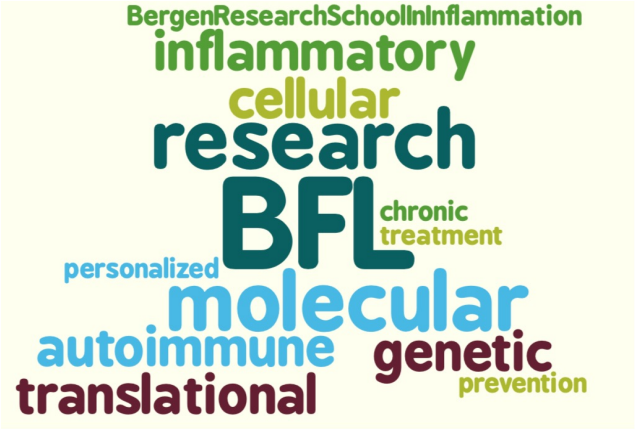
Annual Report 2021

Broegelmann Research Laboratory
University of Bergen



Photos: Silke Appel, Anne Sidsel Herdlevaer, Karl A. Brokstad, Roland Jonsson, Kim E. Andreassen, Helena Erlandsson Harris, UiB. Stefan Bladh

Front cover illustration by Kjerstin Jakobsen

Editor: Helena Erlandsson Harris

Content

Director’s comment

Silke Appel, Dr. rer. nat.
Acting head of Broegelmann Research Laboratory, 2021

Broegelmann Research Laboratory has also in 2021 been influenced by the ongoing Corona pandemic. Periods with mandatory home-office for scientific and administrative staff not dependent on laboratory work. This resulted in fewer physical meetings and social activities. We still managed to keep our spirits up and maintained regular joint activities as hybrid meetings. Despite the difficult situation, three of our PhD candidates (Dag Heiro Yi: Monocyte-derived dendritic cells in cancer immunotherapy- Considerations on their applicability; Anders Krogh Aarebrot: Single cell signalling and immune cell profiling in psoriasis; Magdalena Keindl: Interleukin-2 receptor in the pathogenesis of diabetic complications and Sjögren's syndrome) as well as three master students (Manpreet Kaur Hans:Immune cell profiling in COVID-19 recovered patients using mass cytometry; Ingvild Øye Bueide: Effects of herring roe oil on immune cells and cytokines in treatment of mild psoriasis; Victoria Marie Samuelsen: Investigation of immune cells in psoriasis patients treated with infliximab) defended their thesis in 2021.

Regarding the teaching situation we were able to maintain most of our Research School activities, both on campus and as hybrid seminars. Only the practical courses had to be cancelled due to the restrictions given by the pandemic.

Our long-standing employee Karl Albert Brokstad moved on to an associate professor position at the University College Vestland but stayed affiliated with Broegelmann Research Laboratory until the end of September 2021 in a 20% position.

2021 was a successful year regarding securing external funding. Both Yenan Bryceson and Marie Wahren Herlenius received grants from NFR, and Piotr Mydel was granted funding from the EEA research program.

Saving the best for last: After a long and strenuous pursuit for Roland Jonsson's successor as Head of the Broegelmann Research Laboratory, we managed to recruit professor Helena Erlandsson Harris from the Karolinska institutet, starting from January 1st 2022.

With these introductory words we proudly present our annual report 2021.

Silke Appel

New Director appointed

In August, a new director for the Broegelmann research laboratory was appointed.

Helena Erlandsson Harris, PhD, will start her position as Broegelmann Chair and professor at the University of Bergen 1st January 2022.

At present, Helena Erlandsson Harris is professor of rheumatological inflammation research at Karolinska Institutet and director for the Center for molecular medicine there.

'' I am really exciting about this opportunity to join the Broegelmann Research Laboratory and together with researchers there further develop BRL as a hub for research on inflammatory diseases. My goal is to ensure that the tradition of translational immunological research is continued and expanded by utilising the modern, state-of-the-art facilities available at UiB. Not only is this important in the quest to improve treatment and care of those affected by chronic inflammatory conditions, it is also the foundation for high quality doctoral education ''

Photo: Stefan Bladh

Vision and Research Areas

'' To pave the way for personalized treatment and ultimately prevention of rheumatic diseases and their associated co-morbidities''

The researchers at the Broegelmann Research Laboratory have a mutual interest in translational research on chronic inflammatory and autoimmune diseases. The research performed spans from molecular and genetic studies, cellular studies and experimental models as well as studies on clinically well-characterized patient samples.

The mutual ambition is to understand the molecular mechanisms active in different inflammatory diseases and their subgroups, their underlying risk factors and triggers. This paves the way for better, personalized treatment and ultimately to prevention of disease.

Current major areas of research:

Translational studies in autoimmunity; autoantibodies and biomarkers

Functional genomics and genetic basis of the autoimmune exocrinopathy (Sjögren's syndrome)

Dendritic cells in immunotherapy

Host microbe interactions (P- gingivalis – arthritis, Alzheimer)

Hyperinflammatory primary immunodeficiency syndromes

Cancer

The Board

Strandgaten 5 Photo: Helena Harris

The Broegelmann Foundation Board 2021
(Kjøbmand J.P. Broegelmanns Legat)

Left to right: Chairman, Managing Associate ***Bernt Jacob Pettersen****, Professor* ***Robert Bjerknes*** *MD, PhD, Senior consultant at BRL Kate Froland (not member of the board), Professor* ***Lars A. Akslen*** *MD, PhD. Photo: Helena Harris*

Our Researchers

Head of Laboratory

Acting head 2021
Silke Appel, Dr. rer. nat.
Professor of Immunology

Academic staff/senior researchers /postdoctoral fellows

Head Bergen Research School in Inflammation (BRSI)
Silke Appel, Dr. rer. Nat. (prof I)
(cellular/molecular immunology)

Veronica Binder, PhD (post doc)
(biochemistry)

Yenan Bryceson, PhD (prof II)
(cellular/molecular immunology)

Richard Davies, PhD (post doc)
(cellular/molecular immunology)

Tim Holmes, PhD (post doc)
(cellular/molecular immunology)

Roland Jonsson, DMD, PhD (Prof emeritus)
(rheumatology/immunology)

Marta Kaminska, PhD (post doc)
(biochemistry)

Piotr Mydel, MD, PhD (prof I)
(biochemistry/immunology)

Marie Wahren-Herlenius, MD, PhD (prof II)
(rheumatology/immunology)

Trainees
(supervisors in parentheses)

Anders Krogh Aarebrot, PhD candidate
(Appel/Holmes/Sandvik)

Ingvild Øye Bueide, master student
(Petrovic/Bergum/Appel)

Manpreet Kour Hans, master student
(Skavland/Appel)

Ylva Bratterud Helgesen, master student
(Appel/Bergum)

Urszula Kalucka, PhD candidate
(Mydel/Appel)

Magdalena Keindl, PhD candidate
(Lyssenko/Appel/Jain)

Dorentina Osmani, PhD candidate
(Fossen/Appel)

Aleksandra Petrovic, PhD candidate
(Appel/Jonsson/Solberg)

Victoria Marie Samuelsen, master student
(Holmes/Petrovic/Bergum/Appel)

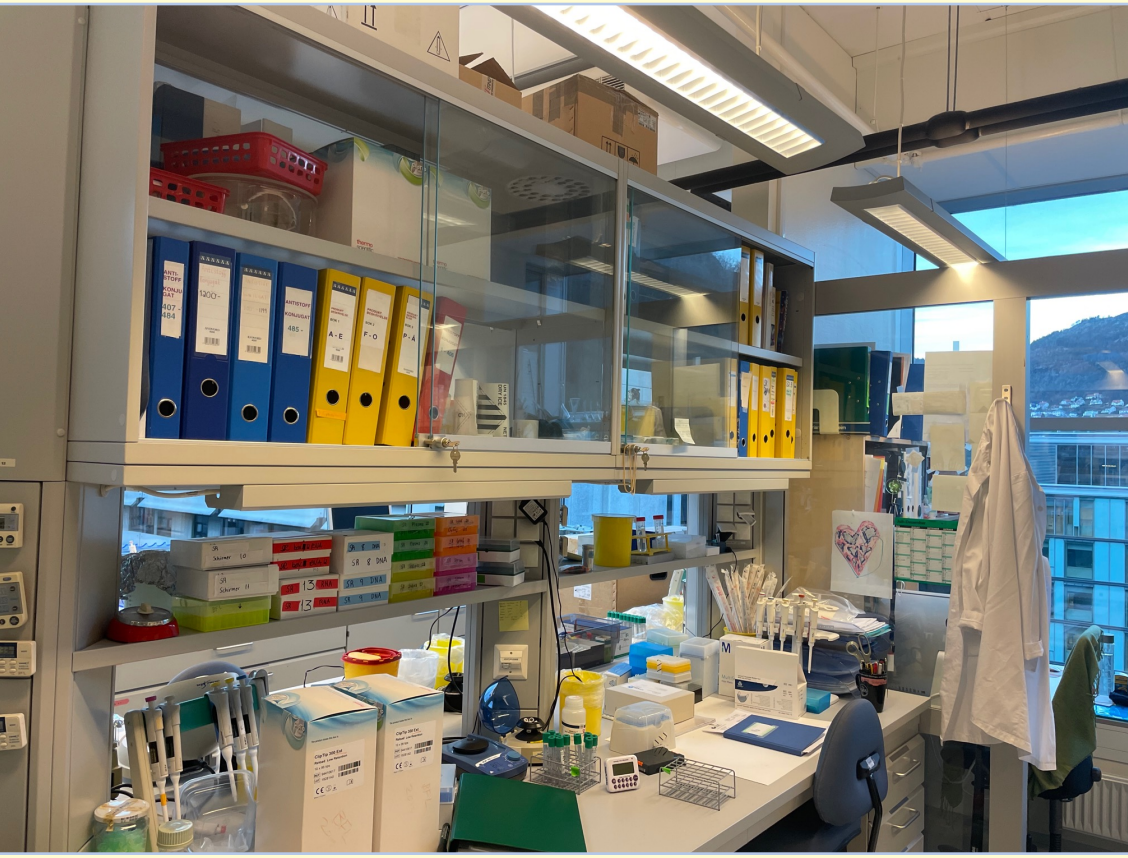
Dag Heiro Yi, PhD candidate
(Appel/Jonsson)

Technical and administrative staff

Kate Froland, office manager

Marianne Eidheim, laboratory manager

Kjerstin Jakobsen, laboratory manager



ADDITIONAL SCIENTISTS/ KEY-COLLABORATORS AT UIB AFFILIATED WITH THE LABORATORY

Brith Bergum, PhD
Dept of Clinical Science

Johan G. Brun, Professor,
Department of Clinical Science

Rebecca Cox, Professor Influenza Centre,
Department of Clinical Science

Torgils Fossen, Professor
Department of Chemistry

Eva Gerdts, Professor,
Department of Clinical Science

Daniel Hammenfors, MD
Haukeland University Hospital

Stephanie Le Hellard, Professor,
Department of Clinical Science

Erik Johnsen, Professor,
Department of Clinical Medicine

Malin V. Jonsson, Professor,
Department of Clinical Dentistry

Karl-Henning Kalland, Professor,
Department of Clinical Science

Valeriya Lyssenko, Professor,
Department of Clinical Science

Rune Kroken, Assoc Professor,
Department of Clinical Medicine

Hans Peter Marti, Professor
Department of Clinical Medicine

Roald Omdal, Professor emeritus,
Department of Clinical Science

Lene Frøyen Sandvik, Assoc Professor,
Department of Clinical Medicine

Kathrine Skarstein, Professor,
Department of Clinical Medicine

Jørn Skavland, PhD
Department of Clinical Science

Silje Solberg, Assoc. Prof.
Department of Clinical Medicine

Principal Investigators

Silke Appel

Yenan Bryceson

Piotr Mydel

Marie Wahren Herlenius

Silke Appel
Professor

Due to the outstanding capacity of dendritic cells (DC) to process and present antigenic peptides to T lymphocytes, several approaches have been developed for their application in cancer immunotherapy. DC-based immunotherapy has been shown to be safe, but so far, clinical impact has been lacking. By improving the quality of the DC populations used in the clinic, we hope to succeed in generating better DC-based immunotherapies.

Another focus of our research is single cell network profiling of distinct immune subsets to allow for analysis of pathway specific activity of patient samples at the single cell level. This will enable us to stratify different categories of patients and develop personalized therapies.

About Silke Appel:

Head of Research, Dept Clinical Science, UiB
Head of the core facility for flow cytometry, UiB

During the past year, we used mass cytometry analyses of psoriasis patients treated with various biopharmaceuticals (anti-TNF, anti-IL-17 or anti-IL-12/23) to show that immune cell composition and signaling profile differed between responders and non-responders (Solberg et al., Eur J Immunol, 2021). The overall aim of our research is to further unravel the mechanisms by which DC modulate T cell responses, both in autoimmune diseases such as Sjögren's syndrome and psoriasis as well as tumor immunity. Our results will lead to a better understanding of the cellular mechanisms involved in antigen presentation, T cell stimulation and tolerance induction, thereby revealing new tools for diagnosis and targets for therapy of patients with cancer, autoimmune and infectious diseases as well as patients undergoing stem cell transplantation. Thus, it might lead to an increased survival and better quality of life for patients.

GROUP MEMBERS

Anders Krogh Aarebrot, MD, PhD candidate
Tamandeep Kaur Bharaj, master student
Richard Davies, PhD, postdoc
Ylva Bratterud Helgesen, master student
Roland Jonsson, professor emeritus
Magdalena Keindl, MSc, PhD candidate
Dorentina Osmani, MSc, PhD candidate
Aleksandra Petrovic, MD, PhD candidate
Dag Heiro Yi, MD, PhD candidate

Yenan Bryceson Professor II

Our laboratory studies the molecular regulation of cytotoxic lymphocyte function in the context of inflammatory disease as well as cancer. Defects in cytotoxic lymphocyte function are associated with often-fatal hyperinflammatory primary immunodeficiency syndromes in infants, but many such patients cannot be explained by current molecular insights. Furthermore, harnessing lymphocyte differentiation and function represent a promising avenue increasing the efficacy of cellular immunotherapy of cancer.

About Yenan Bryceson:

Yenan Bryceson did his undergraduate training at the University of Oslo and PhD at the National Institutes of Health, Rockville, MD, USA. He was appointed professor II at the University of Bergen in 2012. He is also a professor at Karolinska Institutet, Stockholm, Sweden.

Our laboratory studies the molecular regulation of cytotoxic lymphocyte function in inflammation. Cytotoxic lymphocytes are broadly categorized into cytotoxic CD8+ T cells and natural killer (NK) cells. Defects in cytotoxic lymphocyte function are associated with often-fatal hyperinflammatory primary immunodeficiency syndromes in infants. These hyperinflammatory syndromes are also associated with an increased risk of developing hematological malignancies. Recently, adoptive transfer of NK cells as well as NK cells or T cells engineered to express chimeric activating receptors (CARs) have shown efficacy in clinical trials against hematological malignancies, but improving their persistence and potential utility against solid tumors remains a major challenge.

We are working to decipher the molecular regulation of cytotoxic lymphocyte differentiation and function in blood and tissues using cutting-edge single cell techniques, including advanced flow cytometry and sorting combined with high-throughput sequencing. A particular focus of ours is on how specific transcription factors can be harnessed to manipulate NK cell differentiation and potentiate function for improved immunotherapy of cancer.

GROUP MEMBERS
Timothy Holmes, PhD (post doc)

Piotr Mydel
Professor

The group believes in interdisciplinary cooperation with medical and dental clinicians, epidemiologists, bio-scientists, industrial scientists to achieve our goals of elucidating the role of post-translational modifications in the aetiology of auto immune diseases.

About Piotr Mydel:

Taking into account that up to 30% of the adult population worldwide suffers from severe periodontitis, the impact of this disease on human health is immense. Periodontitis (PD) is largely caused by infection, in which *Porphyromonas gingivalis* is a major pathogen, and is the most prevalent infectious inflammatory disease of mankind.

Mounting evidence suggests a causative link between PD and rheumatoid arthritis (RA), as well as periodontitis and cardiovascular disease. *P. gingivalis* is the only bacterium expressing the enzyme peptidylarginine deiminase (PAD) which converts arginine to citrulline, a process referred to as citrullination. Antibodies torwards such citrullinated proteins, i.e ACPAs/aCCP, are of central importance in RA a chronic autoimmune disease which affect 0.5-1% worldwide. The presence of ACPAs or aCCP autoantibodies is not only highly specific for RA but the presence is also related to a more severe and destructive disease progression.

We hypothesise that anti-citrullinated protein antibodies can be generated, in genetically susceptible individuals, as a consequence of P.gingivalis-induced citrullination in the gingiva.

GROUP MEMBERS
Veronika Binder, PhD (researcher)
Urszula Zofia Kalucka, MSc, PhD candidate
Marta Kaminska, PhD, postdoc
Noemie Dudzińska, PhD candidate

Marie Wahren-Herlenius
Professor II

The majority of autoimmune diseases are more common in women than in men, but the molecular basis for this sex-bias remains poorly understood. In our projects we focus on the autoimmune exocrinopathy Sjögren's syndrome which has among the highest observed female-to-male ratios, to dissect the genetic and hormonal contribution to sex-dependent immune regulation at single cell resolution and how these differences may lead to autoimmune disease.

About Marie Wahren Herlenius:

Marie Wahren-Herlenius did part of her PhD training and a postdoctoral period at the Broegelmann Research Laboratory. She was appointed professor II, University of Bergen in 2020. She is also a professor at Karolinska Institutet, Stockholm, Sweden

Women are at much higher risk of developing autoimmune disease, with the most extreme numbers in systemic disorders such as SLE and Sjögren's syndrome for which more than nine out of ten patients are women. There is a clear genetic contribution to these diseases and genome-wide studies have identified polymorphisms associated with Sjögren's syndrome. Interestingly, many of the associated genetic variants lead to differential gene regulation. However, the influence of sex, or why these immune-pathways and related genes would become dysregulated specifically in women is not clear.

In our projects, we build on the observation that genetic polymorphisms associated with Sjögren's syndrome that we identify dramatically increase the likelihood for the disease to develop in women carrying these genetic traits compared to men. Consequently, the context "female sex" may lead to a different functional impact of the genetic polymorphisms associated with systemic autoimmunity than the context "male sex". Our projects aim to identify sex-influenced eQTLs, and dissect the genetic and hormonal contribution to sex-dependent immune regulation at single cell resolution and how these differences may lead to autoimmune disease.

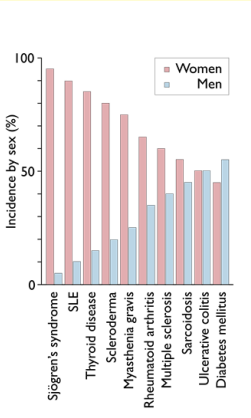


Figure 1. Sex distribution of the major Autoimmune diseases.

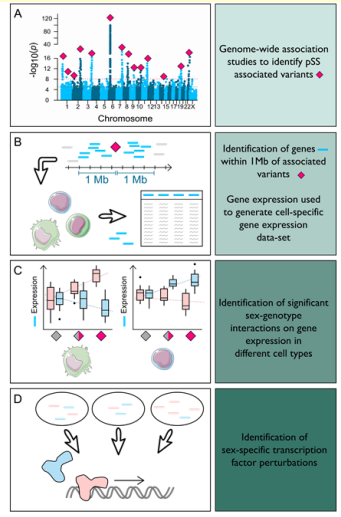


Figure 2. Steps to identify sex-influenced eQTLs and their mechanistic basis.

Graduations

PhD:

Dag Heiro Yi

Monocyte-derived dendritic cells in cancer immunotherapy - Considerations on their applicability

Supervisors: Silke Appel, Roland Jonsson

Philosophiae doctor (PhD), thesis defence February 17, 2021

Anders Krogh Aarebrot

Single cell signalling and immune cell profiling in psoriasis

Supervisors: Silke Appel, Lene Frøyen Sandvik, Timothy Holmes, Roland Jonsson

Philosophiae doctor (PhD), thesis defence February 19, 2021

Magdalena Keindl

Interleukin-2 receptor in the pathogenesis of diabetic complications and Sjögren's syndrome

Supervisors: Valeryia Lyssenko, Silke Appel, Ruchi Jain

Philosophiae doctor (PhD), thesis defence December 14, 2021

Master:

Manpreet Kaur Hans – Master of Pharmacy

Immune cell profiling in COVID-19 recovered patients using mass cytometry

Supervisors: Jørn Skavland, Silke Appel

Ingvild Øye Bueide – Master of Pharmacy

Effects of herring roe oil on immune cells and cytokines in treatment of mild psoriasis

Supervisors: Aleksandra Petrovic, Brith Bergum, Silke Appel

Victoria Marie Samuelsen – Master of Pharmacy

Investigation of immune cells in psoriasis patients treated with infliximab

Supervisors: Timothy Holmes, Aleksandra Petrovic, Brith Bergum, Silke Appel

External funding - major grants

2016 – 2021
Piotr Mydel: National Science Centre (Sonata Bis). Carbamylation as a Modulator of Immune Response, Total 330 000 €

2018 – 2021
Piotr Mydel: Polish National Science Centre (Opus) „Serum PAD-activity: Risk Factor in Development and Novel Biomarker in Rheumatoid Arthritis" 3.9 mill NOK

2019 – 2024
Piotr Mydel: National Institutes of Health (RO1 DE022597) "Bacterial peptidylarginine deiminase, a link between gums and joint disease", Total 6.4 mill NOK

2020-2023
Foundation for Research in Rheumatology (FOREUM) "Genetic variants associated with Sjögren's syndrome leading to differential gene expression in males and females and their functional impact on the immune system"; Karolinska Institutet v/Marie Wahren Herlenius er coordinator, UiB og Harvard er partnere. Appel/Jonsson Totalt 1 500 000 NOK

2020 – 2023
Piotr Mydel: National Science Center Poland (2019/33/B/NZ4/01889) "Protein Carbamylation in Hemostatic Dysfunctions in Chronic Kidney Disease"; Total 505 000 €

2020 – 2023
Piotr Mydel: EU Joint Programme – Neurodegenerative Disease Research (EC/JPND; ES655895) "Alzheimer's disease as a co-morbidity of chronic periodontitis with *Porphyromonas gingivalis* as a causative link between both diseases" Total 575 000 €

2021 – 2024
Piotr Mydel: EC/Grieg “Novel mechanisms of PAD activity regulation. Substrate specificity and activation of peptidyl arginine deiminases in the context of RA” Total 499 000 €

2019-2024
Roland Jonsson: The European Commission Horizon 2020 contract NECESSITY (IMI2-JU/EU/H2020 nr. 806975) “New Clinical Endpoints in primary Sjögren’s Syndrome: an Interventional Trial based on stratifying patients”

2021-2025
Yenan Bryceson: Norwegian Research Council ‘’Engineering NK cells for improved functionality in immunotherapy’’ Total 12 mill NOK

2021-2025
Marie Wahren Herlenius: Norwegian Research Council ‘’The molecular basis of sex differences in Sjögren’s syndrome’’ Total 10 mill NOK

Bergen research school in inflammation (BRSI)

BRSI, coordinated by Silke Appel, is open to PhD candidates at UiB and encompasses activities such as courses, seminars, journal clubs – all with the aim to provide subject-specific knowledge to the participants.
Furthermore BRSI is an important platform for the interaction between PhD candiates and experienced scientists, to build networks, provide imput on research projects and facilitate informal mentoring on research careers.

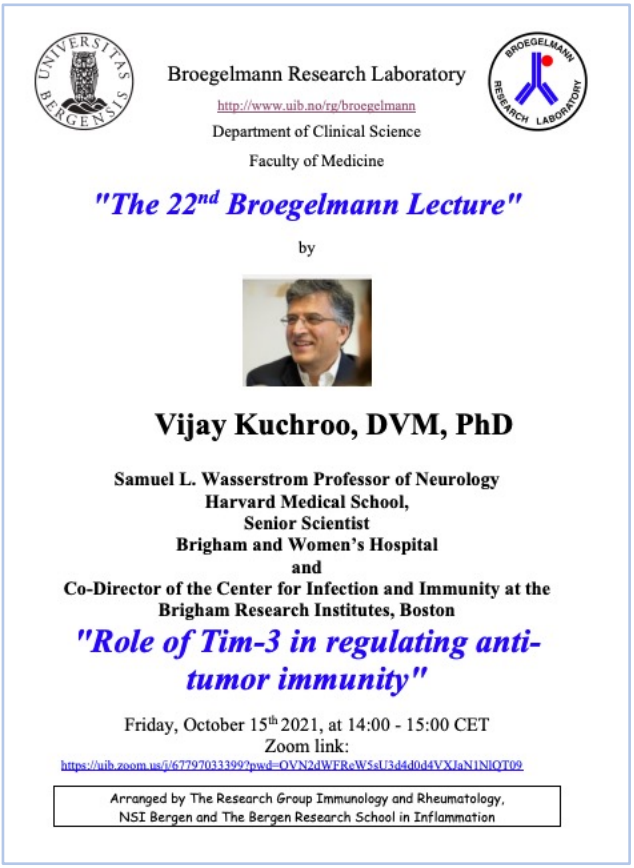
Due to the lock down, practical courses had to be cancelled during 2021, while other activities could be held in a digital format.

Courses given during 2021

- **HUIMM320** – Basic Immunology (5 ECTS)
- **HUIMM903** – Human Immunobiology (10 ECTS)
- **HUIMM901** – Translational Immunology/project seminars (3 ECTS)
- **HUIMM902** – Journal club (3 ECTS)

Meetings and Dissemination

The 22nd Broegelmann Lecture



This year's Broegelmann lecture was given by Professor Vijay Kuchroo, Harvard Medical School. Due to the travel restrictions during the pandemic, the lecture was digital.

International Publications 2021

- Ambrosi A, Thorlacius GE, Sonesson SE, Wahren-Herlenius M. Interferons and innate immune activation in autoimmune congenital heart block. *Scand J Immunol.* 2021 Jan;93(1):e12995. PMID: 33188653

- Sandling JK, Pucholt P, Hultin Rosenberg L, Farias FHG, Kozyrev SV, Eloranta ML, Alexsson A, Bianchi M, Padyukov L, Bengtsson C, Jonsson R, Omdal R, Lie BA, Massarenti L, Steffensen R, Jakobsen MA, Lillevang ST; ImmunoArray Development Consortium and DISSECT consortium, Lerang K, Molberg Ø, Voss A, Troldborg A, Jacobsen S, Syvänen AC, Jönsen A, Gunnarsson I, Svenungsson E, Rantapää-Dahlqvist S, Bengtsson AA, Sjöwall C, Leonard D, Lindblad-Toh K, Rönnblom L. Molecular pathways in patients with systemic lupus erythematosus revealed by gene-centred DNA sequencing. Ann Rheum Dis. 2021 Jan;80(1):109-117. Epub 2020 Oct 9. PMID: 33037003

- Niewold TB, Meves A, Lehman JS, Popovic-Silwerfeldt K, Häyry A, Söderlund-Matell T, Charlesworth CM, Madden B, Lundberg IE, Wahren-Herlenius M, Svenungsson E, Oke V. Proteome study of cutaneous lupus erythematosus (CLE) and dermatomyositis skin lesions reveals IL-16 is differentially upregulated in CLE. *Arthritis Res Ther* 2021, 23:132.

- Thorlacius GE, Hultin-Rosenberg L, Sandling JK, Bianchi M, Imgenberg-Kreuz J, Pucholt P, Theander E, Kvarnström M, Forsblad-d'Elia H, Bucher SM, Norheim KB, Johnsen SJA, Hammenfors D, Skarstein K, Jonsson MV, Baecklund E, Aqrawi LA, Jensen JL, Palm Ø, Morris AP; DISSECT consortium; the ImmunoArray consortium, Meadows JRS, Rantapää-Dahlqvist S, Mandl T, Eriksson P, Lind L, Omdal R, Jonsson R, Lindblad-Toh K, Rönnblom L, Wahren-Herlenius M, Nordmark G. Genetic and clinical basis for two distinct subtypes of primary Sjögren's syndrome. *Rheumatology* 2021 Feb 1;60(2):837-848

- Solberg SM, Aarebrot AK, Sarkar I, Petrovic A, Sandvik LF, Bergum B, Jonsson R, Bryceson YT, Appel S. Mass cytometry analysis of blood immune cells from psoriasis patients on biological therapy. *Eur J Immunol* 2021 Mar;51(3):694-702
- Björk A, Da Silva Rodrigues R, Richardsdotter Andersson E, Ramírez Sepúlveda JI, Mofors J, Kvarnström M, Oke V, Svenungsson E, Gunnarsson I, Wahren-Herlenius M. Interferon activation status underlies higher antibody response to viral antigens in patients with systemic lupus erythematosus receiving no or light treatment. *Rheumatology* (Oxford). 2021 Mar 2;60(3):1445-1455. PMID: 33006609
- Asano, Takaki, Bertrand Boisson, Fanny Onodi, Daniela Matuozzo, Marcela Moncada-Velez, Majistor Raj Luxman Maglorius Renkilaraj, Peng Zhang, et al. X-Linked Recessive TLR7 Deficiency in ~1% of Men under 60 Years Old with Life-Threatening COVID-19. *Science Immunology* 6, no. 62 (August 19, 2021): eabl4348.
- Azeem W, Bakke RM, Gabriel B, Appel S, Øyan AM, Kalland KH.Evaluation of β-Catenin Inhibition of Axitinib and Nitazoxanide in Human Monocyte-Derived Dendritic Cells. *Biomedicines*. 2021 Aug 3;9(8):949. PMID: 34440153
- Jonsson R. Henrik Sjögren (1899-1986): the syndrome and his legacy. Ann Rheum Dis. 2021 Sep;80(9):1108-1109. Epub 2021 Jun 21. PMID: 34385154.
- Bąbol-Pokora, Katarzyna, Magdalena Wołowiec, Katarzyna Popko, Aleksandra Jaworowska, Yenan T. Bryceson, Bianca Tesi, Jan-Inge Henter, et al. Molecular Genetics Diversity of Primary Hemophagocytic Lymphohistiocytosis among Polish Pediatric Patients. *Archivum Immunologiae Et Therapiae Experimentalis* 69, no. 1 (October 22, 2021): 31. PMID: 34677667

- Bahr Greenwood, Tatiana von, Bernhard Holzgraefe, Samuel C. C. Chiang, Yini Wang, Bianca Tesi, Yenan T. Bryceson, and Jan-Inge Henter. Clinical and Laboratory Signs of Haemophagocytic Lymphohistiocytosis Associated with Pandemic Influenza A (H1N1) Infection in Patients Needing Extracorporeal Membrane Oxygenation: A Retrospective Observational Study. *European Journal of Anaesthesiology* 38, no. 7 (July 1, 2021): 692–701. PMID: 33186307
- Bharaj TK, Aqrawi LA, Fromreide S, Jonsson R, Brun JG, Appel S, Skarstein K. Inflammatory Stratification in Primary Sjögren's Syndrome Reveals Novel Immune Cell Alterations in Patients' Minor Salivary Glands. *Front Immunol.* 2021 Jul 12;12:701581. eCollection 2021.PMID: 34322130
- Ivanchenko M, Thorlacius GE, Hedlund M, Ottosson V, Meneghel L, Björkander S, Ossoinak A, Tingström J, Bremme K, Sverremark-Ekström E, Gemzell-Danielsson K, Sonesson SE, Chemin K, Wahren-Herlenius M. Natural killer cells and type II interferon in Ro/SSA and La/SSB autoantibody-exposed newborns at risk of congenital heart block. *Ann Rheum Dis* 2021, 80:194-202.
- Hetemäki, Iivo, Meri Kaustio, Matias Kinnunen, Nelli Heikkilä, Salla Keskitalo, Kirsten Nowlan, Simo Miettinen, et al. Loss-of-Function Mutation in IKZF2 Leads to Immunodeficiency with Dysregulated Germinal Center Reactions and Reduction of MAIT Cells. *Science Immunology* 6, no. 65 (November 26, 2021): eabe3454. PMID: 34826260
- Holmes, Tim D., Ram Vinay Pandey, Eric Y. Helm, Heinrich Schlums, Hongya Han, Tessa M. Campbell, Theodore T. Drashansky, et al. The Transcription Factor Bcl11b Promotes Both Canonical and Adaptive NK Cell Differentiation. *Science Immunology* 6, no. 57 (March 12, 2021): eabc9801. PMID: 33712472

- Thorlacius GE, Hultin-Rosenberg L, Sandling JK, Bianchi M, Imgenberg-Kreuz J, Pucholt P, Theander E, Kvarnström M, Forsblad-d'Elia H, Bucher SM, Norheim KB, Johnsen SJA, Hammenfors D, Skarstein K, Jonsson MV, Baecklund E, Aqrawi LA, Jensen JL, Palm Ø, Morris AP; DISSECT consortium; the ImmunoArray consortium, Meadows JRS, Rantapää-Dahlqvist S, Mandl T, Eriksson P, Lind L, Omdal R, Jonsson R, Lindblad-Toh K, Rönnblom L, Wahren-Herlenius M, Nordmark G. Genetic and clinical basis for two distinct subtypes of primary Sjögren's syndrome. *Rheumatology* (Oxford) 2021, 60:837-848.
- Ramos-Casals M, Acar-Denizli N, Vissink A, Brito-Zerón P, Li X, Carubbi F, Priori R, Toplak N, Baldini C, Faugier-Fuentes E, Kruize AA, Mandl T, Tomiita M, Gandolfo S, Hashimoto K, Hernandez-Molina G, Hofauer B, Mendieta-Zerón S, Rasmussen A, Sandhya P, Sene D, Trevisani VFM, Isenberg D, Sundberg E, Pasoto SG, Sebastian A, Suzuki Y, Retamozo S, Xu B, Giacomelli R, Gattamelata A, Bizjak M, Bombardieri S, Loor-Chavez RE, Hinrichs A, Olsson P, Bootsma H, Lieberman SM; Sjogren Big Data Consortium*. Childhood-onset of primary Sjögren's syndrome: phenotypic characterization at diagnosis of 158 children. *Rheumatology* (Oxford) 2021, 60:4558-4567.
- Horne, AnnaCarin, Tatiana von Bahr Greenwood, Samuel C. C. Chiang, Marie Meeths, Caroline Björklund, Maria Ekelund, Peter Erensjö, et al. Efficacy of Moderately Dosed Etoposide in Macrophage Activation Syndrome-Hemophagocytic Lymphohistiocytosis. *The Journal of Rheumatology* 48, no. 10 (October 2021): 1596–1602. PMID: 33589555
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Social Activities

Summer lunch

Christmas lunch

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