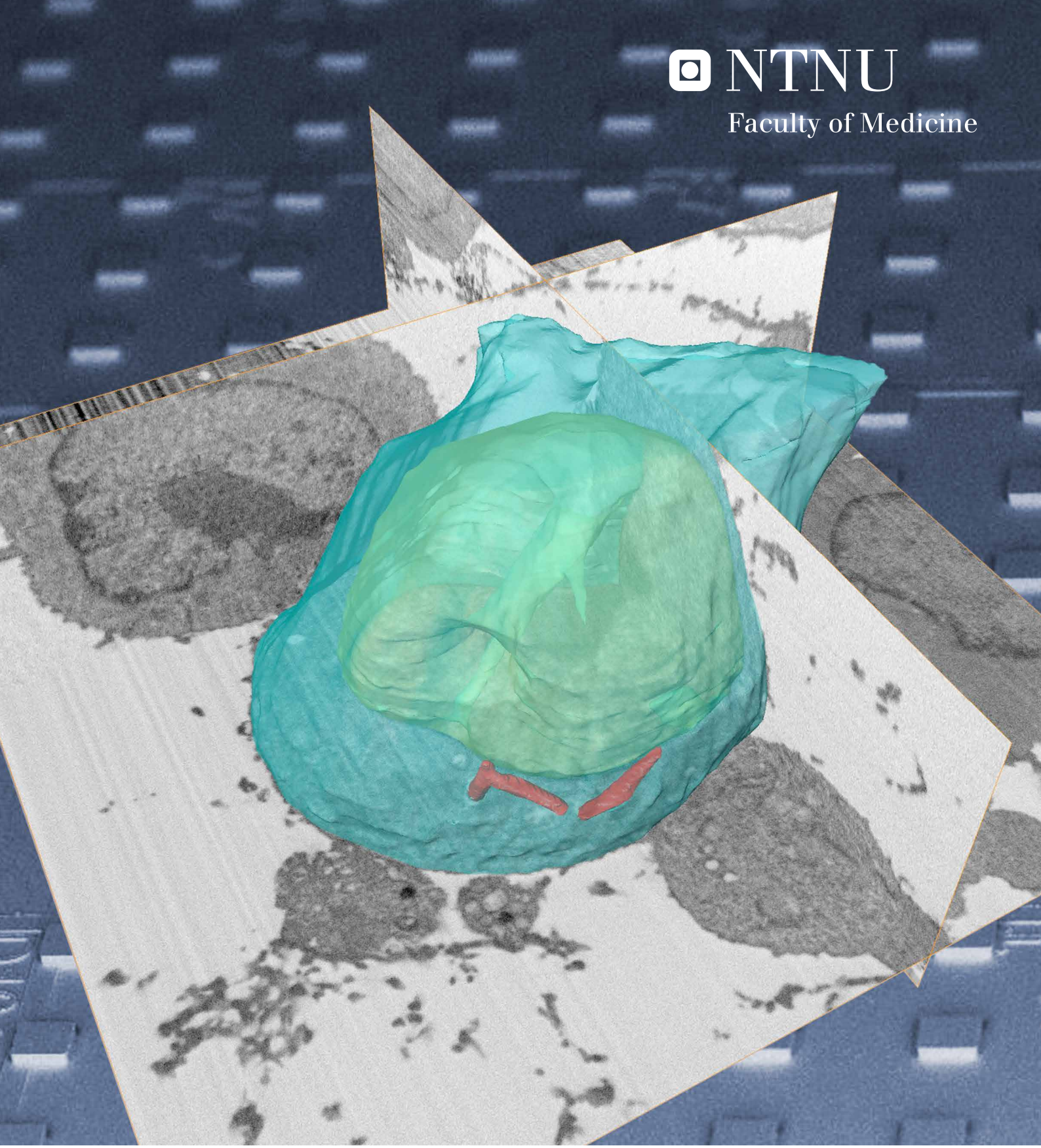

NTNU
Faculty of Medicine

CEMIR
Centre of Molecular Inflammation Research

Annual Report 2013

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Cover photo made by Marianne Sandvold Beckwith: In the background is a Scanning Electron Microscope (SEM) image of a silicon stamp, which can be used to mold aclar films into microwells of size 100µm. The reference system enables localization of cells grown in the aclar wells with both light and electron microscopy. In front is a macrophage infected with *Mycobacterium avium* reconstructed from a Focused Ion Beam (FIB)/SEM tomography experiment, with plasma membrane traced in cyan, nucleus in yellow and bacteria in red. The model is overlaid on the SEM images used for reconstruction.

Director's Comment

CEMIR was established on January 1, 2013 as part of the Research Council of Norway's third round of Centres of Excellence. 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.

A central question in CEMIR's research is how inflammation can be so closely connected to many seemingly different chronic diseases. CEMIR's research programme has a hypothesis that the key to new therapeutic targets for chronic inflammatory diseases can be found in the early stages of the inflammatory response where sensors in the innate immune system are activated.

In its first year CEMIR has emphasized the importance of establishing a unified research group in which multidisciplinary research cooperation is encouraged and stimulated. In June 2014 all CEMIR research activity will be located in the new Knowledge Centre at Øya Campus in Trondheim. The location of the Centre gives us an excellent basis for establishing a unified environment and the exchange of ideas across the research groups. At the same time the Centre remains close to our host department (the Department of Cancer Research and Molecular Medicine) in the neighbouring Gastro Centre and the clinic, St.Olavs University Hospital, which makes it easy to cooperate both organizationally and translationally. The localization of CEMIR in an integrated university hospital environment facilitates translational research on human disease.

CEMIR recruited a number of Norwegian and international researchers during the first year. We also established close collaboration with excellent researchers from other institutions by recruiting six outstanding scientists in the fields of cell biology and innate immunity from universities in Boston, Los Angeles, Bonn and Oslo. They are all high profile scientists that publish their work in leading international journals, and I am very pleased that they all have signed work contracts with CEMIR throughout the project period. They will contribute to the research programme at the Centre, and also supervise our PhD students and postdoctoral fellows who will spend extended periods in their labs.

At the end of 2013, 63 people (including master's students) were associated with the Centre. CEMIR will continue to grow in 2014. We are in the process of recruiting several postdoctoral fellows and PhDs, and we look forward to having even more talented and motivated people in our Centre.

In October 2013, we arranged a scientific opening seminar with contributions from our national and international collaborators. The seminar was a great success with more than 100 participants, including researchers from the universities in Oslo and Bergen.

2013 has been a year with several scientific breakthroughs and findings that can lead to new therapeutic tools for inflammatory diseases. These are some of the highlights:

- In a recent study CEMIR researchers have taken a closer look at the anti-inflammatory effects of High-density lipoprotein (HDL). The study will provide a greater understanding of the mechanisms behind the anti-inflammatory effect of HDL, and has laid the foundation for understanding the regulatory mechanisms that control inflammation in atherosclerosis and other chronic inflammatory diseases.

- Another main finding is that a receptor which is part of the innate immune system, Toll-like receptor 3 (TLR3), appears to be important in the production of cytokines,

chemokines and antibacterial peptides in Inflammatory Bowel Disease (IBD).

- CEMIR researchers have also shown that treatment with inhibitors of CD14 and complement activation components have a good effect on serious infections.

CEMIR initiated two PhD courses in 2013, and yet another will start in 2014. They are all part of NTNU's PhD programme in Molecular Medicine. "Receptor Signaling and Trafficking" is an advanced course that describes the mechanisms of receptor signalling and the most commonly used methods for studying them. The course "Molecular Mechanism of Inflammation" gives an overview of mechanisms and signaling pathways involved in inflammatory processes. The third course "Advanced Cellular Imaging Techniques" will provide the theoretical background for diverse imaging techniques that can be applied to study innate immune activation.

CEMIR researchers have contributed to a large number of scientific papers and outreach activities in 2013. There have been 97 contributions to scientific publications, conferences, presentations and media (including newspapers and blogs).

Three CEMIR PhD students defended their thesis and successfully completed their PhDs in 2013. These were Atle Van Beelen Granlund, Jane Atesoh Awuh and Marte Singsås Dragset. It is a great benefit for CEMIR that all of them will continue their research at CEMIR as postdoctoral fellows.

I am very pleased to conclude that CEMIR has completed a productive and consolidating first year. I feel confident that CEMIR has established a strong foundation to continue the work for novel discoveries in the field of inflammation in the years to come.

Terje Espevik
Centre Director

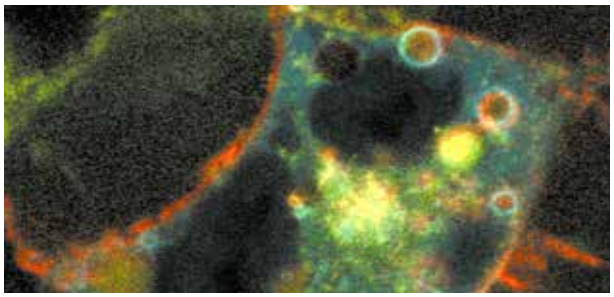
CEMIR is located in the new Knowledge centre at Øya Campus.

CEMIR Research Activity

Toll-Like Receptor Trafficking

Theme Manager:
Professor Terje Espevik

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, though the exact biological effects of these cytokines during bacterial infections are still unclear. The aim of this theme is to find new principles of TLR signaling resulting in type I interferons from endosomes and phagosomes.



Main activities in 2013

In 2013 we have had a focus on the small GTPase Rab11a. We have investigated mechanisms by which Rab 11a and the Rabb11-family interacting proteins (RabFIPs) modulate IFNβ production *E. coli* by specifically focusing on inflammatory signaling events from endosomes and phagosomes. We have also characterized the mechanisms behind *Staphylococcus aureus* – induced IFNβ production in human monocytes. Moreover, we have had a close collaboration with the Mollnes group on a project with the purpose of constructing and characterizing CD14 Abs with minimal ability to activate complement and bind to FcγRs.

Major achievements in 2013

- Showed that Rab11a integrates TRAM trafficking between trans Golgi network and endosome in LPS induced TRAM-TRIF-signaling.
- Demonstrated that *Staphylococcus aureus* induces IFNβ production in human monocytes by a TLR8-TAK1-IKKβ-IRF5 pathway which is antagonized by TLR2 signaling.
- Generated recombinant anti-porcine and anti-human CD14 Abs endowed with the IgG2/IgG4 hybrid Fc region. These Abs are unique tools for future studies of CD14 inhibition using porcine in vivo models, and pave the way for human therapy with CD14 inhibition, preferentially in combination with complement inhibition.

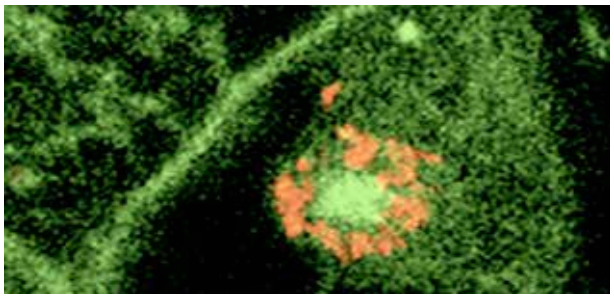
Ambitions for 2014

- To identify the molecular mechanisms of TLR8-TAK1-IKKβ-IRF5 signalling and explore its role in phagocyte activation by different types of bacteria.
- To understand the detailed role of Rab11a and Rab-11FIPs in regulating *E.coli*-induced cytokine responses.
- To establish the role of CD150/SLAM in regulating TLR4 trafficking and *E.coli*-induced cytokine responses.
- To reveal new components that regulate trafficking of TLR9 from endoplasmic reticulum to the endolysosomes.
- To test the efficacy of combined CD14 and complement inhibition in a polymicrobial sepsis study in mice

The Molecular Basis for Inflammasome Activation

Theme Manager:
Professor Egil Lien

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 this theme is focused on describing mechanisms leading to inflammasome activation, and to study implications in infectious and non-infectious inflammation.



Main activities in 2013

The work during this year, the first with CEMIR activities, has focused on describing mechanisms for inflammasome activation induced by *Salmonellae,* and the human-pathogenic *Yersiniae*, these are Gram-negative bacteria containing a type III secretion system. We use *Yersinia pestis*, the causative agent of plague, as a model system for bacterial activation and evasion of immune responses. We have found that IL-18 mediated innate immune defences are critical to limit pneumonia induced by *Y. pestis*, and that NLRP12 and NLRP3 contribute to host resistance in the airways. Furthermore, our results suggest a pathway that mediates rapid cell death upon bacterial infection, which involves kinases RIP1 and RIP3, together with caspase-8. Interestingly, this pathway also appears to control NF-κB activation and inflammasome activation. Other activities have involved studies of the role of NLR proteins in sterile inflammation induced during obesity.

Major achievements in 2013

- Showed that IL-18, NLRP12 and NLRP3 regulate host defenses in the lungs during bacterial infection.
- Our results indicate that NLRP12 and NLRP3 co-operate for optimal resistance to *Y. pestis* in the airways.
- Found that RIP1, RIP3 and caspase-8 regulate inflammasome activation, NF-κB activation and induction of cell death during infection with human-pathogenic *Yersiniae*. *Salmonellae* mainly use other pathways. Mice lacking caspase-8 and RIP3 are highly susceptible to bacterial infection.

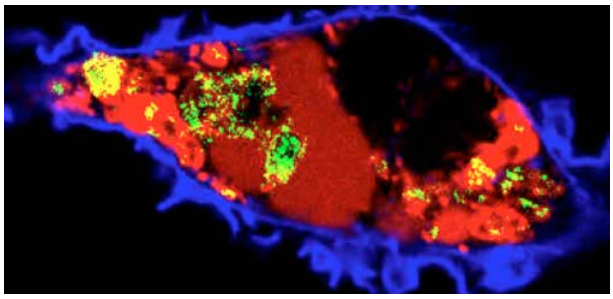
Ambitions for 2014

- Complete studies of inflammasome triggering and implications of this activation during bacterial pneumonia
- Finalize studies of the role of RIP1, RIP3 and caspase-8 in regulation of cell death and innate immune activation after *Yersinia* infection
- Evaluate the broader roles of RIP kinases and caspase-8 in inflammasome activation and cell death mediated by both infectious and non-infectious inflammation.
- Establish novel model systems for immune activation by human-pathogenic *Salmonellae*.

Inflammatory Responses induced by Cholesterol

Theme Manager:
Professor Jan Kristian Damås

High cholesterol levels in blood constitute the most prominent risk factor for atherosclerotic coronary artery disease. Cholesterol itself can cause inflammation in its crystalline form by activating the NLRP3 inflammasome. Priming is needed for NLRP3 activation and one aim of this theme is to uncover the mechanisms by which cholesterol crystals prime monocytes and induce inflammatory responses.



Major achievements in 2013

- Showed that cholesterol crystals induce complement-dependent inflammasome activation and cytokine release.
- Discovered that high-density lipoprotein (HDL) uses transcriptional regulator ATF3 to inhibit TLR-induced inflammatory responses.
- Initiated a clinical study with a interleukin-6 receptor antagonist in patients with myocardial infarction.

Main activities in 2013

In 2013 a research focus has been on the role of complement activation for cholesterol crystal (CC) induced inflammatory responses. We show that CC induced robust complement activation in human serum, revealed by activation products from the alternative and terminal pathways.

Moreover, CC induced cytokine release in whole blood, which were efficiently attenuated by complement inhibitors. Combined C5a and TNF potently primed CC-induced IL-1β release in peripheral mononuclear cells (PBMC) and monocytes by increasing IL-1β transcription. Based on the findings in this study we suggest that complement inhibition might be an interesting therapeutic approach for treatment of atherosclerosis. Moreover, we have initiated the study "Effect of the interleukin-6 receptor antagonist tocilizumab in non-ST elevation myocardial infarction". This is a double-blinded, randomized, placebo controlled study with tocilizumab (RoActemra, 240 mg i.v.) or placebo. Patients (120) have been recruited at two study centres; Oslo University Hospital Rikshospitalet, Oslo and St. Olavs Hospital, Trondheim. Effect of treatment will be assessed by measuring levels of inflammatory cytokines as well as myocardial damage.

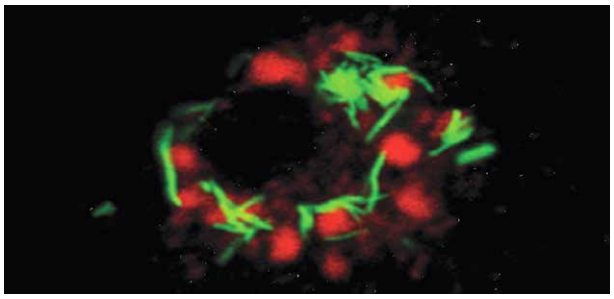
Ambitions for 2014

- To identify and characterize the molecular mechanisms behind the complement activation induced by cholesterol crystals.
- To perform characterisation of the molecular mechanisms underlying the inhibitory effect of HDL on cholesterol crystal-induced inflammation.
- To test the effect of cholesterol crystal dissolution in mouse models of atherosclerosis.
- To establish the role of the coagulation system in cholesterol crystal-induced inflammation.
- To complete a clinical study with an IL-6 receptor antagonist for treatment of atherosclerosis.

Inflammation & Autophagy

Cells frequently experience stress with increased levels of reactive oxygen species (ROS). ROS may contribute in activation of the NLR inflammasomes or induction of autophagy, an evolutionary conserved catabolic process in where damaged organelles, protein aggregates or intracellular pathogens are enclosed into an autophagosome and degraded after fusion to lysosomes. Autophagy is essential for cellular homeostasis and defects lead to disorders like degenerative diseases, cancers, infections, inflammation and cardiovascular disease. In CEMIR theme 4 we aim to define novel relations between oxidative stress, signaling through pattern recognition receptors and autophagy in inflammatory diseases, including mycobacterial infections.

Theme Manager:
Trude Helen Flo, Senior Research Scientist



Main activities in 2013

Several projects were initiated and progressed in 2013. We were investigating the role of a key oxidative stress protein in mycobacterial infections, a work to be continued in 2014 and extended to also include patients with bacterial sepsis. We also worked on mycobacterial virulence factors, including iron acquisition systems and the ESX-3 secretion system, and on high-resolution imaging techniques for visualization of pathogenic mycobacteria within host macrophages. In several separate projects we studied the role of autophagy in prevention and development of age-related disease, and if n-3 polyunsaturated fatty acids (PUFAs) regulate oxidative stress and autophagy. In 2013 we recruited five PhD students and one post doc, and seven master students are currently working on theme 4 projects. There were two PhD dissertations within the theme in 2013.

Major achievements in 2013

- Characterized a role for an oxidative stress protein in regulation of inflammatory signaling and killing of pathogenic mycobacteria in host macrophages.
- Developed tools for inducible expression of proteins in mycobacteria.
- Established protocols to facilitate studies of intracellular processes in mycobacterium-infected macrophages using Focused Ion-Beam Scanning Electron Microscopy (FIB-SEM) at NTNU nanolab.
- Elucidated that n-3 polyunsaturated fatty acids (PUFAs) induce changes in autophagy and the oxidative stress defense system coordinated by Nrf2

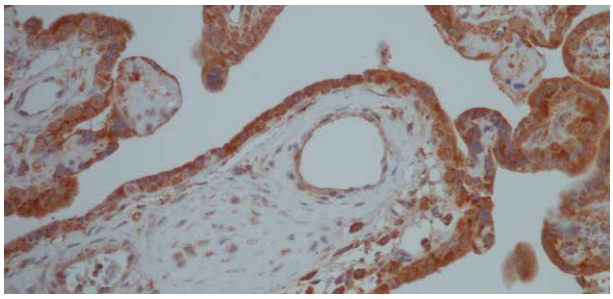
Ambitions for 2014

- Dissect mechanisms of regulation by the oxidative stress protein and possible clinical relevance in sepsis patients.
- To visualize pathogenic mycobacteria in relation to autophagosomes and lysosomes within host macrophages using correlative light and FIB-SEM microscopy techniques.
- Elucidate on the role of lipid metabolism in HIV disease susceptibility and progression.
- Elucidate on the role of autophagy in macrophages and T-cells during infection.
- Establish routines and training to work with M. tuberculosis in the new Biosafety Level 3 lab to be opened in 2014 in Kunnskapssenteret.
- Dissect the relation between oxidative stress, autophagy and the anti-inflammatory roles of n-3 PUFAs and establish if n-3 PUFAs can affect the development of proteinopathies.
- Investigate the putative role of systemically activated autophagy in patients that develops cancer cachexia.
- Establish cell models that will allow screening of compounds, conditions and factors that affect autophagy.

Inflammation underlying Atherosclerosis and Pregnancy

Cardiovascular disease (CVD) is a major cause of human illness and death worldwide where inflammation plays a key role. Women with preeclampsia have increased risk for laterCVD, suggesting shared underlying mechanisms for disease. Soluble inflammatory mediators like microbial products, oxidized lipoproteins and cholesterol crystals are implicated, but with unknown molecular action. We hypothesize that pattern recognition receptor (PRR) ligands are initiators of both the pathogenesis and gender-specificity of CVD. In CEMIR theme 5A we aim to investigate how PRR-initiated inflammatory processes of preeclampsia in pregnancy are related to later development of CVD.

Theme Manager:
Ann-Charlotte Iversen, Senior Researcher



Main activities in 2013

Several projects in theme 5A have had a good start in 2013 and the work includes collection and clinical phenotyping of pregnancy-related Biobanks, studies of the phenotypic, metabolomic and genetic relation between development of preeclampsia and cardiovascular diseases, as well as molecular analyses of PRR involvement in the inflammation of pregnancy. Overall, this work has added new knowledge to the phenotypic relation between development of preeclampsia and CVDs, and the discovery of a broad PRR expression in fetal trophoblasts of early pregnancy, establishes the importance of further unraveling the role of PRRs in pathological pregnancies.

Major achievements in 2013

- Discovered broad Toll-like receptor expression and functions in primary trophoblasts, defining an immunologic role for trophoblasts in placental development and pregnancy.
- Established use of NMR profiling of maternal serum and urine for detailed detection of pregnancy and disease related metabolic variations. Revealed changes in lipid metabolites relating preeclampsia to cardiovascular disease.
- Found that preeclamptic risk genes are associated with cardiovascular risk traits in preeclamptic mothers and children born from preeclamptic pregnancies.
- A serologic study of cytomegalovirus infection in pregnant Norwegian women revealed strong geographical differences, and that cytomegalovirus seroprevalence in Norway seems to be increasing.

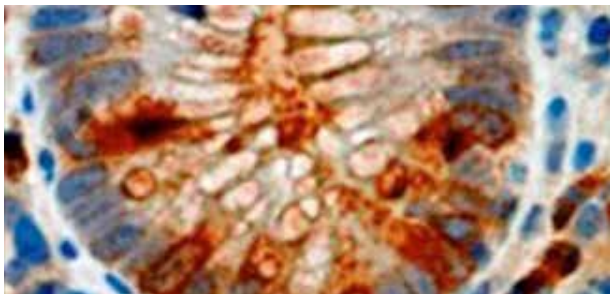
Ambitions for 2014

- Collection and characterization of pregnancy-related Biobanks at St. Olavs Hospital and Haukeland University Hospital.
- Elucidate specific PRR mechanisms mediating the harmful inflammation of preeclampsia, focusing on fetal trophoblasts.
- To improve prediction models and subgrouping of preeclampsia, and to find new etiologic clues to the disease by inflammatory and metabolomics profiling of week 11-13 pregnancies.
- Identification of gene variants (SNPs) of relevance to the pathogenesis and inheritance of preeclampsia and cardiovascular diseases.
- Identification of preeclampsia risk genes through genome wide association studies of women with or without preeclamptic pregnancies.

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 100 mutations 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 CEMIR theme 5B is to understand central mechanisms for mucosal homeostasis, how this is disrupted in active IBD disease and subsequently restored in remission.

Theme Manager:
Professor Arne Kristian Sandvik



Main activities in 2013

Within the CEMIR theme on Inflammatory bowel disease (IBD) work in 2013 proceeded along two lines; studying the role of REG (regenerating islet-derived) peptides in IBD, and TLR3 mediated immune mechanisms in the colonic mucosa. The studies have yielded very interesting results with possible clinical relevance, and these factors are now the focus for CEMIR related research within the IBD group. There was one PhD dissertation within the theme in 2013, and another thesis was delivered for assessment in December.

Major achievements in 2013

- Discovered that REG peptides are potently regulated by the inflammatory process in vivo. The mechanisms behind this and the impact of REG on the inflammatory process are unknown, and subject to ongoing studies.
- Established that a TLR3 agonist regulates cytokines, chemokines and antimicrobial peptides in vitro, corresponding well with the gene expression (mRNA and protein) pattern seen in biopsies from patients with IBD.

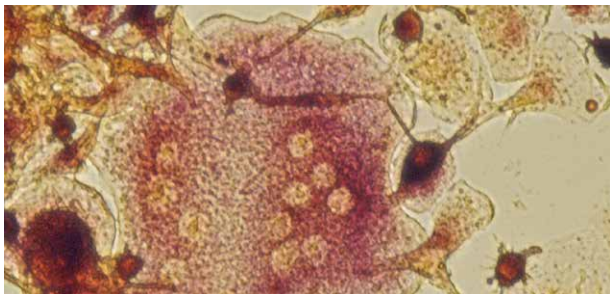
Ambitions for 2014

- To elucidate the detailed role of TLR3 and REG in IBD using animal models (standard animal IBD models and studies on transgenic animals) and in vitro. Patient material will be used to secure a human correlate to experimental observations, and also to assess the utility of a number of biomolecules in noninvasive IBD diagnostics.

Inflammation underlying Bone Destruction

Chronic inflammation is a common characteristic of diseases such as multiple myeloma, rheumatoid arthritis and inflammatory bowel disease. Thus, mechanisms for the bone destruction associated with these diseases might be similar. The main hypothesis in CEMIR theme 5C is that activation of pattern recognition receptors and autophagy in bone cells influences bone remodeling in conditions like multiple myeloma and rheumatoid arthritis.

Theme Manager:
Therese Standal, Senior Research Scientist



Main activities in 2013

In 2013 we worked mainly on two projects: 1) To identify TLR agonist activity in synovial fluids from patients with rheumatoid arthritis and psoriatic arthritis, and 2) To clarify how TLR-signaling influence cytokine and RANKL expression in human mesenchymal stem cells. In addition, theme leader Therese Standal worked as a visiting scientist at St. Vincent's Institute in Melbourne, Australia, on a project aiming to understand the role of gp130 in osteocytes for intermittent parathyroid hormone-induced bone formation. One of the PhD students was in Prof. Anton Martens laboratory in Utrecht, the Netherlands, to learn a novel mouse model of multiple myeloma. There was one PhD thesis delivered for assessment.

Major achievements in 2013

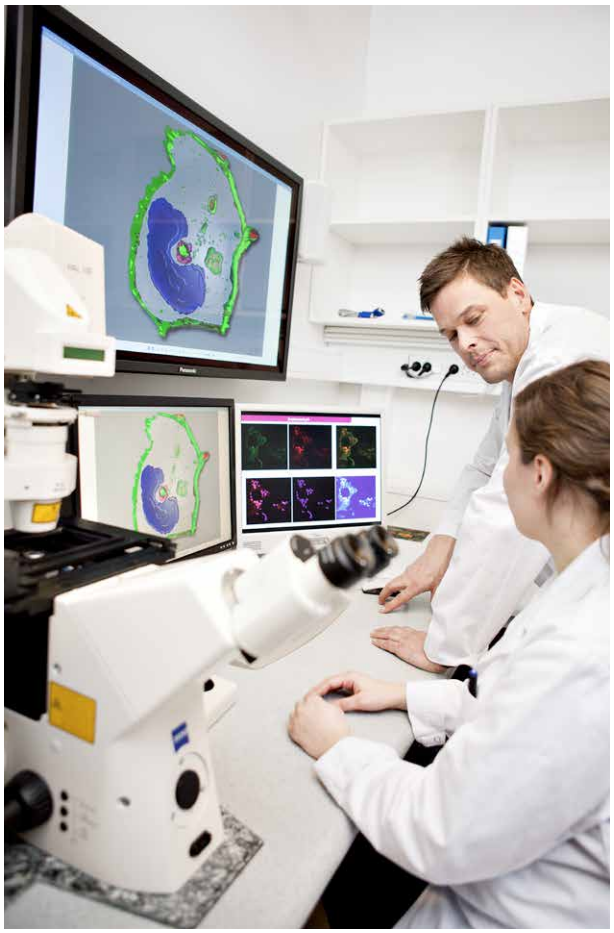
- Showed that synovial fluid from some arthritis patients contains TLR3 and TLR9 ligands. Levels of TLR9 agonists correlate with levels of hepatocyte growth factor, previously shown to be negatively associated with bone health in rheumatoid arthritis and multiple myeloma.
- Established that TLR3 and TLR4-signaling triggers cytokine and RANKL production in human bone marrow derived mesenchymal stem cells.

Ambitions for 2014

- To understand mechanisms for TLR-induced RANKL expression in mesenchymal stem cells.
- To identify inflammation-related genes relevant for myeloma bone destruction by screening tissue RNA isolated from myeloma patients with and without bone disease using Nanostring technology.
- To identify and characterize crystals in bone marrow from myeloma patients and synovial fluids from rheumatoid arthritis patients. Examine effects of crystals on osteoclast activation in vitro and on bone formation in vivo.
- To establish at CEMIR a humanized mouse model of multiple myeloma.

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 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 the inflammatory responses induced by cholesterol crystals. The aim of this subproject is to identify and characterize molecular mechanisms of inflammatory responses that can be targeted for the design of 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 a scientific leader for the Imaging Core Facility at NTNU (http://www.ntnu.edu/dmf/cmic). This core facility is now acquiring the most recent state of the art high-resolution laser confocal microscopes that will be installed in the new CEMIR laboratories in 2014. 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 (Sandvik and Damås).

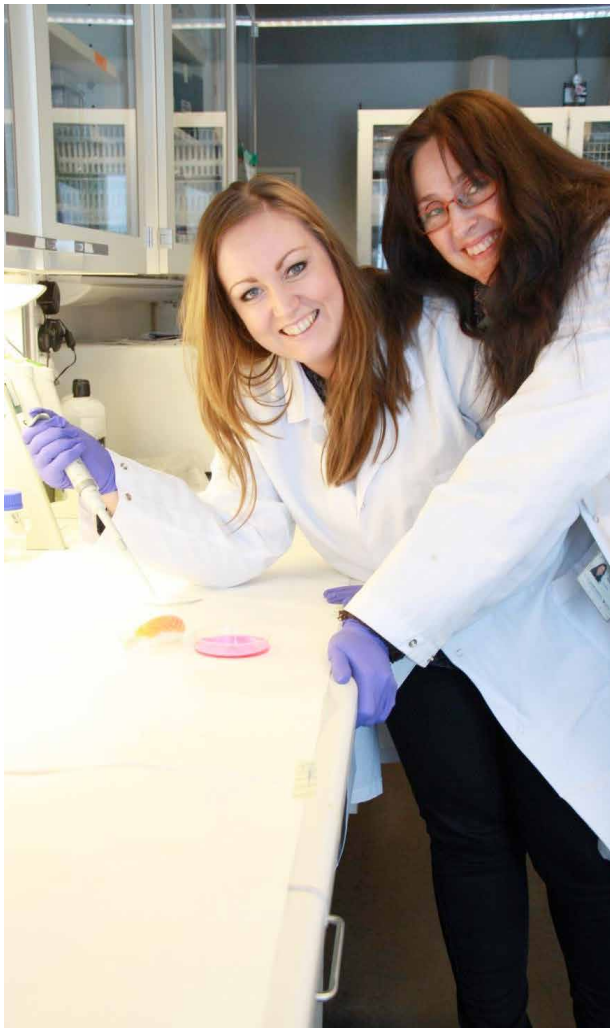
The research group is led by Terje Espevik and currently consists of 22 persons including 5 PhD students, 7 post docs, 6 research scientists and 4 staff engineers. The group has close collaborations with the CEMIR affiliated professors, Mollnes, Lien, Fitzgerald, Stenmark and Latz. Moreover, the group is also actively involved in collaborative projects at national (Aukrust and Yndestad, University of Oslo) and international levels (G. Teti, University of Messina, Italy, and M. McCaffrey, University of Cork, UK).

The Research Group on Molecular Mechanisms of Mycobacterial Infections

Tuberculosis kills more than 1.5 million people worldwide each year, and an estimated 2 billion individuals carry latent *Mycobacterium tuberculosis* (Mtb) infection. 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 iron metabolism, pattern recognition receptor signaling 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 the pathogen. There has been an increase in TB following the HIV epidemic. T cell effector functions in patients co-infected with mycobacteria and HIV are impaired and we currently study the impact of concomitant HIV-infection on anti-mycobacterial host defenses, including lipid metabolism and autophagy in T-cells. 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, two post docs, three PhD students, one staff engineer and master students. We have developed expertise, methods and tools to study mycobacteria and the host innate and adaptive immune defenses both in vitro and in vivo in mice. We have strains of Mtb, *M. avium* and *M. smegmatis* available with fluorescence and firefly luciferase, and we will have a confocal microscope in our new BSL-3 facility at Kunnskapssenteret for live imaging of Mtb 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 but 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 establish nanoscale high resolution imaging of intracellular mycobacterial 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 Autophagy and Oxidative Stress Defense Group



The autophagy group focus on the role of this intracellular degradation route in the prevention and development of age-related diseases. In preventive settings we are particularly 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 defence system coordinated by Nrf2. We also study if these responses are involved in the anti-inflammatory roles of n-3 PUFAs and if these lipids can affect the development of proteinopathies. For the disease promoting functions of autophagy and oxidative stress responses, we particularly study the formation of aggressive tumours and try to decipher how these cytoprotective processes are turned into mechanisms that support growth and survival of cancer cell sunder stressful conditions. Finally, the group investigate the putative role of systemically activated autophagy in patients that develops cancer cachexia. Particularly, the role of tumour derived pro-inflammatory signalling substances in the activation of lysosomal protein degradation in muscle cells and tissues are investigated.

The group is led by Professor Geir Bjørkøy and consists of one and a half senior technicians, four PhD students and four master students. The group have established several cellular models of both normal and cancerous cells to study regulation of autophagy by both protein analyses, imaging approaches and flow cytometry. In addition, the group recently published a paper describing a novel approach to quantify signalling in the autophagy regulating PI3K pathway in cancers and how this could be used to guide targeted treatment. The group is also involved in determining bioactivity for novel targeted kinase inhibitors designed and synthesized by a collaborating group at NTNU and HiST (B. Hoff and E. Sundby). A close collaboration with the Jebsen centre on Myelomatosis Research headed by A. Sundan at NTNU allows studies of the role of oxidative stress responses and autophagy in patients treated with proteasomal inhibitors. External collaborators include the groups of T. Johansen (UiT), P.E. Lønning (UiB), K. Fearon (Univ of Edinburgh) and M. Komatsu (Tokyo Metropolitan Univ.).

The Research Group on Inflammation and Genetics in Pregnancy

The Research Group of Inflammation and Genetics in Pregnancy is closely linked to CEMIR themes focusing on the molecular studies of lipids and cholesterol crystals and activation of inflammasomes, TLR2 and TLR4 (Professors Espevik and Damås). The inflammation underlying preeclampsia closely resembles central atherosclerotic processes and in the placenta, the fetal trophoblasts are shown to possess a strong panel of functional PRRs. The Research Group further aims to unravel the inflammatory role for atherosis in preeclamptic pregnancies, and to define the maternal systemic inflammatory mediators contributing to preeclampsia and later risk for heart diseases. Several pregnancy-based Biobanks are collected and administered by the Research Group and provide unique materials for the molecular inflammation analyses.

The broad research approach involving biobanking, molecular studies, genetics and metabolomics, is made possible by a strong collaboration between clinical departments and basic researchers. Central collaborators include Professor Line Bjørge at Haukeland University Hospital, The Women's Clinic at St Olavs Hospital, Professor Kjell Salvesen at Lund University, and at NTNU, Professor Tone Bathen and the Core Facility CMIC. Professor Eric Moses at University of Western Australia is a crucial international collaborator. 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 and the relation to cardiovascular risk traits, based on the world's largest pregnancy based cohort collaboration for genetic studies.

In 2013 in collaboration with Professor Torstein Vik at NTNU, an epidemiologic study of the link between cerebral palsy and being born from a preeclamptic pregnancy have been completed and published in the esteemed British Medical Journal. MD PhD student Kristin Melheim Strand in the Research Group revealed that exposure to preeclampsia is associated with an increased risk for cerebral palsy in the child, and that this is mediated through the children being born preterm or small for gestational age.

The Research Group is led by Senior Researcher Ann-Charlotte Iversen and Professor Rigmor Austgulen and counts eleven persons, of which five are PhD students and one Staff Engineer. Two Medical Students completed the Medical Students Research Program and one new master student joined the group in 2013.

The Inflammatory Bowel Diseases Research Group

The research group started at NTNU/St. Olav's University Hospital in 2007 as a close collaboration between clinical medicine and basal laboratory research. The IBD research projects aim at understanding central mechanisms for mucosal homeostasis and how this is 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, and how the diffuse neuroendocrine system interacts with immune signaling in IBD. The group has a close collaboration with other CEMIR research groups working with innate immune mechanisms (professor Espevik, professor Damås).

The IBD group draws much of its strength from a close connection with clinical medicine; the two group leaders are professors at NTNU and clinical gastroenterologists. A large clinical biobank was established several years ago, and during 2014 a Health Authority supported region-wide project will result in a substantial expansion of the biobank. A large project integrating the immune and the diffuse neuroendocrine systems, done in collaboration with Yale University, has been funded. One of the two IBD group leaders also administers the 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.

The IBD research group is led by two professor I (in gastroenterology) with side affiliations as senior consultants in clinical medicine, Drs Arne Sandvik and Bjørn Gustavsson. The group has recruited two postdocs (one in 2013, another coming in 2014) and plans to recruit three PhD students the coming year. One research branch medical student does her project within the group. Other staff is one senior researcher and one associate professor working partly within IBD. The group has recruited one adjunct professor from Yale University.

The Bone Disease Group

The research is focused on how cancer and inflammation influence bone, and we are in particular interested in understating the molecular mechanisms for the bone destruction associated with multiple myeloma and rheumatoid arthritis. The group is affiliated with the KG Jebsen center for myeloma research and profit from a close collaboration with clinicians and researchers at this center. 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. By the end of 2013 we have established a mouse model for multiple myeloma here in Trondheim, which will give us new opportunities in terms of in vivo experiments.

The bone disease group is led by senior research scientist Therese Standal and currently includes one post doctor and two PhD students. By mid-2014 another post doc will be recruited to the group.

CEMIR Affiliated Adjunct Professors

CEMIR has recruited six outstanding researchers as adjunct professors. They will organize three PhD courses for the centre, and will be tightly involved with the centre by supervising our PhD and postdoctoral candidates who will spend extended periods in their laboratories. We are proud to briefly present our adjunct professors below:

Harald Stenmark, Professor and director of the Centre of Cancer Biomedicine, University of Oslo. Stenmark is an expert in the field of intracellular sorting and trafficking mechanism. His research focus is on basic cell biological mechanisms of endocytosis, autophagy, cytokinesis and tumour suppressors. The Stenmark Lab studies the molecular mechanisms that promote or suppress cancer, a disease that involves uncontrolled proliferation and invasiveness of specific cell types of the body.

Eicke Latz, Professor and Director of the Institute of Innate Immunity, University of Bonn, Germany. The Latz Lab is interested in understanding how innate immune receptors interact with their ligands and how this molecular interaction leads to receptor activation and immune responses. An important goal of his research is to devise means to pharmacologically interfere with the activation of innate immune receptors in order to develop novel approaches to treat inflammatory diseases such as atherosclerosis.

Tom Eirik Mollnes, Professor, University of Oslo and University of Tromsø. A primary research goal for the Mollnes Lab is to elucidate the role of complement as a primary inducer of the inflammatory reaction and thereby form a basis for a future therapeutic approach in complement-mediated disease processes. His work has focus on inflammatory diseases with emphasize on infection, sepsis and inflammatory response syndrome and ischemia-reperfusion injury.

David Underhill, Professor at Cedars-Sinai Medical Center, Los Angeles, USA. Underhill has studied basic mechanisms of innate immunity for more than a decade. In particular, his Lab has clarified the role of phagocytosis in modulating inflammatory signaling in macrophages and dendritic cells. In addition, his lab has defined the role of microbial degradation in triggering innate immune responses, including inflammasome activation. Underhill is now focusing on how innate immune signaling pathways shape inflammatory responses and are dysregulated in inflammatory bowel disease.

Kate Fitzgerald, Professor at University of Massachusetts, USA. Research in the Fitzgerald Lab is focused on understanding, in mole-cular detail, the mechanisms by which the innate immune response recognizes and responds to challenge with pathogenic microbes. Expertise in this regard relates to the study of Toll-like receptors, NOD-like receptors and cytosolic RNA/DNA sensors in orchestrating early innate defenses and inflammation.

Egil Lien, Professor at University of Massachusetts, USA. The laboratory of Egil Lien is primarily focused on understanding the innate immune recognition of pathogens, such as Gram-negative bacteria, by Toll-like receptors (TLRs) and inflammasomes. His work has provided greater understanding of microbial activation and evasion of innate immunity and has pointed to new therapies and vaccines against infectious diseases. The Lien Lab is also studying mechanisms of inflammation that is involved in the development of diabetes and obesity.

Close Collaboration with Clinical Departments and Biobanks

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 in much of our research. We benefit from the close integration between NTNU and St.Olavs Hospital and the location of both institutions at Øya Campus.

The Integrated University Hospital

A controlled inflammatory response is needed to fight infections and to heal wounds, but it can become detrimental and cause disease if it is dysregulated. There are numerous studies showing associations between chronic inflammation and several diseases, including obesity, cancer, cardiovascular disease (CVD), diabetes and inflammatory bowel disease (IBD). CEMIR's research program will detail the molecular and cell biological principles for initiation and regulation of inflammatory responses through the use of basic research, in vitro- and in vivo models.

Importantly, we have access to several biobanks for inflammatory diseases which will be instrumental in identifying new biomarkers and novel clinically therapeutic targets. In particular The Nord-Trøndelag Health Study (HUNT 1-3) will be used for examination of association between preeclampsia and CVD. For cardiovascular specimens, atherosclerotic plaques from coronary and carotid arteries, serum/plasma/blood cells from patients with acute coronary syndromes (unstable angina and acute myocardial infarction) are available through collaboration with Rikshospitalet National Hospital.

For IBD-specimens, a large biobank of intestinal tissue, sera and blood cells has been collected from patients with Crohn's disease or ulcerative colitis and healthy controls, and is continuously expanded through collaboration with the largest gastrointestinal endoscopy units in Midt-Norge.

For bone destruction specimens, the national biobank for multiple myeloma will be used. The material includes bone marrow aspirates, serum as well as clinical data that are stored at St.Olavs Hospital.

In collecting and expanding these biobanks, a close collaboration with the clinical departments at St. Olav's Hospital is essential. In defining novel biomarkers from these biobanks, the clinical characterization is essential, often involving clinical chemistry, analyses of biopsies and radiological investigations. For identification of new therapeutic targets, interventional studies will be initiated with the knowledge from basic and clinical sciences. The close collaboration between the hospital and CEMIR will clearly be of benefit for both institutions.

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 was less complement dependent. CD14 is a co-receptor for a number of Toll-like receptor molecules 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 combined. 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 for endogenous danger like meconium that induces a serious inflammation in newborns, which initially is sterile. 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 on 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.

The principle of double-blockage of complement and CD14 to attenuate inflammation has been patented by one of the CEMIR researchers (TE Mollnes). Moreover, CEMIR researchers at NTNU have developed the anti-CD14 that is effective in the combined treatment. The vision is to test this principle in clinical therapeutic settings in collaboration with Inven2, the Innovation Company at University of Oslo, and NTNU Technology Transfer AS.

Completed PhDs in 2013

CEMIR has the ambition to educate a large number of PhD candidates during the 10-year period as a Centre of Excellence. In 2013, 17 PhDs were doing their research at CEMIR. Three of them defended their theses and successfully completed their PhDs in 2013: Atle Van Beelen Granlund, Jane Awuh and Marte Singsås Dragset:

Atle Van Beelen Granlund

Granlund defended his thesis «Colonic mucosal gene expression in inflammatory bowel disease – From whole genome to *REG* gene family expression» on April 11, 2013 at the Norwegian University of Science and Technology (NTNU). The work was carried out at Institute of Cancer Research and Molecular Medicine, Faculty of Medicine. Professor Arne K. Sandvik supervised the work, and Professor Terje Espevik was co-supervisor.

Marte Singsås Dragset

Dragset defended her thesis «Riding the Ferrous Wheel: Study and Identification of Genes Involved in Mycobacterial Iron Acquisition» on December 11, 2013 for the degree of Philosophiae Doctor at the Norwegian University of Science and Technology (NTNU), Department of Biotechnology. The experimental work was conducted at Department of Biotechnology and CEMIR, Department of Cancer Research and Molecular Medicine at NTNU and the Department of Immunology and Infectious Diseases at Harvard School of Public Health, with Professor Svein Valla as supervisor and Magnus Steigedal (researcher) and Trude Helen Flo (senior researcher) as co-supervisors.

Jane Awuh

Awuh defended her thesis «Host Defence Mechanisms in *M. avium* Infection» on April 22, 2013 for the degree of Philosophiae Doctor at Norwegian University of Science and Technology (NTNU). The work was conducted at CEMIR, Department of Cancer Research and Molecular Medicine with Trude H. Flo (senior researcher) as supervisor and Professor Jan Kristian Damås as co-supervisor.

All three have advanced in their careers at CEMIR after completing their PhDs. They have continued as postdoctoral fellows in their respective research groups.

Educational Activities

PhD courses

CEMIR initiated two PhD courses in 2013, and yet another will start in 2014. They are all part of NTNUs PhD programme in Molecular Medicine and open for PhD students nationally and internationally that are interested in molecular inflammation:

"Receptor Signaling and Trafficking" is an advanced course that describes the most commonly used methods for studying receptor signaling and discusses cell signaling downstream of the most important receptor classes.

The course *"Molecular Mechanism of Inflammation"* gives an overview of mechanisms and signaling pathways involved in inflammatory processes, mainly connected to activities at CEMIR. This is inflammation related to infections, but also sterile inflammation.

The third course *"Advanced Cellular Imaging Techniques"* focus on light microscopy and electron microscopy and students will learn about molecular imaging techniques with a focus on imaging innate immune cell activation. The course will provide the theoretical background for diverse imaging techniques that can be applied to study innate immune activation.

Master of Science in Molecular Medicine

NTNU offers an International Master of Science (MSc) programme in Molecular Medicine. The purpose of the MSc programme is to develop knowledge and skills in cellular and molecular biology.

CEMIR offers master's thesis projects for the MSc in Molecular Medicine and researchers affiliated with CEMIR also contribute with lectures and seminars.

Medical Student Research Programme

The Medical Student Research Programme (MSRP) is a national research education and grant scheme for medical students who wish to carry out research. These students are interested in medical research and willing and motivated to do research besides their regular studies. CEMIR offers supervision for MSRP students doing course work and thesis.

CEMIR Outreach Activities

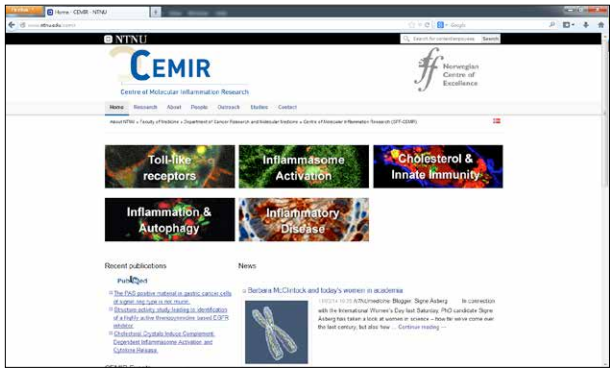
At CEMIR we aim to make the public aware of and understand our research on inflammation, and how our research can contribute to the development of new treatments and diagnostic tools. We are involved in many outreach activities.

Media Highlights

In March, Terje Espevik and Trude Helen Flo were interviewed by the regional newspaper Adresseavisen about their research and being selected as a Norwegian Centre of Excellence.

New website

In 2013 we launched our new and redesigned website: www.ntnu.edu/cemir



Blogging

In 2013 we wrote several blogs for the #NTNUmedicine blog

Looking for the perfect immune response - Blogger: Trude Helen Flo
Why study chronic intestinal inflammation? Bloggers: Arne Kristian Sandvik og Jan Kristian Damås
Sugar + inflammation = true? Blogger: Eivind Samstad
What does inflammation have to do with global health? Blogger: Trude Helen Flo
Plagues and illness – what's the connection between the plague and being overweight? Blogger: Egil Lien
You can read the blogs here: http://blog.medisin.ntnu.no/tag/cemir-en

«Kunnskapsbyen» with Trude

In November, Trude Helen Flo, gave a talk on "Betent kunnskap" (Inflamed knowledge) to about 70 Citizens of Trondheim at Suhmhuset. Her talk was on how knowledge on inflammation can help us find better treatment for cancer, Alzheimer and diabetes.


6 Nyheter

Onsdag 13. mars 2013 Adresseavisen

Mus og mennesker: Forsker Trude Flo bruker mus til å studere betennelsesreaksjoner. Prosessene er i stor grad de samme som hos mennesket. I bakgrunnen professor Terje Espevik.

Krigercellene gir ny viten

En hoven finger, litt feber ved en infeksjon. Betennelser beskytter oss. – Hadde systemet fungert perfekt, ville vi aldri blitt syke, sier Trude Flo.

Betennelse oppstår når cellene i kroppens immunforsvar oppfatter fare og sender ut signaler.

Realiserer drømmer

Nødvendige betennelser

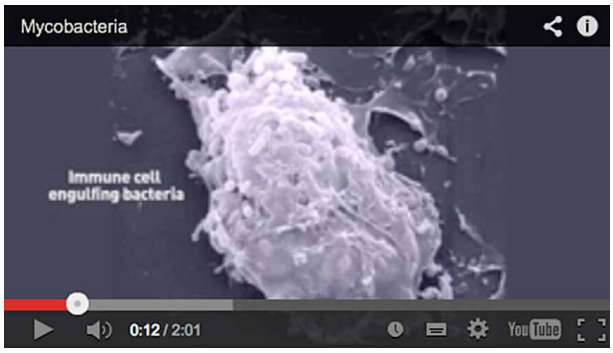
Varsler om fare

– Jeg tror ikke det helt har sunket inn hvor stort dette er. Men prestisjen forplikter også.

TRUDE FLO, forsker

Youtube-film

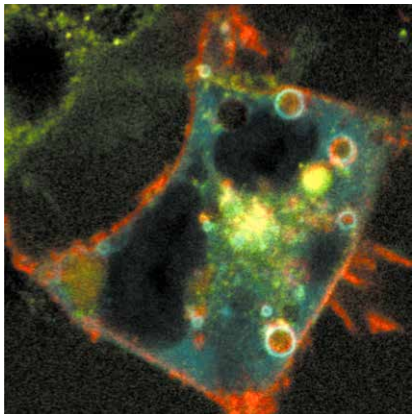
Co-Director Trude Helen Flo featured in at film by NTNU on understanding mycobacteria to fight tuberculosis. You can find the film on our website:



http://www.ntnu.edu/cemir/outreach

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 DMF, NTNU. https://www.ntnu.edu/dmf/cmic



Confocal microscopes

Confocal microscopy studies at CEMIR include live-cell imaging, fluorescence recovery after photobleaching (FRAP), the study of intracellular trafficking of pathogens and immune receptors and their adaptor molecules.

LSM 510 META LIVE and FCS

This microscope has an incubator to regulate temperature, humidity and gas for live-cell imaging. It also has a fast-scanning module based on a line-scanner with which a scanning speed of up to 120 confocal frames per second. We also have access to fluorescence correlation spectroscopy which makes it possible to study diffusion of labeled receptors in live cells. Also the interaction between receptors and ligands can be studied with FCS.

Confocal Spinning Disk

The combination of a spinning disk and a highly sensitive EMCCD camera (Evolve 512) makes it possible that live cells can be imaged at video-rate without any photo-damage caused to the cells. In this way, the trafficking of individual endosomes containing e.g. Toll-like receptors can be studied for minutes, without any bleaching observed. In combination with a patch-clamp, fast studies of calcium release are possible.

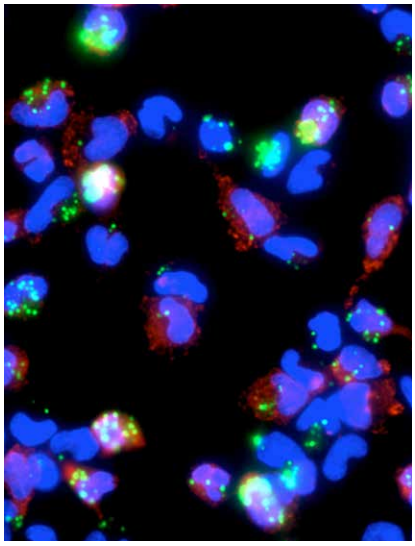
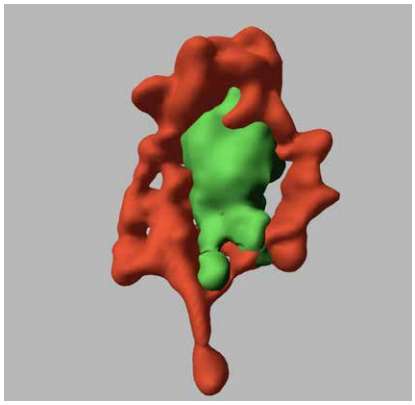


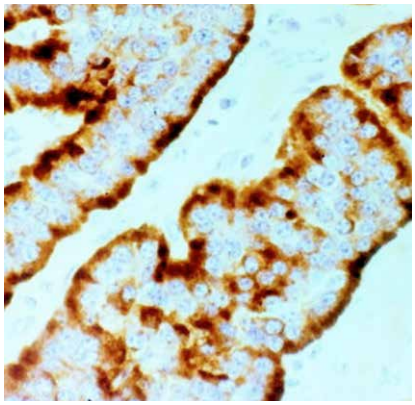
Image-based screening station: Olympus Scan^R

Scan^R offers fully automated high-throughput image acquisition including time-lapse (in environmental chamber) and automated analysis e.g. to sort out populations, for assay development and high-content screening. Illumination is performed with a xenon-mercury lamp in combination with an excitation filter wheel, which enables high speed imaging. Scan^R is equipped with a hardware autofocus and a Hamamatsu CCD camera. Four combination emission filters are available for all common fluorophores. Polarisation analysis can be performed in order to e.g. detect crystals. Examples of CEMIR applications: cell transfection efficiency studies, intracellular transport and location studies, RNA interference and bacterial infection studies.



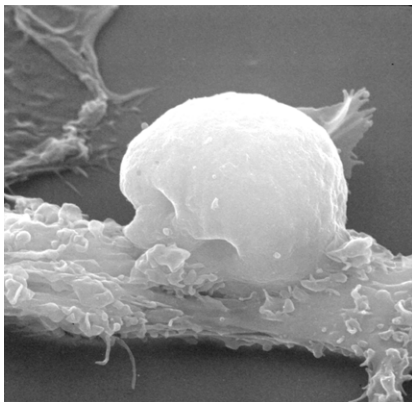
Imaris-Image visualization software

This software enables 3D visualization of confocal images and image analysis. The program is ideal for measuring co-localization of molecules and to follow trafficking of endosomes.



Histochemistry

Also, histological studies are being performed by CEMIR scientists in the CMIC labs. The used techniques include embedding, sectioning and staining, either HES staining or immunohistochemical staining of cells and tissue.

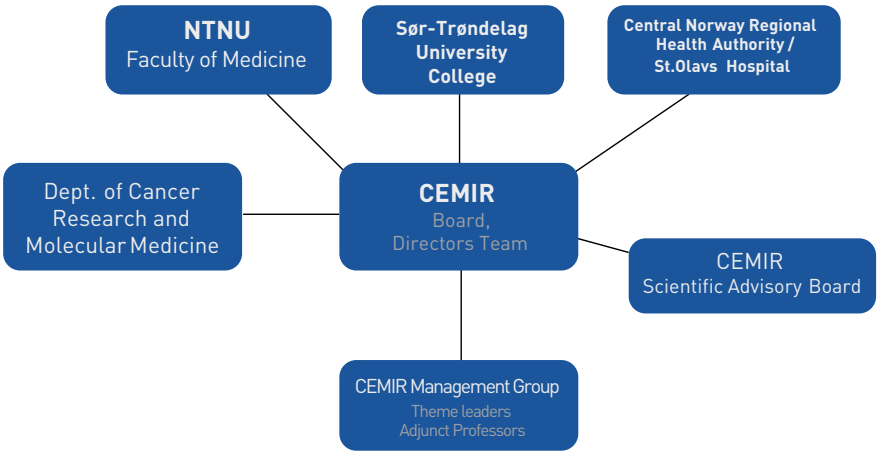


Electron microscopy

Both SEM and TEM are becoming important tools in CEMIR research. Preparation of samples for imaging in the Focused-Ion Beam Scanning Electron Microscope (FIB-SEM, part of NTNU Nanolab) is also performed at CMIC EM lab.

CMIC is in the process of purchasing new equipment including a state of the art confocal microscope that has the possibility of Super Resolution Microscopy and a TIRF microscope for imaging events in and close to the plasma membrane. The microscope will have sensitive detectors, making it possible to observe structures that are not highly overexpressed in cells, and also facilitating long-term imaging because low-laser power can be used in these very sensitive microscopes. A white-light laser enables choosing excitation wavelengths for 'all' possible dyes and fluorescent proteins.

CEMIR Organisation



CEMIR is closely connected to the host department, Department of Cancer Research and Molecular Medicine, at Faculty of Medicine, NTNU. CEMIR has two consortium participants that contribute by performing research activities and providing financing: Sør-Trøndelag University College and The Central Norway Regional Health Authority/St.Olavs Hospital.

The Centre is headed by Professor Terje Espevik (Director) and Senior Researcher Trude (co-director). The Centre management is supported by Head of Administration, Kari Håland. CEMIR activity integrates 7 research themes headed by Professor Terje Espevik, Professor Arne Kristian Sandvik, Professor Jan Kristian Damås, Professor Egil Lien, Senior Research Scientist Trude Helen Flo, Researcher Ann-Charlotte Iversen and Researcher Therese Standal.

The theme leaders meet for discussions and decision making on a regular basis.

The CEMIR board

The authority of the board is to ensure that the intensions and terms of contract described in the contract are fulfilled within the time frameworks. The board is to ensure that cooperation proceeds smoothly between the centre, the host institution and the consortium participants.

The board has 5 members:
Stig A. Slørdahl - Dean, Faculty of Medicine, NTNU
Magne Børset - Head of Department of Cancer Research and Molecular Medicine, NTNU
Einar Hjorthol -Dean, Faculty of Technology, Sør-Trøndelag University College (HiST)
Petter Aadahl - Research director, St. Olavs Hospital
Anne Borg - Dean, Faculty of Natural Sciences and Technology, NTNU

The Scientific Advisory Board, SAB

SAB's mandate is to critically evaluate and advice on the Centre's scientific performance and progress, and to support the Centre with valuable input on strategy and science.

SAB has 5 members:


Professor Alan Aderem, Seattle Biomedical Research Institute


Professor Douglas Golenbock, University of Massachusetts Medical School


Professor Göran Hansson, Karolinska Institutet


Professor Lynda Stuart, B&M Gates Foundation


Professor Stefanie Vogel, University of Maryland Medical Center

Collaboration

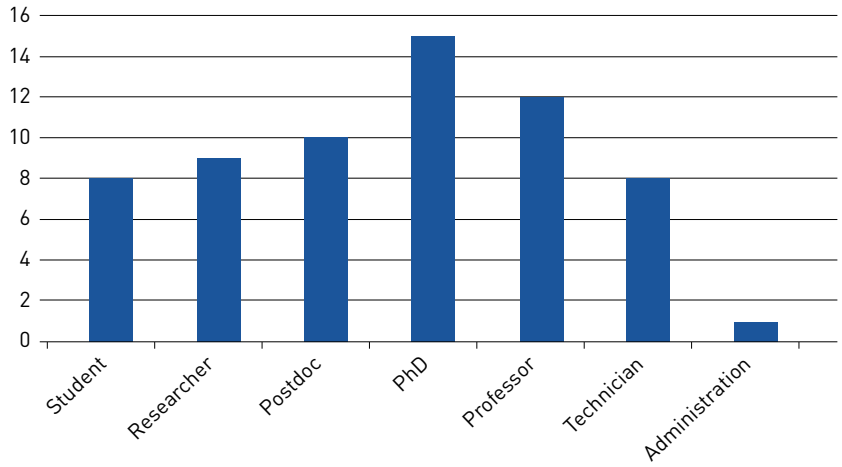
NATIONAL

Name	Institution
Gudmund Skjåk-Bræk	NTNU
Tone Bathen	NTNU/St.Olavs Hospital
Torstein Vik	NTNU/St.Olavs Hospital
Björn Gustafsson	NTNU/St.Olavs Hospital
Anders Waage	NTNU/St.Olavs Hospital
Otto Nygård	Univ. of Bergen/Haukeland Univ. Hospital
Grethe Tell	Univ. of Bergen
P E Lønning	Univ. of Bergen
Andreas Brech	Univ. of Oslo
Harald Stenmark	Univ. of Oslo
Pål Aukrust	Univ. of Oslo
Arne Yndestad	Univ. of Oslo
Oddmund Bakke	Univ. of Oslo
Tom Eirik Mollnes	Univ. of Oslo and Tromsø
Terje Johansen	Univ. of Tromsø
Jon Florholmen	Univ. of Tromsø
Egil Lien	Univ. of Massachusets, USA

INTERNATIONAL

Name	Institution
Robin Ingalls	Boston University, USA
Eric Rubin	Harvard School of Public Health, USA
Anderssen	Harvard Univ., USA
Chris Benedict	La Jolla Institute, USA
Alan Aderem	Seattle Biomed, USA
Masaaki Komatsu	Tokyo Metropolitan Univ., Japan
Joan Mecsas	Tokyo Univ. of Foreign Studies, Japan
Luke O`Neill	Trinity, Univ. of Oslo
Eicke Latz	Univ. of Bonn, Germany
Mary McCaffrey	Univ. of Cork, UK
Ken Fearon	Univ. of Edinburgh, UK
Kate Fitzgerald	Univ. of Massachusets, USA
Jon Goguen	Univ. of Massachusets, USA
Giuseppe Teti	Univ. of Messina, Italy
Harry LT Mobley	Univ. Of Michigan Medical School, USA
Eric Moses	Univ. of Western Australia
Thomas Hawn	University of Washington, USA
Kenneth Kidd	Yale, USA
European Myeloma Network	

CEMIR Staff and Students



By the end of 2013 65 people (included master's students) were associated with the centre.

Name		Postition	Nationality	Research Group
Ajayi	Clement Olufemi	Master's student	Nigeria	Inflammation
Andersen	Sonja	Technician	Norway	Autophagy
Aune	Marie Hjelmseth	Postdoctor	Norway	Inflammation
Austgulen	Rigmor	Professor	Norway	Pregnancy
Awuh	Jane	PhD candidate	Cameroon	Mycobacteria
Bakke	Siril Skaret	Postdoctor	Norway	Inflammation
Beckwith	Marianne	PhD candidate	Norway	Mycobacteria
Bergstrøm	Bjarte	Postdoctor	Norway	Inflammation
Bjørkøy	Geir	Professor	Norway	Autophagy
Bjørnvall	Christina Dybdrodt	Master's student	Norway	Mycobacteria
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
Espevik	Terje	Professor	Norway	Inflammation
Fitzgerald	Kate	Professor II	USA	
Flo	Trude Helen	Senior Researcher	Norway	Mycobacteria
Granlund	Atle Van Beelen	Postdoctor	Norway	IBD
Grøvdal	Lene Melsæther	Postdoctor	Norway	Inflammation
Hannam	Ryan	Master's student	England	Mycobacteria
Haug	Markus	Postdoctor	Germany	Mycobacteria
Husebye	Harald	Researcher	Norway	Inflammation
Håland	Kari	Head of admin.	Norway	
Ibrahim	Hany	Master's student	Egypt	Mycobacteria
Iversen	Ann-Charlotte	Senior Researcher	Norway	Pregnancy
Johansson	Ida	PhD candidate	Norway	Autophagy
Kannan	Nisha	PhD candidate	India	Mycobacteria
Khoshkalam	Omid	Master's student	Iran	Mycobacteria
Klein	Dionne	Technician	Netherlands	
Latz	Eicke	Professor II	Germany	
Lien	Egil	Professor II	Norway	
Marstad	Anne	Technician	Norway	Mycobacteria
Mildenberger	Jennifer	PhD candidate	Germany	Autophagy
Mollnes	Tom Eirik	Professor II	Norway	

Name		Postition	Nationality	Research Group
Neckmann	Ulrike	PhD candidate	Germany	Autophagy
Nilsen	Nadra	Researcher	Norway	Inflammation
Niyonzima	Nathalie	PhD candidate	Burundi	Inflammation
Nonstad	Unni	Technician	Norway	Inflammation, autophagy
Paulsen	Julie	PhD candidate	Norway	Inflammation
Pettersen	Kristine	PhD candidate	Norway	Inflammation
Rokstad	Anne Mari	Researcher	Norway	Inflammation
Rollnes	Haakon Berg	Master's student	Norway	Inflammation
Ryan	Liv	Technician	Norway	Inflammation
Samstad	Eivind	PhD candidate	Norway	Inflammation
Sandvik	Arne	Professor	Norway	IBD
Shrestha	Birendra Kumar	Researcher	Nepal	Mycobacteria
Silvia	Gabriela	Master's student	Brazil	Inflammation
Skei	Bente	Technician	Norway	Pregnancy
Skjesol	Astrid	Postdoctor	Norway	Inflammation
Standal	Therese	Senior Researcher	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
Stødle	Guro	PhD candidate	Norway	Pregnancy
Sundan	Anders	Professor	Norway	Bone disease
Tangerås	Line	PhD candidate	Norway	Pregnancy
Underhill	David	Professor II	USA	
Vik	Randi	Technician	Norway	Inflammation
Waagsbø	Bjørn	PhD candidate	Norway	Inflammation
Wang	Nelson	Master's student	Canada	Mycobacteria
Yurchenko	Mariia	Postdoctor	Norway	Inflammation
Ørning	Mathias Pontus	PhD candidate	Sweden	Inflammation
Østvik	Ann Elisabeth	PhD candidate	Norway	IBD
Åsberg	Signe	PhD candidate	Norway	Mycobacteria

CEMIR has an international environment. 16 countries are represented in our staff.

Results 2013: Publications, Academic Presentations and Media Coverage

CONFERENCE LECTURE AND ACADEMIC PRESENTATION:

- **Aune, Marie Hjelmseth; Samstad, Eivind O.; Niyonzima, Nathalie; Nymo, Stig; Ryan, Liv; Lappegård, Knut Tore; Brekke, Ole-Lars; Lambris, John D.; Damås, Jan Kristian; Latz, Eicke; Mollnes, Tom Eirik; Espevik, Terje.** Cholesterol crystals induce complement-dependent inflammasome activation. Inflammasomes in health and disease; 2013-06-24 - 2013-06-25. HIF, NTNU, UiO og UiT
- **Austdal, Marie; Skråstad, Ragnhild; Gundersen, Astrid; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte.** Metabolomic Biomarkers in Serum and Urine in Women with Preeclampsia. ISSHP European Congress; 2013-06-12 - 2013-06-14. NTNU
- **Austdal, Marie; Skråstad, Ragnhild; Gundersen, Astrid; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte.** Metabolomic Biomarkers in Serum and Urine of Preeclamptic Women. ESMRMB; 2013-10-03 - 2013-10-05. NTNU
- **Beckwith, Marianne.** Electron Microscopy Techniques for Biological Applications. Seminar on Biological TEM; 2013-09-05. NTNU
- **Bugge, Marit; Nilsen, Nadra; Espevik, Terje.** A potential role for TLR3 expression and TLR3 mediated responses in the progression of colorectal cancer. Keystone Symposia on Cancer Immunology and Immunotherapy; 2013-01-27 - 2013-02-01. NTNU og UiO
- **Chappell, Sally; Lee, Wai Kwong; Shooter, S; McGinnis, Ralph; Austgulen, Rigmor; Iversen, Ann-Charlotte; Morgan, Linda; The InterPregGen Consortium, on behalf of.** Evaluation of GWAS chip-genotyping of fetal DNA extracted from umbilical cord tissue and WGA-DNA extracted from filter paper bloodspots. The European Society of human genetics (ESHG) Conference; 2013-06-08 - 2013-06-11. NTNU
- **Dragset, Marte Singsås; Steigedal, Magnus; Valla, Svein; Flo, Trude Helen.** Riding the Ferrous Wheel: Identification and Study of Genes Involved in Mycobacterial Iron Acquisition. Department seminar at the Department of Biotechnology; 2013-11-13. NTNU
- **Espevik, Terje.** CEMIR - a new centre of excellence on inflammation research. CEMIR opening seminar, NTNU; 2013-10-14. NTNU
- **Espevik, Terje.** CEMIR - Centre of Molecular Inflammation Research. Offisiell åpning av de 4 nye SFF sentrene ved NTNU; 2013-06-10. NTNU
- **Espevik, Terje.** Centre of Molecular Inflammation Research. SFF forum, Oslo; 2013-11-05. NTNU
- **Espevik, Terje.** Cholesterol crystal-mediated inflammation: relationship to development of atherosclerosis. 6th International Conference on Complement Therapeutics; 2013-06-18 - 2013-06-23. NTNU
- **Espevik, Terje.** Complement dependency of cholesterol crystal induced inflammation. Gjesteforelesning ved University of Massachusetts; 2013-01-15. NTNU
- **Espevik, Terje.** Immunrespons ved sepsis. Infeksjonsmøte, Oslo; 2013-11-08. NTNU
- **Espevik, Terje.** Inflammation responses. MBI 8001 PhD kurs Universitetet i Tromsø; 2013-06-05. NTNU
- **Espevik, Terje.** Introduction to Innate Immunity. PhD course Innate Immunity, University of Copenhagen; 2013-01-20. NTNU
- **Espevik, Terje.** Involvement of cholesterol crystals in atherosclerosis. Gjesteforelesning ved Boston University; 2013-01-16. NTNU
- **Espevik, Terje.** Kolesterolkrystaller som årsak til inflammasjon ved aterosklerose. Åpning av Jebsen senter, Universitetet i Oslo; 2013-10-25. NTNU
- **Espevik, Terje.** Staphylococcus aureus triggers IFN-beta induction in human monocytes by phagosomal TLR8 signaling. 10th International Conference on Innate Immunity; 2013-06-25. NTNU
- **Espevik, Terje.** TLRs, NLRs, PAMPs and DAMPS in innate immunity. PhD course Innate Immunity, University of Copenhagen; 2013-03-23. NTNU
- **Espevik, Terje.** Toll-like receptor signalling in innate and adaptive immunity. PhD kurs: Mechanisms of cellular signal transduction, Universitetet i Oslo; 2013-10-29. NTNU
- **Flo, Trude Helen.** Betent kunnskap. Kunnskapsbyen; 2013-11-06. NTNU
- **Flo, Trude Helen.** Lipocalin 2 in mucosal immunity. Workshop on Infectious Diseases and Molecular Methods; 2013-01-08 - 2013-01-08. NTNU
- **Flo, Trude Helen.** Molecular mechanisms of mycobacterial infections. An overview. Norwegian Society for Immunology 30th anniversary meeting; 2013-11-30. NTNU
- **Flo, Trude Helen; Awuh, Jane Atesoh; Haug, Markus; Steigedal, Magnus; Damås, Jan Kristian; Halaas, Øyvind; Marstad, Anne; Shrestha, Birendra Kumar; Do, Ngoc Phuc Chau.** The role of a stress-related protein in inflammatory signalling and intracellular survival of mycobacteria. Keystone symposium: Keystone Symposium: Host Response in Tuberculosis; 2013-03-13 - 2013-03-18. NTNU og STO
- **Flo, Trude Helen; Haug, Markus; Steigedal, Magnus; Awuh, Jane Atesoh; Marstad, Anne; Shrestha, Birendra Kumar.** Mycobacterial survival and killing in host macrophages. CEMIR opening seminar; 2013-10-14. NTNU
- **Haug, Markus; Awuh, Jane Atesoh; Steigedal, Magnus; Kojen, June Frengen; Marstad, Anne; Halaas, Øyvind; Flo, Trude Helen.** T regulatory and T helper 17 cells in mouse Mycobacterium avium infection. Keystone Symposium: Host Response in Tuberculosis; 2013-03-13 - 2013-03-18. NTNU og UiO

- **Haug, Markus; Chonchoro A., Habtamu; Awuh, Jane Atesoh; Steigedal, Magnus; Marstad, Anne; Halaas, Øyvind; Flo, Trude Helen.** Mycobacteria-specific Immunity in HIV-infected Individuals and Healthy Controls. Workshop on Infectious Diseases and Molecular Methods; 2013-01-08. NTNU
- **Haug, Markus; Flo, Trude Helen; Høgset, Anders; Halaas, Øyvind.** Photochemical internalization (PCI) as novel strategy to enhance efficacy of vaccines. Instituttseminar IKM; 2013-02-27. NTNU UiO
- **Iversen, Ann-Charlotte.** Inflammation in preeclampsia and cardiovascular diseases. EU FP7 project InterPregGen Annual Meeting; 2013-04-16 - 2013-04-17. NTNU
- **Iversen, Ann-Charlotte.** Inflammatory mechanisms in preeclampsia. International Society for the Study of Hypertension in Pregnancy Congress 2013; 2013-06-11 - 2013-06-14. NTNU
- **Johansson, Ida; Bjørkøy, Geir; Monsen, Vivi; Pettersen, Kristine; Schønberg, Svanhild Margrethe Arentz.** Targeting autophagy in Disease Prevention; Effects of Marine Lipids in normal cells. 2nd NordForsk Autophagy meeting; 2013-10-01. HIST, NTNU og UiT
- **Johansson, Ida; Monsen, Vivi; Pettersen, Kristine; Schønberg, Svanhild Margrethe Arentz; Bjørkøy, Geir.** Targeting Autophagy in Disease Prevention and Theraphy; Effect of PUFAs in Normal and Cancer cells. EMBO Autophagy conference; 2013-05-05 - 2013-05-09. UiT, HIST og NTNU
- **Johansson, Ida; Monsen, Vivi; Pettersen, Kristine; Schønberg, Svanhild Margrethe Arentz; Bjørkøy, Geir.** Targeting Autophagy in Disease Prevention and Theraphy; Effect of PUFAs in Normal and Cancer cells. 2nd NordForsk Autophagy meeting; 2013-10-01 - 2013-10-03 UiT, HIST og NTNU
- **Klein, Dionne; Espevik, Terje.** Cellular and Molecular Imaging Core Facility (CMIC). The Annual Meeting of the Nordic Microscopy Society SCANDEM 2013; 2013-06-10 - 2013-06-14. NTNU
- **Klein, Dionne; Kers, Esther; Espevik, Terje; Husebye, Harald.** Dynamics of toll-like receptor 4 and its adaptor protein TRAM. The Annual Meeting of the Nordic Microscopy Society SCANDEM 2013; 2013-06-10 - 2013-06-14. NTNU
- **Løset, Mari; Johnson, Matthew P; Melton, P; Ang, W; Marsh, J; Huang, RC; Mori, T; Beilin, L; Pennell, CE; Roten, Linda Tømmerdal; Iversen, Ann-Charlotte; Austgulen, Rigmor; East, CE; Blangero, John; Brennecke, Shaun P.; Moses, Eric K.** A SNP associated with susceptibility to preeclampsia near the Inhibin, beta B gene, is also associated with cardiovascular disease risk traits. European Congress of the International Society for the Study of Hypertension in Pregnancy; 2013-06-12 - 2013-06-14. NTNU
- **Moen, Siv Helen; Nørgaard, Nikolai Nordberg; Westhrin, Marita; Størdal, Berit Fladvad; Hella, Hanne; Sundan, Anders; Standal, Therese.** TLR agonists induce expression of cytokines in mesenchymal stem cells and pre-osteoblasts promoting osteoclast activation and MM-cell growth. International Myeloma Workshop 2013; 2013-04-03 - 2013-04-07. NTNU
- **Skjesol, Astrid; Starheim, Kristian Kobbenes; Klein, Dionne C.G.; McCaffrey, Mary; Espevik, terje; Husebye, Harald.** The small GTPase Rab11a integrates TRAM trafficking between TGN and endosome in LPS induced TRAM-TRIF-signaling. Systems Dynamics in Endocytosis; 2013-09-29 - 2013-10-04. NTNU
- **Steigedal, Magnus; Siegrist, Sloan; Dragset, Marte Singsås; Haug, Markus; Ahmad, Rushdy; Rubin, Eric J; Flo, Trude Helen.** EspG Contributes to Mycobactin-Mediated Iron Acquisition and Protein Secretion in Mycobacteria. Keystone symposia: Tuberculosis: Understanding the enemy; 2013-03-13 - 2013-03-18. NTNU
- **Steigedal, Magnus; Siegrist, Sloan; Dragset, Marte Singsås; Haug, Markus; Ahmad, Rushdy; Rubin, Eric J; Flo, Trude Helen.** EspG of Esx-3 contributes to Mycobactin-mediated Iron Acquisition and Protein secretion in Mycobacteria. Norwegian Bichemical Society Contact Meeting 2013; 2013-01-31 - 2013-02-03. NTNU
- **Stødle, Guro; Tangerås, Line; Olsen, Guro Dalheim; Gundersen, Astrid; Leknes, Ann-Helen; Ryan, Liv; Steinkjer, Bjørg; Skei, Bente; Vikdal, Anne Jorunn; Myklebost, Merete; Langaas, Mette; Austgulen, Rigmor; Iversen, Ann-Charlotte.** Activation of endosomal Toll-like receptors in first trimester trophoblasts. The International Society for the Study of Hypertension in Pregnancy (ISSHP) European Congress 2013; 2013-06-12 - 2013-06-14. NTNU og STO
- **Stødle, Guro; Tangerås, Line; Olsen, Guro Dalheim; Gundersen, Astrid; Leknes, Ann-Helen; Ryan, Liv; Steinkjer, Bjørg; Skei, Bente; Vikdal, Anne Jorunn; Myklebost, Merete; Langaas, Mette; Austgulen, Rigmor; Iversen, Ann-Charlotte.** Activation of endosomal Toll-like receptors in first trimester trophoblasts. Translational Science in Perinatal Biology Graduate Course; 2013-03-24 - 2013-03-29. NTNU og STO
- **Tangerås, Line; Stødle, Guro; Olsen, Guro Dalheim; Gundersen, Astrid; Leknes, Ann-Helen; Ryan, Liv; Steinkjer, Bjørg; Skei, Bente; Vikdal, Anne Jorunn; Myklebost, Merete; Langaas, Mette; Austgulen, Rigmor; Iversen, Ann-Charlotte.** Cell surface Toll-like receptors in primary trophoblasts from first trimester placentas. The International Society for the Study of Hypertension in Pregnancy (ISSHP) European Congress 2013; 2013-06-12 - 2013-06-14. NTNU og STO
- **Tangerås, Line; Stødle, Guro; Olsen, Guro Dalheim; Gundersen, Astrid; Ryan, Liv; Steinkjer, Bjørg; Skei, Bente; Austgulen, Rigmor; Iversen, Ann-Charlotte.** First Trimester Trophoblasts Mediate Potent Inflammatory Responses through Activation of Toll-Like Receptors. Translational Science in Perinatal Biology Graduate Course; 2013-03-24 - 2013-03-29. NTNU
- **Tangerås, Line; Stødle, Guro; Olsen, Guro Dalheim; Leknes, Ann-Helen; Gundersen, Astrid; Skei, Bente; Vikdal, Anne Jorunn; Ryan, Liv; Steinkjer, Bjørg; Myklebost, Merete; Langaas, Mette; Ausgtulen, Rigmor; Iversen, Ann-Charlotte.** Functional toll-like receptors in primary first trimester trophoblasts. The 13th International Federation of Placenta Associations (IFPA) Meeting; 2013-09-11 - 2013-09-15. NTNU og STO
- **Thomsen, Liv Cecilie Vestrheim; Melton, Philip E.; Sun, Chen; Tollaksen, Kjersti; Lyslo, Ingvill; Solberg, Per; Roten, Linda Tømmerdal; Gundersen, Astrid S.; Nygård, Ottar; Iversen,**

Ann-Charlotte; Ausgtulen, Rigmor; Moses, Eric K; Bjørge, Line. Arvelighet av kardiovaskulær sykdom i en familiekohort med økt forekomst av preeklampsi. Norsk Gynekologisk Forenings årsmøte; 2013-10-24 - 2013-10-26 HAUKELAND, HNT, NTNU, SUS og UiB

- **Thomsen, Liv Cecilie Vestrheim; Melton, Philip E.; Tollaksen, Kjersti; Lyslo, Ingvill; Solberg, Per; Roten, Linda Tømmerdal; Gundersen, Astrid S.; Odland, Maria Lisa; Strand, Kristin Melheim; Nygård, Ottar; Sun, Chen; Iversen, Ann-Charlotte; Austgulen, Rigmor; Moses, Eric K; Bjørge, Line.** Heritability of cardiovascular diseases in a preeclampsia family cohort. 63rd Annual Meeting of The American Society of Human Genetics; 2013-10-22 - 2013-10-26 HAUKELAND, HNT, NTNU, SUS og UiB
- **Åsberg, Signe; Birendra, Kumar Shrestha; Flo, Trude Helen; Haug, Markus; Awuh, Jane Atesoh.** The interplay of C-type lectins and Toll-like receptors in shaping host-responses to mycobacteria. Practical course: Current Methods in Cell Biology; 2013-09-29 - 2013-10-04. NTNU

INFORMATION MATERIAL(S)

- **Espevik, Terje.** CEMIR sitt forskningstema er inflammasjon. NTNU
- **Espevik, Terje.** CEMIR's research topic is inflammation. NTNU
- **Flo, Trude Helen.** Hva har betennelse med global helse å gjøre? NTNU
- **Flo, Trude Helen.** What does inflammation have to do with global health? NTNU
- **Lien, Egil.** Pest og plager - kva er samanhengen mellom pest og overvekt? NTNU
- **Lien, Egil.** Plagues and illness – what's the connection between the plague and being overweight? NTNU
- **Niyonzima, Nathalie; Samstad, Eivind.** Det gode kolesterolet ble akkurat enda bedre. NTNU
- **Samstad, Eivind.** Sugar + inflammation = true? NTNU
- **Samstad, Eivind.** Sukker + inflammasjon = sant? NTNU
- **Sandvik, Arne; Damås, Jan Kristian.** Hvorfor forske på kroniske tarmbetennelser? UiO og NTNU
- **Sandvik, Arne; Damås, Jan Kristian.** Why study chronic instestinal inflammation? UiO og NTNU
- **Sandvik, Arne; Damås, Jan Kristian.** Why study chronic intestinal inflammation? UiO og NTNU

MEDIA CONTRIBUTION

- **Flo, Trude Helen; ntnuinfo, ntnuinfo.** Mycobacteria. [Internet] 2013-07-03. NTNU
- **Jakobsen, Siw Ellen; Espevik, Terje; Flo, Trude Helen.** Når forsvarerne blir fienden. Bladet Forskning [Business/trade/industry journal] 2013-09-01. NTNU
- **Monsen, Tor; Flo, Trude Helen.** Leter etter ny vaksine. Universitetsavisa [Newspaper] 2013-12-18. NTNU
- **Weisser, Agnethe; Espevik, Terje.** Senter for Molekylær Inflammasjonsforskning. [Newspaper] 2013-03-13. NTNU
- **Weisser, Agnethe; Espevik, Terje; Flo, Trude Helen.** Se krigercellene gå til angrep. Adressa [Newspaper] 2013-03-15. NTNU

REPORT/THESIS

- **Awuh, Jane Atesoh.** Host defense mechanisms in Mycobacterium avium infection. : NTNU 2013 (ISBN 978-82-471-4319-3) 100 p. NTNU
- **Dragset, Marte Singsås.** Riding the Ferrous Wheel: Identification and Study of Genes Involved in Mycobacterial Iron Aquisition. Trondheim: Institutt for bioteknologi, NTNU 2013 (ISBN 978-82-471-4836-5) 228 p. NTNU
- **Granlund, Atle Van Beelen.** Colonic mucosal gene expression in inflammatory bowel disease. NTNU: NTNU 2013 (ISBN 978-82-471-4322-3) 100 p. NTNU

JOURNAL PUBLICATION

- **Austdal, Marie; Skråstad, Ragnhild; Gundersen, Astrid; Ausgtulen, Rigmor; Bathen, Tone; Iversen, Ann-Charlotte.** Changes in Levels of Metabolomic Biomarkers in Serum and Urine in Women with Preeclampsia. Magnetic Resonance Materials in Physics, Biology and Medicine 2013 ;Volume 26.(1) Suppl. 1 p. 287-287. NTNU
- **Austdal, Marie; Skråstad, Ragnhild; Gundersen, Astrid; Austgulen, Rigmor; Bathen, Tone Frost; Iversen, Ann-Charlotte.** Metabolomic biomarkers in serum and urine of preeclamptic women. Pregnancy Hypertension 2013 ;Volume 3.(2) p. 67-68. NTNU
- **Brenna, Øystein; Furnes, Marianne Waldum; Drozdov, Ignat; Granlund, Atle Van Beelen; Flatberg, Arnar; Sandvik, Arne Kristian; Zwiggelaar, Rosalie; Mårvik, Ronald; Nordrum, Ivar Skjåk; Kidd, Mark; Gustafsson, Björn.** Relevance of TNBS-Colitis in Rats: A Methodological Study with Endoscopic, Historical and Transcripttomic Characterization and Correlation to IBD. PLoS ONE 2013 ;Volume 8.(1) p. NTNU og STO
- **Espevik, Terje.** Sensorer som setter i gang betennelse: hvordan virker de og hvorfor trenger vi dem?. Årbok / Det norske videnskaps-akademi 2013 . NTNU
- **Grandaunet, Berit Helen Jensen; Syversen, Silje Watterdal; Hoff, Mari; Van der Hejde, Désirée; Haugeberg, Glenn; Kvien, Tore Kristian; Standal, Therese.** Dickkopf-1 is associated with periarticular bone loss in patients with rheumatoid arthritis. Open Journal of Rheumatology and Autoimmune Diseases 2013 (3) p. 216-220. DIAKON, NTNU, SSHF, STO og UiO
- **Granlund, Atle Van Beelen.** Nye doktorgrader - Atle van Beelen Granlund. NBS-nytt 2013 (3) p. 30-30. NTNU
- **Granlund, Atle Van Beelen; Flatberg, Arnar; Østvik, Ann Elisabet; Drozdov, Ignat; Gustafsson, Björn; Kidd, Mark; Beisvag, Vidar; Torp, Sverre Helge; Waldum, Helge; Martinsen, Tom Christian; Damås, Jan Kristian; Espevik, Terje; Sandvik, Arne Kristian.** Whole Genome Gene Expression Meta-Analysis of Inflammatory Bowel Disease Colon Mucosa Demonstrates Lack of Major Differences between Crohn's Disease and Ulcerative Colitis. PLoS ONE 2013 ;Volume 8.(2) p. NTNU og STO
- **Grebe, Alena; Latz, Eicke.** Cholesterol crystals and inflammation. Nature reviews. Immunology 2013

- **Grimstad, Øystein; Husebye, Harald; Espevik, Terje.** TLR3 mediates release of IL-1 beta and cell death in keratinocytes in a caspase-4 dependent manner. Journal of dermatological science (Amsterdam) 2013 ;Volume 72.(1) p. 45-53. NTNU og STO
- **Haug, Markus; Awuh, Jane Atesoh; Steigedal, Magnus; Kojen, June Frengen; Marstad, Anne; Nordrum, Ivar Skjåk; Halaas, Øyvind; Flo, Trude Helen.** Dynamics of immune effector mechanisms during infection with Mycobacterium aviumin C57BL/6 mice. Immunology 2013 ;Volume 140.(2) p. 232-243. NTNU og STO
- **Iversen, Ann-Charlotte.** Inflammatory mechansism in preeclampsia. Pregnancy Hypertension 2013 ;Volume 3.(2) p. 58. NTNU
- **Latz, Eicke; Xiao, T. Sam; Stutz, Andrea.** Activation and regulation of the inflammasomes. Nature reviews. Immunology 2013 ;Volume 13.(6) p. 397-411. NTNU
- **Lau, Corinna; Gunnarsen, Kristin Støen; Høydahl, Lene Støkken; Andersen, Jan Terje; Berntzen, Gøril; Pharo, Anne Margrethe; Lindstad, Julie Katrine; Ludviksen, Judith K; Brekke, Ole Lars; Barratt-Due, Andreas; Nielsen, Erik Waage; Stokes, Christopher R.; Espevik, Terje; Sandlie, Inger; Mollnes, Tom Eirik.** Chimeric Anti-CD14 IGG2/4 Hybrid Antibodies for Therapeutic Intervention in Pig and Human Models of Inflammation. Journal of Immunology 2013 ;Volume 191.(9) p. 4769-4777 NLSH, NTNU, OUS, UiO og UiT
- **Løset, Mari; Johnson, MP; Melton, P; Ang, W; Marsh, J; Huang, RC; Mori, T; Beilin, L; Pennell, C.; Roten, Linda Tømmerdal; Iversen, Ann-Charlotte; Austgulen, Rigmor; East, CE; Blangero, J; Brennecke, SP; Moses, Eric.** A SNP associated with susceptibility to preeclampsia near the Inhibin, beta B gene, is also associated with cardiovascular disease risk traits. Pregnancy Hypertension 2013 ;Volume 3.(2) p. 63-63. NTNU
- **Marty-Roix, Robyn; Lien, Egil.** De-oiling inflammasomes. Immunity 2013 ;Volume 38. p. 1088-1090. NTNU
- **Mollnes, Tom Eirik; Barratt-Due, Andreas; Pischke, Søren Erik; Sandanger, Inger; Nilsson, Pernille; Lambris, J; Nunn, Miles A.; Denk, Stephanie; Espevik, Terje; Huber-Lang, Markus.** Double-blockade of CD14 and complement component C5 abolish the inflammatory storm and improve survival in mouse polymicrobial sepsis. Molecular Immunology 2013 ;Volume 56.(3) p. 294-294. NTNU, OUS og UiO
- **Nymo, Stig Haugset; Samstad, Eivind; Niyonzima, Nathalie; Aune, Marie Hjelmseth; Bergseth, Grete; Ryan, Liv; Brekke, Ole Lars; Latz, E; Lambris, J.D.; Espevik, Terje; Mollnes, Tom Eirik.** Cholesterol crystals activate the complement system and are phagocytosed in a complement-dependent manner. Molecular Immunology 2013 ;Volume 56.(3) p. 246-246. NLSH, NTNU, UiO, UiT og OUS
- **Odland, Maria Lisa; Strand, Kristin Melheim; Nordbø, Svein Arne; Forsmo, Siri; Ausgtulen, Rigmor; Iversen, Ann-Charlotte.** Changing patterns of cytomegalovirus seroprevalence among pregnant women in Norway between 1995 and 2009 examined in the Norwegian Mother and Child Cohort Study and two cohorts from Sør-Trøndelag County: a cross-sectional study. BMJ Open 2013 ;Volume 3. NTNU og STO
- **Rokstad, Anne Mari; Brekke, Ole Lars; Steinkjer, Bjørg; Ryan, Liv; Kolláriková, Gabriela; Strand, Berit Løkensgard; Skjåk-Bræk, Gudmund; Lambris, John D.; Lacík, Igor; Mollnes, Tom Eirik; Espevik, Terje.** The induction of cytokines by polycation containing microspheres by a complement dependent mechanism. Biomaterials 2013 ;Volume 34.(3) p. 621-630. NLSH, NTNU, OUS, UiO og UiT
- **Rokstad, Anne Mari; Strand, Berit Løkensgard; Espevik, Terje; Mollnes, Tom Eirik.** Biocompatibility and Biotolerability Assessment of Microspheres Using a Whole Blood Model. Micro and Nanosystems 2013 ;Volume 5.(3) p. 177-185. NLSH, NTNU og UiO
- **Samstad, Eivind; Niyonzima, Nathalie; Nymo, Stig Haugset; Aune, Marie Hjelmseth; Ryan, Liv; Brekke, Ole Lars; Sandanger, I; Aukrust, Pål; Damas, Jan Kristian; Latz, Eicke; Lambris, J.D.; Mollnes, Tom Eirik; Espevik, Terje.** Cholesterol crystals induce inflammasome activation and cytolcine release in a complement-dependent manner. Molecular Immunology 2013 ;Volume 56.(3) p. 260-260. NLSH, NTNU, OUS, UiO og UiT
- **Sandanger, Øystein; Ranheim, Trine; Vinge, Leif Erik; Bliksøen, Marte; Alfsnes, Katrine; Finsen, Alexandra; Dahl, Christen Peder; Askevold, Erik Tandberg; Florholmen, Geir; Christensen, Geir Arve; Fitzgerald, Katherine A.; Lien, Egil; Valen, Guro; Espevik, Terje; Aukrust, Pål; Yndestad, Arne.** The NLRP3 inflammasome is up-regulated in cardiac fibroblasts and mediates myocardial ischaemia-reperfusion injury. Cardiovascular Research 2013 ;Volume 99.(1) p. 164-174. NTNU, OUS og UiO
- **Stødle, Guro; Tangerås, Line; Olsen, Guro Dalheim; Leknes, Ann-Helen; Gundersen, Astrid; Ryan, Liv; Steinkjer, Bjørg; Skei, Bente; Vikdal, Anne Jorunn; Myklebost, Merete; Langaas, Mette; Austgulen, Rigmor; Iversen, Ann-Charlotte.** Activation of endosomal Toll-like receptors in first trimester trophoblasts. Pregnancy Hypertension 2013 ;Volume 3.(81). NTNU og STO
- **Tangerås, Line; Stødle, Guro; Olsen, Guro Dalheim; Gundersen, Astrid; Leknes, Ann-Helen; Ryan, Liv; Steinkjer, Bjørg; Skei, Bente; Vikdal, Anne Jorunn; Myklebost, Merete; Langaas, Mette; Austgulen, Rigmor; Iversen, Ann-Charlotte.** Cell surface Toll-like receptors in primary trophoblasts from first trimester placentas. Pregnancy Hypertension 2013 ;Volume 3.(81). NTNU og STO
- **Tangerås, Line; Stødle, Guro; Olsen, Guro Dalheim; Leknes, Ann-Helen; Gundersen, Astrid; Skei, Bente; Vikdal, Anne Jorunn; Ryan, Liv; Steinkjer, Bjørg; Myklebost, Merete; Langaas, Mette; Ausgtulen, Rigmor; Iversen, Ann-Charlotte.** Functional Toll-like receptors in primary first trimester trophoblasts. Placenta 2013 ;Volume 34.(9) p. A33-A33. NTNU og STO
- **Thomsen, Liv Cecilie Vestrheim; Melton, Philip E.; Sun, Chen; Tollaksen, Kjersti; Lyslo, Ingvill; Solberg, Per; Roten, Linda Tømmerdal; Gundersen, Astrid; Nygård, Ottar; Ivers-**

en, Ann-Charlotte; Ausgtulen, Rigmor; Moses, Eric; Bjørge, Line. Arvelighet av kardiovaskulær sykdom i en familiekohort med økt forekomst av preeklampsi. Gynekologen 2013 ;Volume 26.(3) p. 43-44. HNT, NTNU, SUS, UiB og UIS

- **Vladimer, G; Marty-Roix, R; Ghosh, S; Weng, D; Lien, Egil.** Inflammasomes and host defenses against bacterial infections. Current Opinion in Microbiology 2013 ;Volume 16.(1) p. 23-31. NTNU
- **Østvik, Ann Elisabet; Flo, Trude Helen; Granlund, Atle Van Beelen; Espevik, Terje; Torp, Sverre Helge; Beisvag, Vidar; Damås, Jan Kristian; Flatberg, Arnar; Waldum, Helge; Sandvik, Arne Kristian.** Expression of Toll-like receptor-3 is enhanced in active inflammatory bowel disease and mediates the excessive release of lipocalin 2. Clinical and Experimental Immunology 2013 ;Volume 173.(3) p. 502-511. NTNU og STO
- **Østvik, Ann Elisabet; Granlund, Atle; Bugge, Marit; Nilsen, Nadra; Torp, Sverre Helge; Waldum, Helge; Damås, Jan Kristian; Espevik, Terje; Sandvik, Arne Kristian.** Enhanced expression of CXCL10 in inflammatory bowel disease: Potential role of mucosal toll-like 3 receptor stimulation. Inflammatory Bowel Diseases 2013 ;Volume 19.(2) p. 265-274. NTNU og STO

Funding and Expenditures 2013

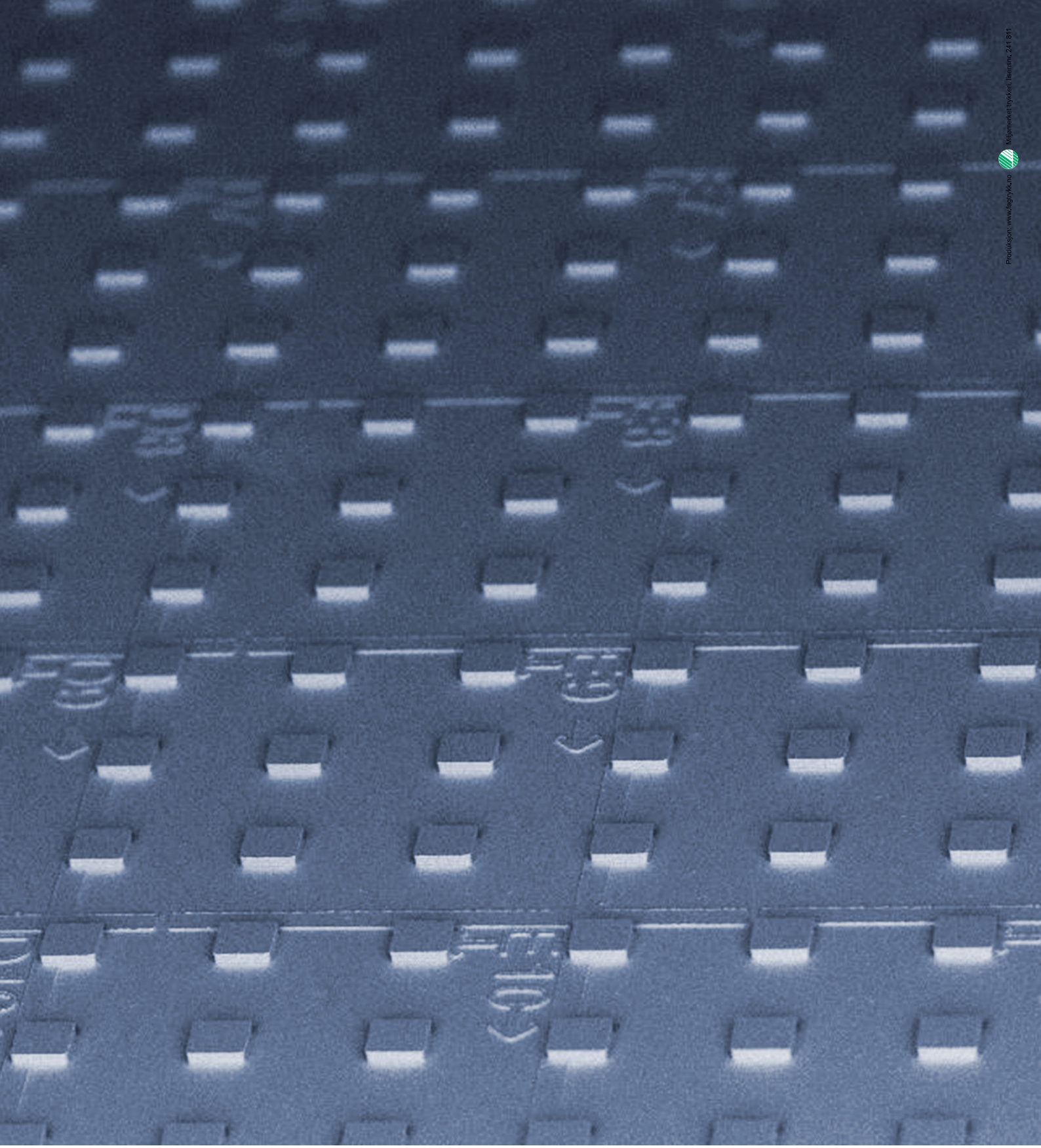
Funding (1000 NOK)	2013
NTNU	6 197
Research Council of Norway (RCN) – Centre of Excellence grant	4 793
Other RCN funding	8 470
Other public funding	8 800
Total funding	28 260

Expenditures (1000 NOK)	2013
Personnel and indirect costs	22 028
Procurement of R&D services	0
Equipment	1 440
Other operating costs	4 792
Total expenditures	28 260

Microscope photos:
Page 5: Harald Husebye
Page 6: Terje Espevik
Page 7: Eicke Latz
Page 8: Øyvind Halaas
Page 9: Guro Stødle
Page 10: Ann Elisabeth Østvik
Page 11: Marita Westhrin

Microscope photos page 24-25:
In order:
Harald Husebye
Marie Aune
Sverre Torp
Terje Espevik

Photos:
Photo on page 4: Helsebygg Midt-Norge
Photo on page 19: Helsebygg Midt-Norge/Synlig
Photos on page 3, 12, 13, 15, 16, 17 and 22: NTNU/Geir Mogen
Black/white portrait on page 5, 7, 8, 9,10 og 11: NTNU/Geir Mogen



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HELSE MIDT-NORGE