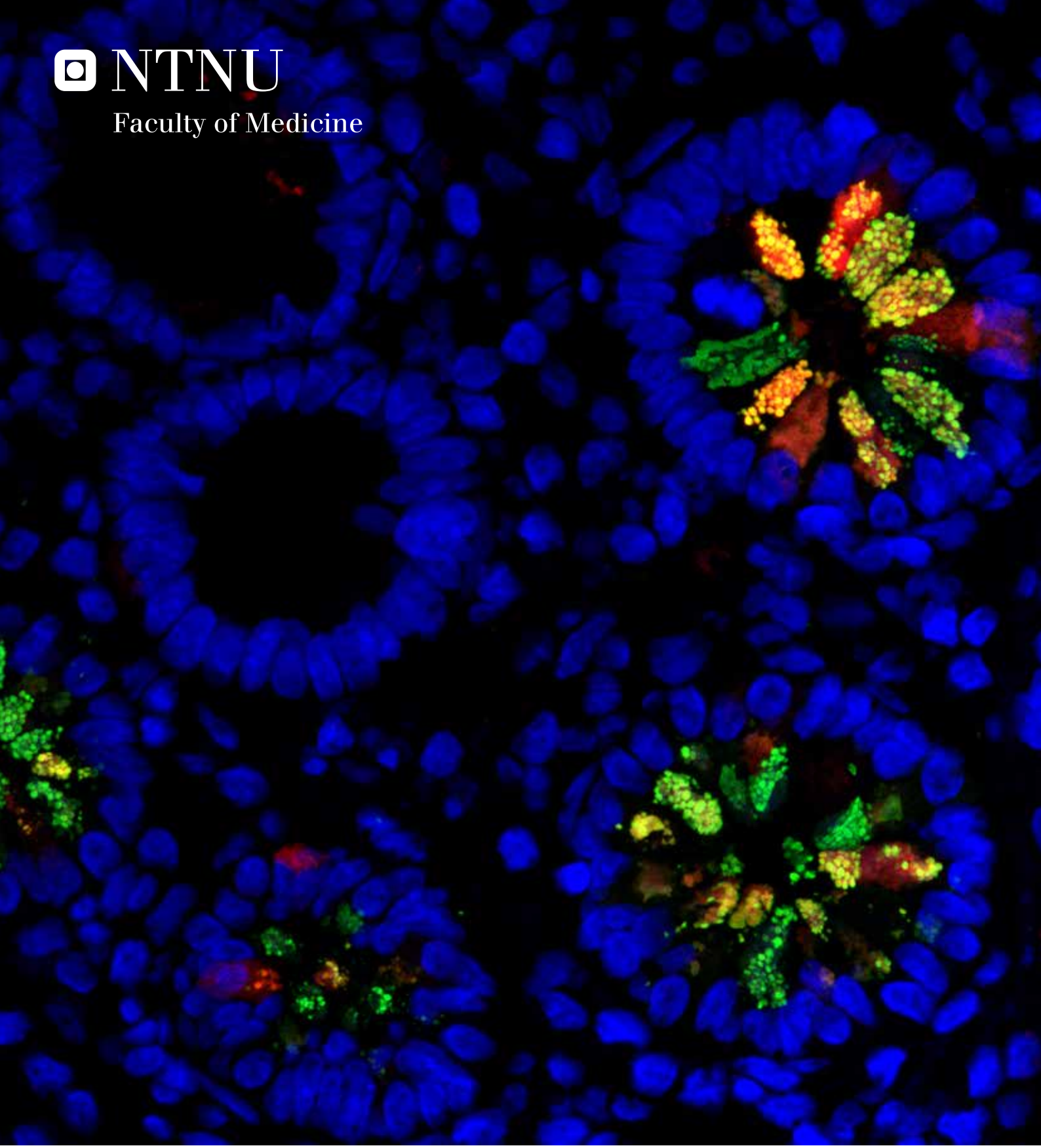
NTNU
Faculty of Medicine



CEMIR
Centre of Molecular Inflammation Research

Annual Report 2015

Table of Contents

Cover photo made by Ingunn Bakke and Bjørnar Sporsheim:
Double immunofluorescence staining of human intestinal mucosa from a patient with inflammatory bowel disease (IBD) showing Neutrophil Gelatinase-Associated Lipocalin (NGAL) (red) partly overlapping (yellow) with the Paneth cell marker Defensin 5 (green). Nucleic DNA is stained with DAPI (blue). The pictures were taken using Olympus IX71 inverted microscope (40× objective) with a digital monochrome XM10 camera and the P^cell software (Olympus). (Thorsvik S, Bakke I (photo), Sandvik AK et al., unpublished results). The image on the back is composed of the individual color channels in red, green and blue separately.

DIRECTOR'S COMMENT

The vision of CEMIR is to find out how sensors in the innate immune system initiate and regulate inflammatory responses. This new knowledge will be used in disease models to identify new therapeutic targets and diagnostic tools for inflammatory diseases.

Throughout 2015 CEMIR has continued to perform research in the important field of inflammation. Inflammation is a host response that is triggered by noxious stimuli arising during infection and tissue injury. A controlled inflammatory response is needed to fight infections and to heal wounds, but can become detrimental if dysregulated. CEMIR performs basic and clinical inflammation research, and our aim is to unite scientists across disciplines for breaking new grounds in inflammation research.

CEMIR was established as a Centre of Excellence January 1, 2013. In its first years we emphasized the importance of establishing a unified research group in which multi-disciplinary research cooperation is encouraged and stimulated. By the end of 2015 65 scientific staff members, 12 technicians, 12 students and an administrative coordinator were associated with the centre. We have over the last year wanted to improve and strengthen the scientific quality and scope of our centre and as a result of this we recruited two new group leaders in 2015. The positions were announced as *Group leaders with startup-package*. We were searching for persons with excellent scientific background to complement and strengthen existing CEMIR research groups and improve the scientific expertise further, especially within the fields of proteomics, bioinformatics and models of inflammatory diseases. We considered several candidates and our primary focus was on potentially successful ERC applicants. Two qualified persons were accepted for the positions. Richard Kandasamy started in December 2015, and Menno Oudhoff joins CEMIR in March 2016. The startup-package contains positions (PhD candidate, Post doctor), laboratory support as well as consumables and access to highly advanced scientific equipment and core facilities.

CEMIR is located in the Knowledge Centre at Øya Campus in Trondheim, owned by St.Olavs Hospital and NTNU. The Knowledge Centre hosts first-class laboratories with state of the art cellular imaging instruments. In October 2015 we opened a new BSL3-laboratory, offering the highest level of security for research on viruses and bacteria in Norway. The new lab contains an advanced Leica SP8 confocal microscope making it possible to study immune cells infected with viable mycobacteria and HIV virus.

The scientific activities at CEMIR have proceeded with very good progress. In 2015 77 papers have been published. CEMIR researchers have published a total of 144 articles since 2013, several in high quality journals like *Journal of Immunology, Nature, Nature Immunology, Autophagy and PNAS*. Eight PhD students completed their theses at the centre in 2015, one man and seven women. These are some of the scientific highlights in 2015:

- Flo and co-workers published a paper in PNAS demonstrating new mechanisms explaining how pathogenic mycobacteria can survive inside macrophages. They found that Kelch-like ECH-associated protein 1 (Keap1) is a negative regulator of inflammatory responses in *M.avium* infected macrophages which can result in increased growth of the bacteria.

- Bjørkøy and co-workers reported in *Autophagy* that the n-3 polyunsaturated fatty acid, DHA, induces endogen anti-oxidant production and mobilizes a selective autophagy response against miss-folded proteins. These mechanisms could be relevant to reduce the risk of developing aggregate--associate diseases

- Iversen and co-workers published in *Arterioscler Thromb Vasc Biol* a study where they identified early pregnancy differences in serum cytokine profiles for gestational hypertension and preeclampsia.

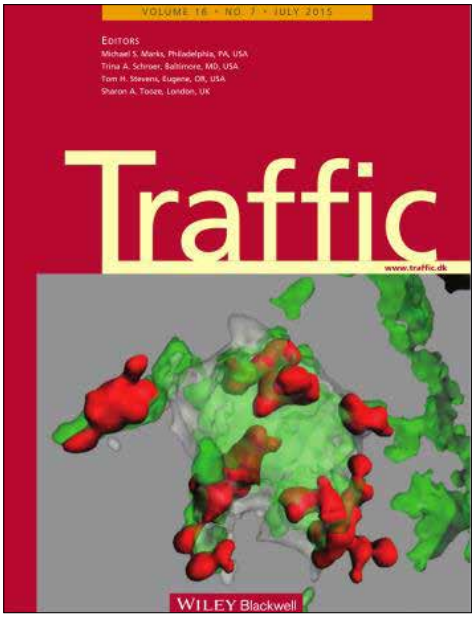
- Stenvik and co-workers published in *J. Immunol* that Toll-like receptor 8 is an essential sensor for detection of the bacterium *S. aureus* in human primary monocytes and macrophages.

- Husebye and co-workers reported new findings in *Traffic* on how the sorting adaptor protein TRAM is transported in cells towards the endocytic recycling compartment. This result adds new information to our understanding of how Gram-negative bacteria induce inflammatory responses in macrophages. The theme of this paper was displayed on the front page of the journal in July 2015.

In September/October 2015 the conference Toll 2015 Targeting Innate Immunity was arranged in Marbella, Spain, with more than 700 participants. A number of CEMIR researchers were involved in the organization of the Toll conference. CEMIR researchers also contributed as plenary speakers and with poster presentations. This was a great opportunity to make CEMIR more visible and to share our research with a large international audience.

May 30th – June 2nd 2016 CEMIR arranges an international conference in Trondheim: *Conference on Molecular Mechanisms of Inflammation*. Outstanding international researchers will give presentations, and this will be a unique opportunity to expand our insight into processes of inflammatory disorders. We expect about 250 participants from all over the world and are looking forward to hosting excellent international scientists from this important field of research.

Every year brings new opportunities and plans for progress. In 2016 we will continue to work hard to achieve our goals and further increase our understanding in the field of inflammation. As a center of excellence we aim a bit higher and try to publish some of our work in high impact journals such as in the Cell- and Nature journals. Such efforts are encouraged and strongly supported from the centre management. It is very inspiring to lead a center with so many highly competent colleagues!



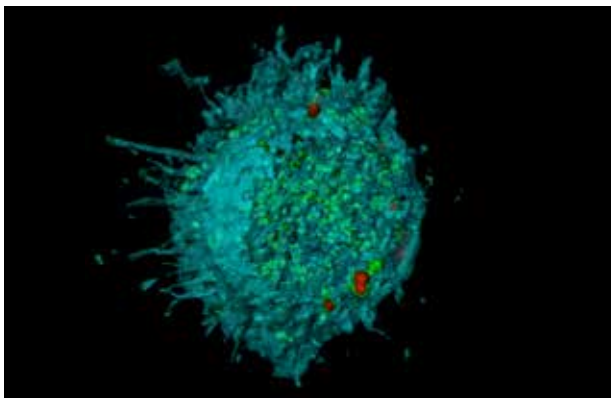
In July 2015 a publication by Husebye and Espevik et al. was displayed on the front page of *Traffic*.

CEMIR RESEARCH ACTIVITY

Theme Manager:
Professor Terje Espevik

Toll-like Receptor Trafficking and Inflammatory Responses induced by Bacteria

In the presence of systemic infection, microbial pathogens induce strong inflammatory- and coagulation activation, leading to sepsis and septic shock. Also, an anti-inflammatory response is induced during sepsis that can contribute to secondary infections. Severe bacterial infections may lead to high amounts of type I IFNs that can result in production of immunosuppressive molecules increasing the risk for secondary infections. The main aim of this theme is to find new principles of Toll-like receptor (TLR) signalling resulting in type I interferons from endosomes and phagosomes. A second aim is to find ways to inhibit inflammatory responses by targeting TLRs and the complement system.



MAIN ACTIVITIES IN 2015

Type I IFNs are classically known as potent antiviral cytokines. More recently the induction of type I IFNs by various types of bacteria in different immune cells has gained increased attention. The impact of type I IFNs on bacterial infections is not clear and spans from immune stimulation to immune suppression which may contribute to the progression of septic shock. Lipopolysaccharide (LPS) from Gram-negative bacteria is recognized by TLR4 and activates two distinct signalling pathways. One of them needs the adapter proteins TRAM and TRIF for inducing IFN-β. In 2015 we have investigated the location and mobility of TRAM towards the *E.coli* phagosome and how the small GTPase Rab11a and its effector molecule FIP2 regulate TRAM trafficking. We have found that FIP2 plays an essential role in the IFN-β response mediated by *E.coli* in human primary macrophages.

TLR2 is activated by lipoproteins and are though to mediate signalling through the MyD88 dependent pathway. We have found a new role for TRAM and TRIF also in TLR2 regulation and signaling. The findings broaden our understanding of how Toll/interleukin-1 receptor adaptor proteins may participate in signaling downstream from TLR2.

Moreover, we have delineated the molecular mechanisms on how TLR8 and TLR2 control *Staphylococcus aureus*- induced IFN-β production in human monocytes. CEMIR scientists have also revealed that combined inhibition of CD14 and complement is a promising treatment for both Gram-positive and Gram-negative sepsis.

MAJOR ACHIEVEMENTS IN 2015

- Published data showing that Rab11a regulates TLR4 mediated IFN-β production through its ability to transport TRAM form Golgi to endocytic recycling compartments and further onto endosomes.
- Demonstrated a physiological role of TLR8 in the sensing of entire *S. aureus* in human primary phagocytes, including the induction of IFN-β and IL-12 production via a TAK1 -: IKKβ -: IRF5 pathway that can be inhibited by TLR2 signaling.
- Published data showing that combined inhibition of complement factor C5 and CD14 significantly improved survival, hemodynamic parameters and inflammation in a blinded, randomized trial of porcine polymicrobial sepsis.
- Published data demonstrating that human endothelial cell activation by *E. coli* and *S. aureus* is mediated by TNF and IL-1β secondarily to activation of C5 and CD14 in whole blood.
- Published results showing a novel function of TRAM and TRIF in TLR2-mediated signal transduction.

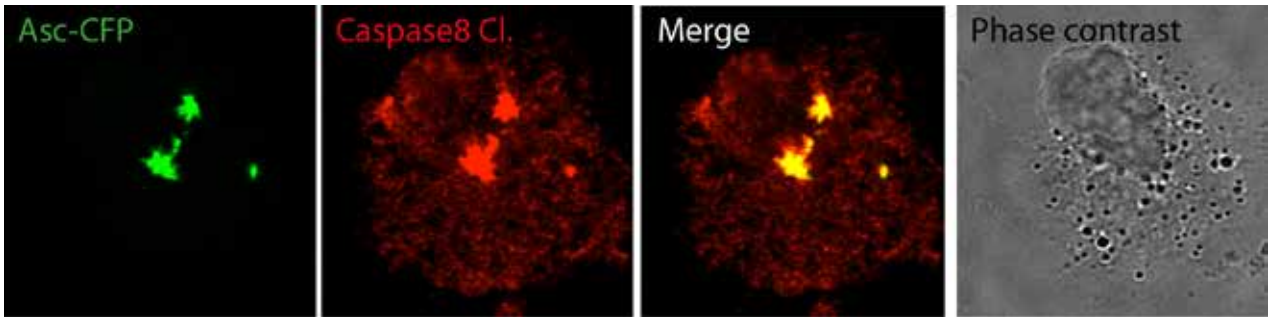
AMBITIONS FOR 2016

- To identify the molecular mechanisms behind cross talks between TLR8 and TLR2 signalling in monocytes and macrophages.
- To understand the detailed role of Rab11FIP2 in regulating phagocytosis and *E.coli*-induced cytokine responses.
- To establish the role of CD150/SLAM in regulating TLR4 and TRAM trafficking and *E.coli*-induced cytokine responses.
- To reveal new components that control trafficking of TLR9 from endoplasmic reticulum to the endolysosomes.
- To identify mechanisms behind the improved combined CD14 and complement inhibition of inflammatory responses induced by Gram-positive and Gram-negative bacteria.

Theme Manager:
Professor Egil Lien

The Molecular Basis for Inflammasome Activation

Inflammasomes are multi-molecular complexes that process pro-caspase-1 into the active enzyme. Caspase-1 mediates maturation of pro-forms of cytokines IL-1β and IL-18 into active forms. These cytokines play key roles in the host defenses towards a number of infections, but can also be harmful in some inflammatory disorders. The work in Theme 2 is focused on describing mechanisms leading to inflammasome activation, and to study implications and regulation of infectious and non-infectious inflammation.



MAIN ACTIVITIES IN 2015

Our work has focused on mechanisms for inflammasome activation, manipulation of inflammasomes and cytokine release by bacterial pathogens, and on linking inflammasome activation and vaccinations with clinically relevant vaccine adjuvants. We showed that a QS-21 saponin adjuvant used in exploratory and licensed vaccines (among others, the new RTS,S malaria vaccine) triggered inflammasome activation and IL-1β/IL-18 release via NLRP3, when co-delivered with another adjuvant, the TLR4-activating compound Monophosphoryl Lipid A. However, the *in vivo* role of this pathway may be inhibitory on vaccination effects using HIV-1 gp120.

During many infections, IL-1β and IL-18 have strong anti-bacterial effects, and hence, it could be desirable to minimize their production. *Yersinia pestis*, the plague bacterium, manipulates the innate immune system. It harbors a powerful type III secretion system (T3SS), a syringe nano-machine that can actively deliver bacterial effector proteins into the host cell via a needle protruding from the bacteria and a pore generated in the host cell membrane. These T3SS effector proteins can in turn affect a variety of signaling pathways. Yersinia effectors YopJ and YopM were believed to have opposite roles in inflammasome activation: YopJ is activating caspase-1 via caspase-8, whereas YopM inhibits caspase-1 activation. However, we found that the sum of YopM and YopJ actions is suppressive on IL-1β release. In the absence of YopM, YopJ does not play a major role in activating caspase-1. Deleting both effectors significantly reduced *Y. pestis* virulence, and attenuation was dependent on IL-1β, IL-18 and caspase-1.

Additional work has focused on Yersinia and Salmonella T3SS and impact on other aspects of inflammation, inflammasomes and cell death.

MAJOR ACHIEVEMENTS IN 2015

- Completed and published a paper on molecular mechanisms on QS-21 saponin adjuvant triggering IL-1β and IL-18 release via the NLRP3 inflammasome
- Studied the role of the NLRP3 pathway in vaccinations with QS-21 and HIV-1 gp120
- Identified surprising roles for bacterial T3SS effectors in manipulating inflammasomes
- Deleting both Yersinia T3SS effectors YopJ and YopM gives significant attenuation, dependent upon IL-1β/IL-18/caspase-1

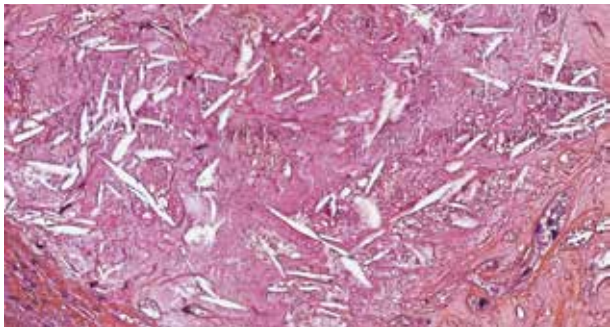
AMBITIONS FOR 2016

- Gain a deeper understanding of RIP1kinase and caspase-8 in host anti-bacterial effects
- Further understand bacterial strategies for manipulation of inflammasomes
- Identify new host molecules involved in bacterially induced inflammasome activation and cell death
- Gather new knowledge on the role of lncRNA in inflammation and anti-bacterial responses

Theme Manager:
Professor Jan Kristian Damaas

Inflammatory Responses induced by Cholesterol

Chronic inflammation of the arterial wall is a key element in the development of atherosclerosis, and cholesterol crystals (CC) that accumulate in plaques are associated with initiation and progression of the disease. Inflammation has also become a central focus in atheroma development, and cholesterol itself can cause inflammation in its crystalline form by activating the NLRP3 inflammasome. Our main aim of this theme is to uncover the mechanisms by which CC induce inflammatory responses and to explore novel treatment strategies in atherosclerosis.



Cholesterol crystal clefts in a human atherosclerotic plaque.

MAIN ACTIVITIES IN 2015

A continued research has been on the role of complement activation for CC induced inflammatory responses and how to inhibit these responses. HDL exhibits cardioprotective and anti-inflammatory properties thought to explain its inverse correlation to cardiovascular risk. We have determined the effect of reconstituted HDL (rHDL) on CC-induced inflammation in a human whole blood model. We have investigated how β-cyclodextrin may attenuate CC-induced inflammation. β-cyclodextrin has been shown to remove cholesterol from cultured cells, and we have performed several in vivo and in vitro experiments showing that this substance also may alleviate atherosclerosis in CC-induced inflammation and complement activation.

In parallel to mechanistic studies, we have also investigated the clinical aspects of inflammation in atherosclerosis. We evaluated the association of Single Nucleotide Polymorphisms (SNPs) in genes with the incidence of myocardial infarction in a nested case-control study among participants of the second survey of the HUNT Study. The study population included 1624 cases and 4087 age- and sex-matched controls. We have also examined serum/plasma markers as independent predictors for cardiovascular disease. Finally, we have finished a study on the effect of a single dose of the interleukin-6 receptor antagonist tocilizumab on inflammation and troponin T release in patients with non-ST elevation myocardial infarction. In 2015, two PhD candidates of this theme graduated.

MAJOR ACHIEVEMENTS IN 2015

- We demonstrated and published in *J Immunol* that rHDL bound to CC and inhibited the CC-induced complement activation as measured by soluble terminal C5b-9 formation and C3c deposition on the CC surface. Our results support and extend the notion that CC are potent triggers of inflammation, and that rHDL may have a beneficial role in controlling the CC-induced inflammatory responses by inhibiting complement deposition on the crystals.
- The Latz group together with researchers from CEMIR showed in a paper to be published in Science Translational Medicine, 2016, that cyclodextrin treatment of murine atherosclerosis reduced atherosclerotic plaque size and CC load and promoted plaque regression even under continuing cholesterol-rich diet. Since cyclodextrin treatment in humans is safe and cyclodextrin beneficially affects key pathogenetic factors in atherogenesis it may thus be used clinically to prevent or treat human atherosclerosis.
- We published in DNA Repair that the NEIL3 SNP rs12645561, the TT genotype was associated with increased risk of myocardial infarction both in the genotypic test and in the recessive genetic model. This association may suggest a possible role of attenuated DNA repair, and NEIL3 in particular, in atherogenesis.
- We have shown in a placebo-controlled trial including 117 patients with non-ST elevation myocardial infarction that one single infusion with tocilizumab (a humanised anti-IL-6R antibody) reduces levels of high-sensitivity C-reactive protein and troponin t.

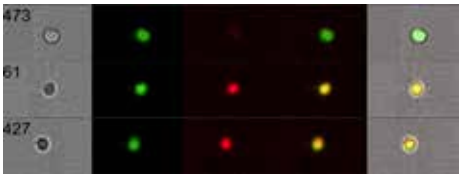
AMBITIONS FOR 2016

- To establish the role of intracellular complement activation for CC-induced responses in monocytes and macrophages
- To examine the effect of cyclodextrin on CC-induced complement activation
- To analyze the involvement of the lectin pathway in CC-induced complement activation and coagulation
- To perform studies of the efficacy of inhibiting complement and CD14 in myocardial infarction models
- To understand role of macrophage survival factor AIM in human atherogenesis
- To start a new clinical study on the effect of the interleukin-6 receptor antagonist tocilizumab as an adjunct to primary percutaneous coronary intervention in ST elevation myocardial infarction study.
- To perform sub-studies on serum/plasma samples from the clinical studies and to explore these findings in experimental models.
- To analyze novel inflammatory markers for cardiovascular disease in the HUNT-database.

Theme Manager:
Professor
Trude Helen Flo

Inflammation & Autophagy

Cells frequently experience stress with increased levels of reactive oxygen species (ROS). ROS may contribute in activation of pattern recognition receptor responses and induction of autophagy, a process that is essential for cellular homeostasis and, if defective, leads to disorders like degenerative diseases, cancers, infections, inflammation and cardiovascular disease. In theme 4 we aim to define novel relations between oxidative stress, signalling through PRRs and autophagy in inflammatory diseases, including mycobacterial infections where the focus is molecular host defence mechanisms involved in immunity to mycobacterial pathogens and virulence strategies employed by mycobacteria to parasitize host cells.



MAIN ACTIVITIES IN 2015

This year we published in PNAS how Keap1 is a negative regulator of inflammatory responses in human primary macrophages, facilitating intracellular growth of *M. avium*. Our data suggest that Keap1 is a general regulator of inflammation and we will continue detailing on the mechanism of regulation, and extend studies to include septic shock. A reliable method was established for correlative imaging of macrophages infected with mycobacteria at an ultra-high resolution and in 3D using FIB/SEM tomography together with confocal fluorescence microscopy. An important activity of 2015 has been to finalize our BSL3 facility and the training of personnel to run the facility. We can now perform experiments on pathogenic organisms like *M. tuberculosis* (Mtb) and HIV, including live confocal imaging (Leica SP8) and drug screening. We have created a useful tool for molecular genetics of mycobacteria by tailoring a gene expression system for protein expression in mycobacteria. In our quest for understanding iron metabolism we also published work describing how a chemical compound inhibits growth of mycobacteria by working as an intracellular iron chelator. During 2015 we also established that omega-3 fatty acids may reduce the risk of neurodegenerative diseases by mobilizing the cellular oxidative stress defence, and published the findings in Autophagy. In cancer cells with downregulated autophagy, we found that the mild and transient oxidative stress induced by omega-3 fatty acids is detrimental. Moreover, we have performed a screen of serum samples from cancer patients and healthy donors for autophagy regulating bioactivities using a novel cell based bioassay. The results suggest that there is a correlation between weight loss (cachexia) and autophagy inducing activity in serum. To better understand how oxidative stress defence and autophagy are deregulated in disease we have established full genome and transcriptome sequencing of a breast cancer metastasis model. Finally, we have studied autophagy and the oxidative stress responses as resistance mechanisms towards proteasomal inhibitors used to treat multiple myeloma.

In 2015 one PhD student of this theme, Ida Johansson, graduated.

MAJOR ACHIEVEMENTS IN 2015

- Established the role of Keap1 as a negative regulator of inflammatory signalling in *M. avium* infected primary human macrophages
- Established a reliable method for correlative imaging of macrophages infected with mycobacteria at an ultra-high resolution and in 3D using Focused Ion Beam/Scanning Electron Microscopy tomography together with confocal fluorescence microscopy
- Established a method for benzoic acid-inducible gene expression in mycobacteria
- Established infection models and routines for working with HIV and Mtb in a BSL3 lab
- Established that n-3 polyunsaturated fatty acids protect retinal epithelial cells from harmful stress by inducing autophagy and oxidative stress defences
- Established that the moderate oxidative stress induced by physiologic concentrations of omega-3 fatty acids is toxic to cancer cells with downregulated autophagy

AMBITIONS FOR 2016

- Establish from which compartments *M. avium* and Mtb induces inflammatory signalling and if endosomal TLRs are involved
- Obtain understanding for HIV infection, disease susceptibility and progression by studying innate T-cell responses and lipid metabolism
- Elucidate on mycobacterial iron metabolism and intramacrophage virulence using *M. smegmatis, M. avium* and Mtb mutants
- Elucidate intra-patient mutations in *M. avium* genomes and how they affect virulence
- Establish screen for novel antimycobacterial compounds targeting Mtb secretion systems
- Identify the signalling pathway and major pro-inflammatory cytokines that seems particularly dampened in response to n-3 fatty acids in cell cultures and in patients
- Based on exom- and transcriptome sequencing of a breast cancer model, identify oxidative stress response genes that drive an aggressive cancer development
- Elucidate how cancer cells secrete factors that stimulate autophagy and determine if serum samples from cachectic patients contain autophagy inducing bioactivities
- Establish the impact of oxidative stress defence responses on therapeutic effects of proteasome inhibitors in myeloma cells

Theme Manager:
Associate Professor
Ann-Charlotte Iversen

Inflammation underlying Preeclampsia and Atherosclerosis

Inflammation plays a key role in cardiovascular disease, a major cause of illness and death worldwide, with gender-specific manifestations. Pregnancy is a natural state of low-grade inflammation and a stress test to the cardiovascular system. Women with preeclampsia have doubled risk for later cardiovascular disease and develop atherosclerosis-like lesions in uterine wall arteries during pregnancy, suggesting shared underlying mechanisms for these vascular diseases. In this theme we aim to define pattern recognition receptor-initiated inflammation underlying preeclampsia and determine the relation to later cardiovascular disease.

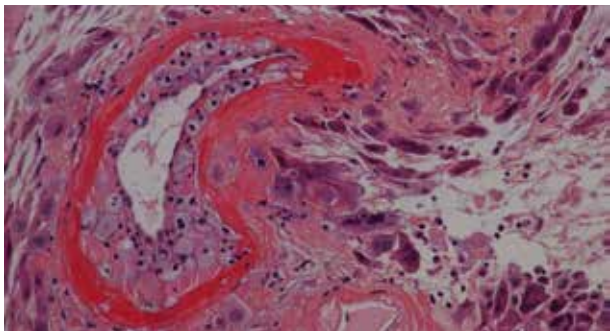


Image of an atherosis in a spiral artery of the uterine wall of a preeclamptic woman. In the atherosis a fibrinoid layer and accumulated foam cells surround the vessel, closely resembling the feature of early atherosclerosis.

MAIN ACTIVITIES IN 2015

Diagnostic validation of the Preeclampsia Biobank has given the basis for an extensive quantitative immunohistochemical analysis comparing placental inflammatory mechanisms in normal and preeclamptic pregnancies. A central role for PRR-mediated inflammation in the preeclamptic placenta is currently being revealed. In uterine wall arteries, the cellular involvement is being addressed and atherosis morphologically defined. Inflammasome NLRP3 and cholesterol accumulation is assessed in both the maternal and fetal portion of the placenta. PRR mechanisms identified in patient samples are being functionally assessed by PRR-activation studies in isolated placental cells and cultured placental explants. Establishment of metabolomic profiling of maternal serum, urine and placental biopsies has revealed a powerful tool for prediction and classification of preeclampsia that is being further developed. Novel maternal and fetal preeclampsia risk genes is being revealed in the largest meta-analysis of GWAS data in preeclampsia, performed in the EU FP7 project InterPregGen where we participate with a cohort of normal and preeclamptic women from the HUNT Study. Overall, this work has added further evidence to the importance of PRR-mediated inflammation in the fetal trophoblasts of the placenta in preeclampsia development, and led to discovery of underlying inflammatory mechanisms, genetic risk factors and novel predictive tools for hypertensive pregnancy disorders.

MAJOR ACHIEVEMENTS IN 2015

- Identified serum cytokine profiling in early pregnancy as a novel tool for identifying differences in inflammatory status before onset of clinical signs in women later developing hypertensive pregnancy disorders. Women later developing gestational hypertension showed a distinct inflammatory cytokine pattern compared to women later developing preeclampsia, pointing to separate etiology for these disorders.
- Showed that NMR profiling of maternal serum in early pregnancy can predict later development of hypertensive pregnancy disorders and that NMR profiling of placental tissue is a sensitive tool for identifying the placental component of preeclampsia.
- Revealed that several widely used trophoblast cell lines do not possess the strong inflammatory capacity of primary first trimester trophoblast, shedding new light on the importance of trophoblast PRR-mediated inflammation and warranting caution for use of trophoblast cell lines.
- Concluded by a meta-analysis of eleven studies that the debated HLA-G 14bp gene polymorphism is not associated to development of preeclampsia.
- Identified that in families with increased occurrence of preeclampsia, other diseases were also heritable, including chronic hypertension, severity of cardiovascular disease, pulmonary disease and fetal growth restriction.

AMBITIONS FOR 2016

- Identify specific PRR mechanisms and cholesterol accumulation in placental villi and in the uterine wall at sites of macrophage and trophoblast interaction and atherotic lesions, relevant for development of preeclampsia.
- Identify shared risk genes and risk traits for subgroups of preeclampsia and cardiovascular disease and mortality.
- Establish novel causal classification of the placental disease in preeclampsia by metabolomic profiling.
- Expanded collection of pregnancy- and obesity-related biobanks for translational inflammation studies.
- Establish animal models for spiral artery atherosis and placental inflammation for functional testing of findings from translational analysis of patient samples.

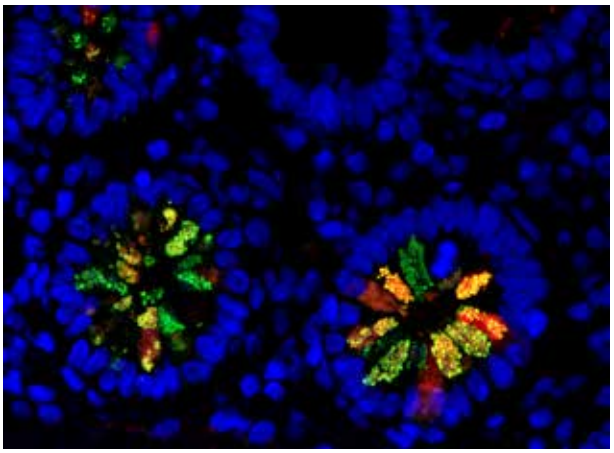
Theme Manager:
Professor Arne Kristian Sandvik

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a major clinical problem, with approximately 2 mill Europeans chronically affected by either ulcerative colitis or Crohn's disease. Current hypotheses on etiology and pathogenesis include dysfunctional inflammatory pathways including PRRs and autophagy, with approximately 200 susceptibility gene loci identified. Hence, we hypothesize that IBD results from an inappropriate inflammatory response to intestinal microbes and endogenous molecules in genetically susceptible hosts. The main aim of this theme is to understand central mechanisms for mucosal homeostasis, how this is disrupted in active disease and subsequently restored in remission.

MAIN ACTIVITIES IN 2015

The research group has further strengthened its focus of studying disease mechanisms in patient material, and the existing IBD biobank has been extended to comprise a total of >600 individuals by late 2015. The projects have concentrated on inflammatory processes in the epithelial monolayer of the gut, establishing and refining methods for these studies, and on applying this knowledge in clinical medicine. Central activities have been to further analyze gene expression features in the epithelial monolayer in diseased and control individuals. Findings from these studies have been used to examine the role of lipocalin 2 (protein name Neutrophil Gelatinase-Associated Lipocalin – NGAL) in IBD, and how NGAL can be used as a fecal inflammation biomarker for primary diagnostics and clinical follow-up. Another specific project has been to examine the role of serotonin in gut inflammation and fibrosis. The group has welcomed two new coworkers; both clinicians in 50% research positions (researcher and postdoc) who pursue in-depth studies on their main fields of interest which are TLR3 mediated mechanisms in IBD and the role of γ-δ lymphocytes in these diseases.



MAJOR ACHIEVEMENTS IN 2015

- Completed a large study on several patient groups showing that fecal NGAL is a sensitive and specific biomarker for IBD
- Performed an in-depth analysis of transcriptome-wide RNASeq data from micro-dissected colonic epithelium in IBD patients and controls, and generated novel hypotheses on the role of the epithelium in IBD
- Analyzed transcriptome data from small intestine and colon to evaluate serotonin dynamics in IBD, and started mechanistic studies in cell lines and animals
- Established methods for isolation of intestinal epithelial crypts, and started work to establish these as permanent organoid cultures for IBD studies

AMBITIONS FOR 2016

- Examine the specificity of fecal NGAL as compared to other biomarkers in patients with non-IBD inflammation and in children with IBD. Finalize studies on NGAL localization, regulation and its molecular forms in IBD
- Add a protein network analysis to the existing epithelial cell transcriptome dataset
- Finalize the cell studies on serotonin release, uptake and degradation as related to innate immune mechanisms, and assess its effects on fibrosis in an animal model
- Penetrate REG4 regulation and function further by WGGE analysis of WT/REG4 KO and supplement with studies on isolated human colonic crypts
- Establish permanent cultures of colonic and small intestinal epithelial organoids and start mechanistic studies related to hypotheses generated from the transcriptome/protein network analyses
- SNP genotype our IBD cohort and merge this with the HUNT population biobank genotyping results, including the IBD subpopulation in HUNT. Utilize the results in relation to transcriptome analysis, and possibly do disease relevant mechanistic studies

Theme Manager:
Professor Therese Standal

Bone Destruction caused by Cancer and Inflammation

Bone remodeling is the reconstruction of the skeleton by osteoclastic bone resorption followed by osteoblastic bone formation. Remodeling is a tightly regulated process, which, however, in some pathological conditions gets out of control. Destruction of bone is common in cancers like multiple myeloma and breast- and prostate cancer metastasizing to bone, in inflammatory diseases such as inflammatory bowel disorder and autoimmune diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus. The main aim of this theme is to reveal underlying mechanisms for bone loss associated with cancer and inflammation.

MAIN ACTIVITIES IN 2015

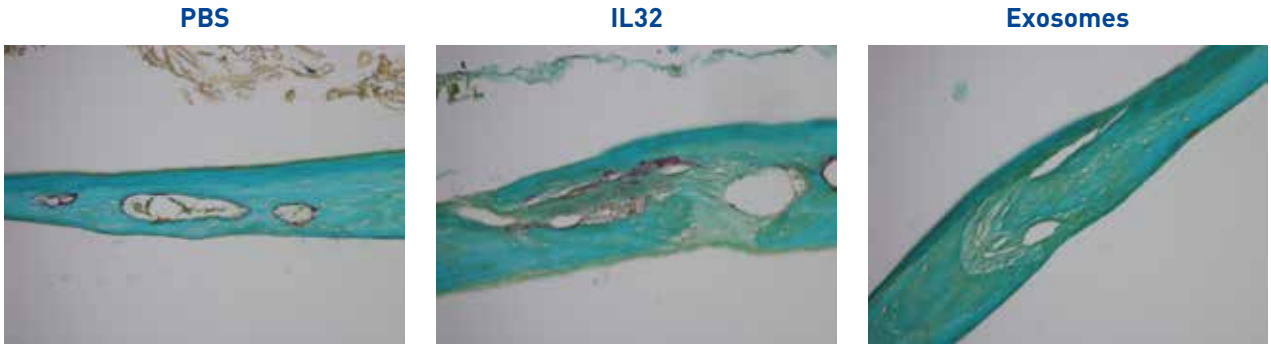
In 2015 we studied how caspase-8 downstream of TLR-TRIF- signaling modulates the expression of pro- and anti-inflammatory cytokines from human bone marrow-derived mesenchymal stromal cells. Further, we identified IL-32 as a novel cytokine produced by malignant plasma cells during hypoxia, and demonstrated that recombinant IL-32 can promote osteoclast differentiation both *in vitro* and *in vivo*. We also found that IL-32 is secreted on extracellular vesicles (EV), and that EVs obtained from myeloma cells expressing IL-32 promote osteoclast differentiation *in vitro* and *in vivo*. We are currently investigating how IL-32 is recruited to the vesicles, and which intracellular signals are regulating the expression and release of IL-32 from myeloma cells. We also addressed the importance of GDF15, a member of the TGFβ superfamily of cytokines, for the bone disease of multiple myeloma. GDF15 was elevated in patients with osteolytic bone disease compared with patients without bone disease, and we showed that GDF15 promotes osteoclast differentiation and at the same time inhibited osteoblast differentiation. Moreover, we obtained exciting preliminary data on the effect of immunoglobulins isolated from bone marrow plasma from myeloma patients on osteoclast differentiation *in vitro*.

MAJOR ACHIEVEMENTS IN 2015

- Demonstrated that caspase-8 downstream of TLR-TRIF may modulate bone marrow stromal cells into gaining a pro-inflammatory phenotype.
- Demonstrated that GDF15 might play a role in myeloma bone disease.
- Identified IL-32 on extracellular vesicles obtained from myeloma cells and that the vesicles potently stimulate osteoclast differentiation.

AMBITIONS FOR 2016

- To continue our studies on the effect of inflammatory signals and hypoxic/ER-stress on mesenchymal stromal cell function, osteoblast and osteoclast differentiation.
- To continue our studies on the role of immunoglobulins for bone health in multiple myeloma.
- To identify and characterize endogenous PRR ligands in bone marrow samples obtained from myeloma patients.
- To continue our studies on the role of IL-32 in multiple myeloma and mechanisms for IL-32 induction and secretion.
- To establish the role of exosomal RANKL for bone remodeling *in vitro* and *in vivo*.



TRAP-staining of mouse calvarial bones treated with PBS control, recombinant IL-32 or exosomes as indicated

CEMIR RESEARCH GROUPS

The Inflammation Research Group

The strategy of the Inflammation Research Group is to study the cellular and molecular mechanisms that inflammasomes, Toll-like receptors (TLRs) and the complement system are using to mount sterile and non-sterile inflammatory responses. The group has a long track record and has made several significant contributions within innate immunity and host defence over the last 25 years. Currently, we have a focus on mechanisms involved in trafficking of TLRs and their adaptor molecules between intracellular compartments where TLR signalling is taking place. This project aims to increase our understanding of how Gram-negative - and Gram-positive bacteria are able to induce inflammatory signalling from different cellular compartments. Moreover, we work on inflammatory responses that occur during the development of atherosclerosis. The aim of this project is to identify the detailed molecular mechanisms of how cholesterol crystals activate the complement system and immune cells. The goal is to design effective therapeutic agents to diagnose and treat atherosclerosis.

The Inflammation Research group has a strong interest in applying and developing molecular and cellular imaging techniques for use in the CEMIR projects. The group leader is also scientific leader for the Imaging Core Facility at NTNU (http://www.ntnu.edu/dmf/cmic). This core facility has recently acquired the most recent state of the art STED super-resolution laser confocal microscope and a TIRF microscope that have been installed in the new CEMIR laboratories. The inflammation Research Group is contributing to several of the basic research oriented CEMIR themes (themes 1-4) as well as having cooperations with the more clinical orientated research themes on inflammatory bowel disease and atherosclerosis (Sandvik and Damås).

The research group is led by Professor Terje Espevik and currently consists of 23 persons including 6 PhD students, 7 post docs, 6 research scientists and 4 staff engineers. The group has close collaborations with the CEMIR affiliated professors, Mollnes, Lien, Fitzgerald, Stenmark and Latz. Moreover, the group is also actively involved in collaborative projects at national (B. Halvorsen, P. Aukrust and A. Yndestad, University of Oslo) and international levels (C. Kemper, Kings College, P. Garred, University of Copenhagen, G. Teti, University of Messina, Italy, and M. McCaffrey, University of Cork, UK).

The Autophagy and Oxidative Stress Defense Group

The autophagy group focuses on the role of this intracellular degradation route in the prevention of age-related diseases and how this mechanism protects against oxidative stress. In the preventive setting we are studying cellular responses towards n-3 polyunsaturated fatty acids (PUFAs) in normal, non-transformed cell models and in primary cells isolated from healthy donors. The responses studied include changes in autophagy and the oxidative stress defense system controlled by the oxidative stress sensor and transcriptional regulator, NFE2L2. On the other side, the function of NFE2L2 can be flipped from being disease preventive into disease promoting when the same mechanisms are utilized by cancer cells to protect themselves from dying. We hypothesize that cancer cachexia, characterized by a severe, and often fatal, loss in body mass is an extreme situation where cancer cells take control over the normal regulation of autophagy. Here we investigate if particular cancer cells may secrete signaling compounds that induce autophagy in normal cells. New understanding of the dualistic roles of both autophagy and oxidative stress defense may open for novel strategies for both disease prevention and diagnostics and therapy of age-related diseases.

The group is led by Professor Geir Bjørkøy and consists of one and half senior technicians, two post-doctor fellows, two PhD- and two master students. The group has established several cellular models of both normal and cancerous cells to study regulation of autophagy and oxidative stress defense by mRNA and protein analyses, imaging approaches and flow cytometry. In addition, we perform next generation sequencing and gene editing to try to decode how autophagy and oxidative stress defense may be controlled normally and deregulated in aggressive cancers. In a close collaboration with the K.G. Jebsen center of Myeloma Research headed by Professor Anders Sundan at NTNU we are studying how oxidative stress responses and autophagy may limit the clinical responses towards proteasomal inhibitors. The aim of these studies is to identify new drug combinations that boost initial responses and limit the development of drug resistance. External collaborators include the groups of Professors T. Johansen (UiT), H. Stenmark (UiO/CEMIR), K. Fearon (Univ of Edinburgh) and K Kaarniranta (Univ of Kuopio).

The Research Group on Molecular Mechanisms of Mycobacterial Infections

Mycobacteria can cause severe disease or life-long infections and pose a global health challenge. Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), kills more than 1.5 million people each year and the prevalence of non-tuberculous mycobacterial infections caused by *M. avium* is increasing in individuals who are immunocompromised due to underlying disease or use of immunosuppressant drugs. Mycobacterial infections require long treatment with antibiotics, and drug resistant strains are emerging. Our primary research focus is the molecular host defense mechanisms involved in immunity to mycobacterial pathogens and virulence strategies employed by mycobacteria to parasitize host cells. The inter-connected roles of trafficking and compartmentalized pattern recognition receptor signaling, iron metabolism and autophagy in mycobacterial survival make these processes attractive targets for drug development and are currently investigated in our lab, both in the host and in the pathogen. There has been an increase in TB following the HIV epidemic. Recently, we are also studying innate properties of the T-cell responses to HIV and mycobacteria. T-cells express PRRs and respond to microbial ligands with cytokine production and induction of autophagy. The significance of this in disease and also in vaccine design is currently not understood and something we are interested in. We believe our basic research strategy may contribute to revealing new therapeutic targets and vaccine development.

The Research Group is led by Trude H. Flo and includes two more research scientists, four post docs, four PhD students, two medical research students and master students. We have developed expertise, methods and tools to study HIV, mycobacteria and the host innate and adaptive immune defenses both in vitro in human primary cells and in vivo in mice. We have strains of Mtb, *M. avium* and *M. smegmatis* available with fluorescence and firefly luciferase, and we have a confocal microscope in our new BSL-3 facility for live imaging of Mtb and HIV infections. Transposon mutant libraries with more than 150 000 mutants in *M. smegmatis, M. avium* and Mtb are available. We are mainly focused on CEMIR theme 4 and collaborate closely with the autophagy group (G Bjørkøy), the inflammation group (T Espevik, JK Damås) and with CEMIR affiliated professor D Underhill. Together with Ø Halaas (NTNU, nanomedicine) we also pioneer the use of Focused Ion-Beam Scanning Electron Microscopy (FIB-SEM) at NTNU Nanolab to perform nanoscale high resolution imaging of intracellular mycobacterial and HIV infections using. Central external collaborators are T Johansen (UiT, autophagy), A Brech (UiO, EM), E Rubin (Harvard School of Public Health, mycobacteria), TR Hawn (U Washington, infections), and A Aderem (Seattle Biomed).

The Research Group of Inflammation in Pregnancy

The Research Group of Inflammation in Pregnancy works closely with other researchers at CEMIR and the core facility CMIC, and is particularly linked to themes focusing on the molecular studies of lipids and cholesterol crystals and activation of inflammasomes, TLR2 and TLR4 (Professors Espevik and Damås). Several pregnancy-based biobanks and an obesity biobank are collected and administered by the research group and provide unique materials for the molecular inflammation analyses.

The broad research approach involving molecular studies, biobanking, metabolomics, epidemiology and genetics is made possible by a strong collaboration between clinical departments and basic researchers in different disciplines both nationally and internationally. Central collaborators include Professor Line Bjørge at Haukeland University Hospital, The Womens's Clinic and Professors Bård Kulseng and Eszter Vanky at St.Olavs Hospital, Professor Kjell Salvesen at the Central Norway Regional Health Authority and Professors Tone Bathen and Torstein Vik at NTNU. Professor Catherine Hedrick at La Jolla Institute for Allergy and Immunology in San Diego hosted Ann-Charlotte Iversen as Visiting Scientist in 2014-2015 for study of mice models of atherosclerosis and pregnancy complications. The Research Group is partner in a large 12-partner EU 7FP project InterPregGen coordinated by Professor Linda Morgan at University of Nottingham, aiming to unravel genetic risk factors for preeclampsia in relation to cardiovascular risk traits, based on the world's largest pregnancy based cohort collaboration for genetic studies, and the research group at CEMIR is involved with a pregnancy cohort from the HUNT Study and are responsible for functional placental risk gene analysis.

In preeclampsia extensive atherotic lesions develop in the uterine wall arteries and these closely resemble atherosclerotic lesions, but a causal role in preeclampsia has not been investigated. The Research Group holds a unique collection of decidual tissues containing atherotic lesions and focus on revealing the inflammatory processes in atherosis and how this influence placental development and eventually preeclampsia. Lessons are learned from the central role of cholesterol crystals and PRR activation in atherosclerosis development and CVD. In addition the central role of the fetal throphoblasts in harmful placental inflammation in preeclampsia is focus for molecular inflammation studies.

The Research Group is led by Associate Professor Ann-Charlotte Iversen. In 2015 the group counted 13 persons; Professor Rigmor Austgulen, 1 post doc, 6 PhD students and 1 staff engineer. Four PhD students defended their thesis and one new PhD student, MD student and Master student joined the group in 2015.

The Inflammatory Bowel Diseases (IBD)

The inflammatory bowel diseases (IBD) research group was established to study disease mechanisms in IBD, and use this knowledge to improve diagnostics and prognostics. Another central aim is to discover novel therapeutic targets. More specifically, the IBD projects concentrate on understanding central mechanisms for mucosal homeostasis and how these are disrupted in active disease and subsequently restored in remission. Example projects are the effect of hypoxia on the epithelium, the role of guanylin/uroguanylin in inflammation, the action and regulation of mucosal antimicrobial peptides and how the diffuse neuroendocrine system interacts with immune signaling in IBD. The CEMIR related projects are done in close collaboration with the CEMIR groups working with innate immune mechanisms.

The IBD group is closely connected with clinical medicine, also through combined university/hospital positions. The group moreover collaborates with clinicians in 7 different hospitals in the Central Norway Health Region, and regional hospital staff is involved in translational research projects. The group staff is cross-diciplinary, in addition to clinicians members also include cell biologists and molecular biologists. One of the two IBD group leaders also administers the faculty Genomics Core Facility (microarray and sequencing), and is experienced within transcriptome analysis and bioinformatics. The group has access to excellent animal experimental facilities, and is among few in the world doing routine colonoscopy on rat and mouse IBD models.

An international collaborative network is under development, and presently includes Immunobiology at Yale University (New Haven), Biomedical Sciences at Cedars-Sinai Hospital (Los Angeles), and Institute of Health Research (FISABIO) (Valencia).

The IBD research group is led by Professor Arne Sandvik.

The Bone Disease Group

Loss of bone is a common feature of different inflammatory diseases as well as for cancers metastasizing to or located within bone. Multiple myeloma is a cancer of plasma cells, located within the bone marrow. The bone disease of multiple myeloma is highly aggressive, and is the cause of pain and reduced quality of life for the myeloma patients. Hypoxic and ER stress and a low grade, chronic inflammation characterizes the myeloma bone marrow. Our research is centered on identifying inflammatory factors present in the bone marrow microenvironment that influence differentiation or activation of bone cells. The underlying hypothesis is that the causes of bone loss associated with inflammatory diseases and cancer might be common.

Our group profits from a close collaboration with clinicians and researchers at the K.G. Jebsen Center for Myeloma Research. Further, in close collaboration with the Department of Rheumatology at St.Olavs Hospital a Biobank for arthritis was established in 2009. Hence, we have access to well characterized samples from both myeloma patients and patients with different subtypes of arthritis. In collaboration with Anton Martens at the VU University Medical Center, Amsterdam, we have established a mouse model for multiple myeloma here in Trondheim. This model allows for a reconstruction of a human hematopoietic environment in scaffolds that are subsequently implanted in mice. This model has given us new opportunities in terms of *in vivo* experiments.

The group is led by Professor Therese Standal and consists of three post doctors, one technician and master students. One PhD student will be recruited during spring 2016.

The Research Group on Cellular and Molecular Mechanisms in Regeneration

Inflammation causes various degrees of damage to tissue that impairs functionality of affected organs. Upon damage, appropriate wound healing and regenerative responses are of the utmost importance to regain organ function and prevent chronic inflammation. Our research group is interested in both the cellular and molecular mechanisms that trigger and execute regenerative processes. Commonly, there is interplay between various cell types, each giving and receiving cues that together orchestrate an optimal response. In addition, there are biomechanical cues such as tissue stiffness that can modulate these responses. Our group combines (bio)-chemical and cell biological tools with *in vivo* mouse and *ex vivo* organoid model systems to study these processes.

Our group will initially have two related research programs. The first research program studies the control of intestinal epithelial cell proliferation and differentiation during regeneration. This program focuses on the molecular control of stem cells in the intestine, which are the cells that fuel the cellular component of repair. This involves the study of several signalling pathways such as Hippo and Wnt, and the control of these pathways by epigenetic modifiers. The second program studies the role of the cytoskeleton and its role in cellular responses. It has been widely recognized that mechanical cues regulate cell behaviour, but how these processes are functioning on a molecular level has not been studied extensively.

The group joined CEMIR in Mach 2016 and is led by group leader Menno Oudhoff, and he will be joined by a post-doctor. In its first year this group will aim to expand with PhD candidates, as well as initiate collaborations both within CEMIR and internationally.

The Systems Inflammation Research Group

Infectious diseases and inflammatory disorders are major contributors to the global burden of disease, thereby having a huge socio-economic impact. Decades of research have unraveled the arsenal of mechanisms by which the host immune system detects an invading microbe and elicit an innate immune response ensuring clearance of the pathogen while exerting a minimal damage to the host. Any failure in this chain could lead to chronic diseases such as Atherosclerosis; as well as devastating conditions like sepsis and sepsis-induced death. It is critical for the host to restore homeostasis and resolve the inflammation upon microbial infections through a collective and meticulous coordination of a number of controlled molecular events such as chromatin remodeling, transcription, translation and post-translational modifications (PTMs). The systems inflammation research group aims to specifically study the role of two major PTMs – phosphorylation and ubiquitinome in antiviral signaling and inflammation using state-of-the-art systems-level approaches. We use 1) mass spectrometry-based proteomics to study the dynamics of phosphorylation and ubiquitination; and 2) CRISPR/Cas9-based targeted genetic screens to identify key regulators; upon various inflammatory stimuli. We believe that our basic research-focused systems-level approaches would yield deeper and broader understanding of inflammatory signaling which will have enormous translational potential.

The research group joined CEMIR in December 2015 and is led by Richard K. Kandasamy. The group currently includes 1 Ph.D. student, 1 post-doc and access to staff engineers. We work in close collaboration with CEMIR research groups led by Terje Espevik, Trude H. Flo and Geir Bjørkøy; as well as Geir Slupphaug (NTNU Proteomics Core), Giulio Superti-Furga (Center for Molecular Medicine, Vienna) and Akhilesh Pandey (Johns Hopkins University, Baltimore).

LABORATORY FACILITIES

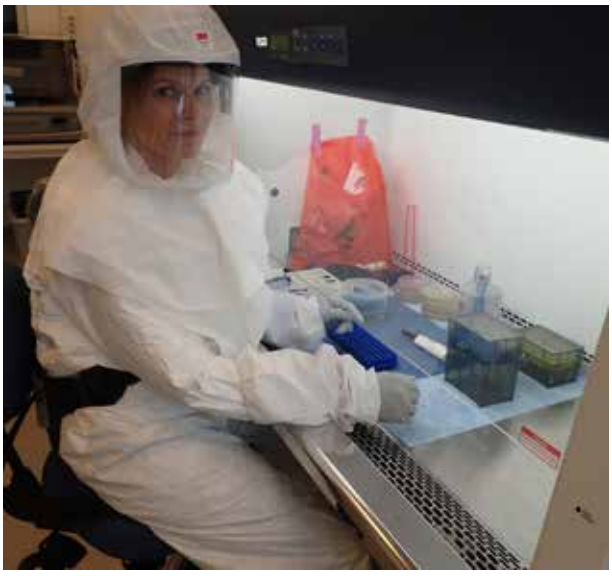
CEMIR is located in the Knowledge Centre and the Gastro Centre at the Øya Campus of St.Olavs Hospital and NTNU in Trondheim, together with the CEMIR-relevant clinical departments of Infectious Diseases (Knowledge Centre) and Gastroenterology and Cancer (Gastro Centre). CEMIR hosts first-class laboratories with state-of-the-art equipment for performing research on cells, tissues and microorganisms:

- a high resolution STED confocal microscope
- total internal reflection fluorescence (TIRF) microscope
- live cell- and spinning disk confocal microscopes
- image flow cytometer
- cell sorter
- a confocal microscope installed in a biosafety level 3 facility

In October 2015 we opened a new Biosafety Level Three (BSL-3) laboratory, offering the highest level of security for research on viruses and bacteria in Norway. The new lab contains an advanced Leica SP8 confocal microscope making it possible to study infections in immune cells with viable Mycobacterium tuberculosis and HIV virus.

Image Flow Cytometer

Leica SP8 Confocal microscope in the BSL3-laboratory



CEMIR personnel wearing protective equipment while working in the BSL-3 laboratory.

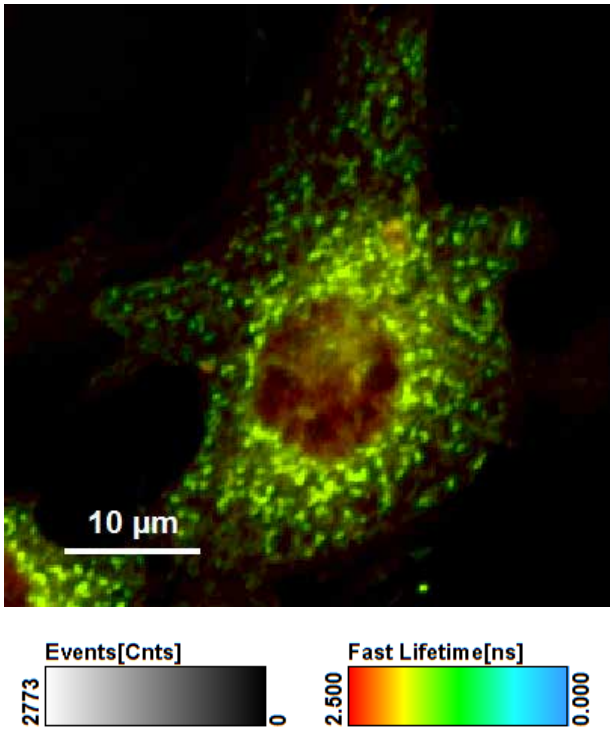
CEMIR-USE OF THE IMAGING CORE FACILITY

Researchers and students at CEMIR have access to a multitude of different imaging techniques, for live cell studies as well as imaging of fixed cells and tissue preparations. These instruments are all part of the recently established Cellular and Molecular Imaging Core Facility, CMIC, at Faculty of Medicine, NTNU. https://www.ntnu.edu/dmf/cmic. In 2014 a super resolution light microscope and a total internal reflection fluorescence microscope were installed at CMIC and placed in the CEMIR laboratories. During the first half of 2016 CMIC will purchase an PicoQuant single molecule detection (SMD) upgrade for our Leica SP8 STED 3X super-resolution microscope.

The Leica SP8 STED 3 X super-resolution microscope gives highly improved resolution and sensitivity in the detection of fluorescence compared to conventional confocal microscopes. Now CMIC will upgrade this system with a PicoQuant package that will open the possibility to quantitate protein-protein interactions, measure fluorescence lifetime, and make dynamic studies of protein trafficking in living cells. The system will then be able to perform microscopy based on fluorescence lifetime (FLIM), which is a very useful method to identify interactions between molecules in cells by applying fluorescence resonance energy transfer (FRET) analysis. The FLIM technology can also measure ion concentrations and pH in intracellular compartments, as well as separating fluorescent molecules with overlapping emission spectra and reduce unwanted background autofluorescence in cells. This method can also be combined with fluorescence correlation-spectroscopy (FCS) to allow advanced measurements of the mobility of molecules and the number of molecules analysed in the focal volume. Since this upgrade will be installed on the Leica STED system it will be possible to measure protein mobility in samples with higher protein concentration compared to what can be done with conventional FCS due to its decreased focal volume introduced by stimulated emission depletion (STED).

PRINCIPLES OF FLUORESCENT LIFE TIME MEASUREMENTS

In confocal laser scanning microscopy laser light at discrete wavelengths is used to excite fluorophores in the sample plane, which then emits fluorescence light. In essence, particles of light called photons get absorbed by the fluorophore (a molecule that are able to fluoresce), causing an electron to transiently move to a higher energy state, called the excited state. Through relaxation to a lower vibrational excited state, the electron drops back to the ground state and the fluorophore can release the excess energy in the form of a emitted fluorescent photon. The time that the electron spends in the excited state before returning back to its ground stade is called the fluorescence lifetime of the fluorophore, which normally is in the ns range. This property can be measured using time-correlated single photon counting (TCSPC), basically measuring the time from the excitation laser pulse to the time point at which the emitted fluorescence photon is detected. This process is repeated many times to build up a lifetime distribution in every pixel of the image



Fast FLIM, showing the average fluorescence lifetime in each pixel of the image.

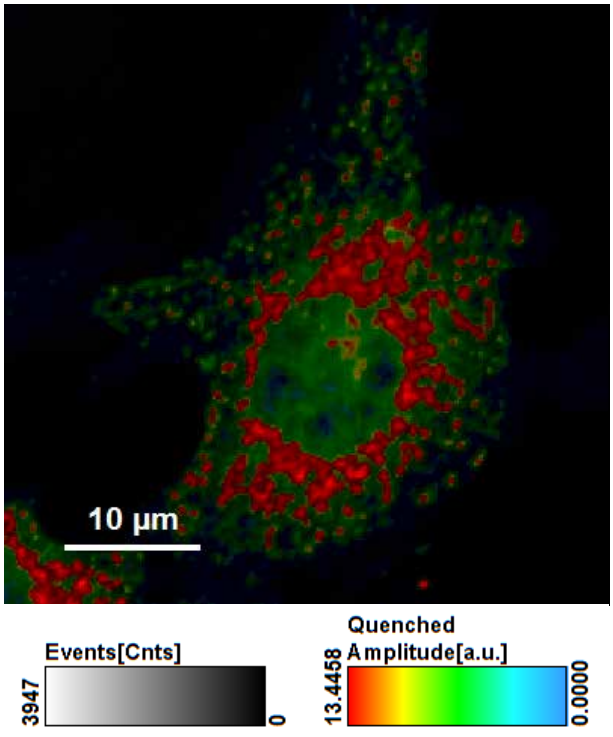


Image of FRET in a cell, represented as quenched amplitude of the donor.

ACTIVITIES IN CLINICAL DEPARTMENTS

Chronic inflammatory processes play an important role in the pathophysiological process in diseases such as atherosclerosis, diabetes, rheumatoid arthritis (RA), inflammatory bowel disease (IBD) and various neurological disorders. During the last years several inflammatory mediators have been identified as novel treatment targets in disorders such as in RA and IBD, and medications blocking or modulating these targets have been very successful. The vision of CEMIR is to lay the foundation for identifying new therapeutic targets and in developing new diagnostic tools for inflammatory diseases through research in molecular innate immune responses.

A close collaboration with the clinical departments is crucial for addressing our goal. CEMIR benefits from a close integration between NTNU and St.Olav's Hospital and the location of both institutions at Øya Campus. Several of our staff members are employed both in the clinic and the university. This close integration between CEMIR and St.Olav's Hospital has also been important in building up several biobanks with clinical specimens from patients with diseases such as coronary artery disease (CAD), IBD, preeclampsia and multiple myeloma. As shown in several papers from 2015, analyses using this material have demonstrated the clinical relevance of results generated in more experimental systems. Many of these patients were also previously included in the HUNT cohort which during 2015 was fully SNP genotyped with genome variability data from around 60.000 individuals. Several studies investigating genetic polymorphisms and plasma levels of cytokines as biomarkers for disease have been performed or are ongoing, hoping to identify novel diagnostic and prognostic tools for chronic inflammatory disorders such as CAD and IBD.

Among other clinically oriented projects, extensive studies were done during 2015 on biomarkers for IBD. In particular, fecal neutrophil gelatinase-associated lipocalin (NGAL) has performed well as a marker for inflammation in patients with ulcerative colitis and Crohn's disease. Upcoming studies uniting clinical and basal groups in CEMIR will further examine the basal mechanisms behind NGAL regulation, and explore the potential of this antimicrobial protein to modulate mucosal inflammation. This type of studies, reaching from bedside to laboratory with real-life material from diseased individuals, is done only in a few places world-wide. This shows that the interaction between CEMIR and the clinical departments is active, leading to novel findings with clinical potential.

Conference on Molecular Mechanisms of Inflammation

May 30th – June 2nd, 2016, Trondheim, Norway

From May 30th – June 2nd CEMIR arrange an international conference on molecular mechanisms of inflammation. The conference will have a particular emphasis on the regulation of inflammation in sterile and infectious diseases. We will bring together experts from basic and clinical inflammation research to promote exchange across disciplines.

The meeting will be interesting to scientists at the group leader, post-doc and PhD level.

Deadline for registration: May 1st 2016

CONFIRMED SPEAKERS

Alan Aderem,
Julie Blander,
Petr Broz,
Terje Espevik,
Kate Fitzgerald,
Richard Flavell,
Trude Helen Flo,
Douglas Golenbock,
Göran Hansson,
Catherine Hedrick,
Harald Husebye,
Jonathan Kagan,
Richard Kandasamy,
Claudia Kemper,
Egil Lien,
Tom Eirik Mollnes,
Kim Newton,
Luke O'Neill,
Alexander Poltorak,
Felix Randow,
Alan Sher,
Harald Stenmark,
Lynda Stuart,
David Underhill,
Stephanie Vogel

MORE INFORMATION:

www.ntnu.edu/cemir/conference2016

NTNU – Trondheim
Norwegian University of
Science and Technology

CEMIR
Centre of Molecular Inflammation Research

Norwegian Centre of Excellence

INTERNATIONAL COLLABORATION

CEMIR has a comprehensive international network, and it's our goal to further develop long-term international cooperation with excellent scientists and institutions.

Six outstanding researchers have been appointed as adjunct professors at CEMIR since 2013, four of them from abroad:

- Professor David Underhill, Cedars-Sinai medical Center, Los-Angeles, USA
- Professor Katherine Fitzgerald, University of Massachusetts, USA
- Professor Eicke Latz, University of Bonn, Germany
- Professor Tom Eirik Mollnes, University of Oslo and University of Tromsø
- Professor Egil Lien, University of Massachusetts, USA
- Professor Harald Stenmark, University of Oslo

The adjunct Professors are responsible for three PhD courses held yearly at NTNU: Advanced Cellular Imaging techniques (held first time in September 2014), Receptor Signalling and Trafficking and Molecular Mechanisms of Inflammation (held first time in 2013).The adjunct professors are also tightly involved with CEMIR by co-supervising our PhD and post-doctoral candidates. Staff members are offered the possibility to spend extended periods in their laboratories. In 2015 several CEMIR members visited researchers in the labs of the adjunct Professors and other international collaborators. This is an important component of the researcher training, networking and internationalization of their research.

Some of them have shared their experience from working abroad:

Kristian Starheim (researcher)

visited UMass Medical School 2014-15

As part of my postdoctoral work at CEMIR I spent two years at Egil Lien's lab at the Division of Infectious Diseases and Immunology, UMass Medical School, USA. My work at the Lien lab focused on how the gram negative bacteria Yersinia pestis induce cell death and inflammasome activation in macrophages. Coming from a cancer background, this introduced me to the field of innate immunity in general, and inflammatory cell death specifically. The stay greatly broadened my scientific repertoire and experience. UMass harbours some of the foremost groups within innate immunity, and during my stay I established contacts that form the basis of present and future collaborations. No doubt, long-term work abroad is crucial for a good integration of Norwegian science into the global scene.

Ann-Charlotte Iversen (Senior researcher)

visited LJI, California 2014-15

I was a Visiting Scientist at prestigious La Jolla Institute for Allergy and Immunology (LJI) in San Diego, California, from August 2014 to July 2015, working closely with Professors Catherine Hedrick and Klaus Ley, leading experts in cholesterol regulation and inflammatory mechanisms in atherosclerosis. I established a collaborative project investigating cholesterol crystal induced inflammasome activation in aortas of mice deficient in ApoE and Nur77, and a novel mouse model for study of atherosis in pregnancy. The cholesterol project will be followed up by a student from CEMIR working at LJI, and the mouse model will be used for functional testing of inflammatory mechanisms involved in atherosis formation in preeclamptic patient samples. Also Professor Hedrick contributes as invited speaker at the CEMIR International Conference in May/June 2016.

Signe Åsberg (PhD candidate)

visited Cedar-Sinai, Los-Angeles 2014-15

From November 2014 to April 2015 I visited my co-supervisor Dr. David Underhill's lab at the Cedar-Sinai Medical Center in Los Angeles. At the time I was investigating the role of C-type lectin receptors (CLRs), autophagy and LC3-associated phagocytosis (LAP) in *M. avium* infection. We decided that I should visit David's lab due to their expertise in Dectin-1 signaling and its relation to autophagy and LAP. «Everything» was different at Cedars so I learned a lot, ranging from laboratory how-to's to new ways of thinking about science. I also got valuable career advice. The amount of paperwork and time that goes into organizing a stay abroad might seem endless but I would not be without this experience. After coming home, I have kept in touch with the scientists I met and they are always extremely helpful.

Siril Skaret Bakke (postdoctor)

visited University of Bonn 2014-15

I worked at Professor Eicke Latz' lab in Bonn, Germany for 6.5 months in 2014/2015. This is one of the leading research groups in the world in the field of inflammation and innate immunity and I learned a lot from working with these experienced scientists and also how other labs outside Norway may work both as a team and as individual scientists. I was really fortunate to be a part of two very interesting projects and they are now soon being published in very good journals. In addition, I brought valuable experiences back to CEMIR to be applied in several projects here. I really appreciate the opportunity I got from CEMIR to work as a post doc in a research group abroad.

Pontus Ørning (PhD candidate)

visiting UMass medical School since 2013

I'm a PhD candidate at NTNU working in the labs of Professors Egil Lien and Kate Fitzgerald at UMass Medical School in Massachusetts, USA. I'm working in the field of innate immunity where I'm investigating how immune cells such as macrophages and dendritic cells use inflammasomes and lncRNA to combat pathogens. This is a great opportunity I have been given to visit one of the leading universities in the field of innate immunity, and it has made it possible for me to interact with renowned professors and researchers helping to push the field forward. More specifically, it has allowed me to work with a huge variety of KO mouse strains, reagents and the most modern equipment and expertise that I can use for my own research.

CEMIR has an international work environment - in 2015, 20 nationalities were represented in our staff. We also hosted a visiting researcher from Italy; A PhD candidate from the lab of Professor Giuseppe Teti, university of Messina, stayed with CEMIR for 12 month, connected to Terje Espevik's research group.

Other central international collaborators in 2015:

Aderem, Alan
Benedict, Chris
DeWan, Andrew T.
European Myeloma Network
Fearon, Ken
Garred, Peter
Goguen, Jon
Hawn, Thomas R.
Ingalls, Robin
Kemper, Claudia
Kidd, Kenneth
Komatsu, Masaaki
McCaffrey, Mary
Mecsas, Joan
Mobley, Harry LT
Moses, Eric
O`Neill, Luke
Rubin, Eric
Teti, Giuseppe
Seattle Biomed, USA
La Jolla Institute, USA
Yale School of Public Health, USA
Univ. of Edinburgh, UK
University of Copenhagen
Univ. of Massachusets, USA
University of Washington, USA
Boston University, USA
King's College London
Yale, USA
Tokyo Metropolitan Univ., Japan
Univ. of Cork, UK
Tokyo Univ. of Foreign Studies, Japan
Univ. Of Michigan Medical School, USA
Univ. of Western Australia
Trinity, Univ. of Oslo
Harvard School of Public Health, USA
Univ. of Messina, Italy

COMPLETED PhDs IN 2015

Cand.med. Eivind Ottersen Samstad defended his thesis "***Molecular Mechanisms of NLRP3 Inflammasome activation by Crystalline Material***" on February 6, 2015 at Norwegian University of Science and Technology (NTNU), Center of Molecular Inflammation Research (CEMIR).

The experimental work was conducted at the Department of Cancer Research and Molecular Medicine at NTNU and St.Olavs hospital with Professor Terje Espevik as supervisor and Professor Eicke Latz as co-supervisor.

Liv Cecilie Vestrheim Thomsen defended her thesis "***Preeclampsia: Specific genetic risk factors and shared predisposition with cardiovascular disease***"on March 13, 2015 at the University of Bergen.

The experimental work was conducted at University of Bergen and University of Western Australia with Professor Line Bjørge as supervisor and Professors Rigmor Austgulen and Associate Professor Ann-Charlotte Iversen (CEMIR) as co-supervisors.

Nathalie Niyonzima defended her thesis "***Role of the complement system in inflammatory responses to cholesterol crystals***"on April 10, 2015 at Norwegian University of Science and Technology (NTNU), Center of Molecular Inflammation Research (CEMIR).

The experimental work was conducted at the Department of Cancer Research and Molecular Medicine with Professor Terje Espevik as supervisor and Professor Jan Kristian Damås as co-supervisor.

Marita Westhrin defended her thesis "***Beauty and the Beast -The Multifaceted Potential of Mesenchymal Stem Cells in Bone Health and Disease***" on June 18, 2015 at Norwegian University of Science and Technology (NTNU), Center of Molecular Inflammation Research (CEMIR).

The experimental work was conducted at the Department of Cancer Research and Molecular Medicine at NTNU and St.Olavs hospital with Professors Therese Standal and Anders Sundan as supervisors.

Kristin Melheim Strand defended her thesis "***Markers of placental insufficiency: etiology and the risk of cerebral palsy - Population based studies of preeclampsia, low birth weight, and abnormal placental weight***" on June 22nd, 2015 at Norwegian University of Science and Technology (NTNU), Department of Laboratory Medicine, Children's and Women's Health and Center of Molecular Inflammation Research (CEMIR).

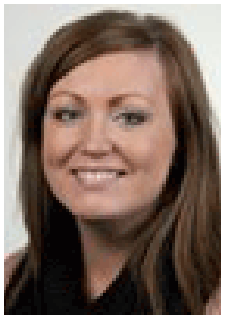
The experimental work was conducted at Department of Laboratory Medicine, Children's and Women's Health with Professors Torstein Vik, Rigmor Austgulen and senior researcher Ann-Charlotte Iversen as supervisors.

Marie Austdal defended her thesis "***Biomarkers for prediction and characterization of preeclampsia using magnetic resonance metabolomics***" September 21st, 2015 at Norwegian University of Science and Technology (NTNU), the Department of Circulation and Medical Imaging and Center of Molecular Inflammation Research (CEMIR).

The experimental work was conducted at the Department of Circulation and Medical Imaging and the Department of Cancer Research and Molecular Medicine, with Professors Tone Frost Bathen, Rigmor Austgulen and senior researcher Ann-Charlotte Iversen as supervisors.

Line Tangerås defended her thesis "***Toll-like receptors and inflammation in pregnancy***"on October 16, 2015 at Norwegian University of Science and Technology (NTNU), Center of Molecular Inflammation Research (CEMIR).

The experimental work was conducted at the Department of Cancer Research and Molecular Medicine at NTNU and St.Olavs hospital with senior researcher Ann-Charlotte Iversen and Professors Rigmor Austgulen and Line Bjørge as supervisors.



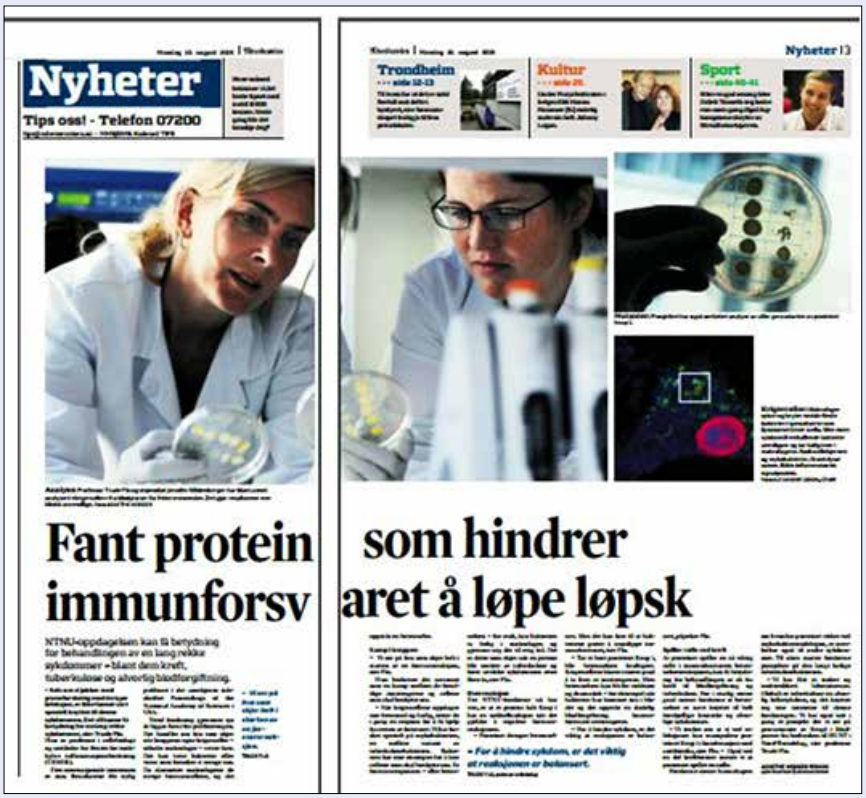
Ida Johansson defended her thesis "***A dual role of autophagy in disease prevention and drug resistance***" Desember 17, 2015 at Norwegian University of Science and Technology (NTNU), Department of Laboratory Medicine, Children's and Women's Health and Center of Molecular Inflammation Research (CEMIR).

The experimental work was conducted at the Department of Laboratory Medicine, Children's and Women's Health and Center of Molecular Inflammation Research (CEMIR) with Professors Geir Bjørkøy and Svanhild Schønberg as supervisors.

CEMIR OUTREACH 2015

At CEMIR we aim to make the public aware of and understand our research on inflammation, and how our research can contribute to the development of new treatments and diagnostic tools. We are involved in many outreach activities.

Website: www.ntnu.edu/cemir


Nyheter

Tips oss! - Telefon 07200

Fant protein immunforsv

som hindrer aret å løpe løpsk

MEDIA HIGHLIGHTS

CEMIR had several media coverage in 2015. In January Trude Helen Flo was interviewed in a TV- show on vaccination (Newton, NRK), and there was several articles on the research, both national and international publications. The publication Jane Atesoh Awuh, et al. *Keap1 regulates inflammatory signaling in Mycobacterium avium-infected human macrophages* in PNAS, got a lot of attention both in science and regular papers. Also articles on the "Good Cholesterol" and why omega -3 lowers the risk of disease had a broad audience due to several articles.

BLOGGING In 2015 we wrote several blogs for the #NTNUmedicine blog

IN ENGLISH, NINE BLOG ARTICLES:

- *Unveiling connections between preeclampsia and cardiovascular disease. (NTNUmedicine)*
- *New anti-inflammatory effects of "the good cholesterol" (Nathalie Niyonzima and Eivind Samstad)*
- *Human Toll-like receptor 8 (TLR8) is a sensor of bacterial infection. (Jørgen Stenvik)*
- *New trafficking dynamics of an innate immune receptor revealed. (Terje Espevik)*
- *ON THE WORLD TUBERCULOSIS DAY 24 March: The surprising mechanism of a new anti-TB compound (Marte Singsås Dragset)*
- *A New Path in the Inflammation Maze. (Nadra J. Nilsen)*
- *What I love about my job. (Signe Åsberg)*
- *When the immune system causes damage. (NTNUmedicine)*
- *I am the herd. (Signe Åsberg)*

IN NORWEGIAN, SIX BLOG ARTICLES

- *Stipend frå Kreftforeningen: Immunforsvaret påverkar kreftutvikling. (Kristian Kobbenes Starheim)*
- *Ny innsikt i hvordan flerumettede omega-3 fettsyrer kan bremse sykdomsutvikling. (Ida Johansson)*
- *Et nytt stoff som dreper tuberkulosebakterien har en overraskende virkningsmekanisme. (Marte Singsås Dragset)*
- *Jeg er flokken (meslingvaksine). (Signe Åsberg)*
- *Når kroppen skyter over mål (krystallinsk materiale). (Hanne Strypet)*
- *Spør en forsker: En sammenheng mellom kronisk infeksjon og brystkreft? (Trude Helen Flo and Tonje Strømmen Steigedal)*

You can read the blogs here:
https://blog.medisin.ntnu.no/tag/cemir-en/?lang=en

RESEARCHERS' NIGHT 2015: FORNUFT OG MAGEFØLELSER, BYSCENEN SEPTEMBER 25TH

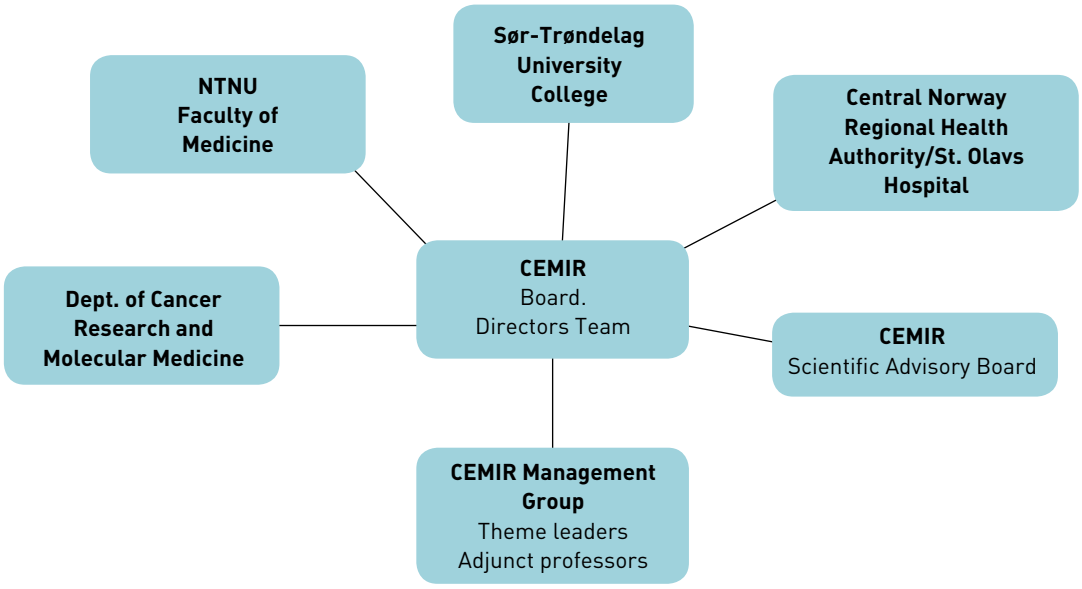
Trude Helen Flo was one of three researchers who participated in the evening talk- show Researchers' Night 2015: Fornuft og mageføelelser at Byscenen in Trondheim city center. The theme of the talk- show was food and its impact on health and the researchers should present and debate different issues from their perspectives. The talk-show host was a well-known Norwegian author, Aslak Nore. The show was a great success with over 230 people of all ages present, Adresseavisen wrote a review. Over 200 people visited the online streaming – and several more will see it as Kunnskapsportalen, NRK will broadcast the talk-show in 2016.

Link to video of the talk-show (full – length):
http://livestream.com/accounts/4172561/events/4371041/videos/100240170

CEMIR PRESENT IN AN EXHIBITION AT THE MEDICAL MUSEUM: CHILDREN AT THE HOSPITAL

CEMIR is present in an exhibition at the Medical Museum that opened in December, in Kunnskapssenteret. The theme is children in the hospital, before and now, and more general health issues relevant for children. Vaccination is one important part of the exhibition, and CEMIR is contributing with their knowledge and is represented in a video on the theme (Trude Helen Flo, from Newton, NRK) and photos.

ABOUT CEMIR



From the start in 2013 CEMIR had two main partners that contribute by performing research activity and providing financing: Sør-Trøndelag University College (HiST) and The Central Norway Regional Health Authority/St.Olavs Hospital. From January 2016 NTNU and HiST merged, and the research group from HiST became an internal NTNU collaborator. The fruitful collaboration continues after the merge and the new Faculty of Technology (Former HiST) continues to be represented in the CEMIR Board.

CEMIR is closely connected to the host department, Department of Cancer Research and Molecular Medicine at the Faculty of Medicine, NTNU. Agreement documents regulate the cooperation with our partners.

The Centre activities integrate 7 research themes and unite researchers across disciplines for breaking new grounds in inflammation research. In addition 6 international researchers are employed at CEMIR as professor II. The Centre management reports to the CEMIR board.

The day-to-day management of CEMIR is performed by Director Terje Espevik, Co-Director Trude Helen Flo and Head of Administration Kari Håland.

CEMIR BOARD

2 board meetings were held in 2015. The board members are:

- Magne Børset – (Board chairman) Head of Dep. of Cancer Research and Molecular Medicine, NTNU
- Björn Gustafsson - Dean, Faculty of Medicine, NTNU
- Terje Meisler - Dean, Faculty of Technology, NTNU
- Petter Aadahl - Research director, St. Olavs Hospital
- Anne Borg - Dean, Faculty of Natural Sciences and Technology, NTNU

CEMIR Scientific Advisory Board (SAB) has five members:

- Professor Douglas Golenbock, University of Massachusetts Medical School
- Professor Alan Aderem, Seattle Biomedical Research Institute
- Professor Göran Hansson, Karolinska Institutet
- Professor Stefanie Vogel, University of Maryland medical Center
- Professor Lynda Stuart, B & M Gates Foundation

The function of SAB is to review the scientific progress of the Centre and to give guidance to future research directions.

EVENTS AT CEMIR

CEMIR now counts more than 80 people from 20 different countries that are sharing labs and office space. This constellation provides ample intellectual stimulation, and as a Centre of excellence we have made a substantial effort to create a common and sharing culture. Important activities to obtain a strong sense of common identity have been:

Annual all-day seminar: Before Christmas we arrange an all-day seminar (retreat). This is an arena for presentations and discussions of ongoing CEMIR research and future topics and projects, and all CEMIR people are invited and encouraged to attend. This year's seminar was held at Frimurerlogen. In addition to scientific talks themes like "what does it take to publish in high-impact papers" were discussed. The seminar was closed with a three-course dinner and social gathering.

Guest lectures: CEMIR aims at inviting a number of guest lectures every year. This is a great opportunity for the Centre members as well as other researchers at Faculty of Medicine to get scientific insight from excellent researchers from other universities. Nobel laureate Bruce Beutler from the University of Texas was awarded an honorary doctorate at NTNU in March and gave a CEMIR-hosted lecture entitled "Real time identification of mutations that cause phenotype" - ending with a total solar eclipse! In June Felix Randow from the MRC laboratory of molecular biology in UK visited and enchanted CEMIR scientists with an exciting talk "autophagy in host-pathogen interactions" about cell autonomous immunity to intracellular bacteria. We all remember how Shigella undress! CEMIR also had the pleasure to host the following guest lecturers: Joerg Koehl, University of Lübeck, who talked about "Cross-talk between complement and IgG Fc receptors in autoimmunity". Guttorm Haraldsen, University of Oslo gave a talk on: "Notch signalling in vascular quiescence and inflammation", Claudia Kemper, Kings College London presented exiting new findings on intracellular complement activation: "New tricks for an Old Dog: unexpected roles for complement in basic cellular processes", Sanjay Ram, University of Massachusetts, who presented: "Harnessing the sialylation machinery of Neisseria gonorrhoeae to design novel immunotherapeutics against multidrug-resistant gonorrhea".

Toll 2015: In September 2015 the conference Toll 2015 Targeting Innate Immunity was arranged in Marbella, Spain, with more than 700 participants. A number of CEMIR researchers were involved in the organization of the conference. CEMIR researchers also contributed as plenary speakers and with poster presentations. This was a great opportunity to make CEMIR more visible and to share our research with a large international audience.

International Conference in 2016: May 30th – June 2nd 2016 CEMIR arranges an international conference in Trondheim: Conference on Molecular Mechanisms of Inflammation. Outstanding international researchers will give presentations, and this will be a unique opportunity to expand our insight into processes of inflammatory disorders. We expect about 250 participants from all over the world and are looking forward to hosting excellent international scientists from this important field of research. Read more about the conference on page 23.

Professors Bruce Beutler and Trude Helen Flo

Professors Claudia Kemper, Kings College London, and Sanjay Ram, University of Massachusetts, gave a guest lecture when visiting NTNU as an opponent for PhD Nathalie Niyonzima in April 2015

CEMIR members at the Toll 2015 conference in Marbella, Spain

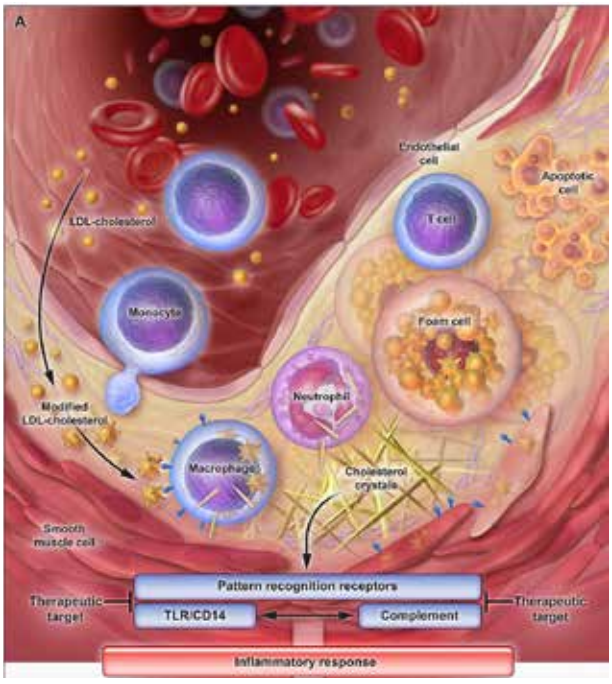
INNOVATION AND PATENTS

The concept of double-blockade of complement and CD14 to attenuate inflammation

Microbial as well as sterile inflammation is initiated by pattern recognition. This is the initial and most upstream event for the inflammatory response, which subsequently leads to activation of a broad inflammatory network with release of innumerable of mediators. Using specific complement inhibitors of the central components C3 and C5 we observed that certain branches of inflammation was substantially inhibited, including granulocyte activation with surface receptor up-regulation and oxidative burst, whereas other mediators including a number of cytokines were less complement dependent. CD14 is a co-receptor for several of the Toll-like receptor molecules, in particular TLR4 and TLR2 and thus could be another key target for inhibition. Using specific antibodies to block CD14 we documented a marked reduction in a broad panel of cytokines and monocyte-mediated responses, differential from the complement-dependent responses.

Based on these observations we combined complement inhibitors (C3 or C5) with anti-CD14 and found these to be crucial "bottle-neck" molecules which virtually abolished the whole inflammatory response when inhibited in combination. This was shown for both exogenous danger signals like Gram-negative and Gram-positive bacteria in vitro (human) and in vivo (pigs and baboons), for polymicrobial sepsis in mice and pigs, and for endogenous danger like meconium, which is sterile and induces a serious inflammation in newborns. In a whole genome array we documented that 70% of all Gram-negative bacterial induced genes (a total of >2000) were reversed by an average of >80% signal by combined inhibition of C3 and CD14. Thus, blocking of two "bottle-neck" molecules (C3 or C5 of complement) and CD14, at the very first step of danger recognition might be a potent therapeutic strategy to attenuate undesired inflammation occurring in a number of pathophysiological states leading to different disease conditions. Eritoran (E5564) is a specific inhibitor of the TLR4-MD4 complex. Although promising results were initially observed in human sepsis, the study was closed in phase III due to lack of improved survival. Importantly, we recently shown that anti-CD14 was more efficient in inhibiting bacterial-induced inflammation than eritoran, in particular for the monocytes, and that the combined inhibition of CD14 and complement was substantially more efficient than eritoran, supporting the broad-acting role for CD14 and complement in the innate immune response.

The principle of double-blockage of complement and CD14 to attenuate inflammation was proposed, and has been driven by one of the CEMIR researchers (TE Mollnes). Moreover, CEMIR researchers at NTNU (T Espevik et al) have developed the anti-CD14 antibody 18D11 that is effective in the combined treatment and currently is under production as a recombinant humanized antibody for therapeutic use. Three patents have been posted related to this scientific project. A formal collaboration contract has been made with a company producing a C5 inhibitor for clinical use. The vision is to test this principle in clinical therapeutic settings in collaboration with Inven2 (the TTO at University of Oslo), and NTNU Technology Transfer AS. The project received grants from the BIOTEK program from The Research Council of Norway for the period 2015-2017.



Potential role for inhibition of innate immunity in atherosclerosis. The atherosclerotic plaque is characterized by immune cells including monocytes, macrophages, granulocytes, T-cells and foam cells. LDL-cholesterol is retained in the intima where it is oxidized or otherwise enzymatically modified. There is also formation of cholesterol crystals known to activate the innate immune system. The changes in the vessel wall induce innate immune activation through pattern recognition receptors including toll-like receptors and the complement system. These systems cross-talk extensively including both positive and negative feedback mechanisms. (From: Mollnes et al. The complement system and toll-like receptors as integrated players in the pathophysiology of atherosclerosis. Atherosclerosis 241, 480–494, 2015).

PRICES AND AWARDS 2015

PROFESSOR HARALD STENMARK – MØBIUS AWARD 2015

Harald A. Stenmark, director of the Centre for Cancer Biomedicine at UIO and Professor II at CEMIR won the 2015 "Møbius award" - the annual prize for excellent research from the Research Council of Norway. The award is granted on the basis of documented results, and is intended to encourage further research activity. The award amounts to 1 mill. NOK and was distributed Wednesday September 23rd 2015 in Oslo Konserthus. We congratulate Professor Stenmark with the prestigious award!

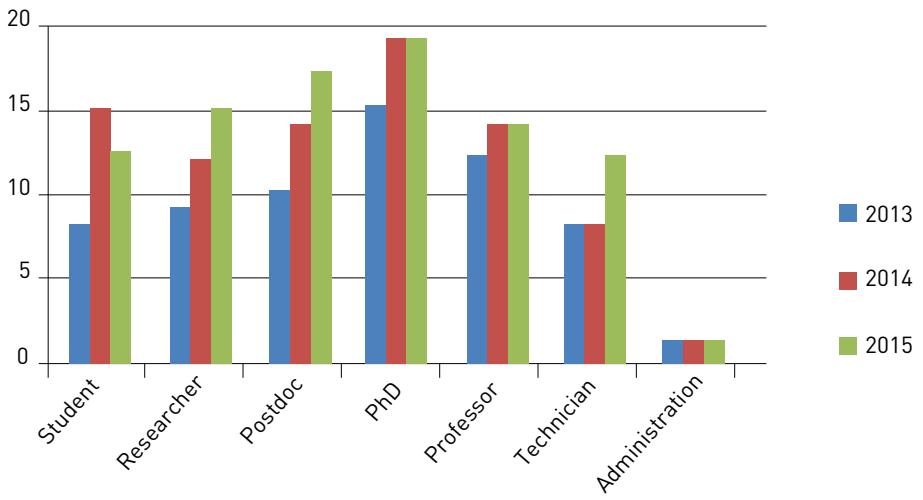
Rector Gunnar Bovim, Professor Bruce Beutler, Dean Stig Slørdahl, Head of Department Magne Børset, Professor Anders Waage and CEMIR director Terje Espevik

PROFESSOR BRUCE BEUTLER – HONORARY DOCTORATE AT NTNU

In March 2015 The Board of the Norwegian University of Science and Technology, NTNU, awarded Professor Bruce Beutler the degree of doctor honoris causa (honorary doctorate) to NTNU. The appointment of Beutler recognizes his significant contributions to understanding how innate immune cell receptors regulate inflammatory responses. He discovered an important family of sensors in immune cells called Toll-like receptors that allow us to sense danger signals from microbes and damaged cells. Bruce Beutler's groundbreaking discoveries about sensors in our innate immune system that recognize bacteria have led to an explosion of research on this theme. In 2011 he received Nobel Prize in Physiology or Medicine. Bruce Beutler's work has greatly inspired scientists at CEMIR and we are looking forward to further interactions with him.

CEMIR STAFF AND STUDENTS

CEMIR was established as a Centre of Excellence January 1, 2013. We have emphasized the importance of establishing a unified research group in which multidisciplinary research cooperation is encouraged and stimulated. By the end of 2015 65 scientific staff members, 12 technicians, 12 students and an administrative coordinator were associated with the centre.



Name		Position	Nationality	Research Group
Agliano	Federica	PhD candidate	Italy	Inflammation
Andersen	Sonja	Technician	Norway	Autophagy
Aune	Marie Hjelmseth	Postdoctor	Norway	Inflammation
Austgulen	Rigmor	Professor	Norway	Pregnancy
Awuh	Jane	Postdoctor	Cameroon	Mycobacteria
Bakke	Siril Skaret	Postdoctor	Norway	Inflammation
Beckwith	Marianne Sandvold	PhD candidate	Norway	Mycobacteria
Bergstrøm	Bjarte	Postdoctor	Norway	Inflammation
Bjørkøy	Geir	Professor	Norway	Autophagy
Bözl	Korbinian Michael	PhD candidate	Germany	System Inflammation
Boyartchuk	Victor	Researcher	Ukraine	Inflammation
Bugge	Marit	PhD candidate	Norway	Inflammation
Damaas	Jan K	Professor	Norway	Inflammation
Dragset	Marte Singsås	Postdoctor	Norway	Mycobacteria
Egeberg	Kjartan	Technician	Norway	Inflammation
Ehrnstrøm	Birgitta	PhD candidate	Sweden	Inflammation
Espevik	Terje	Professor	Norway	Inflammation
Fitzgerald	Kate	Professor II	USA	
Flo	Trude Helen	Professor	Norway	Mycobacteria
Gidon	Alexandre	Postdoctor	France	Mycobacteria
Gierman	Lobke	Postdoctor	Netherlands	Pregnancy
Ginbot	Zekarias	Researcher	Eritrea	Mycobacteria
Granlund	Atle Van Beelen	Postdoctor	Norway	IBD
Grøvdal	Lene Melsæther	Postdoctor	Norway	Inflammation
Haug	Markus	Researcher	Norway	Mycobacteria
Husebye	Harald	Researcher	Norway	Inflammation
Håland	Kari	Head of administration	Norway	
Ibrahim	Hany	PhD candidate	Egypt	Mycobacteria
Iversen	Ann-Charlotte	Associate Professor	Norway	Pregnancy
Johansson	Ida	PhD candidate	Norway	Autophagy
Kandasamy	Richard Kumaran	Researcher	India	System Inflammation
Kannan	Nisha	PhD candidate	India	Mycobacteria
Kojen	June Frengen	Technician	Norway	Inflammation
Latz	Eicke	Professor II	Germany	
Lien	Egil	Professor II	Norway	
Louet	Claire	Technician	France	Mycobacteria
Marstad	Anne	Technician	Norway	Mycobacteria
Mildenberger	Jennifer	PhD candidate	Germany	Autophagy
Moharrami	Neda Nejati	PhD candidate	Iran	Inflammation
Mollnes	Tom Eirik	Professor II	Norway	
Mundal	Siv Boon	PhD candidate	Norway	Pregnancy
Mærk	Mali	Postdoctor	Norway	Mycobacteria
Neckmann	Ulrike	PhD candidate	Germany	Autophagy
Nilsen	Nadra	Researcher	Norway	Inflammation
Niyzima	Nathalie	Postdoctor	Burundi	Inflammation
Nonstad	Unni	Technician	Norway	Inflammation

Ostrop	Jenny	Postdoctor	Germany	Regeneration
Paulsen	Julie	PhD candidate	Norway	Inflammation
Pervaiz	Zhara	Student	Pakistan	Pregnancy
Pettersen	Kristine	PhD candidate	Norway	Autophagy
Rokstad	Anne Mari	Researcher	Norway	Inflammation
Ryan	Liv	Technician	Norway	Mycobacteria
Samstad	Eivind	Researcher	Norway	Inflammation
Sandvik	Arne	Professor	Norway	IBD
Silva	Gabriela Brettas	PhD candidate	Brazil	Pregnancy
Skei	Bente	Technician	Norway	Pregnancy
Skjesol	Astrid	Postdoctor	Norway	Inflammation
Standal	Therese	Professor	Norway	Bone disease
Starheim	Kristian K.	Postdoctor	Norway	Inflammation
Steigedal	Magnus	Researcher	Norway	Mycobacteria
Steinkjer	Bjørg	Technician	Norway	Inflammation
Stenmark	Harald	Professor II	Norway	
Stenvik	Jørgen	Researcher	Norway	Inflammation
Strand	Trine Aakvik	Technician	Norway	Mycobacteria
Stødle	Guro	PhD candidate	Norway	Pregnancy
Sundan	Anders	Professor	Norway	Bone disease
Tangerås	Line	PhD candidate	Norway	Pregnancy
Thorsvik	Silje	PhD candidate	Norway	IBD
Underhill	David	Professor II	USA	
Vik	Randi	Technician	Norway	Inflammation
Waagsbø	Bjørn	PhD candidate	Norway	Inflammation
Yurchenko	Mariia	Postdoctor	Ukraine	Inflammation
Zahoor	Muhammad	Postdoctor	Pakistan	Bone disease
Ørning	Mathias Pontus	PhD candidate	Norway	Inflammation
Østvik	Ann Elisabeth	Researcher	Norway	IBD
Åsberg	Signe	PhD candidate	Norway	Mycobacteria
Waagsbø	Bjørn	PhD candidate	Norway	Inflammation
Wilson	Ernest	Master's student	Ghana	Mycobacteria
Yurchenko	Mariia	Postdoctor	Ukraine	Inflammation
Zahoor	Muhammad	Postdoctor	Pakistan	Bone disease
Ørning	Mathias Pontus	PhD candidate	Sweden	Inflammation
Østvik	Ann Elisabeth	Postdoctor	Norway	IBD
Åsberg	Signe	PhD candidate	Norway	Mycobacteria

RESULTS 2015: PUBLICATIONS, THESIS AND ACADEMIC PRESENTATIONS

JOURNAL PUBLICATIONS

Arlov, Øystein; Aachmann, Finn Lillelund; Feyzi, Emadoldin; Sundan, Anders; Skjåk-Bræk, Gudmund. The impact of chain length and flexibility in the interaction between sulfated alginates and HGF and FGF-2. Biomacromolecules2015 ;Volum 16.(11) s.3417-3424 NTNU STO

Asprusten, Tarjei Tørre; Fagermoen, Frode Even; Sulheim, Dag; Skovlund, Eva; Sørensen, Øystein; Mollnes, Tom Eirik; Wyller, Vegard Bruun. Study findings challenge the content validity of the Canadian Consensus Criteria for adolescent chronic fatigue syndrome. Acta Paediatrica 2015;Volum 104.(5) s.498-503 AHUS NLSH NTNU OUS SI UiO UiT

Austdal, Marie; Tangerås, Line Haugstad; Skråstad, Ragnhild; Salvesen, Kjell Å; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte. First trimester urine and serum metabolomics to predict preeclampsia and gestational hypertension. Pregnancy Hypertension 2015 ;Volum 5. s.248 NTNU STO

Austdal, Marie; Tangerås, Line Haugstad; Skråstad, Ragnhild; Salvesen, Kjell Å; Austgulen, Rigmor; Iversen, Ann-Charlotte; Bathen, Tone Frost. First Trimester Urine and Serum Metabolomics for Prediction of Preeclampsia and Gestational Hypertension: A Prospective Screening Study. International Journal of Molecular Sciences 2015;Volum 16.(9) s.21520-21538 NTNU STO

Austdal, Marie; Thomsen, Liv Cecilie Vestrheim; Tangerås, Line Haugstad; Skei, Bente; Mathew, Seema; Bjørge, Line; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte. Metabolic profiles of placenta in preeclampsia using HR-MAS MRS metabolomics. Placenta 2015; Volum 36. (12) s.1455-1462 HAUKELAND NTNU STO UiB

Beckwith, Marianne; Beckwith, Kai Sandvold; Sikorski, Pawel; Skogaker, Nan Elisabeth Tostrup; Flo, Trude Helen; Halaas, Øyvind. Seeing a mycobacterium-infected cell in nanoscale 3D: Correlative imaging by light microscopy and FIB/SEM tomography. PLoS ONE 2015;Volum 10:e0134644.(9) NTNU

Bergstrøm, Bjarte; Aune, Marie Hjelmseth; Awuh, Jane Atesoh; Kojen, June Frengen; Blix, Kjetil Jordahl; Ryan, Liv; Flo, Trude Helen; Mollnes, Tom Eirik; Espevik, Terje; Stenvik, Jørgen. TLR8 senses Staphylococcus aureus RNA in human primary monocytes and macrophages and induces IFN- production via a TAK1-IKK-IRF5 signaling pathway. Journal of Immunology 2015 ;Volum 195.(3) s.1100-1111 NLSH NTNU OUS UiO UiT

Brenna, Øystein; Bruland, Torunn; Furnes, Marianne Waldum; Granlund, Atle Van Beelen; Drozdov, Ignat; Emgård, Johanna; Brønstad, Gunnar; Kidd, Mark; Sandvik, Arne Kristian; Gustafsson, Björn. The guanylate cyclase-C signaling pathway is down-regulated in inflammatory bowel disease. Scandinavian Journal of Gastroenterology 2015;Volum 50.(10) s.1241-1252 NTNU STO

Broderick, Lori; De Nardo, Dominic; Franklin, Bernardo S; Hoffman, Hal M; Latz, Eicke. The inflammasomes and autoinflammatory syndromes. Annual Review of Pathology 2015 ;Volum 10. s.395-424 NTNU

Cebulla, Jana; Huuse-Røneid, Else Marie; Pettersen, Kristine; van der Veen, Anna; Kim, Eugene; Andersen, Sonja; Prestvik, Wenche S; Bofin, Anna M.; Pathak, Arvind P; Bjørkøy, Geir; Bathen, Tone Frost; Moestue, Siver Andreas. MRI Reveals the in Vivo Cellular and Vascular Response to BEZ235 in Ovarian Cancer Xenografts with Different PI3-Kinase Pathway Activity. British Journal of Cancer 2015 ;Volum 112.(3) s.504-513 HIST NTNU STO

Chan, Jennie; Atianand, M; Jiang, Z; Carpenter, S.; Aiello, Daniel; Elling, Roland; Fitzgerald, Katherine A.; Caffrey, DR. Cutting edge: A natural antisense transcript, AS-IL-1, controls inducible transcription of the proinflammatory cytokine IL-1. Journal of Immunology 2015 ;Volum 195.(4) s.1359-1363 NTNU

Dragset, Marte Singsås; Barczak, Amy K.; Kannan, Nisha; Mærk, Mali; Flo, Trude Helen; Valla, Svein; Rubin, Eric J.; Steigedal, Magnus. Benzoic Acid-Inducible Gene Expression in Mycobacteria. PLoS ONE 2015 ;Volum 10.(9) NTNU

Dragset, Marte Singsås; Poce, Giovanna; Alfonso, Salvatore; Padilla-Benavides, Teresita; Ioerger, Thomas R.; Kaneko, Takushi; Sacchettini, James C.; Biava, Mariangela; Parish, Tanya; Argüello, José M.; Steigedal, Magnus; Rubin, Eric J. A novel antimycobacterial compound acts as an intracellular iron chelator. Antimicrobial Agents and Chemotherapy 2015;Volum 59.(4) s.2256-2264 NTNU

Egge, Kjetil Hagene; Barratt-Due, Andreas; Nymo, Stig Haugset; Lindstad, Julie Katrine; Pharo, Anne Margrethe; Lau, Corinna; Espevik, Terje; Thorgersen, Ebbe Billmann; Mollnes, Tom Eirik. The anti-inflammatory effect of combined complement and CD14 inhibition is preserved during escalating bacterial load. Clinical and Experimental Immunology 2015;Volum 181.(3) s.457-467 NLSH NTNU OUS UiO UiT

Egge, Kjetil Hagene; Thorgersen, Ebbe Billmann; Pischke, Søren Erik; Lindstad, Julie Katrine; Pharo, Anne Margrethe; Bongoni, Anjan K.; Rieben, Robert; Nunn, Miles A.; Barratt-Due, Andreas; Mollnes, Tom Eirik. Organ inflammation in porcine Escherichia coli sepsis is markedly attenuated by combined inhibition of C5 and CD14. Immunobiology 2015;Volum 220.(8) s.999-1005 NLSH NTNU OUS UiO UiT

Fadila, Cero; Hillestad, Vigdis; Sjaastad, Ivar; Yndestad, Arne; Aukrust, Pål; Ranheim, Trine; Lunde, Ida Gjervold; Olsen, Maria Belland; Lien, Egil; Zhang, Lili; Haugstad, Solveig Bjærum; Løberg, Else Marit; Christensen, Geir Arve; Larsen, Karl-Otto; Skjønsberg, Ole Henning. Absence of the inflammasome adaptor ASC reduces hypoxia-induced pulmonary hypertension in mice. American Journal of Physiology – Lung cellular and Molecular Physiology 2015;Volum 309.(4) s.L378-L387 NTNU OUS UiO

Fadila, Cero; Hillestad, Vigdis; Sjaastad, Ivar; Yndestad, Arne; Aukrust, Pål; Ranheim, Trine; Lunde, Ida Gjervold; Olsen, Maria Belland; Lien, Egil; Zhang, Lili; Haugstad, Solveig Bjærum; Løberg, Else Marit; Christensen, Geir Arve; Larsen, Karl-Otto; Skjønsberg, Ole Henning. Absence of the inflammasone adaptor ASC reduces hypoxia-induced pulmonary hypertension in mice. American Journal of Physiology - Lungcellular and Molecular Physiology 2015;Volum 309. s.L378-L387 NTNU OUS UiO

Florholmen, Jon; Sandvik, Arne Kristian. Achievements and challenges in the management of inflammatory bowel disease. Scandinavian Journal of Gastroenterology 2015;Volum 50.(1) s.1-2 NTNU UiT

Follin-Arbelet, Virginie; Misund, Kristine; Naderi, Elin Hallan; Ugland, Hege Katrin; Sundan, Anders; Blomhoff, Heidi Kiil. The natural compound forskolin synergizes with dexamethasone to induce cell death in myeloma cells via BIM. Scientific Reports 2015;Volum 5:13001. NTNU UiO

Gidon, Alexandre; Feinstein, Timothy N.; Xiao, Kunhong; Vilardaga, Jean-Pierre. Studying the regulation of endosomal cAMP production in GPCR signaling. Methods in Cell Biology 2015 NTNU

Gierman, Lobke; Stødle, Guro; Tangerås, Line Haugstad; Austdal, Marie; Olsen, Guro Dalheim; Follestad, Turid; Skei, Bente; Rian, Kristin; Gundersen, Astrid; Austgulen, Rigmor; Iversen, Ann-Charlotte. Functional screening of toll-like receptors in seven trophoblast cell lines. Pregnancy Hypertension 2015;Volum 5. s.229 NTNU STO

Gierman, Lobke; Stødle, Guro; Tangerås, Line Haugstad; Austdal, Marie; Olsen, Guro Dalheim; Follestad, Turid; Skei, Bente; Rian, Kristin; Gundersen, Astrid; Austgulen, Rigmor; Iversen, Ann-Charlotte. Toll-like receptor profiling of seven trophoblast cell lines warrants caution for translation to primary trophoblasts. Placenta 2015;Volum 36.(11) s.1246-1253 NTNU STO

Goll, Rasmus; Granlund, Atle Van Beelen. Intestinal barrier homeostasis in inflammatory bowel disease. Scandinavian Journal of Gastroenterology 2015;Volum 50.(1) s.3-12 NTNU UNN

Hallstensen, Randi; Bergseth, Grete; Foss, Stian; Jæger, Steinar; Gedde-Dahl, Thobias; Holt, jan; Christiansen, Dorte; Lau, Corinna; Brekke, Ole Lars; Armstrong, Elina; Stefanovic, Vedran; Andersen, Jan Terje; Sandlie, Inger; Mollnes, Tom Eirik. Eculizumab treatment during pregnancy does not affect the complement system activity of the newborn. Immunobiology 2015;Volum 220.(4) s.452-459 NLSH NTNU OUS UiO UiT

Hein, E; Munthe-Fog, Lea; Thiara, Amrit Paul Singh; Fiane, Arnt E; Mollnes, Tom Eirik; Garred, P. Heparin-coated cardiopulmonary bypass circuits selectively deplete the pattern recognition molecule ficolin-2 of the lectin complement pathway in vivo. Clinical and Experimental Immunology 2015;Volum 179.(2) s.294-299 NLSH NTNU OUS UiO UiT

Holien, Toril; Misund, Kristine; Olsen, Oddrun Elise; Baranowska, Katarzyna Anna; Buene, Glenn; Børset, Magne; Waage, Anders; Sundan, Anders. MYC amplifications in myeloma cell lines: Correlation with MYC-inhibitor efficacy. OncoTarget 2015;Volum 6.(26) s.22698-22705 NTNU STO

Hovland, Anders; Jonasson, Lena; Garred, Peter; Yndestad, Arne; Aukrust, Pål; Lappegård, Knut Tore; Espevik, Terje; Mollnes, Tom Eirik. The complement system and toll-like receptors as integrated players in the pathophysiology of atherosclerosis. Atherosclerosis 2015;Volum 241.(2) s.480-494 NLSH NTNU OUS UiO UiT

Johansson, Ida; Monsen, Vivi Anita Talstad; Pettersen, Kristine; Mildenberger, Jennifer; Misund, Kristine; Kaarniranta, Kai; Schønberg, Svanhild Margrethe Arentz; Bjørkøy, Geir. The marine n-3 PUFA DHA evokes cytoprotection against oxidative stress and protein misfolding by inducing autophagy and NFE2L2 in human retinal pigment epithelial cells. Autophagy 2015;Volum 11.(9) s.1636-1651 HIST NTNU

Jung, Kwan-Young; Wang, Huabo; Teriete, Peter; Yap, Jeremy L; Chen, Lijia; Lanning, Maryanna E; Hu, Angela; Lambert, Lester J; Holien, Toril; Sundan, Anders; Cosford, Nicholas D P; Prochownik, Edward V; Fletcher, Steven. Perturbation of the c-Myc-Max Protein-Protein Interaction via Synthetic -Helix Mimetics. Journal of Medicinal Chemistry 2015;Volum 58.(7) s.3002-3024 NTNU

Khan, Faraz Hameed; Pharo, Anne Margrethe; Lindstad, Julie Katrine; Mollnes, Tom Eirik; Tønnessen, Tor Inge; Pischke, Søren Erik. Effect of Perfusion Fluids on Recovery of Inflammatory Mediators in Microdialysis. Scandinavian Journal of Immunology 2015;Volum 82.(5) s.467-475 NLSH NTNU OUS UiO UiT

Klein, Dionne; Skjesol, Astrid; Kers-Rebel, Esther D.; Sherstova, Tatyana; Sporsheim, Bjørnar; Egeberg, Kjartan Wøllo; Stokke, Bjørn Torger; Espevik, Terje; Husebye, Harald. CD14, TLR4 and TRAM Show Different Trafficking Dynamics During LPS Stimulation. Traffic : the International Journal of Intracellular Transport 2015;Volum 16.(7) s.677-690 NTNU

Landsem, Anne; Fure, Hilde; Christiansen, Dorte; Nielsen, Erik Waage; Østerud, Bjarne; Mollnes, Tom Eirik; Brekke, Ole Lars. The key roles of complement and tissue factor in Escherichia coli-induced coagulation in human whole blood. Clinical and Experimental Immunology 2015 Volum 182.(1) s.81-89 UIN NLSH NTNU OUS UiO UiT

Lau, Corinna; Nygård, Ståle; Fure, Hilde; Olstad, Ole Kristoffer; Holden, Marit; Lappegård, Knut Tore; Brekke, Ole Lars; Espevik, Terje; Hovig, Johannes Eivind; Mollnes, Tom Eirik. CD14 and complement crosstalk and largely mediate the transcriptional response to Escherichia coli in human whole blood as revealed by DNA microarray. PLoS ONE 2015;Volum 10.(2) NLSH NR NTNU OUS UiO UiT

Lau, Corinna; Olstad, Ole Kristoffer; Holden, Marit; Nygård, Ståle; Fure, Hilde; Lappegård, Knut Tore; Brekke, Ole Lars; Espevik, Terje; Hovig, Johannes Eivind; Mollnes, Tom Eirik. Gene expression profiling of Gram-negative bacteria-induced inflammation in human whole blood: The role of complement and CD14-mediated innate immune response. Genomics Data 2015;Volum 5. s.176-183 NLSH NR NTNU OUS UiO UiT

Lindenskov, Paal Helge H.; Castellheim, Albert; Saugstad, Ola Didrik; Mollnes, Tom Eirik. Meconium aspiration syndrome: Possible pathophysiological mechanisms and future potential therapies. Neonatology 2015;Volum 107.(3) s.225-230 NLSH NTNU OUS UiO UiT

Marty-Roix, Robyn; Vladimer, Gregory; Pouliot, Kimberly; Weng, Dan; Buglione-Corbett, Rachel; West, Kim; MacMicking, John; Chee, Jonathan; Wang, Shixia; Lu, Shan; Lien, Egil. Identification of QS-21 as an inflammasome-activating molecular component of saponin adjuvants. Journal of Biological Chemistry 2015;Volum 291.(3) s.1123-1136 NTNU

Morgan, Linda; McGinnis, Ralph; Steinthorsdottir, Valgerdur; Svyatova, Gulnara; Zakhidova, Nodira; Lee, Wai Kwong; Iversen, Ann-Charlotte; Magnus, Per; Walker, James; Casas;,Juan Pablo; Sultanov, Saidazim; Laivuori, Hannele; on behalf of the. InterPregGen Consortium. Clinical features of preeclampsia in. 2613 Central Asian women and babies recruited for genetic studies.

Nilsen, Nadra; Gregory I., Vladimer; Stenvik, Jørgen; Ørning, Mathias Pontus; Zeid-Kilani, Maria Vanessa; Bugge, Marit; Bergstrøm, Bjarte; Conlon, Joseph; Husebye, Harald; Amy, Hise; Fitzgerald, Katherine A.; Espevik, Terje; Lien, Egil. A role for the adaptor proteins TRAM and TRIF in toll-like receptor 2 signaling. Journal of Biological Chemistry 2015;Volum 290.(6) s.3209-3222 NTNU

Niyonzima, Nathalie; Samstad, Eivind; Aune, Marie Hjelmseth; Ryan, Liv; Bakke, Siril Skaret; Rokstad, Anne Mari; Wright,

Samuel; Damås, Jan Kristian; Mollnes, Tom Eirik; Latz, Eicke; Espevik, Terje. Reconstituted high-density lipoprotein attenuates cholesterol crystal-induced inflammatory responses by reducing complement activation. Journal of Immunology 2015;Volum 195.(1) s.257-264 HMR NLSH NTNU OUS UiO UiT

Olsen, Oddrun Elise; Wader, Karin Fahl; Hella, Hanne; Mylin, Anne K.; Turesson, Ingemar; Nesthus, Ingerid; Waage, Anders; Sundan, Anders; Holien, Toril. Activin A inhibits BMP-signaling by binding ACVR2A and ACVR2B. Cell Communication and Signaling 2015;Volum 13.(1) s.27 HAUKELAND NTNU STO

Otterdal, Kari; Haukeland, John Willy; Yndestad, Arne; Dahl, Tuva Børresdatter; Holm, Sverre; Segers, Filip; Gladhaug, Ivar Prydz; Zbigniew, Konopski; Damås, Jan Kristian; Halvorsen, Bente; Aukrust, Pål. Increased serum levels of LIGHT/TNFSF14 in nonalcoholic fatty liver disease: Possible role in hepatic inflammation. Clinical and Translational Gastroenterology 2015;Volum 6:e95. NTNU OUS STO UiO

Pabalan, Noel; Jarjanazi, H; Sun, Chen; Iversen, Ann-Charlotte. Meta-analysis of the human leukocyte antigen-G (HLA-G) 14bp insertion/deletion polymorphism as a risk factor for preeclampsia. Tissue Antigens 2015;Volum 86.(3) s.186-194 HAUKELAND NTNU

Paulsen, Julie; Mehl, Arne; Askim, Åsa Susanne; Solligård, Erik; Åsvold, Bjørn Olav; Damås, Jan Kristian. Epidemiology and outcome of Staphylococcus aureus bloodstream infection and sepsis in a Norwegian county 1996-2011: An observational study. BMC Infectious Diseases2015 ;Volum 15.(1) HNT NTNU STO

Pettersen, Kristine; Monsen, Vivi Anita Talstad; Pettersen, Caroline Hild; Overland, Hilde Bremseth; Pettersen, Grete Klippenvåg; Samdal, Helle; Tesfahun, Almaz Nigatu; Lundemo, Anne Gøril; Bjørkøy, Geir; Schønberg, Svanhild Margrethe Arentz. DHA-induced stress response in human colon cancer cells - Focus on oxidative stress and autophagy. Free Radical Biology & Medicine 2015;Volum 90. s.158-172 HIST NTNU

Prebensen, Christian; Ueland, Thor; Michelsen, Annika; Lind, Andreas; Pettersen, Frank Olav; Mollnes, Tom Eirik; Aukrust, Pål; DyrholRiise, Anne Ma; Kvale, Dag. High MIP-1b Levels in Plasma Predict Long-Term Immunological Nonresponse to Suppressive Antiretroviral Therapy in HIV Infection. Journal of Acquired Immune Deficiency Syndromes 2015;Volum 69.(4) s.395-402 NLSH NTNU OUS UiO UiT

Raiborg, Camilla; Wenzel, Eva; Stenmark, Harald Alfred. ER-endosome contact sites: Molecular compositions and functions. EMBO Journal 2015;Volum 34.(14) s.1848-1858 NTNU OUS UiO

Rustad, Even Holth; Dai, Hong Yan; Hov, Håkon; Coward, Eivind; Beisvag, Vidar; Myklebost, Ola; Hovig, Johannes Eivind; Nakken, Sigve; Vodak, Daniel; Meza, Leonardo Zepeda; Sandvik, Arne Kristian; Wader, Karin Fahl; Misund, Kristine; Sundan, Anders; Aarset, Harald; Waage, Anders. BRAF V600E mutation in early-stage multiple myeloma: good response to broad acting drugs and no relation to prognosis. Blood Cancer Journal 2015;Volum 15. NTNU OUS STO UiO

Sharma, Shruti; Campbell, Allison M; Chan, Jennie; Schattgen, Stefan A; Orlowski, Gregory M; Nayar, Ribhu; Huyler, Annie H; Nundel, Kerstin; Mohan, Chandra; Berg, Leslie J; Shlomchik, Mark J; Marshak-Rothstein, Ann; Fitzgerald, Katherine A.. Suppression of systemic autoimmunity by the innate immune adaptor STING. Proceedings of the National Academy of Sciences of the United States of America 2015;Volum 112.(7) s.E710-E717 NTNU

Skarpengland, Tonje; Laugsand, Lars Erik; Janszky, Imre; Gomez, Luisa Fernanda Luna; Halvorsen, Bente; Platou, Carl Geoffrey Parrinder; Wang, Wei; Vatten, Lars Johan; Damås, Jan Kristian; Aukrust, Pål; Bjørås, Magnar; Åsvold, Bjørn Olav. Genetic variants in the DNA repair gene NEIL3 and the risk of myocardial infarction in a nested case-control study. The HUNT Study. DNA Repair 2015;Volum 28. s.21-27 HNT NTNU OUS STO UiO

Skjeflo, Espen Waage; Sagatun, Caroline; Dybwik, Knut; Aam, Sturla; Urving, Sven Haakon; Nunn, Miles A.; Fure, Hilde; Lau, Corinna; Brekke, Ole Lars; Huber-Lang, Markus; Espevik, Terje; Barratt-Due, Andreas; Nielsen, Erik Waage; Mollnes, Tom Eirik. Combined inhibition of complement and CD14 improved outcome in porcine polymicrobial sepsis. Critical Care 2015;Volum 19:415. UIN NLSH NTNU OUS UiO UiT

Skovdahl, Helene Kolstad; Granlund, Atle Van Beelen; Østvik, Ann Elisabet; Bruland, Torunn; Bakke, Ingunn; Torp, Sverre Helge; Damås, Jan Kristian; Sandvik, Arne Kristian. Expression of CCL20 and its corresponding receptor CCR6 is enhanced in active inflammatory bowel disease, and TLR3 mediates CCL20 expression in colonic epithelial cells. PLoS ONE 2015;Volum 10:e0141710.(11) NTNU STO

Sponaas, Anne-Marit; Moen, Siv Helen; Liabakk, Nina-Beate; Feyzi, Emadoldin; Holien, Toril; Kvam, Solveig; Grøseth, Lill Anny Gunnes; Størdal, Berit Fladvad; Buene, Glenn; Espevik, Terje; Waage, Anders; Standal, Therese; Sundan, Anders. The proportion of CD16+CD14dim monocytes increases with tumor cell load in bone marrow of patients with multiple myeloma. Immunity,Inflammation and Disease 2015;Volum 3.(2) s.94-102 NTNU STO

Sponaas, Anne-Marit; Nejati Moharrami, Neda; Feyzi, Emadoldin; Standal, Therese; Rustad, Even Holth; Waage, Anders; Sundan, Anders. PDL1 expression on plasma and dendritic cells in myeloma bone marrow suggests benefit of targeted anti PD1-PDL1 therapy. PLoS ONE 2015;Volum 10:e0139867.(10) NTNU STO

Tangerås, Line Haugstad; Austdal, Marie; Skråstad, Ragnhild; Salvesen, Kjell Åsmund; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte. Distinct First Trimester Cytokine Profiles for Gestational Hypertension and Preeclampsia. Arteriosclerosis, Thrombosis and Vascular Biology 2015;Volum 35.(11) s.2478-2485 NTNU STO

Tangerås, Line Haugstad; Stødle, Guro; Silva, Gabriela; Thomsen, Liv Cecilie Vestrheim; Gierman, Lobke; Skei, Bente; Collett, Karin; Myklebost, Merete; Beversmark, Anne Lise; Skråstad, Ragnhild; Austgulen, Rigmor; Bjørge, Line; Iversen, Ann-Charlotte. The inflammatory role of HMGB1 in preeclampsia. Pregnancy Hypertension 2015;Volum 5. s.229 HAUKELAND NTNU STO UiB

Thomsen, Liv Cecilie Vestrheim; McCarthy, Nina; Melton, Philip E.; Cadby, Gemma; Austgulen, Rigmor; Moses, Eric; Bjørge, Line; Iversen, Ann-Charlotte. Identifying a novel link between preeclampsia and chronic hypertension in the MTHFR gene using the population based Norwegian HUNT Study. Pregnancy Hypertension 2015;Volum 5. s.243-244 NTNU UiB

Thomsen, Liv Cecilie Vestrheim; McCarthy, Nina; Melton, Philip E.; Tollaksen, Kjersti; Lyslo, Ingvill; Solberg, Per; Roten, Linda Tømmerdal; Nygård, Ottar; Cadby, Gemma; Austgulen, Rigmor; Moses, Eric; Iversen, Ann-Charlotte; Bjørge, Line. A genetic connection between preeclampsia and chronic hypertension in Norwegian families. Pregnancy Hypertension 2015;Volum 5. s.138-139 HNT NTNU SUS UiB UIS

Thomsen, Liv Cecilie Vestrheim; Melton, Philip E.; Tollaksen, Kjersti; Lyslo, Ingvill; Roten, Linda Tømmerdal; Odland, Maria Lisa; Strand, Kristin Melheim; Nygård, Ottar; Sun, Chen; Iversen, Ann-Charlotte; Austgulen, Rigmor; Moses, Eric; Bjørge, Line. Refined phenotyping identifies links between preeclampsia and related diseases in a Norwegian preeclampsia family cohort. Journal of Hypertension 2015;Volum 33.(11) s.2294-2302 HAUKELAND NTNU SUS UiB

Tian, Erming; Børset, Magne; Sawyer, Jeffrey R; Brede, Gaute; Våtsveen, Thea Kristin; Hov, Håkon; Waage, Anders; Barlogie, Bart; Shaughnessy, John D.; Epstein, JS; Sundan, Anders. Allelic mutations in noncoding genomic sequences construct novel transcription factor binding sites that promote gene overexpression. Genes, Chromosomes and Cancer 2015;Volum 54.(11) s.692-701 NTNU STO

Vanaja, Sivapriya K.; Rathinam, Vijay A.K.; Fitzgerald, Katherine A. Mechanisms of inflammasome activation: Recent advances and novel insights. Trends in Cell Biology 2015;Volum 25.(5) s.308-315 NTNU

Vange, Pål; Bruland, Torunn; Beisvag, Vidar; Erlandsen, Sten Even; Flatberg, Arnar; Doseth, Berit; Sandvik, Arne Kristian; Bakke, Ingunn. Genome-wide analysis of the oxyntic proliferative isthmus zone reveals ASPM as a possible gastric stem/progenitor cell marker overexpressed in cancer. Journal of Pathology 2015 (237) s.447-459 NTNU STO

Vatn, Morten H; Sandvik, Arne Kristian. Inflammatory bowel disease. Scandinavian Journal of Gastroenterology 2015;Volum 50.(6) s.748-762 NTNU OUS STO UiO

Vietri, Marina; Schink, Kay Oliver; Campsteijn, Coen; Wegner, Catherine E Sem; Schultz, Sebastian; Christ, Liliane Florence; Bratlie, Sigrid; Brech, Andreas; Raiborg, Camilla; Stenmark, Harald. Spastin and ESCRT-III coordinate mitotic spindle disassembly and nuclear envelope sealing. Nature 2015;Volum 522.(7555) s.231-235 NTNU OUS UiO

Volokhina, Elena B.; van de Kar, Nicole C.A.J.; Bergseth, Grethe; van der Velden, Thea J.A.M.; Westra, Dineke; Wetzels, Jack F.M.; van den Heuvel, Lambertus P.; Mollnes, Tom Eirik. Sensitive, reliable and easy-performed laboratory monitoring of eculizumab therapy in atypical hemolytic uremic syndrome. Clinical Immunology 2015;Volum 160.(2) s.237-243 NLSH NTNU OUS UiO UiT

Wang, Huabo; Teriete, Peter; Hu, Angela; Raveendra-Panickar, Dhanya; Pendelton, Kelsey; Lazo, John S; Eiseman, Julie; Holien, Toril; Misund, Kristine; Oliynyk, Ganna; Arsenian-Henriksson, Marie; Cosford, Nicholas DP; Sundan, Anders; Prochownik, Edward V. Direct inhibition of c-Myc-Max heterodimers by celastrol and celastrol-inspired triterpenoids. OncoTarget 2015;Volum 6.(32) s.32380-32395 NTNU

Wergeland, Ida; Pullar, Nadine Durema; Assmus, Jörg; Ueland, Thor; Tonby, Kristian; Feruglio, Siri; Kvale, Dag; Damås, Jan Kristian; Aukrust, Pål; Mollnes, Tom Eirik; Dyrhol-Riise, Anne Ma. IP-10 differentiates between active and latent tuberculosis irrespective of HIV status and declines during therapy. Journal of Infection 2015;Volum 70.(4) s.381-391 HAUKELAND NLSH NTNU OUS STO UiB UiO UiT UNN

Westhrin, Marita; Moen, Siv Helen; Holien, Toril; Mylin, Anne K.; Heickendorff, Lene; Olsen, Oddrun Elise; Sundan, Anders; Turesson, Ingemar; Gimsing, Peter; Waage, Anders; Standal, Therese. Growth differentiation factor 15 (GDF15) promotes osteoclast differentiation and inhibits osteoblast differentiation and high serum GDF15 levels are associated with multiple myeloma bone disease. Haematologica 2015;Volum 100.(12) s. e511-e514 NTNU

Westhrin, Marita; Xie, Minli; Olderøy, Magnus Ø.; Sikorski, Pawel; Strand, Berit Løkensgard; Standal, Therese. Osteogenic differentiation of human mesenchymal stem cells in mineralized alginate matrices. PLoS ONE 2015;Volum 10.(3) NTNU

Wilks, Jessica; Lien, Egil; Jacobson, Amy N; Fischbach, Michael A.; Qureshi, Nilofer; Chervonsky, Alexander V; Golovkina, Tatyana V. Mammalian Lipopolysaccharide Receptors Incorporated into the Retroviral Envelope Augment Virus Transmission. Cell Host and Microbe 2015;Volum 18.(4) s.456-462 NTNU

Williams, Nicholas; Dudbridge, Frank; Chapell, Sally; Iversen, Ann-Charlotte; Franklin, Chris; McGinnis, Ralph; The InterPregGen Consortium, on behalf of. Investigation of the genetics of preeclampsia and its relationship with other phenotypes. European Journal of Human Genetics 2015;Volum 23. s.65 NTNU

Wyller, Vegard Bruun; Sørensen, Øystein; Sulheim, Dag; Fagermoen, Frode Even; Ueland, Thor; Mollnes, Tom Eirik. Plasma cytokine expression in adolescent chronic fatigue syndrome. Brain, behavior, and immunity 2015;Volum 46. s.80-86 AHUS NLSH NTNU OUS SI UiO UiT

Ystgaard, Martin Bogale; Sejersted, Yngve; Løberg, Else Marit; Lien, Egil; Yndestad, Arne; Saugstad, Ola Didrik. Early upregulation of NLRP3 in the brain of neonatal mice exposed to hypoxia-ischemia: No early neuroprotective effects of NLRP3 deficiency. Neonatology 2015;Volum 108. s.211-219 NTNU OUS UiO

Zub, Kamila; Sousa, Mirta; Sarno, Antonio; Sharma, Animesh; Dikic, Aida; Rao, Shalini; Young, Clifford; Aas, Per Arne; Ericsson, Ida; Sundan, Anders; Jensen, Ole Nørregaard; Slupphaug, Geir. Modulation of cell metabolic pathways and oxidative stress signaling contribute to acquired Melphalan resistance in multiple myeloma cells. PLoS ONE 2015;Volum 10.(3) NTNU

THESIS

Austdal, Marie. Biomarkers for prediction and characterization of preeclampsia using magnetic resonance metabolomics. NTNU 2015

Johansson, Ida. A role of Autophagy in Disease Prevention and Drug Resistance. NTNU 2015

Niyonzima, Nathalie. Role of the complement system in inflammatory responses to cholesterol crystals. NTNU 2015

Samstad, Eivind. Molecular Mechanisms of NLRP3 Inflammasome activation by Crystalline Material. NTNU 2015

Kristin Melheim Strand. Markers of placental insufficiency: etiology and the risk of cerebral palsy - Population based studies of preeclampsia, low birth weight, and abnormal placental weight. NTNU 2015

Tangerås, Line Haugstad. Toll-like receptors and inflammation in pregnancy. NTNU 2015

Liv Cecilie Thomsen. Preeclampsia: Specific genetic risk factors and shared predisposition with cardiovascular disease. UiB og NTNU 2015

Westhrin, Marita. Beauty and the Beast - The Multifaceted Potential of Mesenchymal Stem Cells in Bone Health and Disease. NTNU 2015

ACADEMIC PRESENTATIONS

Arlov, Øystein; Aachmann, Finn L.; Sundan, Anders; Espevik, Terje; Skjåk-Bræk, Gudmund. Heparin Analogs from Sulfated Alginates. 8th European Symposium on Bioploymers; 2015-09-15 - 2015-09-18 NTNU

Askim, Åsa Susanne; Mehl, Arne; Paulsen, Julie; Åsvold, Bjørn Olav; Damås, Jan Kristian; Solligård, Erik. Epidemiology and outcome in adult patients with Streptococcus pneumoniae sepsis in Nord-Trøndelag 1993-2011: An observational study. Forskningskonferanse; 2015-06-09 - 2015-06-10 NTNU

Aune, Marie Hjelmseth; Niyonzima, Nathalie; Samstad, Eivind; Bakke, Siril Skaret; Ryan, Liv; Rokstad, Anne Mari; Nymo, Stig Haugset; Damås, Jan Kristian; Latz, Eicke; Mollnes, Tom Eirik; Espevik, Terje. Crystalline cholesterol is found in atherosclerotic plaques and induces complement mediated inflammation. 15th European Meeting on Complement in Human Disease; 2015-06-27 - 2015-06-30 NTNU UiO UiT

Aune, Marie Hjelmseth; Niyonzima, Nathalie; Samstad, Eivind; Nymo, Stig; Ryan, Liv; Bakke, Siril Skaret; Damås, Jan Kristian; Latz, Eicke; Mollnes, Tom Eirik; Espevik, Terje. Cholesterol crystals activate the complement system to induce crystal phagocytosis and inflammation. 17TH International Congress on Atherosclerosis 2015; 2015-05-22 - 2015-05-26 NTNU UiO

Austdal, Marie; Tangerås, Line Haugstad; Skråstad, Ragnhild; Salvesen, Kjell Å; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte. First trimester urine and serum metabolomics to predict preeclampsia and gestational hypertension. EUROISSHP 2015; 2015-09-24 - 2015-09-26 NTNU STO

Austdal, Marie; Tangerås, Line; Skråstad, Ragnhild Bergene; Salvesen, Kjell Å; Austgulen, Rigmor; Iversen, Ann-Charlotte; Bathen,Tone Frost. First Trimester Urine and Serum Metabolomics to Predict Preeclampsia and Gestational Hypertension. 51st Norwegian Biochemical Society Contact Meeting; 2015-02-09 - 2015-02-13 NTNU STO

Austdal, Marie; Thomsen, Liv Cecilie Vestrheim; Tangerås, Line; Skei, Bente; Mathew, Seema; Bjørge, Line; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte. Metabolic profiles of placenta in preeclampsia using HR-MAS MRS metabolomics. Regional forskningskonferanse i Helse Midt-Norge; 2015-06-09 - 2015-06-10 HAUKELAND NTNU STO UiB

Bakke, Siril Skaret; Aune, Marie Hjelmseth; Niyonzima, Nathalie; Ryan, Liv; Damås, Jan Kristian; Latz, Eicke; Mollnes, Tom Eirik; Espevik, Terje. - Cyclodextrin reduces cholesterol crystal-induced inflammation through modulating omplement activation. Toll 2015; 2015-09-30 - 2015-10-03 NTNU UiO

Bakke, Siril Skaret; Aune, Marie Hjelmseth; Niyonzima, Nathalie; Ryan, Liv; Damås, Jan Kristian; Mollnes, Tom Eirik; Latz, Eicke; Espevik, Terje. Beta-cyclodextrin reduces cholesterol crystal-induced inflammation through modulating complement activation. European Meeting on Complement in Human Disease; 2015-06-27 - 2015-06-30 NTNU UiO

Bergstrøm, Bjarte; Aune, Marie Hjelmseth; Awuh, Jane Atesoh; Kojen, June Frengen; Ryan, Liv; Flo, Trude Helen; Mollnes, Tom Eirik; Stenvik, Jørgen; Espevik, Terje. TLR8 is a sensor for Staphylococcus aureus RNA in human monocytes and macrophages. 12th International Conference on Innate Immunity; 2015-06-19 - 2015-06-24 NTNU UiO

Bergstrøm, Bjarte; Ryan, Liv; Espevik, Terje; Stenvik, Jørgen. Emerging behaviour in multi-PRR signaling. TOLL 2015; 2015-09-30 - 2015-10-03 NTNU

Bugge, Marit; Solli, Helene; Kjønstad, Ingrid F.; Stenvik, Jørgen; Espevik, Terje; Nilsen, Nadra J. Metastatic Intestinal Epithelial Cells Express Surface Toll-Like Receptor 3. Toll 2015 Targeting Innate Immunity; 2015-09-30 - 2015-10-03 NTNU

Egeberg, Kjartan Wøllo; Sporsheim, Bjørnar; Espevik, Terje. STED microscopy of ASC speck inflammasome formation in mouse macrophages. EMBL Symposium "Seeing is Believing"; 2015-10-06 - 2015-10-10 NTNU

Flo, Trude Helen; Awuh, Jane Atesoh; Haug, Markus; Damås, Jan Kristian; Marstad, Anne; Steigedal, Magnus; Halaas, Øyvind; Stenvik, Jørgen; Mildenberger, Jennifer. Inflammatory signaling in mycobacterium avium infected human macrophages. Toll 2015: Targeting Innate Immunity; 2015-09-30 - 2015-10-03 HIST NTNU

Flo, Trude Helen; Awuh, Jane Atesoh; Haug, Markus; Steigedal, Magnus; Marstad, Anne; Mildenberger, Jennifer; Damås, Jan Kristian; Halaas, Øyvind; Louet, Claire; Stenvik, Jørgen. Keap1 regulates inflammatory signaling in M. avium infected human macrophages. Keystone symposium: Innate Immunity and Determinants of Microbial Pathogenesis; 2015-04-19 - 2015-05-24 HIST NTNU

Gierman, Lobke; Stødle, Guro; Tangerås, Line Haugstad; Austdal, Marie; Olsen, Guro Dalheim; Follestad, Turid; Skei, Bente; Rian, Kristin; Gundersen, Astrid; Austgulen, Rigmor; Iversen, Ann-Charlotte. Functional screening of Toll-like receptors in seven trophoblast cell lines. EUROISSHP 2015; 2015-09-24 - 2015-09-26 NTNU STO. Awarded 3rd best oral presentation.

Gierman, Lobke; Stødle, Guro; Tangerås, Line Haugstad; Austdal, Marie; Olsen, Guro Dalheim; Follestad, Turid; Skei, Bente; Rian, Kristin; Gundersen, Astrid; Austgulen, Rigmor; Iversen, Ann-Charlotte. Functional screening of Toll-like recep-tors in trophoblast cell lines. NBS contact meeting; 2015-02-10 - 2015-02-13 NTNU STO

Gierman, Lobke; Stødle, Guro; Tangerås, Line Haugstad; Olsen, Guro Dalheim; Austdal, Marie; Follestad, Turid; Skei, Bente; Rian, Kristin; Gundersen, Astrid; Austgulen, Rigmor; Iversen, Ann-Charlotte. Functional screening of Toll-like receptors in trophoblast cell lines. Society for Reproductive Investigation Annual Scientific Meeting; 2015-03-25 -2015-03-28 NTNU STO

Granlund, Atle van Beelen; Flatberg, Arnar; Østvik, Ann Elisabet; Bakke, Ingunn; Bruland, Torunn; Sandvik, Arne Kristian. Antigen presentation activity of the Intestinal Epithelial Cells. AIBD 2015; 2015-12-08 - 2015-12-12 NTNU

Granlund, Atle van Beelen; Thorsvik, Silje; Beisvag, Vidar; Flatberg, Arnar; Bakke, Ingunn; Sandvik, Arne Kristian. Exploring the barrier; RNA sequencing of laser microdissected epithelium from IBD patients. 10th congress of European Crohn's and Colitis Organisation; 2015-02-18 - 2015-02-21 NTNU

Haug, Markus; Ibrahim, Hany; Brede, Gaute; Flo, Trude Helen; Høgset, Anders; Halaas, Øyvind. Photochemical internalization as novel vaccination technology to enhance antigen-specific CD8+ T cell responses. 4th European Congress of Immunology (ECI 2015); 2015-09-06 - 2015-09-09 NTNU

McGinnis, Ralph; Dudbridge, Frank; Lawlor, L; Kemp, Caroline; Iversen, Ann-Charlotte; Franklin, Chris; Williams, Nicholas; on behalf of the InterPregGen Consortium. Investigation of DNA variants responsible for preeclampsia. ASHG 2015 meeting; 2015-10-06 - 2015-10-10 NTNU

Nilsen, Nadra J.; Espevik, Terje; Gjerdingen, Thea Johannne; Bugge, Marit; Kjønstad, Ingrid Fadum. A toll-like receptor 7/8 ligand secreted by myeloma cells induces primary bone marrow stromal cells to produce cytokines that promote myeloma survival. Toll2015 Targeting Innate Immunity; 2015-09-30 - 2015-10-03 NTNU UiO

Nilsen, Nadra J.; Espevik, Terje; Vladimer, G; Stenvik, Jørgen; Orning, M. Pontus A.; Zeid-Kilani, Maria Vanessa; Bugge, Marit; Bergstrøm, Bjarte; Conlon, Joseph; Husebye, Harald; Fitzgerald, Katherine A.; Lien, Egil; Hise, Amy G. The adaptor proteins tram and trif mediate toll-like receptor 2 signaling. Innate Immune Memory; 2015-03-18 - 2015-03-20 NTNU

Nilsen, Nadra J.; Espevik, Terje; Vladimer, G; Ørning, Mathias Pontus; Zeid-Kilani, Maria Vanessa; Bugge, Marit; Bergstrøm, Bjarte; Conlon, Joseph; Husebye, Harald; Hise, Amy G; Fitzgerald, Katherine A.; Lien, Egil. The adaptor proteins tram and trif mediate toll-like receptor 2 signaling. Toll2015 Targeting Innate Immunity; 2015-09-30 - 2015-10-03 NTNU

Rokstad, Anne Mari. The complement c3 deposition depends on the alginate microspheres composition and determinds the cytokine profile. Functional polymers at bio-material interfaces, 79th Prague meeting on macromolecules; 2015-06-28 - 2015-07-02 NTNU

Samstad, Eivind. When the immune system causes damage. NTNU

Silva, Gabriela; Tangerås, Line Haugstad; Stødle, Guro; Thomsen, Liv Cecilie Vestrheim; Gierman, Lobke; Skei, Bente; Austgulen, Rigmor; Bjørge, Line; Iversen, Ann-Charlotte. The inflammatory role of HMGB1 in preeclampsia. NBS møte; 2015-02-09 - 2015-02-13 NTNU STO UiB

Skjesol, Astrid; Patane, Francesco; Yurchenko, Mariya; Aune, Marie Hjelmseth; McCaffrey, Mary; Espevik, Terje; Husebye, Harald. The small GTPase Rab11a and its partner Rab11FIP2 affect TLR4 signaling pathways. TOLL 2015 Targeting innate immunity; 2015-09-30 -2015-10-03 NTNU

Skjesol, Astrid; Patane, Francesco; Yurchenko, Mariya; Aune, Marie Hjelmseth; McCaffrey, Mary; Espevik, Terje; Husebye, Harald. The small GTPase Rab11a and its partner Rab11FIP2 regulate TLR4 signaling pathways. 15th annual meeting of the European Light Microscopy Initiative (ELMI); 2015-05-19 - 2015-05-21 NTNU

Sporsheim, Bjørnar; Egeberg, Kjartan Wøllo; Espevik, Terje. STED microscopy of ASC speck inflammasome formation in mouse macrophages. 15th International ELMI meeting; 2015-05-19 - 2015-05-22 NTNU

Sporsheim, Bjørnar; Egeberg, Kjartan Wøllo; Klein, Dionne; Espevik, Terje. STED microscopy at the Cellular and Molecular Imaging Core facility. NBS kontaktmøte; 2015-02-09 - 2015-02-13 NTNU

Standal, Therese. GDF15 in multiple myeloma. 10th myeloma workshop in Brno; 2015-11-11 - 2015-11-12 NTNU

Stødle, Guro; Silva, Gabriela; Tangerås, Line Haugstad; Thomsen, Liv Cecilie Vestrheim; Lilledahl, Magnus Borstad; Skei, Bente; Collett, Karin; Myklebost, Merete; Austgulen, Rigmor; Aune, Marie Hjelmseth; Bjørge, Line; Iversen, Ann-Charlotte. The NLRP3 inflammasome in placentas from preeclamptic and healthy pregnancies. Toll 2015; 2015-09-30 - 2015-10-03 HAUKELAND NTNU STO UiB

Tangerås, Line Haugstad; Gierman, Lobke; Stødle, Guro; Silva, Gabriela; Thomsen, Liv Cecilie Vestrheim; Skei, Bente; Skråstad, Ragnhild; Austgulen, Rigmor; Bjørge, Line; Iversen, Ann-Charlotte. The inflammatory role of HMGB1 in preeclamptic and normal pregnancies. Toll 2015; 2015-09-30 - 2015-10-03 NTNU STO UiB

Tangerås, Line Haugstad; Stødle, Guro; Silva, Gabriela; Thomsen, Liv Cecilie Vestrheim; Gierman, Lobke; Skei, Bente; Skråstad, Ragnhild; Austgulen, Rigmor; Bjørge, Line; Iversen, Ann-Charlotte. The inflammatory role of HMGB1 in preeclampsia. EUROISSHP 2015; 2015-09-24 - 2015-09-26 NTNU STO UiB

Thomsen, Liv Cecilie Vestrheim; McCarthy, Nina; Melton, Philip E.; Cadby, Gemma; Austgulen, Rigmor; Moses, Eric; Nygård, Ottar; Bjørge, Line; Iversen, Ann-Charlotte. Identifying a novel link between preeclampsia and chronic hypertension in the MTHFR-gene using the population based Norwegian HUNT Study. EUROISSHP 2015; 2015-09-24 - 2015-09-26 NTNU UiB. Awared best poster.

Thorsvik, Silje; Damås, Jan Kristian; Granlund, Atle van Beelen; Flo, Trude Helen; Bakke, Ingunn; Østvik, Ann Elisabet; Sandvik, Arne Kristian. Fecal Neutrophil Gelatinase Associated Lipocalin as a biomarker for Inflammatory Bowel Disease. AIBD 2015; 2015-12-08 - 2015-12-12 NTNU

Westhrin, Marita; Moen, Siv Helen; Holien, Toril; Olsen, Oddrun Elise; Sundan, Anders; Waage, Anders; Standal, Therese. Growth differentiation factor 15 (GDF15) promotes osteoclast differentiation and inhibits osteoblast differentiation and high serum GDF15 levels are associated with multiple myeloma bone disease. 15th international myeloma workshop; 2015-09-23 - 2015-09-25NTNU

Williams, Nicholas; Dubridge, F; Chapell, Sally; Franklin, Chris; Iversen, Ann-Charlotte; Morgan, Linda; McGinnis, Ralph; The InterPregGen Consortium, on behalf of. Investigation of the polygenic genetics of preeclampsia and its relationship with other phenotypes. ESHG Conference; 2015-06-06 - 2015-06-09 NTNU

Østvik, Ann Elisabet; Granlund, Atle van Beelen; Flatberg, Arnar; Damås, Jan Kristian; Bruland, Torunn; Sandvik, Arne Kristian. Waves of epithelial TLR5 and TLR3 signaling in the pathogenesis of inflammatory bowel disease (IBD). TOLL 2015 Targeting Innate Immunity; 2015-09-20 - 2015-10-03 NTNU

FUNDING AND EXPENDITURES 2015

Funding (1000 NOK)	2015
NTNU	21 119
Research Council of Norway (RCN) – Centre of Excellence grant	15 899
Other RCN funding	6 035
Other public funding	17 263
Other private funding	1 220
Total funding	**61 536**

Expenditures (1000 NOK)	2015
Personnel and indirect costs	46 258
Equipment	202
Other operating costs	15 076
Total expenditures	**61 536**

Microscopy photos:
Front page: Ingunn Bakke, IKM and Bjørnar Sporsheim, CEMIR
Page 5: Harald Husebye, CEMIR
Page 6: Kristian Starheim, CEMIR
Page 7: Bjørnar Sporsheim, Ingunn Nervik, Bente Halvorsen, CMIC
Page 8: Markus Haug, CEMIR
Page 9: Gabriela Brettas Silva, CEMIR
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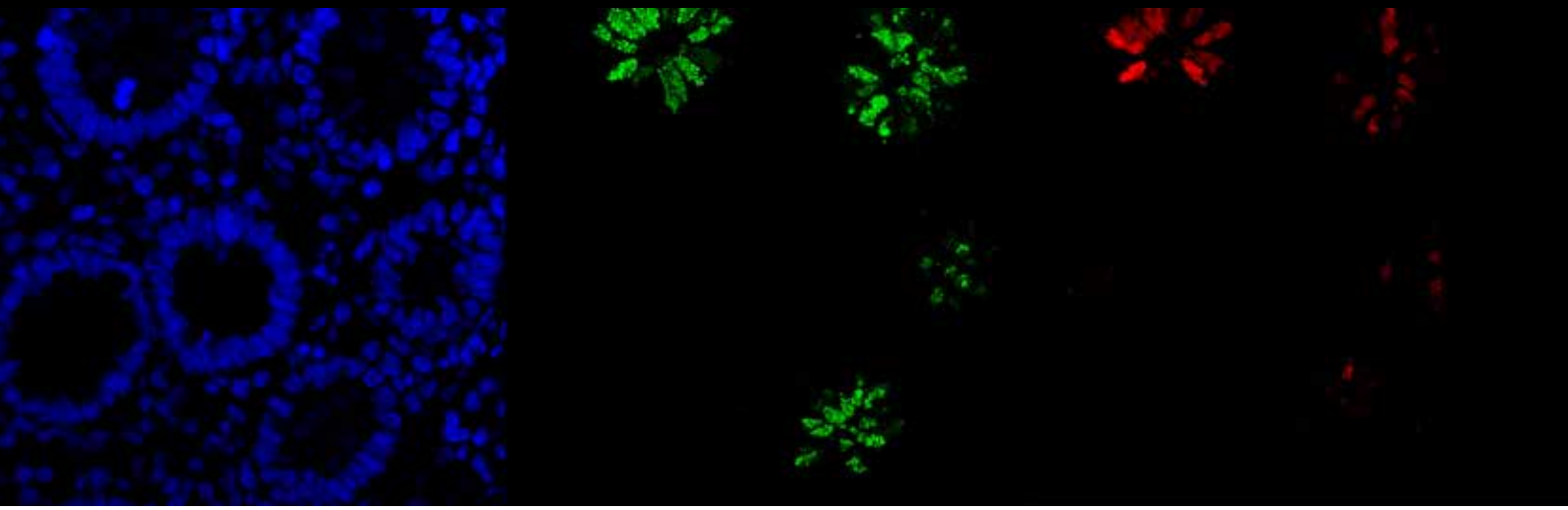

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