THE DANISH SOCIETY FOR MATRIX BIOLOGY

Newsletter

No. 6, October, 2018

From the Chairman

Welcome to our 6th Newsletter!

In July, several participants from Denmark and DSMB members attended the well-arranged 2018 MBE (European) conference in Manchester, UK. René Svensson from Institute of Sports Medicine, Copenhagen represented Denmark in the Dick Heinegård young investigator award session (please read his joyful experience of 2018 MBE below). René did not win, but Raphael Reuten from BRIC representing Germany shared the award together with Karl - Emil Tykkeson from Lund University, Sweden. Also, Chloé Yeung from Institute of Sports Medicine, Copenhagen participated in the award session representing Britain with an excellent presentation.

Also earlier in April this year, the 1st Tendon UK meeting, hosted by the University of Oxford was held at the beautiful grounds of the Worchester College. The focus was Translation Tendon science - a large group from Institute of Sports Medicine, Copenhagen also participated, which including a couple of young talented investigators, who were in the young investigator award session and Adam Jørgensen, MD from Institute of Sports Medicine, Copenhagen won with a brilliant presentation.

At the moment, the DSMB board is working hard on arranging the 1st Joint Nordic matrix meeting, which will take place on March 14 – 15th 2019 at Copenhagen. This meeting will run straight after the PhD matrix course "Extracellular Matrix and Proteolysis in Disease" organised by our DSMB board members Marie Kveiborg and Niels Behrendt. In addition, Chloé Yeung, is also arranging a matrix PhD course with focus on exercise at the Institute of Sports Medicine, Copenhagen. These courses were huge successes last year, so be sure to sign up soon if you would like to participate.

In this newsletter, we present the lab and research from Daniel Madsen. We are looking forward to seeing you at our upcoming meetings, and we hope that you also will enjoy our newsletter.

Sincerely,
Christian Couppé

Meeting and conference reports

2018 Matrix Biology Europe Meeting (50th Anniversary of FECTS) 21st-24th July, University of Manchester, UK

I attended this year's MBE conference in Manchester, competing for the Dick Heinegård young investigator award on behalf of the Danish Society for Matrix Biology. Although I did not win, it was a great pleasure to attend, and I have to congratulate the two winners Raphael Reuten and Karl Tykesson from the German and Swedish societies. Considering their fantastic presentations, there was no shame in losing.

René Svensson presenting in the Dick Heinegård young investigator award session

As a biomechanicist I particularly enjoyed the work by Viola Vogel on fibronectin mechanics and especially the novel molecular strain probe that she presented, a kind of tool that I would love to have for my own research on tendon nano-mechanics. I was a bit surprised that there wasn't much other mechanics work being presented, but in no way was I disappointed since the molecular and biochemical work was of an outstanding quality. For someone like me who usually attend more mechanics focused meetings, the MBE provided ample food for thought on expanding my own research from mechanics into more molecular biology.

Overall I really enjoyed the meeting, it was well organized and since many of the speakers and attendees knew each other well there was an informal atmosphere that I personally find conductive to scientific discussion.

René B. Svensson
Postdoc, Institute of Sports Medicine Copenhagen, Bispebjerg Hospital

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I work on the cellular aspect of matrix biology, studying cancer associated fibroblasts, so I was honoured to be chosen as best presenter at the DSMB meeting in April and very excited to attend the MBE conference in Manchester.

The conference had more than 300 attendees, flustering the photographer when the conference group photo was being taken. With around 200 posters, and scientific sessions jam-packed with invited and selected talks the, MBE 2018 provided a comprehensive dose of matrix biology research for me and the rest of the attendees. Due to flight delays the original key note speaker Reinhard Fässler couldn't make it in time, so Janine Erler from BRIC, University of Copenhagen, stepped in with short notice and gave a great opening talk.

During the coffee breaks the discussion was lively overall, I met some great people and one of my colleagues left the conference having forged multiple new collaborations, calling MBE 2018 the most fruitful meeting he ever attended.

MBE 2018 in Manchester was my trial by fire into the international community for matrix biology research. Personally, having drinks under the ancient skeleton of a T-rex during the welcome reception in the Manchester Museum was an unexpected but fun first! I am very grateful for having had the opportunity to jump head first into, for me, a fairly unknown research field, and feeling so

welcomed by a great gathering of enthusiastic scientists. Keep up the good work and the great spirit all of you!

Freja A. Venning
PhD Student, Biotech Research and Innovation Centre (BRIC), University of Copenhagen

2018 MBE Group photo

The Lord Mayor of Manchester, Councillor June Hitchen, welcomed everyone at the Manchester Museum

Tour of the Old Trafford Manchester football stadium before the conference dinner (also at the Old Trafford)

Group photo of DSMB Danish delegates at MBE
(3 delegates missing in this photo)

Dick Heinegård Young Investigator Award presenters

Poster award winners

Dick Heinegard YIA was shared between
Raphael Reuten and Karl Emil Tykesson

See you all in Florence for MBE 2020

Group Highlights

Daniel Hargbøl Madsen, PhD – Junior Group Leader of the Tumor Stroma and Matrix Immunology Group, Center for Cancer Immune Therapy, Herlev Hospital

In my research group at the Center for Cancer Immune Therapy, Herlev Hospital, we try to understand how different components of the tumor microenvironment, including the extracellular matrix (ECM), affect the activity of tumor-infiltrating T cells. Consequently, our research belongs in the cross-field between matrix biology, immunology, and cancer biology and requires insight into each of these three fields. The goal is to identify molecular mechanisms that could lead to new cancer therapies or improvements of existing cancer immunotherapy.

Our research group, which we have named Tumor Stroma and Matrix Immunology (TSMI) group, currently consist of one postdoc, two PhD students and two Master's students. Our research is dependent on external funding and especially the Danish cancer society has been instrumental for the establishment of my research group. For the composition of the group I am interested in having people with diverse backgrounds, expertise, and interests. In combination with an open-minded and curious approach to the projects, I hope this will stimulate a dynamic environment where innovative projects of high quality are carried out.

Research:
Cancer immunotherapy is a collection of therapies, which exploit the ability of immune cells to combat the cancer [1,2]. These include checkpoint-inhibitors (anti-PD1, anti-PD-L1, and anti-CTLA-4), adoptive cell transfer, vaccines, and genetically modified T cells (CAR T cells). Immunotherapy has been a breakthrough in the treatment of cancer and has led to remarkable responses for patients with otherwise untreatable cancer. Still, however, the majority of patients do not respond to immunotherapy or only experience a partial response followed by relapse. The tumor microenvironment (TME), consisting of non-malignant cells, such as fibroblasts and macrophages, as well as the extracellular matrix (ECM), has strong suppressive effects on the tumor-infiltrating T cells [3,4]. This immunosuppressive microenvironment is considered an important reason for the lack of efficacy for many patients. However, mechanisms by which the TME suppresses T cell activity are incompletely understood.

Tumor progression is accompanied by dramatic remodeling of the surrounding ECM leading to the formation of a tumor-specific ECM, which has a different composition and is often more collagen-rich and of increased stiffness [5–7]. The altered ECM of the tumor supports cancer growth and metastasis [8] but it is unknown if this effect involves modulation of T cell activity.

In my research group we are investigating if the tumor-specific alterations of the ECM can influence the activity of the tumor-infiltrating T cells and thereby limit the efficacy of immunotherapy (Figure 1). Initially, we are using 3D culture systems to study the effects of collagen-density on T cell activity and on macrophage polarization. Additionally, we are starting to use transgenic mouse models in which we can modulate collagen levels in the tumors by either reducing collagen synthesis or limiting collagen degradation. To study non-collagen components of the ECM we are using cell-derived matrices which are deficient of single ECM components and investigating how these matrices affect T cell activity. Altogether we hope that our research can reveal new immunosuppressive mechanisms in the tumors and perhaps even identify new therapeutic targets.

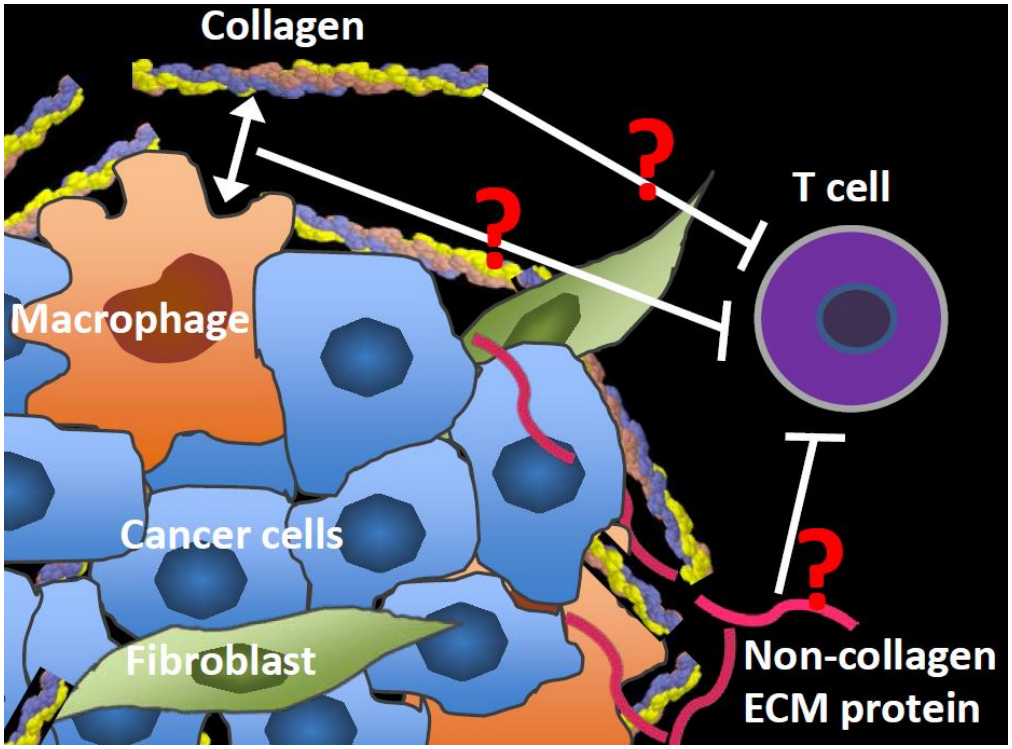

Figure 1. How does the tumor microenvironment affect the activity of tumor-infiltrating T cells?
The tumor microenvironment (TME) consists among other things of non-malignant cells such as cancer-associated fibroblasts (CAFs) and tumor-associated macrophages (TAMs) as well as the extracellular matrix (ECM). These components of the TME are known to influence tumor progression but the underlying mechanisms behind this effect are largely unknown. In our research group we aim to elucidate mechanisms by which the TME modulates the activity of infiltrating T cells.

Center for Cancer Immune Therapy:
Our research is conducted at the Center for Cancer Immune Therapy (CCIT) at Herlev Hospital, which is a research center trying to bridge basic and clinical immune therapy research (https://www.herlevhospital.dk/ccit-denmark/Sider/default.aspx). The center comprises five research groups and a total of approximately 40 researchers. The center conducts many clinical trials, with several of them originating from the center's own basic research. The different research groups at CCIT work on distinct research questions which all are related to cancer immunology and immunotherapy. The complementary expertise of the different research groups is a great strength of the center and many collaborative projects between the groups are ongoing.

Research career:
The most defining step in my scientific career was the decision to move to the USA after finishing my PhD. During my PhD at the Finsen Laboratory in the group of Niels Behrendt I had studied molecular mechanisms of collagen degradation with main emphasis on intracellular collagen degradation mediated by an endocytic receptor named uPARAP (or Endo180). The project involved a collaboration with Thomas Bugge at the National Institutes of Health (NIH) and as part of my PhD I had visited his laboratory. After my PhD I moved to the USA together with my wife and two small children to work as a postdoc in the research group of Thomas Bugge. In Thomas' group I continued my work on collagen degradation, but also worked on other projects spanning topics

such as regulation of epithelial integrity, protease-activated toxins for cancer treatment, and bone development and homeostasis. Most of the projects involved mouse genetics and transgenic mouse models.

After 4 years in the USA, we decided to move back to Denmark in the summer 2015. I had several ideas for new research projects and I started contacting research centers and departments that I believed could be interested in these projects. Luckily the CCIT were interested in providing a platform in the form of lab and office space for me to establish a research group. Initially, the "group" only consisted of myself, but gradually funding allowed for the establishment of an actual research group. I am sure that the process of finding a host institution and obtaining funding for starting up a research group had been much more difficult if I had not been abroad and gained valuable expertise that I could bring back to Denmark. In addition, we had a wonderful time in the Washington DC area, and based on personal experience I can only encourage people to consider going abroad to experience life and research in another country.

References:

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Membership

Our membership (100 dkr) includes free registration to our annual meeting, 3-4 newsletters a year, updates on position openings and conferences as well as eligibility for travel grants to local and international matrix meetings. We also appreciate any extra donations and will acknowledge your contribution in our next newsletter. **Please remember to EMAIL your name and receipt of your payment to our treasurer Abbas Jafari (ajafari@sund.ku.dk).** You can pay by:

1) Transferring via MobilePay to **46151** (Danish Society for Matrix Biology) *OR*

2) Transferring to the DSMB bank account: Reg: 1551 Account: 1227130 (Danske bank). Please indicate "DSMB membership" on your bank transfer *OR*

3) Email our treasurer Abbas Jafar (ajafari@sund.ku.dk) if you need to transfer from an international account

Courses for PhD students (local and overseas) at University of Copenhagen

1. Matrix Biology - physiology and function of extracellular matrix

7th-9th November, 2018 at Faculty of Health and Medical Sciences, University of Copenhagen
https://phdcourses.ku.dk/DetailKursus.aspx?id=104921&sitepath=SUND
ECTS credits 3.00
Enrolment deadline: 01/10/2018
Enrolment handling/course organiser PhD administration email: fak-phdkursus@sund.ku.dk

Aim

1. Gain insight into the basics of matrix biology and relate this to his/her own field of research
2. Understand analytical methods used in matrix biology and critically appraise published articles in this field of research
3. Understand what methods are suitable for testing different study hypotheses.

Content

The role of the extracellular matrix in physiological, pathophysiological and pathological situations will be the main focus, and specifically the cell-matrix interaction, the formation of collagen and other matrix tissue, and the coupling between matrix structure and function in health and disease will be taught. The newest matrix research will be reported from areas like the musculo-skeletal system (bone, cartilage, tendon, muscle), skin, vasculature and cancer.

All participants will have the opportunity to present and discuss their PhD projects, and we will discuss and evaluate relevant articles from the field of matrix biology research.

2. Extracellular Matrix and Proteolysis in Disease

11th-15th March, 2019 at BRIC, Copenhagen Biocenter and Panum Instititue, University of Copenhagen
ECTS credits 4.00
Enrolment deadline: end of 2018
Course coordinators: A/Prof. Marie Kveiborg (marie.kveiborg@bric.ku.dk) and Niels Behrendt

Aim

The extracellular matrix and its dynamic remodeling are decisive factors in several cellular functions and, when dysregulated, give rise to several types of disease. In addition to the essential scaffolding function of extracellular matrix molecules, these structures also harbor secreted or shed proteins, such as growth factors, chemokines and cytokines, and interact with membrane-anchored proteins, including adhesion and growth factor receptors. The consequences of extracellular matrix remodeling are wide-ranging, resulting in activation or inactivation of substrate proteins, or modulation of the substrate's functional properties. Thus, it is not surprising that the implicated proteases play key roles in normal tissue development and repair, as well as in the pathogenesis of a plethora of diseases.

Content

The course will address a number of structural, biochemical, and cell biological properties of extracellular matrix proteins and the associated proteases, including cutting-edge methodological development in this field of research. Furthermore, it will provide important examples of the contribution of extracellular proteolysis to development and disease - with particular focus on cancer and inflammatory disorders.

The course concludes with the participants attending and presenting their individual research projects at a *joint scientific conference of the Nordic Societies of Matrix Biology* (refer to the flyer below)

Upcoming meetings

tebu-bio
Innovative Lab Services & Reagents

THE DANISH SOCIETY FOR MATRIX BIOLOGY

ASMB

2018 American Society of Matrix Biology Biennial Meeting
ECM Microenvironments in Disease, Aging and Regeneration
14th-18th October 2018, Red Rock Casino, Las Vegas, NV, USA
http://www.asmb.net/current-meeting

MBI
MATRIX BIOLOGY IRELAND

5th Annual Matrix Biology Ireland Meeting
Matrix Pathophysiologies and Reparative Therapies
21st-23rd November 2018, Galway, Ireland
http://www.mbi.ie/meeting-2018/home

11th Asia and Pan-pacific Connective Tissue Society Symposium & 3rd National Conference of CSMB
16st-20th November 2018, Hangzhou, China
http://pptcss2018.org/en/index.html

Matrix Biology Society of Australia and New Zealand

2018 Annual MBSANZ meeting
4-5th Dec, Auckland, New Zealand
http://mbsanz18.nz/

BSMB

MBI
MATRIX BIOLOGY IRELAND

2019 BSMB Spring meeting & Matrix Biology Ireland Meeting
Stroma, Niche, and Repair
8-9th April 2019, Liverpool, UK
http://www.bsmb.ac.uk/