthrodial joints caused by multiple risk factors and is characterized by articular cartilage destruction as well as changes in other articular tissues. Semaphorin 3A (Sema3A), known to be a chemo-repellent for sensory nerve fibers, has recently been implicated in cartilage OA pathophysiology. We demonstrated that the expression of SEMA3A and its receptor neuropilin-1 (NRP1) are synchronously upregulated in chondrocytes isolated from knee cartilage of OA patients compared to non-OA*

control chondrocytes. In addition, we observed that during in vitro passaging of OA chondrocytes, the Nrp-1 level increases, whereas the Sema3A level decreases. In this study, we aimed to uncover how Sema3A-Nrp-1 signaling affects metabolism and viability of OA chondrocytes via siRNA-mediated inhibition of Nrp-1 expression. We observed a decreased proliferation rate and an increase in adhesion and senescence after Nrp-1 silencing. Moreover, MMP13 gene expression was reduced by approximately 75% in NRP1 knockdown OA chondrocytes, whereas MMP13 expression was induced by Sema3A treatment in control (nt siRNA) OA chondrocytes, accompanied by an impaired AKT phosphorylation. These findings suggest a potential catabolic function of Sema3A signaling in OA chondrocytes by inducing MMP13 expression and by compromising pro-survival AKT activation. We propose that targeting the Sema3A-Nrp-1 signaling axis might be an opportunity to interfere with OA pathogenesis and progression.

Decorin improves human pancreatic β-cell function and regulates ECM expression in vitro.
Urbanczyk M, Jeyagaran A, Zbinden A, Lu CE, Marzi J, Kuhlburger L, Nahnsen S, Layland SL, Duffy G, Schenke-Layland K. Matrix Biol. 2022 Dec 30:S0945-053X(22)00154-8. doi: 10.1016/j.matbio.2022.12.005.
Corresponding author: katja.schenke-layland@uni-tuebingen.de
Abstract: *Transplantation of islets of Langerhans is a promising alternative treatment strategy in severe cases of type 1 diabetes mellitus; however, the success rate is limited by the survival rate of the cells post-transplantation. Restoration of the native pancreatic niche during transplantation potentially can help to improve cell viability and function. Here, we assessed for the first time the regulatory role of the small leucine-rich proteoglycan decorin (DCN) in insulin secretion in human β-cells, and its impact on pancreatic extracellular matrix (ECM) protein expression in vitro. In depth analyses utilizing next-generation sequencing as well as Raman microspectroscopy and imaging identified pathways related to glucose metabolism to be upregulated in DCN-treated cells, including oxidative phosphorylation within the mitochondria as well as proteins and lipids of the endoplasmic reticulum. We further showed the effectiveness of DCN in a transplantation setting by treating collagen type 1-encapsulated β-cell-containing pseudo-islets with DCN. Taken together, in this study, we show the potential of DCN to improve* the function of insulin-secreting β-cells while reducing the expression of ECM proteins affiliated with fibrotic capsule formation, making DCN a highly promising therapeutic agent for islet transplantation.

Influence of the Peripheral Nervous System on Murine Osteoporotic Fracture Healing and Fracture-Induced Hyperalgesia.
Wank I, Niedermair T, Kronenberg D, Stange R, Brochhausen C, Hess A, Grässel S. Int J Mol Sci. 2022 Dec 28;24(1):510. doi: 10.3390/ijms24010510.
Corresponding author: susanne.graessel@ukr.de
Abstract: *Osteoporotic fractures are often linked to persisting chronic pain and poor healing outcomes. Substance P (SP), α-calcitonin gene-related peptide (α-CGRP) and sympathetic neurotransmitters are involved in bone remodeling after trauma and nociceptive processes, e.g., fracture-induced hyperalgesia. We aimed to link sensory and sympathetic signaling to fracture healing and fracture-induced hyperalgesia under osteoporotic conditions. Externally stabilized femoral fractures were set 28 days after OVX in wild type (WT), α-CGRP- deficient (α-CGRP -/-), SP-deficient (Tac1-/-) and sympathectomized (SYX) mice. Functional MRI (fMRI) was performed two days before and five and 21 days post fracture, followed by µCT and biomechanical tests. Sympathectomy affected structural bone properties in the fracture callus whereas loss of sensory neurotransmitters affected trabecular structures in contralateral, non-fractured bones. Biomechanical properties were mostly similar in all groups. Both nociceptive and resting-state (RS) fMRI revealed significant baseline differences in functional connectivity (FC) between WT and neurotransmitter-deficient mice. The fracture-induced hyperalgesia modulated central nociception and had robust impact on RS FC in all groups. The changes demonstrated in RS FC in fMRI might*

potentially be used as a bone traumata-induced biomarker regarding fracture healing under pathophysiological musculoskeletal conditions. The findings are of clinical importance and relevance as they advance our understanding of pain during osteoporotic fracture healing and provide a potential imaging biomarker for fracture-related hyperalgesia and its temporal development. Overall, this may help to reduce the development of chronic pain after fracture thereby improving the treatment of osteoporotic fractures.

Role of Macrophages in Wound Healing.
Willenborg S, Injarabian L, Eming SA. Cold Spring Harb Perspect Biol. 2022 Dec 1;14(12):a041216. doi: 10.1101/cshperspect.a041216.
Corresponding author: sabine.eming@uni-koeln.de
Abstract: *Monocytes/macrophages are key components of the body's innate ability to restore tissue function after injury. In most tissues, both embryo-derived tissue-resident macrophages and recruited blood monocyte-derived macrophages contribute to the injury response. The developmental origin of injury-associated macrophages has a major impact on the outcome of the healing process. Macrophages are abundant at all stages of repair and coordinate the progression through the different phases of healing. They are highly plastic cells that continuously adapt to their environment and acquire phase-specific activation phenotypes. Advanced omics methodologies have revealed a vast heterogeneity of macrophage activation phenotypes and metabolic status at injury sites in different organs. In this review, we highlight the role of the developmental origin, the link between the wound phase-specific activation state and metabolic reprogramming as well as the fate of macrophages during the resolution of the wounding response.*

Meeting announcements

The American and the International Society for Matrix Biology are offering a joint e-Symposium on January 26, 2023
09:00 AM in Eastern Time (US and Canada)

It is **FREE** and open to all. Register at
https://us02web.zoom.us/webinar/register/WN_XC-GTAAFQyKRB23lx7gE5g

MAKE IT OR BREAK IT: How ECM production and degradation fuels disease
A collaborative event with ISMB, Organized by: Valerio Izzi (Finland) and Raphael Reuten (Germany)

Roles of fibroblast/ECM functional units in pancreatic cancer, Edna Cukierman, *Fox Chase Cancer Center (USA)*

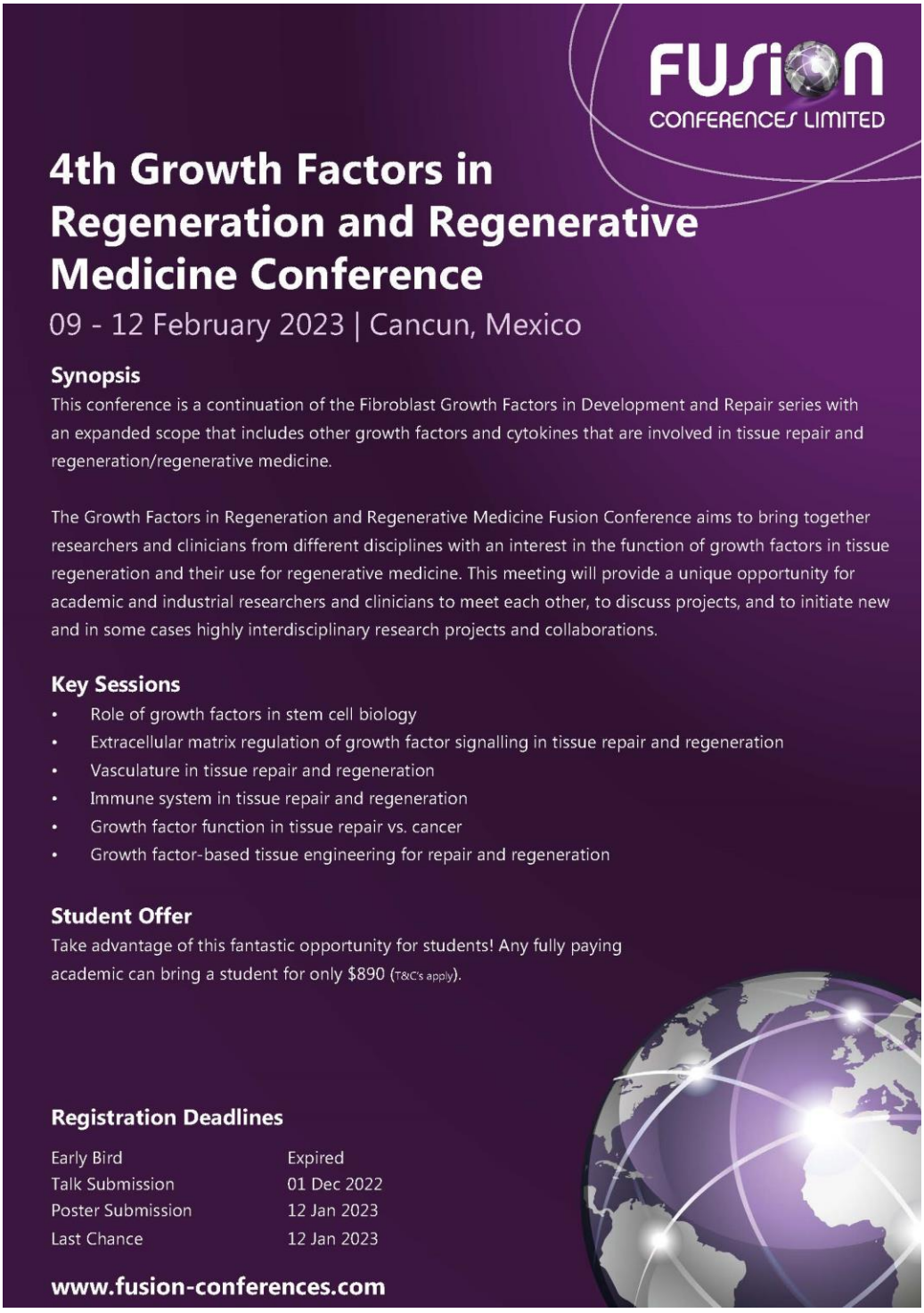
CAF metabolism coordinates tumour ECM production, Sara Zanivan, *University of Glasgow (UK)*

Dysregulated matrix remodeling emerges as important pathophysiological disease biomarker, Irit Sagi, *Weizmann Institute of Science (Israel)*

Roles of the ECM in tumor metastasis and drug resistance, Madeleine Oudin, *Tufts Unviersity (USA)*

4th Growth Factors in Regeneration and Regenerative Medicine Conference
9 - 12 February 2023, Cancun, Mexico

Chairs: Sabine Werner (ETH Zurich Institute of Molecular Health Sciences, Switzerland)
David Ornitz, Washington University (USA)
https://www.fusion-conferences.com/conference/116



The International Society for Hyaluronan Sciences (ISHAS) meeting - Hyaluronan 2023 4-8 June 2023 at the Hilton Portland Downtown, Portland, Oregon, USA.

Title: Hyaluronan 2023

The meeting will consist of ten scientific sessions (below) as well as an opening session with the presentation of the coveted "Rooster Prize", a welcome reception and a conference dinner cruise.

1. HA Metabolism and Synthesis
2. Biophysics and Structural Biology of HA
3. HA in Signaling and Cellular Biology
4. New Therapeutics and Biotechnological Applications of HA
5. HA in Tissue Engineering and Regenerative Medicine
6. HA in Neurobiology
7. HA in Viral Biology
8. HA in Cancer Biology
9. HA in Inflammation and Immunology
10. HA in Development and Aging

Registration can be made through the ISHAS web site (ishas.org), which also details the Invited Speakers in each session as well as information on the conference venue.

Registration will open Nov.15, 2022 and we encourage you to register as soon as possible. Visit https://ishas.org/ha-2023-conference/overview to find more information

Please submit abstracts by 28 February 2023.

We look forward to seeing you in Portland!

Sincerely,

Anthony J Day
ISHAS President

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Crosstalk between the ECM and Proteases from destruction to regeneration

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June 1, 2023

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Ulrich auf dem Keller | DTU - Technical University of Denmark
Christoph Becker-Pauly | Kiel University, Germany
Carl Blobel | HSS Research Institute, USA
Galia Blum | The Hebrew University of Jerusalem, Israel
Antoine Dufour | University of Calgary, Canada
Benjamin Geiger | Weizmann Institute of Science, Israel
Xavier Gomis Ruth | IBMB Barcelona, Spain
Barbara Grunwald | Princess Margaret Cancer Centre, Canada
Steffen Jung | Weizmann Institute of Science, Israel
Nikos Karamanos | University of Patras, Greece
Rama Khokha | University of Toronto, Canada
Moti Klepfish | Anima Biotech, Israel
Roman Krawetz | University of Calgary, Canada
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European Society of Tissue Regeneration in Orthopaedics & Traumatology
3-5 July, 2023, Frankfurt (Germany)

More information can be found here: http://www.estrot.org/

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- Tumor Growth and Metastasis
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- Fibrosis and Tissue Repair
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Gordon Research Conferences
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7th National Matrix Biology Academic Conference of the Chinese Society of Matrix Biology, Lishui, Zhejiang Province, China, August 2023

After discussion, the Committee of Chinese society of matrix biology (CSMB) plans to hold the 7th National Matrix Biology Academic Conference in **Lishui, Zhejiang Province, China**, in **August 2023**. The conference will discuss the matrix microenvironment and development, stem cell differentiation, transmembrane signal transduction, biomechanical characteristics and the relationship with tumors, bone joints, cardiovascular and other diseases from multiple perspectives. Lishui, known as Chuzhou in ancient times, is located in the southwest of Zhejiang Province, covering an area of 17300 square kilometers.

As its name implies, Lishui has incomparably beautiful landscapes. Lishui, with 3573 mountains above 1000 meters above sea level, is also the source of Oujiang River, Qiantang River, Minjiang River, Feiyun River, Lingjiang River and Fu'an River. Lishui is an excellent tourist city in China and a national civilized city. Nanjianyan, Huxian Palace, Baishanzu, Suichang National Mineral Park, etc. are all famous tourist attractions in Lishui. Lishui is also a famous city with profound cultural heritage. It is the first hometown of folk art in a prefecture level city in China, with rich historical and cultural relics. The famous Longquan celadon, Longquan sword and Qingtian stone carving are known as the "Three Treasures of Lishui". Welcome to Lishui, China.

89th Harden Conference
Proteoglycans: Matrix Master Regulators 2023
4 - 7 September 2023
De Vere Horsley Estate, Surrey, UK

https://www.biochemistry.org/events-and-training/events-calendar/89th-harden-conference-proteoglycans-matrix-master-regulators-2023/

Joint Annual Meeting of the German Society and Italian societies of Connective Tissues Münster (Germany) September 22-29, 2023

2023 - October 21-25 ASMB Biennial Meeting

Tissue, Matrix, and Pathobiology is an exciting new multidisciplinary and collaborative joint meeting of the American Society for Matrix Biology (ASMB), The Histochemical Society (HCS), and the American Society for Investigative Pathology (ASIP). This meeting, held in Salt Lake City, UT from Oct. 21–25, 2023, will feature cutting edge basic, clinical, and translational research related to a variety of topics that reflect normal biology of cells and tissues, and the molecular and cellular alterations that drive disease processes and accompany the development of disease.

More information about the program, abstract submission, and registration will be available on the meeting website soon. We hope you will join us next October! https://asmb.memberclicks.net/meetings

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Matrix Biology Europe meeting 2024 Save the date!

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)

Membership
Suneel Apte (USA)

Follow the ISMB on Twitter
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The ISMB correspondents of National Societies for Matrix Biology for Twitter

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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
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