Oslo University Hospital

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Research Institute of Internal Medicine (RIIM)

ANNUAL REPORT 2023

RIIM

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Leader´s corner

Professor Bente Halvorsen
Head of the Research Institute of Internal Medicine

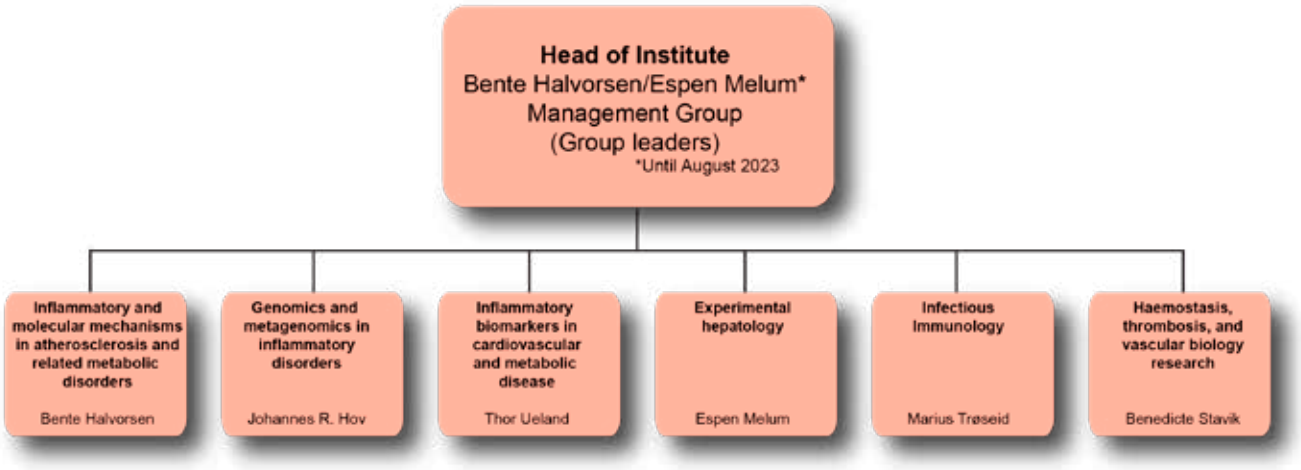
In 2023, The Research Institute of Internal Medicine (RIIM) continued as a leading translational institute, both nationally and internationally. The number of high impact publications is still rising, and several prestigious grants were awarded RIIM scientists in 2023. In addition, RIIM scientist and Institute leader, Prof. Bente Halvorsen received the distinguished OUS`s Excellent Researcher Award 2023. Further, RIIM reached the final round of evaluation as a possible new K.G. Jebsen Center, and although not successful, this was an important milestone for the Institute.

After years with social restrictions due to the Covid 19 pandemic, the annual RIIM Spring Seminar was back in 2023, in a new successful format with a designated "Owren-Stormorken lecture" inviting top level speakers both from Norway and abroad. An important move for a better scientific and social milieu at RIIM.

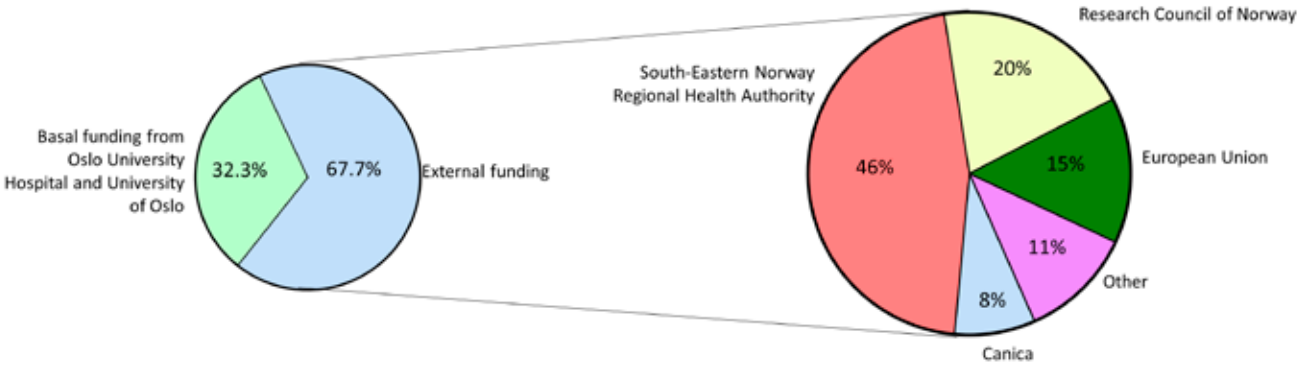
As part of building the new OUH 2030, 2023 became the start of heavy construction work outside RIIM. Further, the reorganization of OUH –resulted in the disruption of Division of Surgery, Inflammatory Medicine and Transplantation, and RIIM was transferred to Division of Head, Neck and Reconstructive Surgery. Also, in 2023 an important decision was made by OUH`s Administrative Director Bjørn Atle Bjørnebeth, after a year with heavy committee work to make the foundation of the gathering of 4 research institutes in the A building. These four institutes comprise Department of Pediatric Research, Institute of Experimental Medical Research, Institute for Surgical Research and RIIM, and when placed together in the A building, this will create a translational research center in the New OUH. This is an important decision for RIIM and a fantastic opportunity to evolve further near other strong scientific milieus situated close to clinical activity. This process has been one of my most important task in my period as head of RIIM, and a strategic move to stay close to clinical activity. To build an even stronger institute, we are dependent on good collaboration with clinical departments and collaborations with complementary skills. Importantly, RIIM must take an even more active role in clinical intervention studies and in the establishing of centers (i.e., K.G. Jebsen Center, Centre of Excellence etc.), and most importantly, RIIM scientist must continue to work hard to compete for ERC grants and funding from EU.

With these milestones for 2023 and visions for 2024, I would like to thank everyone at RIIM including our collaborators at UiO and OUH for all the patience and loyalty you have shown in 2023. And last, but not least – thanks for an inspiring and productive year. Also, thanks to Espen Melum for heading the institute in a strong and enthusiastic manner while I was having a sabbatical year in USA 2022/2023. Thanks to RIIM staff for assisting Espen and me in our management of RIIM. The management team looks into 2024 and the years to come with great enthusiasm for the work and challenges that may come in building our new RIIM - a scientific rock in the new OUH 2030.

ORGANIZATION



ECONOMY / FUNDING



Upper panel: Organizational chart.
Left panel: Funding sources for the institute (basal versus external funding).
Right panel: External funding sources detailed.

FOCUS AREA

AI as a research tool for precision medicine

By Thor Ueland

AI, or Artificial Intelligence, refers to the simulation of human intelligence in machines programmed to think, learn, and problem-solve like humans. While most had some impression of what AI is through science fiction, typically posing an existential threat to humanity, the release of ChatGPT in 2022 and recent availability of AI chatbots has contributed the public's awareness of AI capabilities forcing us to consider these new tools. Indeed, ChatGPT is only a part of a broader ecosystem of AI technologies and applications driving the AI revolution. In the realm of science, AI is becoming an indispensable tool, offering new avenues for discovery, optimization, and understanding of disease mechanisms. With emerging omics technologies generating more data that you can shake a stick at, we can anticipate that proposals for funding will score higher with a well-founded AI component for analysis of these data. Similarly, the government's focus on personalized medicine being an integral part of prevention, diagnostics, treatment, and follow-up further encourages use of AI technologies.

AI technologies can be divided in several fields, but for current medical research purposes, machine learning is the main AI technology utilized, focused on developing algorithms that allow computers to learn from and make predictions or decisions based on data. Machine learning has been used in research for several decades, with its roots dating back to the mid-20th century. Earlier attempts at personalized medicine such as IBM's Watson a decade ago, had an impressive ability to process and analyze vast amounts of data, but had problems understanding context and despite the hype, it ultimately failed to deliver. Hopefully, AI will have more success this time around due to advancements in AI algorithms, data availability and quality, support for integration with healthcare systems and the shift towards a more patient-centered approach.

The aim of personalized medicine is to provide tailored medical care based on an individual's unique genetic, environmental, and lifestyle factors. AI can be crucial in advancing this in several ways: i) Genomic analysis, where AI algorithms analyze large-scale genomic data to identify genetic variations associated with specific diseases, drug responses, and susceptibility to various conditions. This information can be used to develop personalized treatment plans, predict disease risk, and guide preventive measures. ii) Precision diagnostics: AI-powered diagnostic tools can interpret medical images, such as MRI scans, X-rays, and pathology slides, with high accuracy and efficiency. This can lead to earlier and more accurate diagnoses, allowing for timely interventions and improved patient outcomes. iii) Drug Discovery and Development: AI can accelerate the drug discovery process by predicting how different compounds will interact with biological targets and identify potential drug candidates more efficiently. This can lead to the development of targeted therapies tailored to individual patient profiles. iv) Predictive Analytics: AI algorithms can analyze patient data, including medical history, lab results, and real-time monitoring data, to predict disease progression, identify high-risk patients, and recommend personalized interventions. This approach can help in preventing complications and optimizing treatment strategies. AI can promote efficiency in other healthcare sectors as well, but the above represents applications at the intersection of research and clinical practice.

While AI holds great promise in advancing personalized medicine, it also presents challenges related to data privacy, ethical considerations, regulatory compliance, and integration into existing healthcare systems. Addressing these challenges will be essential to realizing the full potential of AI in personalized medicine and ensuring equitable access to personalized healthcare solutions for all patients.

In this report, Simen Hyll Hansen and Jonas Øgaard offer excellent perspectives and examples on use of AI in predictive medicine based on omics data (microbiome) and imaging (histology).

Perspectives on Artificial Intelligence in microbiome research

By Simen Hyll Hansen

Microbiome research was revolutionized in the 2000's with the advent of Next-Generation Sequencing technologies (NGS). In contrast to the traditional Sanger sequencing, NGS outputs millions to trillions of different DNA sequences from every single sample. This makes NGS very well suited for unbiased characterization of all DNA sequences in a sample, as is the desired goal in most microbiome studies. Depending on the exact NGS method, one typically ends up with hundreds to thousands of features (*e.g.* bacterial taxa or genetic functions) in a large dataset. This wealth of information provides research opportunities, but also several difficulties and pitfalls. If the study has recruited a relatively low number of participants (or mice), there is a good chance some features will correlate with any outcome of interest, just by chance. To a certain extent, controlling for the well-known False Discovery Rate (FDR) mitigates this problem. However, given large amounts of sequencing data, simply controlling for the FDR might not be enough:

Consider a synthetic dataset A, consisting of completely random data for 10 cases and 10 controls, simulating a study where there is in fact no relation between the microbiome and the disease of interest. In this simulated experiment, several features were identified as different between the study groups after correcting for the FDR. Using traditional generalized linear models (GLMs), it is easy to create extremely optimistic models with AUC values close to 1 (Table 1). While it could be tempting to apply artificial intelligence (AI) in such a scenario, it is important to acknowledge that AI is no magic solution for insufficient study sizes or bad study design. In fact, while most researchers would identify an AUC value of 1 as a clear sign of overfitting, many would see the AI's average AUC of 0.75 (Table 1) and conclude that their model has found some predictive signal in the microbiome data. Only when the study design includes enough samples will AI behave properly and reflect the actual predictive capacity of the data. Though the optimal size of the dataset depends on many factors, there should at the very least be more samples than features before AI models are created [1]. Continuing the experiment, in the new dataset B we have increased the study size to 10 000 cases and 10 000 controls. As shown in Table 1, GLMs still report moderate predictive capacity from random data in dataset B, even though there is an exceptionally large amount of samples. Meanwhile, the AI methodology outputs an average AUC value of 0.5, correctly reflecting the random relationship between the features and the disease group. This shows that given enough data, AI models can correctly identify noise without overfitting. Similarly, figure 1 shows a parallel experiment with a few features that associate with the outcome, as well as varying amounts of noise. Here, we see that AI only finds the signals among the noise if the study is large enough.

Simulated experiment using random data	Dataset A	Dataset B
Size	10 cases, 10 controls	10 000 cases, 10 000 controls
Number of features	3000	3000
Significant features (FDR-corrected)	Several	None
AUC (GLMs)	~1	~0.72
AUC (AI)	~0.75	~0.5
Correct AUC	0.5	0.5

With the above caveats on study design in mind, AI methodologies within microbiome research has shown great potential in quickly identifying nonlinear patterns between large amounts of features, allowing accurate and reliable estimation of predictive capacity [2]. Within my own research using such models in inflammatory bowel disease (IBD), AI has been employed in the form of gradient boosted decision trees (*e.g.* XGBoost) to create diagnostic and prognostic models. Combining AI with Monte Carlo-based bootstrapping and differing data modalities (*i.e.* switching between using only biochemical features, microbiome features, clinical details on patients, or varying combinations of these), we have assessed the usefulness of microbiome data compared to the biochemical and clinical data already used in clinical practice. In brief, microbiome data seems less useful than traditional biochemical markers when it comes to separating IBD from symptomatic controls, but was the best source of data for within-IBD

diagnostics (*i.e.* separating ulcerative colitis from Crohn's disease) and for predicting future severe disease. The latter is especially interesting, given that early detection of high-risk patients is a critical goal for achieving personalized targeted therapy in IBD [3].

However, even in a future scenario where an AI model does exceptionally well in trials, there are ethical concerns with regards to clinical implications. Specifically, the fact that AI models tend to work as black boxes compared to the more transparent traditional models and clinical scores. For instance, the ELF test (used for estimating fibrosis) contains three markers with static multipliers and constants, while a hypothetical machine learning model for estimating fibrosis might give similar outputs, but without any explanation of why the model reaches its output. This poses an ethical problem, where a clinician that follows the output of an AI for decision making cannot explain or argue why the specific treatment was chosen, other than "*the machine said so*". Solutions to this problem are actively being researched, and one of the solutions I have implemented in my microbiome research is the game-theoretical approach of "SHapley Additive exPlanations", commonly referred to as SHAP [4].

In Figure 2, a SHAP plot is presented for a single person with ulcerative colitis (UC, a type of IBD). This plot represents an interesting case, where the F-calprotectin levels for the patient is actually on the low side, indicating that the person does not have IBD. The plot goes on to explain why the AI model still is fairly sure (with 99.17% certainty) that the person has IBD despite the low F-calprotectin levels. In particular, the combination of very low levels of *Bilophila, Lachnoclostridium* and *Lachnospiraceae* FCS020 led the model to conclude with an IBD diagnosis, even though it also shows that low levels of F-calprotectin contributed to a lower likelihood of IBD (with a moderate value of -0.22 on the x-axis, indicating the SHAP-value). Here a big advantage of AI models becomes apparent; even though an F-calprotectin value of 98 gave a moderately lowered likelihood of IBD in this particular patient, the same value might give a substantially lowered likelihood of IBD in another patient. This might be counter-intuitive at first, but this is simply because the model takes the totality of all variables into account, and the same value of F-calprotectin might mean something totally different given other contexts. To make this point clearer; a height of 150 cm might diagnostically mean something very different given different combinations of the sex and age of a patient. This intuitively makes sense, but when there are hundreds of variables it becomes much harder for humans to incorporate all the information in an objective way. It is in these cases it makes sense to outsource the thinking to AI models, and then interpret the output from these models with systems such as SHAP to make clinical improvements that ultimately benefits the patient in the form of increased diagnostic accuracy and personalized treatment.

All in all, AI systems have been effective at creating useful models, incorporating large amounts of data with hidden interactions. Especially in biological systems like the microbiome, with large amounts of novel taxa and interactions being discovered every year, AI models that automatically discover and incorporate such novel interactions are exceptionally well-suited. By leveraging methods like SHAP, we can peek into the inner workings of each model, casting light into the previously black boxes. With study designs large enough to mirror the vast amounts of data from modern sequencing technologies, AI is increasingly becoming an essential component for further advancing microbiome research.

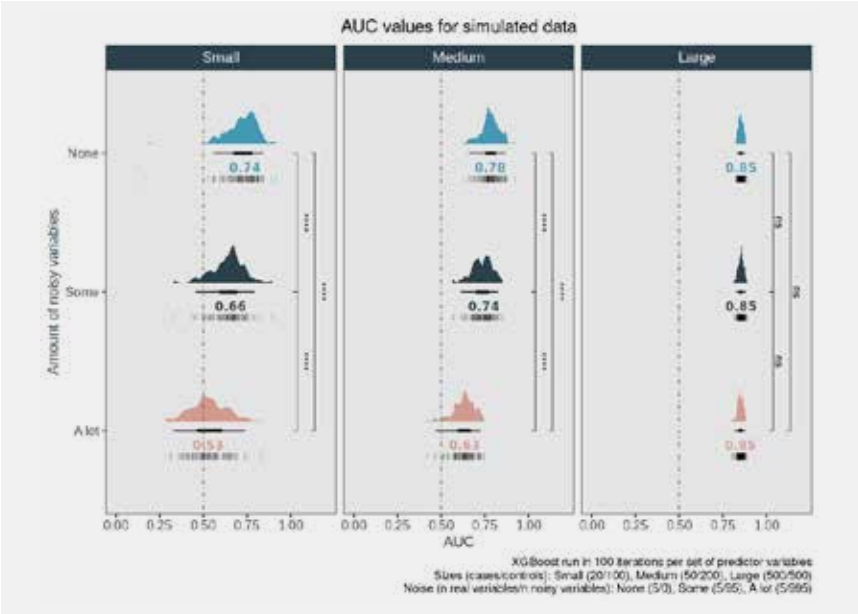


Figure 1. Summary of a synthetic experiment where 5 informative features were mixed with various amount of noisy features, in datasets of variable sizes. The plot shows that AI models (here represented by XGBoost) fails to filter out the signals from the noise in small datasets, but as the number of samples increases to 500 cases and 500 controls, the model could perfectly pick out the 5 informative features, even when the amount of noisy variables was increased to 995. ***** p<0.0001, ns = not significant.*

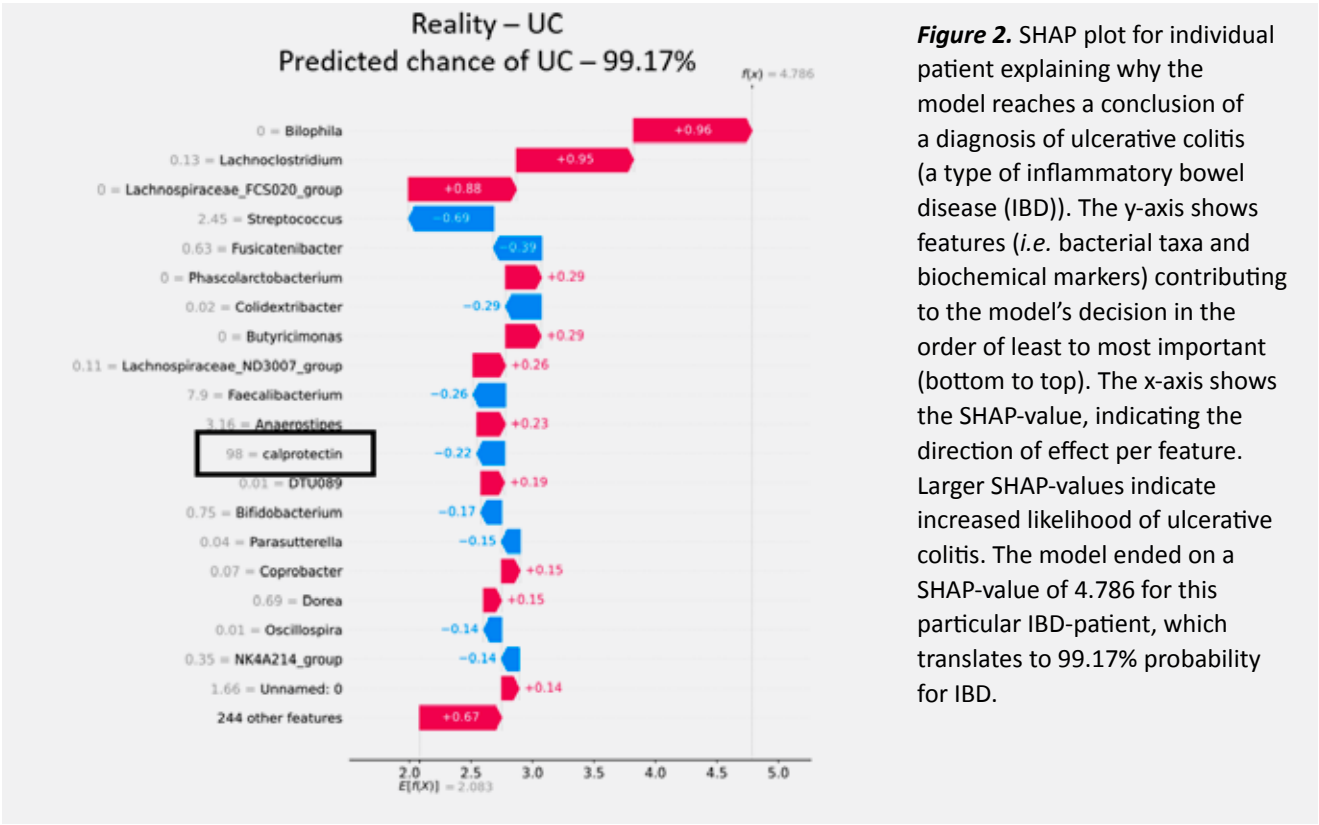


Figure 2. SHAP plot for individual patient explaining why the model reaches a conclusion of a diagnosis of ulcerative colitis (a type of inflammatory bowel disease (IBD)). The y-axis shows features (*i.e.* bacterial taxa and biochemical markers) contributing to the model's decision in the order of least to most important (bottom to top). The x-axis shows the SHAP-value, indicating the direction of effect per feature. Larger SHAP-values indicate increased likelihood of ulcerative colitis. The model ended on a SHAP-value of 4.786 for this particular IBD-patient, which translates to 99.17% probability for IBD.

1. Hua, J., et al., *Optimal number of features as a function of sample size for various classification rules.* Bioinformatics, 2004. **21**(8): p. 1509-1515.

2. Hernández Medina, R., et al., *Machine learning and deep learning applications in microbiome research.* ISME Communications, 2022. **2**(1).

3. Tamboli, C.P., D.B. Doman, and A. Patel, *Current and future role of biomarkers in Crohn's disease risk assessment and treatment.* Clin Exp Gastroenterol, 2011. **4**: p. 127-40.

4. Lundberg, S.M. and S.-I. Lee, *A unified approach to interpreting model predictions.* Advances in neural information processing systems, 2017. **30**.

In situ veritas

By Jonas Øgaard

HISTOLOGY AT RESEARCH INSTITUTE OF INTERNAL MEDICINE

For years, the progress of microscopy techniques relied heavily on scientific breakthroughs within optics, and discoveries of dyes that would stain tissues according to morphological identities. After that, a race for finding high quality, specific antibodies that could target and unique molecules has been – and is still – ongoing.
The past few decades have seen a different transformation of the histological arts, namely in the shape of computerised analysis, and later, with the emergence of in situ transcriptomics histology found an additional purpose. Common for both advancements are a need for handling massive amounts of data, and finding the hidden patterns which may not be perfectly visible at plain sight. Thus, with the addition of machine learning and AI, the field of digital histology has had a colossal bloom the last years, largely contributed to the fact that vision was one of the first complex tasks where the technology made the most progress in the beginning of the AI spring.
Research Institute of Internal Medicine has a long-standing tradition of using histology, both as a means to explore disease mechanisms as well as a tool to confirm findings from other methods of analysis. 10 years ago, we started utilizing WSI (whole-slide imaging – computerised, histological analyses of entire tissue sections), at a time when histological analyses were mostly done by eye, and if quantitative analyses were performed, they were done so on a fractional area of the tissue section (usually in the order of thousands). We quickly developed in-house algorithms to aid us (at this point, few tools were capable of dealing with massive images), created and set up a centralised storage- and analysis system (z9), and in 2017 we started implementing machine learning pipelines to aid WSI-analyses. Shortly after, fully fledged AI pipelines were running.

As the year becomes 2024, we currently employ AI methodologies for two main purposes in the context of histology: Segmentation and classification.

Segmentation
Within image analysis, segmentation is the process of dividing a picture into multiple zones. Transferring this to histology, we are often interested in working with morphologically distinct areas of the tissue separately. As an example, in a liver section, analysing bile ducts separately from parenchyma will give more informative results than taking averaged analytical results from the entire tissue section. In an infarct setting, identifying infarcted tissue from healthy tissue will make us able to focus on two very distinct cell populations. Due to heterogeneity of histological sampling and processing, these analyses are usually optimised per project basis, but since we have our histological data centrally organised, we are working on streamlining such processes to simplify future analyses by extrapolating from prior experiments. Another application of segmentation is separating all individual cells in a histological image from each other. This enables us to analyse the cells in terms of morphology (size, granularity) as well as staining (Haematoxylin-Eosin/ antibody staining/special stain). A typical slide will often contain beyond 100,000 cells, and with the capacity to morphologically describe them automatically yields an enormous advantage. This also allows us to analyse cellular neighborhoods to investigate interactions.

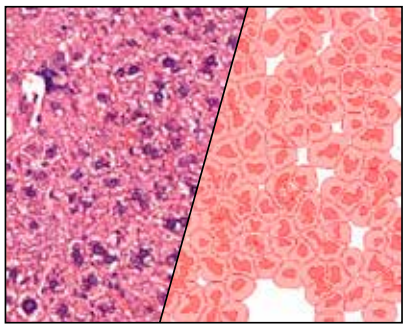


Fig 1: Segmentation of liver HE-stain into its constituent individual cells.

Classification
Classification is a more general concept, which goes hand-in-hand with segmentation. First you would identify out objects (spots, vessels, cells) in your tissue using a segmentation model, and then you can you use a classification model to identify subcategories of such an object. This works particularly well for cells, where we often are interested in finding the quantity of immune cells based on morphology, or specific cell types carrying an antibody tag. Due to the heterogeneity of histology, this feat may be more complex than it seems, as different parts of your tissue may stain differently, or due to variations between samples or batches. Typically we aim for our classification models to achieve a specificity and sensitivity towards 98-99%.

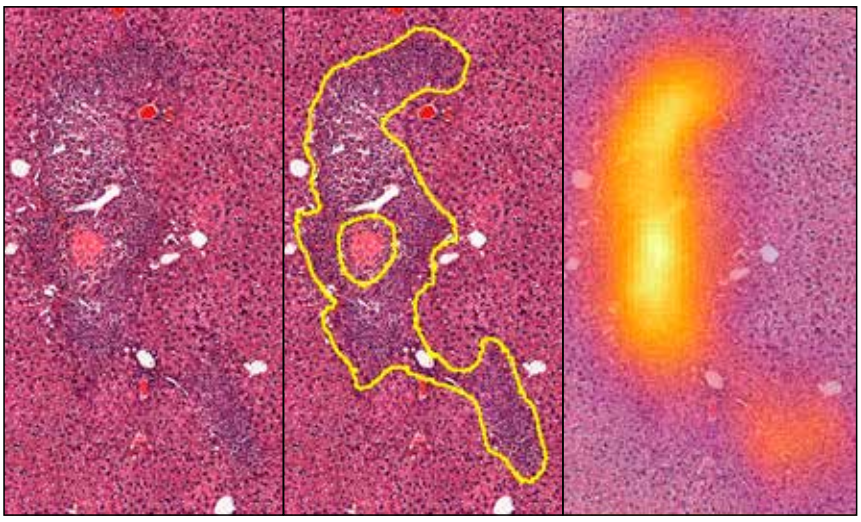


Fig2: Original HE-image (left), segmented image where areas of necrosis is detected (middle), and heatmap of immune infiltration based on the number of cells classified as infiltrating immune cells (right).

Spatial Transcriptomics
Lastly, with the advent of spatial transcriptomics, there is a need to connect tissue morphology with genetic expression levels, i.e. to evaluate to what extent all our genes are turned on and correlate it to positioning within a tissue sample. In this way, we get a map of which genes go on and off, depending on where in the tissue we are looking. To fully utilise this technology, we are again dependent on extracting information from larger tissue sizes and cross referencing them with gene expression. Conventionally such histological examinations are performed by pathologists, but this is both resource demanding and time consuming, which is why we are currently working on semi-automated methods for linking genes and morphology through various projects. Here AI-like technologies also aid us in delineating which cells (from morphology) gives rise to what genes at each spot of analysis (cellular deconvolution).

Infrastructure
We are continuously working on improving infrastructure, keeping our data ready for the coming AI revolution. Part of our accomplishments during 2023 was adapting our 25TB histology database (hosted by Sigma2) for compatibility with state of the art, AI-connected WSI-analysis pipelines. In the same period we also financed and installed upgrades to our microscope utilities that paves the way for AI-supported real time assistance, and we hope to build on the same infrastructure int the future to allow for tighter integration of AI in our workflows. Equivalently, continuous effort is being made to standardize and centralize data storage such that application of current and future tools are supported.

[1] Oldereid, T. S., Jiang, X., Øgaard, J., Schrumpf, E., Bjørnholt, J. V., Rasmussen, H., & Melum, E. (2024). Microbial exposure during early life regulates development of bile duct inflammation. Scandinavian Journal of Gastroenterology, 59(2), 192–201. https://doi.org/10.1080/00365521.2023.2278423
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[3] Chung, B. K., Øgaard, J., Reims, H. M., Karlsen, T. H., & Melum, E. (2022). Spatial transcriptomics identifies enriched gene expression and cell types in human liver fibrosis. Hepatology communications, 6(9), 2538–2550. https://doi.org/10.1002/hep4.2001

DISSERTATIONS 2023

Photo: Ine Eriksen, UiO

MSc. Ruth Elise Dybvik Matlary

Physical activity in young people with haemophilia A in Norway – The HemFitbit study
August 30, 2023
Committee:
1. opponent: Senior Clinical Lecturer in Haematology, Honorary Consultant in Haematology Dan Hart, Queen Mary University of London, UK
2. opponent: Senior Lecturer Sports & Exercise Biomechanics Ryan Mahaffey, St. Mary´s University, UK
3. opponent: Professor II Anne Flem Jacobsen, University of Oslo

Main supervisor: Professor II Pål André Holme, University of Oslo
Summary of PhD project:

Haemophilia A is a rare bleeding disorder where physical activity may pose an increased risk of bleeding, which may lead to joint damage (arthropathy) and functional impairment.

With current efficacious prophylactic medical treatment, people with haemophilia's possibilities to be physically active may be similar to that of people in the general population.

The aims of the thesis were to; describe physical activity (PA) levels in young people with haemophilia A (on prophylaxis) in Norway compared to controls, examine factors associated with PA in these patients, and to investigate the accuracy of the activity tracker Fitbit in measuring PA in this group. Methods included objective measurements of PA, joint status, and other relevant factors.

The Fitbit-measured PA levels of 40 men with haemophilia A aged 13-30 years were similar to that of a large group of peers. People with haemophilia spent some more time in light intensity PA and exercised more frequently than controls. Investigation of factors associated with PA showed that those without signs of arthropathy engaged in some more moderate and vigorous intensity PA than those with signs of arthropathy, and that teenagers who met PA recommendations appeared to have slightly better joint status compared to those who did not.

Comparisons of PA estimates between an ActiGraph accelerometer and a Fitbit activity tracker showed moderate to high correlations between device measurements, but the Fitbit overestimated number of steps and minutes of light and vigorous intensity PA.

These findings demonstrate that PA levels of Norwegian young people with haemophilia A are similar to general population peers, and indicate that presence of haemophilic arthropathy is associated with reduced intensity of PA. Furthermore, the results suggest overestimation of PA estimates by the Fitbit.

Immune regulation in atherosclerosis and other cardio-metabolic diseases

Photo: Åsne Rambøl Hillestad, UiO

From left: Turid M Pedersen, Siva Krishna Vagolu, Sverre Holm, Maria Belland Olsen, Ida Gregersen, Tuva B Dahl, Øystein Sandanger, Vigdis Bjerkeli, Azita Rashidi, Bente Halvorsen, Kari Otterdal, Ylva Schanke, Sarah Louise Mikalsen Murphy, Jonas Øgaard, Xiang Yi-Kong.

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About the group

Cardiovascular disease and related metabolic disorders such as diabetes, obesity and fatty liver disease are major causes of morbidity and mortality worldwide. They have many common features, such as dyslipidemia and inflammation. In our research group, we focus on immune-mediated mechanisms in these conditions. The last years we have also studied these mechanisms in Covid-19, and the association between Covid-19 and risk of cardiovascular disease. By exploring these processes through a translational approach, connecting basic science and the clinic, we wish to build a foundation for the development of new diagnostic and treatment targets for cardiometabolic disease.

Our research group works in the cross-section between molecular biology and biochemistry, and cardiovascular, cerebrovascular, and endocrine medicine. Our ambitious goal is to delineate novel therapeutic targets and biomarkers to change clinical practice.

The group uses different research approaches, ranging from analyses of blood and tissue samples from patients to studies in genetically modified mice and cell culture systems, using advanced cellular and molecular biology. The group consists of people with different educational background and includes medical doctors, nutritionists, biochemists, bioinformatics and engineers. Such multidisciplinary competence is a great strength of our research group.

Activity in 2023
In 2023, the group has reached several important milestones. Prof. Halvorsen received the prestigious yearly "Excellent researcher award" at OUS. Further, the group applied for the establishment of a K.G. Jebsen Centre for Stroke Research lead by Halvorsen, and reached the final round. In 2023, the group had 30 publications, where group members had 10 first or last authorship.

The group runs a large span of interconnected translational projects to study the immunological and molecular mechanisms in obesity, metabolic disorders, cardiovascular disease and Covid-19, and our main projects during 2023 were:

T cells in obesity and metabolic disease. One of the group's largest projects aims to decipher the role of T cells in development of obesity and metabolic disease. We study a transgenic mouse model with altered T cell activation, resulting in increased T cell responsiveness and subsequent obesity development; and is thus a unique model to explore this association. In 2023, the first paper describing this phenotype was finalized and submitted for publication. Herein we present, for the first time, evidence that T cells can cause obesity development in mice; demonstrated by adoptive T cell transfer experiments and bone marrow transplantation experiment of cells from the transgenic mice to several mouse models resulting in obesity in recipient mice. The transgenic mice display increased adipose inflammation and increased T cell activation, however the mechanisms leading to obesity development is still unclear and will be an important research focus in the group for the years to come.

Clinical material and add-on studies to clinical intervention trials. In addition to a wide spectrum of animal models to study cardiometabolic disease, we study molecular mechanisms in patient materials, as a bridge between the lab and the clinic. In 2023, we continued this work and published papers describing altered immune status in patients with cardiovascular disease. We have continued to characterize the immune response of myocardial infarction patients receiving anti IL-6 treatment (in NSTEM and STEMI patients) to identify molecular mechanisms for the beneficial effects of tocilizumab in this group. Further, we have studied stroke the different signatures of atrial fibrillation stroke induced stroke compared to carotid stenosis – or cryptogenic stroke.

Covid-19 and Covid-19 sequalae. In several publications, we have in 2023 described different features of altered immune regulation in patients with Covid-19. We have studied markers of

- LDL aggregation and pro inflammatory proteins
- ECM in association to severity of disease
- Epitranscriptomics
- Coagulopathy

Of particular interest, we have in 2023, published a paper describing altered LDL aggregation as well as pro-inflammatory LDL cholesterol particles 3 months after severe COVID-19. These data point to a possible increased risk of cardiovascular disease in these individuals, persistent for months after recovery. The possible severe cardiovascular sequela of COVID-19 is a great research interest in the group and will be a research focus in the years to come.

Other projects – cooperation. Experience and expertise possessed by our group members lead to fruitful collaborations also in 2023. To mention a few, we planned and performed a pre-clinical study in mice in collaboration with NTNU, where a synthetic peptide was used as a potential new treatment after myocardial infarction. In a different collaboration with Nofima and Division of Clinical Nutrition, UiO, we are now finalizing a pre-clinical study where we found that certain dietary lipids can dampen the development of atherosclerosis in mice. Of clinical collaborations, we are now studying the role of immune cells and inflammation in brain abscesses.

EU-project – PainFACT. We are actively participating in an EU-funded project, PainFACT, investigating the link between pain sensation and immune response. The sensation of pain is an evolutionary adaptation for organism to identify danger. It is a hallmark for injury, inflammation and pathogen invasion, and is mediated through nociceptor sensory neurons. A cross-talk between nociceptors and the immune system is well known, especially the capability of immune modulators to sensitize nociceptors, thus increasing an individual's sensation of pain. The PainFACT consortium integrates pre-clinical and clinical data to investigate the correlation between pain sensitivity/ threshold and risk of cardiovascular events. In 2023, we have further processed biological material from a large-scale pre-clinical study and made them suitable for down-stream analysis to be conducted by the consortium.

Infectious Immunology

Photo: Øystein Horgmo, UiO

From left: Silje Jørgensen, Sajan Raju, Tuva B Dahl, Marius Trøseid, Xiangning Bai, Mai Fraz, Nuriye Basdag Tekin, Hanne Guldsten, Vegard Myhre.

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The Infectious Immunology group was established at the Research institute for Internal Medicine end of 2022. The overall research focus is to characterize and understand the interplay between infections and host immunology, aiming for more targeted and personalized treatment strategies. We perform clinical translational research within Infectious diseases including COVID-19, other respiratory infections and HIV, and primary immunodeficiency including common variable immunodeficiency (CVID). This includes randomized controlled trials (RCTs) and observational studies with biobanking, with a particular focus on innate and adaptive immunity, inflammation as well as the gut microbiota. Our main patient materials are blood, airway and fecal samples, which we use for microbiome analyses, viral analyses, metabolomics, proteomics and other omics analyses, as well as inflammatory profiles and host immunology. Within our HIV and CVID projects, we also perform epigenetic and epitranscriptomic analyses of biopsies from the gastrointestinal tract. Since most of the group`s members have been recruited the last year, we are now in a consolidating phase before planning further expansion. However, a thematic expansion will be increased focus on the airway microbiota, which links previous experience from gut microbiota research with a clinical focus on airway infections as well as respiratory comorbidities within primary immunodeficiencies and people with HIV. Internationalization is also part of our strategy as several ongoing and planned projects are EU funded with possibility for young and senior researchers to visit our collaborators for shorter or longer periods of a project period. Regarding mobility, one post doc has been part time hired in an EU project lead from Madrid, and one senior researcher was recruited from Karolinska Institute in 2023, and is currently performing collaborative projects between these institutions. Funding is exclusively based on competitive funding from NRC, HSØ and EU, and the group has been successful in securing several major grants the last years.

Examples of activity in 2023:

- **COMicS** (Copenhagen-Oslo Comorbidity and Microbiota Study in HIV infection). Planned as the largest prospective microbiome study in HIV-infected individuals. Several papers on 16s DNA microbiota data have been published. Full metagenomic sequencing data were finalized in 2023, which will spark new insight and papers from this unique cohort.

- **Targeting the NLRP3 inflammasome in HIV infection**. The aim is to explore whether inflammasome activation is enhanced during HIV infection, and if so, if inflammasome activation could explain increased cardiovascular risk in HIV-infected individuals. Several papers have been published from this ongoing project based on circulating inflammasome markers, whereas in vitro data have been analyzed during 2023.

- In collaboration with Johannes Hov group we have established the regional research network **ReMicS** (Regional research network for clinical Microbiota Science), encompassing > 25 research groups. In 2023, we hosted the 10th consecutive national microbiota meeting with around 100 participants, and initiated plans for the first Nordic Microbiota meeting (NoMic) starting in 2024.

- We have received funding through the Era-Net for managing a WP on multi-level integrated bioinformatics in the **SCRATCH** consortium (Microbiota-based SCReening of Anal Cancer in HIV-infected individuals), aiming to improve diagnostic screening of HIV-associated anal cancer, taking o clinical practice. This project resulted in a groundbreaking paper published in Nature Medicine 2023, showing that microbiota produced proteins has the potential to markedly improve screening of anal cancer compared to cytology.

- We have also received NRC funding for the project "**Targeting the gut heart axis**". A common theme in this project and SCRATCH is to develop integrated multi-level bioinformatics on metagenomics, metabolomics and proteomics analyses. This project resulted in novel data in 2023, showing that microbiota produced Imidazole propionate links the heart failure-related microbiome with disease severity.

- We have also finalized the first studies over the EU-funded adaptive platform trial for COVID and emerging pandemics, **EU SolidAct**, set up to run phase II and phase III trials in around 15 European countries, with OUH as sponsor. The first phase III trial evaluating baricintib for severe Covid-19 was published in Critical care in 2023, whereas the first phase II trial on bemcentinib was stopped in 2023 due to end of the COVID pandemic. Biobanked material from this platform study is currently being analyzed as part of the HSØ-funded **T3C** (Tailored therapeutics targeting Covid-19 in hospitalized patients) project.
- We have also received an "Open research grant" in 2023 from HSØ on a project entitled "A new approach to disease prevention and therapy in Immunodeficiency". In this project, we will use a unique human biobank material with intestinal biopsies, blood cells, intestinal flora, diet data together with high-tech methods to study changes in DNA and RNA in intestinal biopsies and in inflammatory cells in the blood. The manuscript on **epigenetic** analyses is already submitted.
- In the HSØ -funded post-doc project (HDL beyond atherosclerosis - altered **lipid metabolism** as a driver of inflammation in Common variable immunodeficiency), we have used Common variable immunodeficiency, as a model to study the role cholesterol and fat metabolism have on chronic inflammation without an increased risk of heart disease. This year we have published an article on triglyceride and VLDL-cholesterol (very low-density lipoprotein) in CVID and how increased triglyceride levels in CVID coincided with high inflammatory markers in the blood, and increased microbial imbalance in stool samples, but not heart disease.

Inflammatory Biomarkers in Cardiovascular and Metabolic disease

From left: Kristin Godang, Merisa Abusdal, Thor Ueland, Annika E Michelsen, Maren Wessel, Kari Otterdal, Tove Lekva, Monica Frøystad.

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RESEARCH PROFILE

Many disease states are associated with low-grade chronic inflammation that may result in changes in inflammatory proteins in biological fluid such as serum and plasma. Measurement of these biomarkers will therefore be useful for detecting diseases before the diagnosis and/or offer information on the mechanisms of disease and treatment targets, or be helpful in evaluating treatment responses and predicting outcomes.

A cornerstone in our research is the close collaboration with the Department of Cardiology, and evaluation of biomarkers in heart failure, acute coronary syndromes and aortic stenosis. Biomarkers reflect a wide range of inflammatory processes in the patients and can further predict adverse outcome and treatment responses.
We are evaluating the impact of systemic inflammation in pregnancy on future cardiovascular and metabolic risk. The project "Early detection of preeclampsia and future cardiovascular disease using non-coding RNA" was started in 2023 by Tove Lekva with open support grants from HSØ in collaboration with the Department of Obstetrics, Norwegian Institute of Public Health, Section of Endocrinology and the Department of Cardiology. Our hypothesis is that non-coding RNA is crucial for both development of preeclampsia and later development of cardiovascular disease. Hopefully our research will lead to an early prediction and better monitoring of this condition, in addition to possible new treatment opportunities, and more understanding of the mechanisms of non-coding RNA in the development of preeclampsia and cardiovascular disease.
The endocrine unit is a part of the research group. The main research focuses on the molecular characterization of the pituitary adenomas and finding novel biomarkers to predict the aggressiveness and recurrence, or the response to medical treatment. In addition, we carry several projects on the role of the adipose tissue and bone on the glucose metabolism and cardiovascular risk in different endocrine diseases.

Severe mental disorders like schizophrenia and bipolar disorders are major contributors of morbidity globally and is associated with both cardiovascular and cancer disease. Together with the Norwegian Centre for Mental Disorders Research (NORMENT) we have for more than 10 years analyzed levels of inflammatory molecules in circulation and demonstrated dysregulation of immune cells and endothelial cells. More recently the use of induced pluripotent stem cell (iPSC) models have enabled more mechanistic studies of how brain cells function in mental disorders.

We have an ongoing strong collaboration with TREC, a translational research center at the University of Tromsø, focusing on patient-oriented and population-based research to reveal new risk factors and mechanisms for the formation of venous thrombosis.

In addition, we have strong collaborations with other clinical research, national and international projects.

EXAMPLES OF ACTIVITY IN 2023

- Also, in 2023 we worked on samples collected during the COVID-19 pandemic, resulting in several published papers focusing on biomarkers associated with poor prognosis in hospitalized patients. This work is in collaboration with other research groups at RIIM as well as national and international collaborating hospitals and research units.

- The project "Regulation of non-coding RNAs in preeclampsia and impact on future cardiovascular risk" with grants from the Norwegian Health Association was finalized in 2023. Two papers were published showing decreased anti-ferroptotic activity in maternal leukocytes in women developing preeclampsia that correlated with anti-inflammatory expression. In the extracellular vesicle project, we found platelet-derived and mitochondrial RNA were highly expressed in plasma extracellular vesicles and were decreased in extracellular vesicles isolated from women with preeclampsia. We found the non-coding RNA TUG1 and MT-TA in leukocytes as promising early prediction markers of preeclampsia.

- Kjersti Oppen defended her PhD thesis "Iron-Related Biomarkers as Predictors of Etiology and Prognosis in Pneumonia" where Annika Michelsen contributed as supervisor?

Genomics and metagenomics in inflammatory diseases

Photo: Åsne Rambøl Hillestad, UiO

From left: Georg Schneditz, Jørgen D Rønneberg, Lise Kathrine Engesæther, Petra Hradicka, Simen Hyll Hansen, Johannes R. Hov, Hanne Guldsten, Hanne Lyche Alme, Kristian Holm.
In front: Maria Maseng, Sara Kristina Viberg Tjønnfjord, Mikal J Hole, Peder Braadland, Beate Vestad, Antonio Molinaro.

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RESEARCH PROFILE

The genomics and metagenomics group aim to characterize and understand how the human genome and the gut microbiome influence inflammatory disease, and how this knowledge can be applied clinically. Our general approach is to used nontargeted high-throughput omics like sequencing and metabolomics, followed by targeted our hypothesis-driven methods, supported by bioinformatics and biostatistics including machine-learning. Increasingly, experimental approaches in vitro and in vivo (mouse models) are important to define cause-or-effect and disease mechanisms.

Our main interest is primary sclerosing cholangitis, a disease of the bile ducts of the liver, but we are also involved in research in multiple other conditions relevant for the institute, including heart failure and immunodeficiencies. Our main human materials are blood and fecal samples, but we are also establishing methodology for microbiota profiling in low-biomass material (blood, tissue, bile), while our experimental agenda involves germ-free and conventional mice with induced inflammatory biliary or intestinal disease, in collaboration with the Melum group.

Our current main working hypothesis is that biochemical footprints of microbial activity is driving disease. We aim to define altered functional microbial changes using metagenome sequencing (i.e. the study of all microbial genes) and metabolomics. Our first interesting finding was of altered microbial metabolism of essential nutrients is altered in PSC, with deficiency of vitamin B6 as a potential disease-modifying factor caused by microbiome changes. A clinical trial focusing on translational aspects of vitamin B6 supplementation was approved in 2023 and will recruit the first patients 1st half of 2024 (Pyridoxine in primary sclerosing cholangitis, PiPSC). This represents an example on how we work to identify and potential treat altered microbial functions, defining their clinical impact as biomarkers or in therapy. We are applying this methodology also on recurrence of PSC after liver transplantation, which is a significant clinical problem. This is the underlying idea of the ERC Starting Grant project *StopAutoimmunity*, which directs many of the priorities in the group. With growing data size and complexity, we increasingly depend on bioinformatics and statistics. In our IBD focused projects, now comprising thousands of samples, in collaboration with the Inflammatory Bowel Disease in South-Eastern Norway 3 study, we now apply more advanced bioinformatics and e.g. artificial intelligence to improve the yield from big data from microbiome or metabolome analyses.

The groups also work more disease independent with *Clinical microbiota medicine*, as part of a Strategic research area at Oslo University Hospital awarded to the group in 2019. Interventions targeting the gut microbiome to treat disease may provide evidence of causal relationships between the gut microbiome and disease. In 2023, one important focus was to increase the activity and capacity of the donor bank for fecal microbiota transplants. Finally, the annual National Microbiota conference was a success – the tenth event since 2014. We are excited that from 2024 onward we aim for this to become a Nordic event.

FUNDING

The people in the group were in 2023 funded by one ERC Starting Grant, five grants from Regional Health Authorities of South Eastern Norway, one PhD student following an industrial PhD scheme (funded by Research Council of Norway), one Strategic research area grant in Oslo University Hospital, one postdoc is funded by a grant from UEG, in addition to Canica, funding one bioinformatician, and Nordforsk. In a collaboration with the Experimental group and partners from the Baltic area (driven from Lithuania) we also have funding from the EEA Baltic research funds, which is funding one post doc.

KEY NATIONAL AND INTERNATIONAL COLLABORATORS

Locally, the group has extensive collaborations ongoing within NoPSC and the Research Institute of Internal Medicine, multiple clinical research groups (including in particular the IBD group at the Ullevål campus) as well as pathology and radiology. Regionally and nationally, the group has been working in the ReMicS network (Regional research network for clinical Microbiota Science), with Hanne Guldsten as administrator. Internationally, we continue strong collaborations both within and outside the International PSC Study Group, with the currently strongest links to Swedish groups in Stockholm, Gothenburg and Uppsala.

The Experimental liver research group

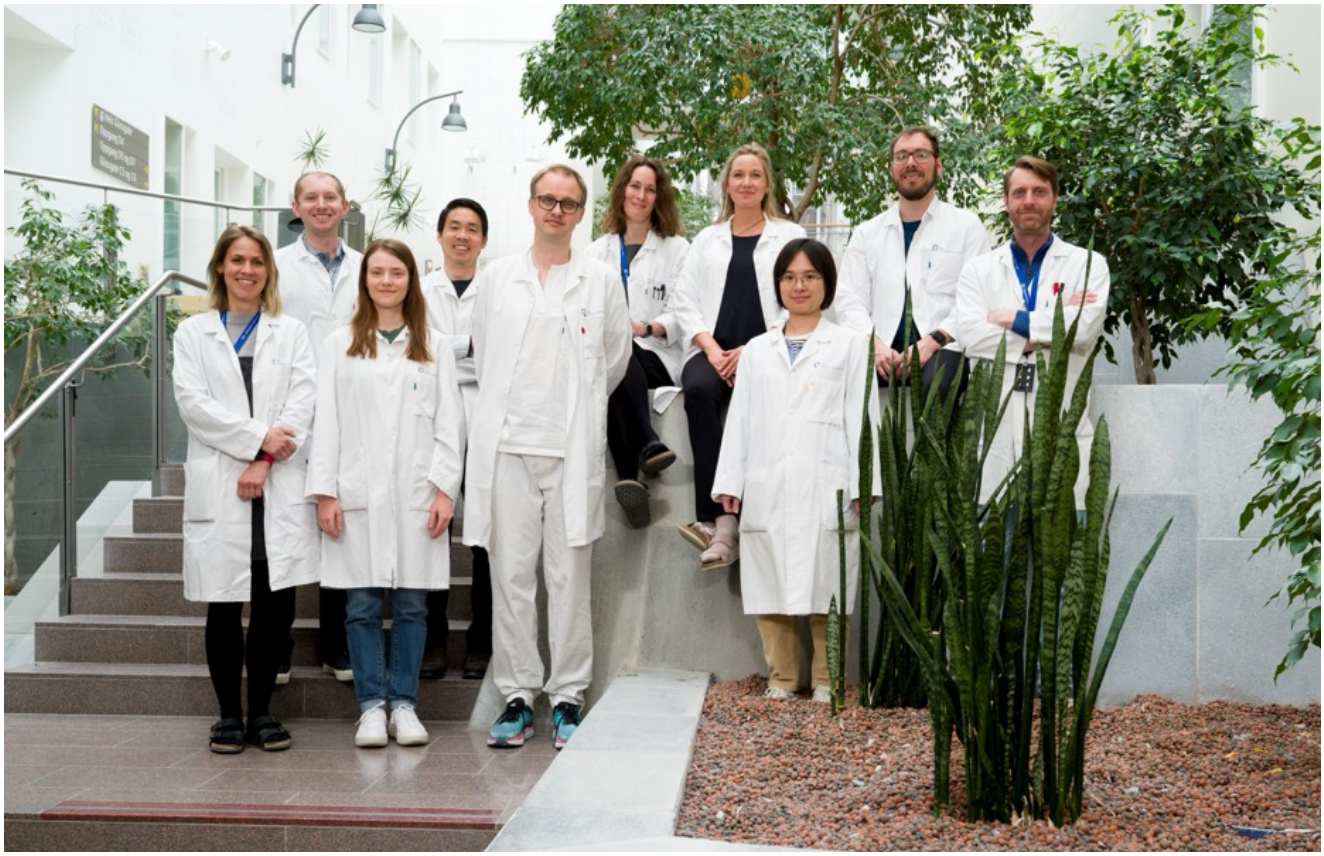

Photo: Åsne Rambøl Hillestad, UiO

From left: Oda Helgesen Ramberg, Henry W Hoyle, Lisa Brynjufsen, Brian Chung, Espen Melum, Kathrine Sivertsen Nordhus, Anna Frank, Xiaojun Jiang, Markus Jördens, Jonas Øgaard.

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RESEARCH PROFILE

The experimental liver research group is focusing on experimental and translational studies related to primary sclerosing cholangitis (PSC). Our laboratory activities take place at the Research institute of Internal Medicine. In 2023 the group consisted of the group leader, four senior researchers, two postdocs, four PhD students, the lab manager, one researcher and two technicians. The overarching topic in the group is to understand mechanisms regulating cholangitis with a clear focus on immunology and the interaction of the immune system with the microbiome and the role of cholangiocytes in propagation of inflammatory processes.

Our strong collaboration with the Hybrid-technology-hub on establishing a bile-bile-duct-on-a-chip continued and in 2023 the project moved from the prototype stage into a system that is useable in a range of experimental conditions. Seeding organoids in the chip now leads to a tight barrier allowing flow of relevant compounds through the duct. We have also tested how this barrier respond to pharmacological substances. The bile-duct-on-a-chip system was also in 2023 accepted into the University of Oslo's SPARK program for commercialization. This project will be led by Dr. Henry W. Hoyle and Dr. Anne Frank from the group. Being admitted to the SPARK program allows us to follow up on the commercial potential of the system and to get a dedicated mentor from the industry. In 2023 we used our experience with organoids coming out of the collaboration with HTH in a large project with Novartis in Basel where we use their automated systems to examine the impact of various pharmacological substances on an induced inflammatory phenotype in the organoids.

In a follow-up study of our previous work on CD100 we got a paper describing a direct interaction of T-cells with cholangiocytes that leads to a clear Th17 profile driving inflammation accepted for publication in Gastroenterology. We also established a joint collaboration with the Seoul National University, SINTEF and OsloMet that was funded through the National Research Foundation of Korea. This project is headed from our side by senior scientist Xiaojun Jiang. A new concept on integration of big data with genetics for patient stratification was funded by a HSØ grant towards the end of the year.

The group also has large projects related to single-cell sequencing and spatial transcriptomics using both human and murine material. The laboratory work and sequencing in several of these projects were finished in 2023 and bioinformatics analyses are currently ongoing. In our project examining liver infiltrating mononuclear cells we finished the sequencing and initial bioinformatics analysis of samples from a range of different liver diseases. Preliminary data from this project was presented at Norwegian Society of Immunology meeting. To comply with the current regulations when expanding our sequencing-based studies in humans we have developed secure bioinformatics pipelines for single cell and spatial transcriptomics data through TSD (Tjenester for sensitive data) at the University of Oslo. All ongoing projects have been adapted to this infrastructure.

Our projects using germ-free animals to assess the importance of timing of microbiome introduction on development of bile duct inflammation using the NOD.c3c4 model and immune maturation in wild-type mice were accepted for publication in 2023. The project using the bile-duct injection model for assessing MAIT-driven inflammation in the bile duct was in 2023 supplemented by a range of immunohistochemical assessments and additional analyses. For investigating the specific role of CD1d on the bile duct epithelium we have established a conditional knock-out mouse model and have used this model together with our bile-duct injection technique using oxazolone to further dissect the role of NKT-cells in the bile ducts.

Haemostasis, Thrombosis, and Vascular Biology Research

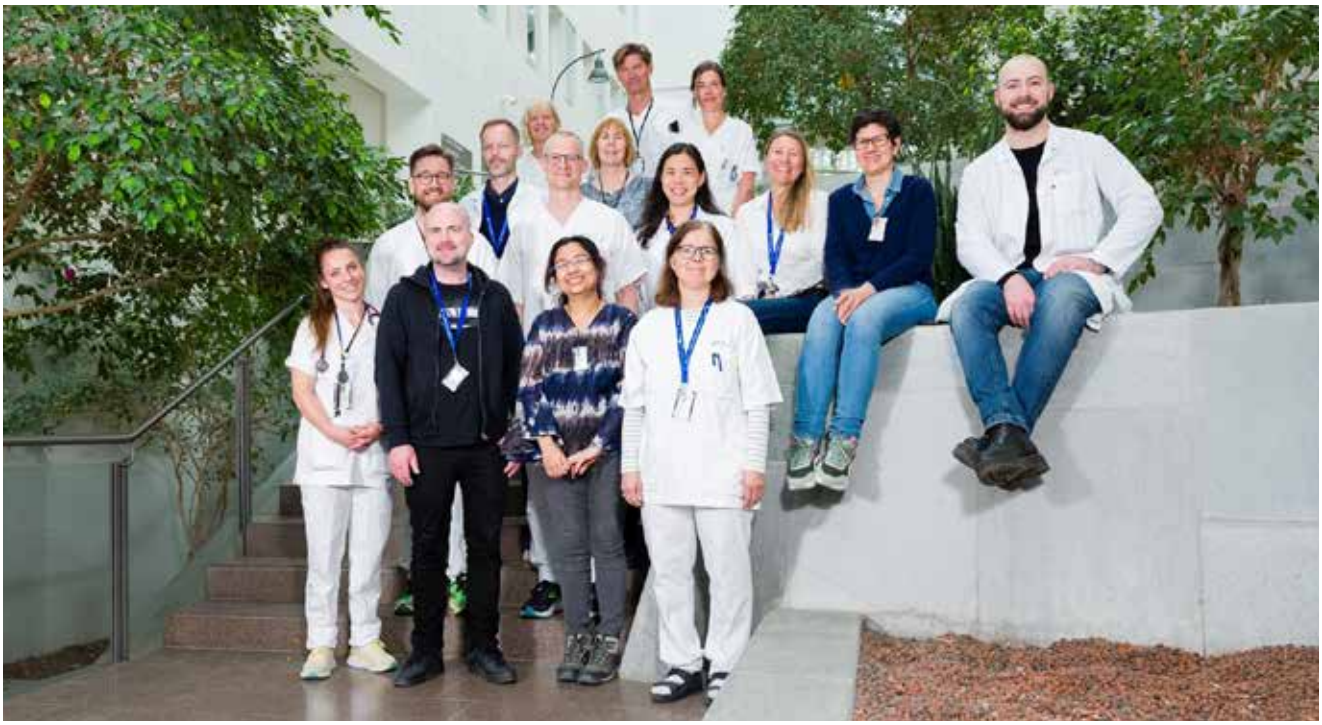

Photo: Øystein Horgmo, UiO

In front, from left: Malu Katalina Marie Lian Hestdalen, Knut Husø Lauritzen, Anindita Bhattacharya, Marie-Christine Raymonde Mowinckel. Second row, from left: Trym Døviken, Jørn Dehli Kristiansen, Xue Yan Cui, Benedicte Stavik, Maria Eugenia Chollet Dugarte, Giacomo Roman. Third row, from left: Christian Qvigstad, Britt Jakobsen. Back row, from left: Marianne Seierstad Andresen, Pål André Holme, Ragnhild Johanne Måseide.

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The group conduct basic, translational, and clinical research within the field of haematology. Last year, several new clinical projects were started up, important project milestones were reached, a PhD was successfully defended, and we hosted the 56th Nordic Coagulation Meeting with >100 participants from the Nordic and Baltic countries. The research group has two areas of interest within haematolgy, one lead by Stavik and Sandset, and one lead by Holme.

RESEARCH PROFILE Sandset/Stavik:

"Coagulation Factors: Role in the Development of Thrombosis, Inflammation and Cancer"

Our group studies the pathophysiological role of blood coagulation proteins in thrombosis and haemorrhage, but also in other pathologic conditions such as inflammation and cancer. Our main goal is to identify how and why components of the blood coagulation process contribute to disease development, and to utilize this knowledge to improve patient care.

Activity in 2023:

Inherited coagulation disorders – ex vivo liver cell models and cell therapy

Inherited deficiency in coagulation proteins can cause mild to severe bleeding or thrombosis in affected individuals. The deficiency is caused by a mutation in the corresponding gene that results in reduced or diminished activity of the protein in plasma. Most coagulation proteins are produced in the liver and secreted to plasma and, with help from our collaborator Gareth Sullivan, we utilize stem cell differentiation techniques to generate stem cell derived liver organoids in the lab to model coagulation protein production and secretion. In 2023, we successfully corrected several mutations in the genes encoding Factor (F) VII and Antithombin in patient-derived induced pluripotent stem cells using CRISPR-CAS9 gene editing. The work required extensive optimization of protocols for gene editing and single cell seeding and culturing, but we have now created a robust and efficient pipeline for the gene correction. With valuable help from colleagues at the institute and collaborators at Kings College Hospital in the UK, we have also moved into the pre-clinical stage of these projects and started to optimize liver organoid transplant procedures in mice.

Bone marrow microenvironment in Multiple Myeloma
Multiple myeloma (MM) is a B cell malignancy where abnormal plasma cells accumulate in the bone marrow. These patients are prone to cancer-related thrombosis already at the precursor stages of the disease and we are deciphering the tumor microenvironment for possible explanations using single cell sequencing. In the last year, sequencing data have been subjected to extensive quality control, clustering and analyses and we are awaiting sequencing of additional samples.

Drug repurposing
Drug repurposing has become a valuable tool to find new treatments to various diseases with low cost and little time. Previous findings in our lab indicated that an approved drug was able to increase the activity of mutated FVII. We therefore performed a larger screen using >1000 FDA approved drugs to identify potential compounds. The screen identified two hits, which have been confirmed in *in vitro* studies in 2023 and a publication on this finding is currently under preparation.

Coagulation proteins in atherosclerotic disease
Atherosclerosis is an inflammatory disease that culminates in thrombotic complications. Using a biobank of human carotid plaques, we are looking into the presence of coagulation factors inside the plaque and investigate their potential role in regulating inflammation and plaque development. The aim is to identify regulatory targets that can reduce the inflammatory burden and, potentially, be beneficial in attenuating atherothrombosis.

Biobanking
Our general biobank for thrombosis and hemostasis research is growing and we have now collected samples from >100 patients with bleeding or thrombosis for future research. We are now setting up the registry that will accompany the biobank.

RESEARCH PROFILE Holme:

"Haemostasis and Bleeding Disorders"
Our scientific interests are focused on clinical and basic aspects of normal and disturbed haemostasis in particular bleeding disorders like hereditary and acquired coagulation disorders.

Oslo University hospital, Rikshospitalet is the only Haemophilia Comprehensive Care Centre in Norway and is one of the biggest haemophilia centres in the Nordic region taking care of more than 1200 persons with bleeding disorders. Several research projects are ongoing besides clinical activity.

Investigator initiated activity in 2023:

Age related comobidities in haemophilia

Our group is the coordinating centre for an epidemiologic European multicentre study on behalf of the ADVANCE (Agerelated-DeVelopments-ANd-Comorbidities-in-hemophilia Working Group) The group is interested in determining, among consecutively screened people with haemophilia (800 pts.), aged ≥40 years with a follow up period of 10 years whether rates of hypertension/renal disease/ and other cardiovascular and malignant comorbidities vary with specific influencing factors in haemophilia. Four papers from the cross-sectional study have already been published and now further followed up in the longitudinal prospective study.

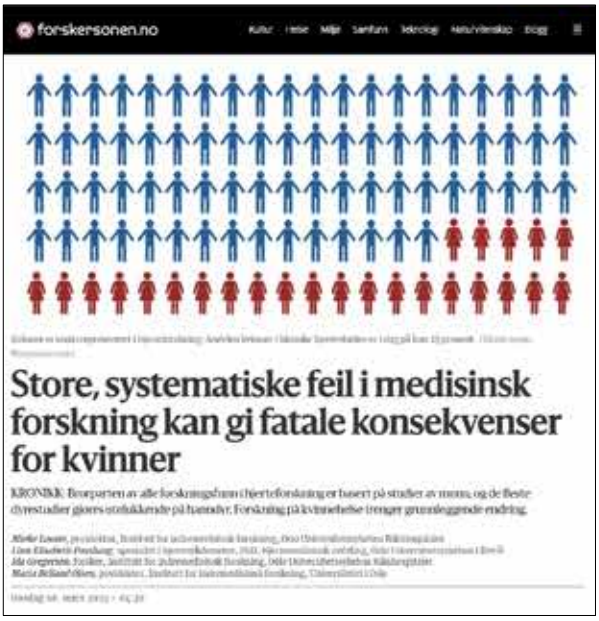
HemFitBit study- Defining Normal Activity in Hemophilia

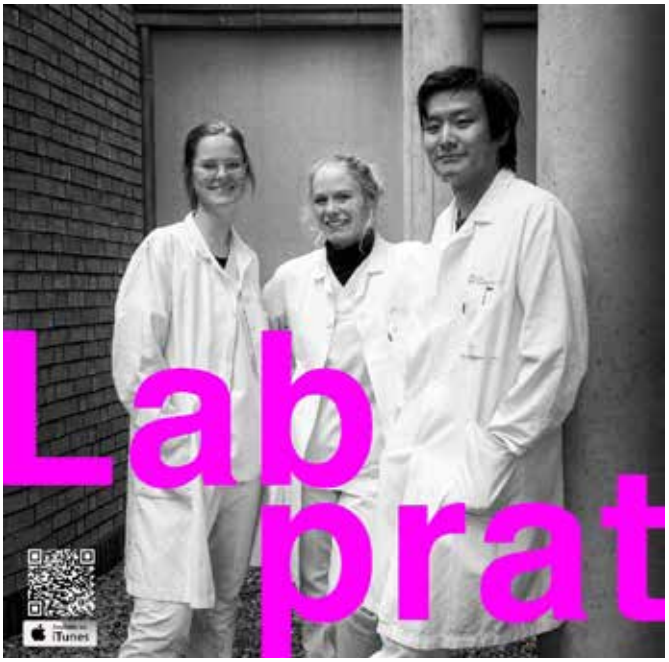
The overarching aim of the HemFitbit study was to investigate aspects related to the habitual physical activity (PA) of young persons with hemophilia A on prophylaxis in Norway. This project has collected information on physical activity levels in 40 patients with haemophilia A aged 12-30 years over a 3-month period using the wearable technology 'Fitbit'. A subgroup of participants has also wear the accelerometer 'ActiGraph' in order to validate the two devices against each other. Through this work we have been able study and (1) to compare PA measurements of the consumer-grade activity tracker Fitbit Charge 3 to the research-grade accelerometer ActiGraph GT3X-BT in young PWH A, (2) to compare objectively measured levels and types of habitual PA among young PWH A on prophylaxis to general population peers over a period of 12 weeks, and to investigate the proportion of study participants meeting the WHO recommendations for weekly MVPA and (3) to investigate factors associated with PA in young people with haemophilia A on prophylaxis. Three papers have been published from this PhD project and Ruth Elise Dybvik Matlary, MSc successfully defended her thesis entitled: Physical activity in young people with haemophilia A in Norway - The HemFitbit study on the 30th of August 2023.

VITT- Vaccine-induced immune thrombotic thrombocytopenia

From March 2021 the group has worked extensively on the SARS-CoV-2 vaccination-related thrombotic complications and thrombocytopenia giving devastating adverse events. This has been done in close collaboration with other groups here at RIIM and Department of immunology, OUS and the Norwegian National Unit for Platelet Immunology, Division of Diagnostics, University Hospital of North Norway. This work lead to the first main publications: Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination. N Engl J Med. 2021;384: 2124-30 and Immune Complexes, Innate immunity, and NETosis in ChadOx1 vaccine-induced thrombocytopenia. Eur Heart J. 2021; 42:4064-72. Further work on this and thrombosis associated with SARS-CoV-2 vaccination is ongoing to study causal relationships including mRNA SARS-CoV-2 vaccines. In 2023, the group published 2 papers on this subject.

PUBLIC OUTREACH





During 2023, Maria Belland Olsen, Ida Gregersen and Xiang Yi Kong have successfully continued producing the podcast “Labprat”. The podcast was started with a desire to reach out with research and knowledge dissemination to the general public, and that it can be used as an advertising or recruitment method for scientific and medical studies. At the same time, parts of research life and research in general that do not always appear in public is presented. It’s rarely just scandals or just magical discoveries, but also a lot of trial and errors and hidden bureaucracy. More than 50 episodes of the podcast is now available for download from most platforms, and “Labprat” is established among the most popular podcasts in its field here in Norway.

AWARDS

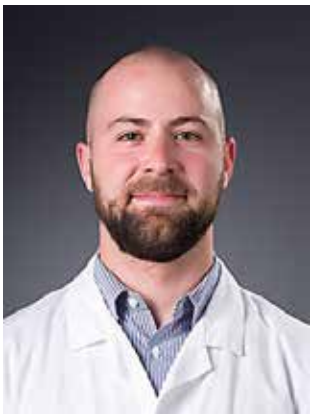
Excellent Researcher Award

Bente Halvorsen, the head of the Research Institute of Internal Medicine (RIIM) was in 2023 awarded the Excellent Researcher award from Oslo University Hospital for her contributions to science.

Committee statement:

«Halvorsen is a professor at the Institute of Clinical Medicine at the University of Oslo and the Head of the Research Institute of Internal Medicine (RIIM) at Oslo University Hospital. She is an authority in the field of atherosclerosis research. She has developed a wide range of methods and models, and combines mouse models with clinical studies in large patient populations. In addition, she masters advanced cell and molecular biology methods. Notably, she has identified a role of the NAD generation pathway in inflammation and metabolism in relation to myocardial infarction, as well as a role for cholesterol crystals in atherogenesis. She has also elucidated important roles of the cytokines CCL19 and CCL21 as inflammatory mediators in clinical and experimental atherosclerosis, and has clarified the mechanisms for the beneficial effects of inhibition of IL-6 in patients with myocardial infarction, with important clinical implications. Recently, Dr Halvorsen has studied the effect of Covid-19 on the epitranscriptome regulation in atherosclerosis and has characterized the immune response to Covid-19 vaccines.

Halvorsen has developed RIIM into a world leading translational research institute with extensive collaborations and unique biobanks and been very effective in promoting the careers for young researchers. She is very successful in obtaining research grants for her studies. The publication record is excellent with more than 300 research papers (29 as first author and 44 as last author). Several of the papers report significant findings and are found in journals of high impact. Professor Bente Halvorsen is an excellent scientist with impressive leadership skills. She has contributed, and continues to contribute, in a profound manner to the research environment at Oslo University Hospital and is a most suitable candidate for the Excellence Researcher Award 2023 at Oslo University Hospital.»



Travel Award

Phd Student Giacomo Roman received $500 USD as an “Early Career Travel Award” for his “highly rated abstract at the 31st Congress of the International Society on Thrombosis and Haemostasis (ISTH) in Montréal, Canada”.

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