Annual report 2013
The negative year-end result is largely explained by the fact that grant instalment frequency vary and major incomes are registered in previous years, whereas costs are relatively equally distributed between years. As outlined in the long term funding plan, planned transfer of funds between fiscal years cover the 2013 deficit and allow for further sound operation.

Compared to 2012 figures, the total funding and cost figures are reduced. In 2013 CIR went through an organisational restructuring, where several members left the CoE to join the newly established K.G. Jebsen Centre for Research on Influenza Vaccines. This affects the 2013 man-year production as well as funding and expenditure figures. External funding, direct- and indirect contributions from both the UiO and OUS, and the associated costs, are reduced in 2013 as a consequence of this change.

1 Centre of Excellence grant.
2 Including value of personnel funded by UiO and indirect costs of infrastructure.
3 Including value of personnel funded by OUS and indirect costs of infrastructure.
4 Including other grants from the RCN and grants from South-Eastern Norway Regional Health Authority.
5 Including grants from the Norwegian Cancer Society, and others.
6 Including ERC advanced grant, EU grants, and others.
7 Including indirect costs.

* Accounting figures from the University of Oslo and Oslo University Hospital.
Vision statement

This centre identifies and investigates novel mechanisms of immune dysregulation to advance the development of therapeutics.

Key accomplishments 2013

- Found that Rab GTP-ases vary greatly during maturation of human dendritic cells, potentially regulating the mature phenotype of these cells.

- Described that Chronic Lymphocytic Leukemia (CLL) cells are regulated by CD4+ T cells.

- Identified a TSLP-responsive DC subset in human nasal mucosa and characterised its role in upper airway allergy.

- Increased our understanding of the interaction between the neonatal Fc receptor (FcRn) and albumin. Designed and characterised novel albumin variants with increased binding to FcRn that will be used to extend the serum half-life of fused biopharmaceuticals.

- Characterised epitopes of transglutaminase 2 (TG2) recognised by autoantibodies of celiac disease patients. The binding of mAbs generated by expression cloning of Ig genes from single plasma cells of the celiac disease lesion was assessed. The mAbs recognise few conformational epitopes that cluster in the N-terminal half of the enzyme.
Yet another year has passed in the life of CIR. 2013 was the first year of the second five-year programme as a Centre of Excellence. We are now closer to the termination than the inauguration day. The perspective of CIR is thus slowly changing.

I ended my comments of last year’s annual report by saying that in January 2014 one of two positions, funded by the Medical Faculty as part of the ‘phasing in scheme’ of our CoE, should be filled by a new group leader at CIR. The ‘phasing in scheme’ has been installed by the Faculty to secure the scientific value and human capital created over the ten-year-period as a CoE. To support CIR in a situation where part of Bjarne Bogen’s group left CIR to form the K.G. Jebsen Centre for Influenza Vaccine Research in 2013, funding for one of CIR’s two new academic positions was approved by the Board of the Medical Faculty already from 2014. The advertisement text to attract a top expert in the area of autoimmunity or allergy was prepared. However, on the decision of CIR’s Board, this position is not yet advertised because of space constraints at the Department of Immunology. Currently there is no possibility to house a professor if she or he is coming from outside bringing a group along. The Board of CIR is actively working to solve the space constraints and find a fine solution. I have great faith in the Board on solving this issue as it is of outmost importance.

Aside of these plans, CIR has got a new group leader – Ludvig Munthe. Ludvig has worked in the group of Bjarne Bogen. Last year Ludvig was appointed professor at the Institute of Clinical Medicine being responsible for the PhD student programme at the Institute, and he now has his own research group. It is my great pleasure to welcome Ludvig to CIR as a group leader. The research programme Ludvig is developing on autoimmunity and T cell and B cell collaboration is a huge asset to CIR. I have great expectations in him, and I hope he will thrive at our centre.

In 2013, CIR scientist authored or co-authored 46 papers in international peer-reviewed journals. I am content with the high publication output, both in terms of volume and quality. The number of CIR researchers is slightly lower than last year due to the above mentioned reorganisation which will likely impact on our productivity in the near future. Five PhD students defended their thesis in 2013. Ole Audun W. Haabeth, Gunnveig Grødeland, Pier Adelchi Ruffini, Kristina Berg Lorvik and Rasmus Iversen successfully completed their PhDs. The candidates and their supervisors do indeed deserve congratulations. I also thank the opponents for their effort in evaluating the work of our candidates.

Our Visiting Professor program had visits from Mark Shlomchik (Yale, USA), Bana Jabri (University of Chicago, USA) and Peter Cresswell (Yale, USA) in 2013. The Visiting Professor program is extremely valuable to CIR. It is also recognised by people outside of CIR. I was recently invited to the leadership of the Medical Faculty at our host institution to inform about it. Clearly the Medical Faculty has ambitions to adopt elements from our Visiting Professor program to other parts of the Faculty. I am very grateful to the Visiting Professors who spent time in Oslo in 2013. I thank them for the insightful advise they have given to the centre researchers, and for their excellent lectures. A general high turnout by non-CIR members at these open lectures signifies that the CIR Visiting Professors are indeed fertilising the grounds outside of CIR. This I am very happy for.

In addition to guest lectures by Visiting Professors, there have been other guest lectures at CIR including those organised by the postdoc committee. Altogether there were seven guest lectures with invited international speakers and CIR hosted or co-hosted five mini-symposia with internal and external speakers. Three of the mini-symposia where organised in collaboration with the Norwegian Society for Immunology and the K.G. Jebsen Centre for Influenza Vaccine Research. The guest lectures and the mini-symposia are described in more detail.
CIR returned to Geilo for the fourth CIR retreat in April 2013. The retreat is a big event for the CIR members. More than 80 participants, an all-time high, attended the retreat. Work at the Centre was presented on posters and in short talks and there were inspirational keynote lectures given by Pavel Tolar, Søren Buus and Allan Mowat. I am very happy with the fruitful scientific discussions and social interaction at the poster sessions, in the workshops and on the ski slopes. I take this opportunity to express my gratitude to the invited guests and the organising committee. The retreat program is also described in more details elsewhere in this report. The CIR management invite all Centre members to a shorter retreat in 2014. The next ‘full scale’ retreat will be held in 2015.

To the CIR members I say: Keep moving, continue to do good science and enjoy the privileges we have as a Centre of Excellence.
Scientific currency

PAPERS
CIR scientist authored or co-authored 46 papers in international peer-reviewed journals in 2013. Of the papers published in 2013, 18 papers appeared in journals with an impact factor above 5.0. Two of these appeared in journals with an impact factor above 10.0, of which 1 had an impact above 30.0. The proportion of papers in journals with medium to high impact factor has increased since last year and with exception of the very strong publication output in 2011, the total number of publications by CIR scientist per year has never been higher. In general the quality and visibility of publications from the centre is high. CIR scientists have extensive collaborations with national and international research groups. More than 50 % of the papers published in 2013 with one or more CIR authors are the result of collaborations with international institutions. Impact factor distribution and publications based on collaborations are illustrated in the figures to the left. CIR publications in 2013 are presented on page 33 of this report. National and international collaborators are listed on page 51.

BOOKS AND BOOK CHAPTERS
CIR members contributed to 7 books or book chapters in 2013. A complete list of books and book chapters is given in the publications section on page 36.

PATENTS
Researchers at CIR have a strong interest in, and record of, innovation and securing of intellectual property rights from research. The accumulated number of patents granted or patent applications filed by CIR scientists since CIR commenced operations is 26. Read more in the innovation and industrialisation section on page 9.

DISSEMINATION OF RESEARCH RESULTS
CIR members gave 25 talks as invited speakers at international scientific meetings in 2013. In addition 12 oral presentations and 12 posters were presented by CIR scientists at international conferences. Furthermore, CIR staff gave 22 lectures and presentations, and published 4 articles, aimed at a targeted audience and the general public. These include postgraduate lectures, research seminars, training courses at universities and hospitals, as well as presentations to patient organisations and professional organisations. Talks, posters and dissemination activities aimed at a targeted audience and the public, as well as media coverage, are listed in the back of this report.

PRIZES AND AWARDS
CIR scientists Aram N. Andersen, Inger Øynebråten and Bjarne Bogen were awarded the 2013 Inven2 idea prize ("Idéprisen"). Inven2 is the technology transfer office at the University of Oslo and Oslo University Hospital. The prize was awarded for their novel technology on HIV and cancer vaccine development and was presented during the Oslo Innovation week (photo).
CONTRIBUTION TO LOCAL RESEARCH ENVIRONMENT

CIR supports the Norwegian Society for Immunology (NSI) and has the ambition to contribute towards the immunological research environment in Oslo. CIR members are collectively members of the NSI and the centre co-host lectures with the society. Importantly, guest lectures and minisymposia hosted by CIR are open to anyone interested and we actively invite the broader immunology community to attend these events. Furthermore, we invite immunologist outside the centre as speakers at these open events.

Centre staff is involved in the education and supervision of basic scientists and clinicians at all levels. CIR scientists have organised or lectured at graduate courses in molecular cell biology and immunology including Basic immunology and immunological techniques and Advanced immunology offered by the University of Oslo.

CIR staff manages and operates advanced technology and share their technical expertise with the surrounding research environment. CIR group leader Oddmund Bakke heads an advanced imaging platform specialising in subcellular studies of live and fixed cells. In 2013, the NorMIC-UiO imaging platform opened as a national facility. CIR scientist Gustavo De Souza heads the proteomics core facility at Oslo University Hospital-Rikshospitalet. The facility offers advanced analysis of proteins and peptides by mass spectrometry.

FOCIS-CoE

CIR is a Federation of Clinical Immunology Societies (FOCIS) Centre of Excellence (FCE) (www.focisnet.org). The FCEs represents an exclusive community of institutions of outstanding clinical and scientific quality. There are 70 FCE’s worldwide, with approximately 45 centres in North-America and 20 in Europe. The FCE status represents an international recognition of the quality and impact of CIR and provides an opportunity for CIR to strengthen our translational immunology activities.

"The Federation of Clinical Immunology Societies (FOCIS) Centers of Excellence (FCE) network creates a community of researchers and clinicians that provides an effective translational training environment by promoting interdisciplinary innovation." www.focisnet.org.
### Innovation and industrialisation

#### VACCIBODY AS
Two of the CIR groups (Bogen and Sandlie) have developed novel vaccine molecules, known as Vaccibodies, which induce superior immune responses in a variety of animals. A spin-out company, Vaccibody AS, was founded in 2007 based on the patented technology. The patent portfolio is continuously strengthened with clinical use and novel targeting units for a variety of applications.

Vaccibodies target antigen presenting cells for efficient delivery of antigen and induction of immune responses. The vaccines are delivered as DNA plasmids administered intramuscularly or intradermally. The muscle or skin cells produce and secrete Vaccibody proteins that target antigen presenting cells and load them with antigen for presentation to lymphocytes.

In 2013 the company made significant progress with its lead product candidate VB 10.16, a therapeutic vaccine against cervical pre-cancerous lesions. VB 10.16 is currently in GLP toxicology.

#### NEXTERA AS
Phage display is the dominating technology for discovery and refinement of novel protein-based diagnostics and therapeutics. An improved version termed SSIp display has been developed by the Sandlie group at CIR, and commercialized by a spin-out company that was established by CIR scientist Geir Åge Løset and Biomedicines Innovation AS in 2009 – Nextera AS. Additional IPR was acquired from Affitech AS in 2012 and Nextera has furthermore inlicensed innovations related to MHC class II through Invenz2. These were jointly developed by the Sandlie and Bogen groups at CIR. Through 2013, Nextera were granted patent rights to WO2009/024591, WO2010/097411, WO2010/097589, WO2011/036555 and WO2011/101681. The core activity of the company is presently focused on phage display of MHC class II molecules, so called Phagemers.

Currently, Nextera AS is performing joint research with the Sollid and Sandlie groups at CIR, partially funded by a major Research Council of Norway BIA grant, using Phagemers with the aim of developing novel therapeutics for Crohn’s disease. In 2013 Nextera raised 550 000€ in private equity which secures continuous funding of research activities, as well as strengthening of the Board of Directors, management and R&D team.

#### EXTENDING IN VIVO HALF-LIFE OF SMALL DRUGS
The efficacy of chemical drugs, peptides, small proteins and engineered antibody fragments are hampered by short serum half-life, ranging from minutes to a few hours. Therefore, strategies to tailor their serum persistence and biodistribution are needed. Postdoc Jan Terje Andersen (Sandlie group) has developed a unique technology that may extend the in vivo half-life of potentially all chemical and protein drugs. This will ultimately result in drugs with stabilised serum levels, which means less side effects and less frequent dosing. Together with Invenz2, they have signed agreements with Novozymes Biopharma, and together with Novozymes, established a very successful research program. So far, six patent families have been filed by Novozymes based on the results of the collaborative research.

As a result of this collaboration, Novozymes has launched two new products named Albufuse Flex and Recombumin Flex. In short, the new products are based on a list of new albumin variants. All have one or more amino acids that differ from normal albumin. They bind the neonatal Fc receptor with a range of different affinities, and when tested in rats and rhesus monkeys show greatly altered half-life. The best binders have increased and the poorest binder decreased half-life. Now, either genetic fusion (peptide or protein) or chemical conjugation of small drugs to either of these albumin variants will greatly alter the serum half-life of the drug. In 2013, new albumin variants have been designed with increased half-life beyond that of earlier versions.

#### PATENTS
Patents and filed patent applications by CIR scientists are listed on page 36.
Core competency at CIR

- A wide variety of cellular and humoral immune assays.
- Advanced methods in molecular biology, proteomics and cellular imaging.
- Disease models in humans and animals. The models are used to understand the molecular mechanisms of immune regulation and autoimmunity.
- Transgenic mouse models.
- Functional characterisation of immune cells in human tissue.
- Study of immune molecules and their intracellular functions in antigen presenting cells.
- Molecular engineering for the development of new therapeutic agents and research reagents.
The centre consists of research groups with complementary scientific expertise. Two groups, headed by Inger Sandlie and Oddmund Bakke, are affiliated with the Department of Biosciences at the Faculty of Mathematics and Natural Sciences. Two research groups, headed by Bjarne Bogen and Ludvig Sollid are affiliated with the Department of Immunology at the Faculty of Medicine. One group, headed by Frode L. Jahnsen, is a member of the Laboratory for Immunohistochemistry and Immunopathology, Department of Pathology, at the Faculty of Medicine.
Tb2 mAb
to da
15K
14L?
FAB 3 ?
Research groups

Bakke group 14
Bogen group 16
Jahnsen group 18
Sandlie group 20
Sollid group 22
Bakke group

Our group has since the early nineties aimed to understand the endocytic pathway and how peptide loading of the MHC class II complexes (MHC II) is regulated. A special focus for the group is to elucidate the contribution of the invariant chain (Ii) to the biogenesis of an antigen-presenting cell (APC) specific endocytic pathway (Landsverk et al., 2009, 2011, 2012).

Ii plays a vital role in MHC II assembly and intracellular transport, but has been attributed an increasing number of additional functions in both antigen presentation, cell signalling and as a vehicle for loading antigens in immunisation protocols. An evolutionary conserved property of Ii is to induce the convergence, or fusion of early endocytic vesicles, and this property may serve vital functions in antigen presentation, cell signalling and beyond. Furthermore we study the influence of other regulatory molecules essential for the antigen loading compartment such as the small Rab GTP-ases (Berg-Larsen et al., 2013). The group consist of 2 researchers, 2 postdocs, 3 PhD students, 6 master students and 2 technicians. The Bakke group also runs the FUGE supported Norwegian Molecular Imaging Consortium, NorMIC-Oslo. NorMIC-Oslo opened as a national imaging facility in 2013.

KEY PROJECT SUMMARIES
The group is focusing on the properties of the endosomal pathway in cells in general and the adaptations to this pathway in immune cells. The projects can be divided into five sub themes:

- Sorting and trafficking of immune molecules in model cell lines and in dendritic cells.
- Regulation of vesicular transport between the Golgi network and the endosomal pathway – searching for new players.
- Study of endosomal maturation and how the antigen loading compartment, the immunendosome, is formed.
- Regulation of receptor signalling by endocytic sorting and endosomal effector kinetics in the endosomal pathway.
- Investigation of the mechanisms by which activated macrophages kill cancer cells in mice and humans.

Our work is primarily focused on understanding the process of antigen uptake, processing and presentation. These events are instrumental to the initiation and propagation of adaptive immune responses. The endocytic pathway common to all cells is uniquely adapted by specific immune cells to achieve this purpose. In order to achieve our ultimate goals with regard to discovering the specifics of immune cell functions, we have invested a large body of research on how the endocytic pathway functions in general in model cell systems. We have contributed to the current understanding of cell biological processes in the endocytic pathway in general and our current goal is to use this foundation to elucidate the unique adaptations to this system in antigen-presenting cells. This will provide the basis to better understand vaccination regimes and protocols for immune therapy of cancers, autoimmune-, and infectious diseases.

Our main strategy employs a wide array of advanced live cell imaging technologies, supplemented by biochemistry, immunological assays and DNA/RNA techniques. The group collaborates in studies within CIR, where we provide the cell biological outlook and essential microscopy expertise. These include:

- Uptake and sorting of targeted antigen (Bogen).
- B lymphoma cells with complementary BCRs delete each other in vitro (Jacobsen/ Bogen).
- Intracellular trafficking of the FcRn receptor (Andersen/ Sandlie).

CENTRAL PUBLICATIONS IN 2013
ACHIEVEMENTS IN 2013
- Showed that Ii carrying antigenic peptides in the CLIP region can promote efficient presentation of the epitopes to CTLs independently of the classical MHC I peptide loading machinery (Eur J Immunol, 2013).
- Found that Rab GTP-ases vary greatly during maturation of human dendritic cells, potentially regulating the mature phenotype (Plos One, 2013).
- Developed a novel strategy for vaccines against HIV and cancer (Inven2 Idea Prize 2013; work performed in Bogen and Bakke groups).

AMBITIONS FOR 2014
- Dissect elements of the molecular mechanisms for sorting to the intracellular antigen loading compartment based on high throughput antigen loading screens.
- Find interactions partners for the Rab modulated transport from late endosomes to the Golgi network.
- Characterise endosomal maturation in dendritic cells and the Meljuso model antigen presenting cells.
- Characterize the immune infiltrate in human non-small cell lung cancer tumors.
Bogen group

The Bogen group runs projects within three areas, 1) Idiotype-driven T-B collaboration and its role in health and disease, 2) The mechanism by which CD4+ T cells can reject cancer cells, 3) Novel vaccine molecules for cancer and infectious diseases (organized in K.G. Jebsen Centre for Research on Influenza Vaccines). Key summaries for the two first research topics only are given below. These two research topics may at first glance seem separate but are in fact closely related. The common theme is immunoglobulins and how these may be recognised by T cells.

KEY PROJECT SUMMARIES

Bogen and co-workers have over the last 25 years painstakingly established a novel type of interaction between T and B lymphocytes where T cells recognise Ig variable region-derived idiotypic (Id) peptides presented on the Major Histocompatibility Class II molecules on the surface of B cells. When the B cell receive help from such Id-specific T cells, and the B cell at the same time recognise a self-antigen with its B-cell receptor for antigen, the B cell, receiving these two separate signals, will be activated, proliferate and differentiate. Our previous work has shown that this mechanism may cause immune dysregulation, autoimmunity and B lymphoma development in mice. In 2012 we started efforts to extend this pathogenic mechanism to patients with Chronic Lymphatic Leukaemia (CLL). This work was published in Cell Report in 2013 (Key accomplishment). At the same time we are extending our studies of the basic mechanisms by having established new strains of knock-in mice that have B cells with anti-Id (in press J Immunol, 2014) and Id+ BCRs, respectively. A project related to elucidation of the ternary Id-specific TCR/Id-peptide/MHC class II (I-Ed) molecule has proven difficult and is in slow progress.

As concerns tumor immunology, a detailed description of CD4+ T cells in tumors and draining lymph nodes was published in 2013. We have studied bystander killing by CD4+ T cells, and detected a mechanism by which tumor cells can escape killing by CD4+ T cells. Further, we have obtained significant results as to how Th1/M1 macrophages kill MHC class II negative tumor cells. The MOPC315.BM model, published by our group in 2012, has now been distributed to a large number (>15) collaborators world-wide.

CENTRAL PUBLICATIONS IN 2013


Bjarne Bogen
ACHIEVEMENTS IN 2013

- Described that Chronic Lymphocytic Leukemia cells are regulated by CD4+ T cells.
- Established an Ig double knock-in mouse with an anti-Id BCR. Used this mouse to show that Id-specific T and B cells can recognise Id+Ig via conventional mechanisms for T-B collaboration. Dendritic cells are not needed.
- Established an Ig VH knock-in mouse, that when bred with \(\lambda^{2315}\)-transgenic mice, establishes a model for an Id+ BCR.
- Developed a model for studying bystander killing of tumor cells mediated by CD4+ T cells.

AMBITIONS FOR 2014

- Define the specificity of CD4+ T cells that help Chronic Lymphocytic Leukemia cells.
- To investigate the importance of BCR-ligation by self-antigen in Idiotype-driven T-B collaboration.
- To explore the mechanism by which CD4+ T cells reject tumour cells.
- To explore the mechanism by which tumor cells escape CD4+ T cells.
- To study interaction of B cells with complementary BCRs by use of the knock-in mice generated in 2013.
Jahnsen group

We study how innate and adaptive immune systems communicate and cooperate on mucosal surfaces in humans. More specifically, we explore the interaction between antigen-presenting cells, CD4+ T cells and stromal cells under steady-state conditions and during inflammation, both chronic and experimentally-induced.

KEY PROJECT SUMMARIES

Antigen presenting cells play a central role in shaping the immune response to foreign antigens at mucosal surfaces. We have characterized these cells in the gut and find that they constitute no less than seven phenotypically distinct subpopulations. We are currently studying their functional properties during steady-state and inflammation. In untreated celiac disease we have observed that cells with phenotypic characteristics of being monocyte-derived (HLA-DR+CD14+CD11c+) are selectively increased in the mucosa. In a recently developed method to track the emigration of leukocytes into the tissue, we directly demonstrate that HLA-DR+CD14+CD11c+ cells in fact are recently recruited blood monocytes. Together, our findings strongly suggest that emigrating CD14+ monocytes are directly involved in the immunopathology of celiac disease. We are currently trying to understand the mechanism for this recruitment and the function of CD14+ monocytes in the disease. We are performing similar studies on macrophages and dendritic cells in the airway mucosa using allergic rhinitis as a model for airway inflammation.

We have an intimate collaboration with clinicians at Oslo University Hospital and other hospitals in the Oslo area. This collaboration puts us in the unique position to get human mucosal tissue for functional studies of resident immune cells under normal conditions. Furthermore, we have several ongoing studies in which we get tissue from experimentally-induced inflammation mimicking celiac disease and hay fever. These are unique models of human disease where we can study the dynamics of the inflammatory reaction.

CENTRAL PUBLICATIONS IN 2013

ACHIEVEMENTS IN 2013

- Performed a fine-grained analysis of monocytes, macrophages and dendritic cells present in the human gut.
- Developed a new method to determine the half-life of antigen presenting cells in the human gut.
- Identified a TSLP-responsive DC subset in human nasal mucosa and characterised its role in upper airway allergy.
- Identified three distinct T cell subsets with regulatory properties in the upper airways.
- Quantified Mycobacterium tuberculosis-reactive CD4+CD45RO+ T cells in latently infected Indian adolescents.

AMBITIONS FOR 2014

- Determine the turn-over rate of antigen presenting cells in the human gut compared with other organs.
- Study the role of monocytes in celiac disease.
- Explore the relationship of immune cells and stromal cells in experimentally-induced allergic rhinitis.
- Explore the relationship of immune cells and stromal cells in active celiac disease.
Sandlie group

The Sandlie group studies the structure and function of antibodies and T-cell receptors, the specific detecting molecules of the adaptive immune system. The purpose of the work is to engineer soluble T-cell receptors, antibodies and antibody derived molecules to be used in therapy and as research reagents.

We focus on two projects: A) Studies of the interaction between Fc receptors, and in particular the neonatal Fc receptor (FcRn), with IgG subclasses and albumin. Key questions are how ligand binding elicits antibody effector functions and regulate biodistribution and serum half-life. B) Expression of soluble T-cell receptors for the detection of complexes between antigenic peptides and HLA molecules, as well as peptide – HLA complexes for detection of T-cell receptors. The focus is on engineering to increase stability and affinity for molecules that are characteristic of disease models in groups at CIR.

KEY PROJECT SUMMARIES

Proteins in blood are short lived and normally degrade within a few hours or days, but the two most abundant proteins, IgG and albumin, are rescued from degradation and have half-lives of three weeks. The rescue mechanism depends on their interaction with the neonatal Fc receptor (FcRn), and it is crucial to understand how FcRn rescues IgG and albumin, and to transfer long half-life to therapeutics, using the same mechanism. We work in collaboration with Novozymes Ltd, UK, who has filed several patent applications and developed the Albufuse Flex technology, a set of human albumin variants designed by us with greatly increased binding affinity for FcRn. Biopharmaceuticals fused to a new albumin variant can have half-life of months, which will decrease dose, administration frequency and toxic side effects.

Furthermore, FcRn directs the transfer of maternal IgG antibodies across the placenta and thus provides the fetus and newborn with protective humoral immunity. Pathogenic maternal IgG antibodies will also be delivered via the placenta and can cause alloimmunity, which may be lethal. In 2013 we have designed a novel strategy to control pathogenic antibodies by administration of a nondestructive IgG antibody that blocks antigen binding while retaining binding to FcRn.

To ask questions regarding the nature of the antigen presenting cell, the location and rate of antigen presentation and the interaction with T cells, specific detection molecules are needed. Soluble T-cell receptors are new tools for such studies in health and disease. We have explored how phage display may be used to improve stability and affinity of soluble T-cell receptors and MHC class II molecules. We have displayed not only soluble T cell receptors, but also MHC class II molecules, so-called “Phagemers”, which will be used as diagnostics for celiac disease. Furthermore, a spin-out company, Nextera AS, commercialises and develops the new phage display- and Phagemer technologies, and utilizes libraries of Phagemers to search for disease causing proteins that drive pathological T cell activation in autoimmune diseases and chronic infections.

CENTRAL PUBLICATIONS AND PATENTS IN 2013

- Andersen JT, Sand KMK and Sandlie I, Human albumin mutants with decreased binding to FcRn (Patent application 2132-13083-US-P2).

The paper by Gunnarsen et al. was selected by Global Medical Discovery as a Key Scientific Article. Global Medical Discovery [ISSN 1929-8536] features breaking research judged by GMD’s advisory team to be of key importance in science and medicine. Papers are selected from over 20,000 published each week from most peer reviewed journals. Link: http://globalmedicaldiscovery.com/key-scientific-articles/chaperone-assisted-thermostability-engineering-of-a-soluble-t-cell-receptor-using-phage-display/
ACHIEVEMENTS IN 2013

- Increased our understanding of the interaction between the neonatal Fc receptor (FcRn) and albumin. Designed and characterised novel albumin variants with increased binding to FcRn that will be used to extend the serum half-life of fused biopharmaceuticals.
- Established a novel strategy for selection of stable protein variants using phage display. A soluble single chain T cell-receptor was stabilised and studied in detail regarding specificity and affinity.
- Designed and characterised a nondestructive IgG antibody variant that has the ability to be transported across the placenta. This will be used to block the activity of maternal IgG antibodies that are harmful to the fetus.

AMBITIONS FOR 2014

- Design improved molecular trackers for specific peptide – MHC complexes to be used in studies of antigen presentation.
- Design molecular trackers for specific T-cell receptors characteristic for gluten specific T cells to be used in diagnostic tests.
- Analyse the fine specificity of the T cell response in celiac disease.
- Understand basic mechanisms that govern transplacental transport of albumin and IgG during pregnancy.
- Understand cellular recycling of IgG and albumin.
Sollid group

Our group is trying to dissect the interplay of environmental factors and genetic factors in chronic autoimmune disorders. We are concentrating on celiac disease as a model to understand the molecular mechanisms leading to chronic inflammatory disease.

This disorder, caused by an inappropriate immune response to cereal gluten proteins, is characterised by a strong HLA association and presence of auto-antibodies specific for transglutaminase 2 (TG2). We have generated a large panel of CD4+ T-cell lines and clones cultured from intestinal biopsy specimens from celiac disease patients. Characterisation of what and how these T cells recognise gluten protein has lead to interesting findings such as the importance of protein structure on antigen processing, how enzyme mediated post-translational protein modification increases antigenicity and how HLA binding specificity and peptide-MHC stability influence T-cell priming. This knowledge does not only impact the understanding of celiac disease pathogenesis, but also reveal general principles of immune regulation that are applicable to other disease models. Currently we have taken up a strong interest in characterising the auto-antibody response of celiac disease. This is the focus of an ERC Advanced Grant project we undertake.

KEY PROJECT SUMMARIES

Our current research on celiac disease immunology takes place in several areas:

Biochemistry of HLA-DQ molecules: We are characterising the biochemistry of the disease associated HLA-DQ molecules. We are doing peptide elution experiments, we are studying peptide binding and we do structural studies. The latter is done in collaboration with the group of Chu-Young Kim at the University of Singapore. We also make MHC tetramers for use in T-cell studies.

Structure and function of transglutaminase 2: We are studying the specificity of TG2 as well as trying to understand where and how TG2 is active in the intestinal celiac lesions. This work is done in collaboration with the group of Chaitan Khosla at Stanford University, Thomas Jørgensen at the University of Southern Denmark as well as several European research groups as part of the EU Marie Curie Training Network TRANS-PATH.

Gluten-reactive T cells: We are studying T-cell receptor specificity and function of gluten reactive T cells of celiac disease patients. MHC tetramers are key tools in these studies.

B cells and plasma cells: In collaboration with the group of Patrick Wilson at the University of Chicago we are cloning and expressing antibody gene of single plasma cells isolated from gut biopsies. This technique has been used to study TG2-specific as well as gluten-specific plasma cells.

Characterisation of B-cell receptors and T-cell receptors of antigen specific cells: High throughput DNA sequencing is implemented to monitor and follow adaptive immune responses.

CENTRAL PUBLICATIONS IN 2013

ACHIEVEMENTS IN 2013

- Characterised epitopes of transglutaminase 2 (TG2) recognised by autoantibodies of celiac disease patients (J Immunol 2013). The binding of mAbs generated by expression cloning of Ig genes from single plasma cells of the celiac disease lesion was assessed. The mAbs recognise few conformational epitopes that cluster in the N-terminal half of the enzyme.
- Measured frequency of gluten reactive T cells in celiac disease lesions by direct cloning and by HLA tetramer staining (Eur J Immunol, 2013). Gluten reactive cells were found in the small intestinal mucosa of all untreated and most treated coeliac disease patients.
- Characterised antigen presenting cells (APCs) in the celiac disease lesion (Mucosal Immunol, 2013). Whether plasmacytoid dendritic cells (PDCs) are the main APCs in the small intestine mucosa is a controversy. By immunohistochemistry and flow cytometry, we found that PDCs represent < 1% of the APCs in normal and celiac disease duodenal mucosa.

AMBITIONS FOR 2014

- Isolate gluten specific plasma cells from coeliac lesions and expression clone monoclonal antibodies from single plasma cells.
- Complete studies using hydrogen/deuterium exchange on assessing activity-regulating structural changes and autoantibody epitopes in TG2.
- Establish high throughput sequencing of B-cell receptors (BCR) and T-cell receptors (TCR) as well as undertaking paired BCR VH–VL and TCR Vw–Vβ sequencing from single cells.
- Complete studies of endogenous peptide ligands of HLA-DQ2.5, HLA-DQ2.2 and HLA-DQ7.5 to understand how the peptide binding motifs of these HLA molecules differ.

Immunofluorescence staining of plasma cells (red, CD138), T cells (green, CD3) and epithelium (blue, cytokeratin) in the small intestinal mucosa of a patient with active celiac disease. Plasma cells are abundant and increased in numbers compared to healthy controls. Photo: Ann-Christin Røberg Beitnes.
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CIR scientists have an extensive international network. A very important element of CIR’s activity is the valuable relations we have formed with our Visiting Professors. These researchers, world leading scientist from renowned institutions, spend an intensive week at the centre. During their site-visit the Visiting Professors give lectures, perform data scrutiny, supervise students and postdocs, and provide valuable input to the research conducted. Following their visit to CIR, the Visiting Professors continue to interact with centre scientists and the program has resulted in fruitful collaborations, exchange of ideas and reagents, as well as researcher mobility and joint publications.

In 2013, Mark Shlomchik (Yale School of Medicine, USA) had his third visit to CIR as a Visiting Professor. In addition, Bana Jabri (University of Chicago, USA) and Peter Cresswell (Yale School of Medicine, USA) joined the Visiting Professor faculty.

We are very proud and happy to announce that Mark M. Davis (Stanford University, USA) will be joining the program and Susan K. Pierce (NIAID NIH, USA) will return to CIR for her second visit in 2014. Bernard Malissen (Centre d’Immunologie de Marseille-Luminy, France) have also accepted the invitation to become Visiting Professor and will be visiting CIR in the spring of 2015.

New Visiting Professors are nominated by CIR staff and additional world-class immunologist will be invited to the centre. CIR is excited about our Visiting Professor program and we are very much looking forward to interacting with these prominent immunologists in 2014 and beyond.

MARK SHLOMCHIK
Dr. Shlomchik is Professor at Yale School of Medicine in New Haven, USA. The main interests of his laboratory are B cell development and immunopathogenesis. They study how autoreactive B cells arise and their role in mediating autoimmune disease. They also have an interest in B cell activation and memory. Shlomchik also run projects investigating the role of memory T cells in graft vs. host disease. During his visit in April, Shlomchik gave two guest lectures entitled “Germinal Center Selection and the Development of Memory B and Plasma Cells” and “NETworks in Lupus: T-B or not T-B, DC is the question”, respectively. Since his visit Dr. Shlomchik has moved and is now Professor and Chair at the Dept. of Immunology at the University of Pittsburgh, USA.

BANA JABRI
Dr. Jabri is a Professor at the University of Chicago, USA. Jabri heads a research group studying mucosal and innate immunity, focusing on the interplay between the immune system and mucosal surfaces. Her group has a particular interest in intestinal inflammatory disorders including celiac disease and inflammatory bowel disease. Her laboratory has expertise in human immunology and is developing mouse models of intestinal inflammation. During her visit in May, Jabri gave a guest lecture entitled “Host, environment and microbes, a love-hate triangle”. Jabri also contributed with a second lecture at a minisymposium entitled “Hot topics in celiac disease” (details on page 27).

PETER CRESSWELL
Dr. Cresswell is a Professor at Yale University School of Medicine, USA, where he heads a research group focusing on molecular mechanisms of antigen processing. The Cresswell laboratory studies the assembly and intracellular transport of CD1, MHC Class I and II molecules, central molecular players in antigen presentation. In addition his group has an interest in antiviral mechanisms of proteins inducible by interferons. Dr. Cresswell gave two guest lectures during his visit in September. The titles of his talks were “Viperin: an interferon-inducible metabolic regulator co-opted by human cytomegalovirus” and “Pathways of MHC class I-restricted Antigen Presentation”. The latter lecture was integrated as a part of MBV4260 - Advanced immunology, a MSc/PhD course at the Faculty of Mathematics and Natural Sciences, Department of Biosciences.
Minisymposia

Minisymposia are an important part of the outreach activity at CIR. In conjunction with visits from our Visiting Professors and other invited guest lecturers, the centre organise seminars aimed at a broader audience interested in clinical- and basic immunology and related disciplines. We actively recruit speakers from outside CIR to these events. In 2013 CIR organised one minisymposium and co-hosted 3 minisymposia in collaboration with the Norwegian Society for Immunology (NSI) and the K.G. Jebsen Centre for Research on Influenza Vaccines.

HOT TOPICS IN CELIAC DISEASE
MAY 30

CONTRIBUTORS AND TITLES: Ludwig M. Sollid, Centre for Immune Regulation, University of Oslo and Oslo University Hospital. “Introduction to immunology of celiac disease”.

Rasmus Iversen, Centre for Immune Regulation, University of Oslo. “Antibody response to transglutaminase 2 in celiac disease”.

Luisa Mearin, Leiden University Medical Center, The Netherlands. “Prevention of celiac disease: Report from an ongoing pediatric trial”.

Melinda Ráki, Centre for Immune Regulation, Oslo University Hospital. “T-cell reactivity to gluten in young children with celiac disease”.

JOINT NSI - CIR MINISYMPOSIUM ON T CELLS
APRIL 9

Norwegian Society for Immunology (NSI) in collaboration with CIR.

CONTRIBUTORS AND TITLES: Thorbald van Hall, Leiden University Medical Center, The Netherlands. “Tumors with processing defects display novel tumor antigens via the non-classical HLA-E”.

Olivier Lantz, Institut Curie, France. “AIT cells, an evolutionarily conserved T cell subset with anti-bacterial reactivity”.

PATHOGENESIS OF B CELL CANCERS
NOVEMBER 28

K.G. Jebsen Centre for Research on Influenza Vaccines, in collaboration with CIR and NSI.


Ludvig A. Munthe, Centre for Immune Regulation, University of Oslo. “T helper cells drive the proliferation of CLL cells, a cancer of anergic autoreactive B cells”.

CANCER IMMUNOTHERAPY
DECEMBER 4

K.G. Jebsen Centre for Research on Influenza Vaccines, in collaboration with CIR and NSI.

CONTRIBUTORS AND TITLES: Per Thor Straten, Copenhagen University Hospital, Denmark. “T cells; magic bullets in cancer therapy?”.

Paul Antony, University of Maryland, USA. “Restoring immune function of tumor associated antigen specific CD4 T cells during recurrence of melanoma”.

Guest lectures

In addition to lectures given by our Visiting Professors and invited speakers at the minisymposia, CIR organise a series of guest lectures. These lectures are chiefly hosted by a postdoc invitation committee. The 2013 committee consisted of Kristin S. Gunnarsen, Omri Snir, Even Fossum, Johanne T. Jacobsen (replaced by Peter C. Huszthy in October), Ole J.B. Landsverk (replaced by Cinzia Progida in October) and Lisa M. Gruber. In 2013, CIR organised 7 guest lectures:

ROBERTA PELANDA visited CIR in February and gave a lecture entitled “Click your heels: you are in the land of B cells”. Dr. Pelanda is a Professor of immunology at National Jewish Health and University of Colorado, USA. Her research group work to uncover the molecular pathways that guide the development, selection and activation of autoreactive and non-autoreactive B cells.

CAETANO REIS E SOUSA visited CIR in June and gave a lecture entitled “A DaNGeRous talk about dendritic cells”. Dr. Reis e Sousa heads a research group at Cancer Research UK, London Research Institute, UK. His laboratory investigates the ontogeny and heterogeneity, as well as activation and modulation, of dendritic cells.

MARK HOGARTH visited CIR in June and gave a lecture entitled “Antibody and Fc-receptor interactions in humans and other primates. Implications for the development of vaccines, therapeutic antibodies and the induction of inflammation”. Professor Hogarth heads a research team at the Burnet Institute, Australia, focusing on fundamental roles of immune cells, their receptors and their antibodies, and how these can be manipulated for the treatment of human disease.

MARC K. JENKINS visited CIR in August and gave a lecture entitled “The CD4+ T cell response to bacterial infection”. Professor Jenkins heads a research group at the University of Minnesota, USA. His laboratory work to improve the basic understanding of activation of CD4+ and B cells in vivo - understanding that can be used to prevent autoimmunity and to improve vaccines.★★
DEBORAH DUNN-WALTERS visited CIR in October and gave a lecture entitled “Spectratype and High Throughput Sequencing analysis of B cell repertoire”. Her laboratory, at King’s College, UK, combines molecular biology techniques with mathematical analyses to investigate the humoral immune system, with particular focus on the B cell repertoire and molecular events involving the immunoglobulin gene during B cell development.

STEN LINNARSSON visited CIR in November and gave a lecture entitled “Unbiased cell-type discovery using large-scale single-cell RNA-seq”. The Linnarsson laboratory at Karolinska Institutet, Sweden, has developed methods for single-cell RNA sequencing that allows for unbiased discovery and characterization of cells based on single-cell transcriptomic analysis.

ANTONIO LANZAVECCHIA visited CIR in December as a PhD thesis opponent and gave a lecture entitled “Dissecting the human antibody response to pathogens and self-antigens”. Lanzavecchia is a Professor at the Swiss Federal Institute of Technology and heads the Institute for Research in Biomedicine, Switzerland. His broad research interests include antigen processing and presentation, dendritic cell biology, lymphocyte activation and trafficking, and T and B cell memory.

PROJECT MEETINGS
To keep the members of the centre up to date on the research within the centre, project meetings are organised monthly. This meeting is an important event that facilitates collaboration, idea generation and critical discussion. Furthermore, the monthly meeting provides a friendly venue for junior scientists less experienced in presenting their own work. The project meeting is also a vital activity aiming to build centre identity and sense of community. In 2013, 9 project meetings were organised. Typically unpublished data from one or two projects are presented. Presentations range from discussion of technical challenges, via preliminary data to publication ready work. Ample time is reserved for discussion following the presentations and discussion is encouraged. At the end of the meeting snacks and soft drinks are served to promote interaction and to continue the discussion in a less formal atmosphere.

CIR ANNUAL RETREAT
The CIR retreat is an important event that facilitates synergies, collaboration and exchange of ideas. The 2013 retreat, the fourth in CIR’s history, took place at Dr. Holms Hotel at Geilo, April 3-5. More than 80 participants, including guest lecturers and a representative from our scientific advisory board, attended the retreat. Three international keynote speakers gave inspiring lectures. Pavel Tolar (MRC National Institute for Medical Research, London, UK) gave a lecture entitled “Mechanical extraction of antigens from the B cell immune synapse: a unique way to measure receptor-ligand affinity”. Allan Mowat (University of Glasgow, UK) delivered a talk on “Local control of dendritic cell and macrophage heterogeneity in intestinal homeostasis and inflammation”. Søren Buus (University of Copenhagen, Denmark), member of the scientific advisory board, gave a talk entitled “Drug hypersensitivity caused by alteration of the MHC-presented self-peptide repertoire. The excellent guest lectures were all very well received and incited questions and debate. Selected CIR scientist presented their work through 16 oral presentations, giving an update and comprehensive overview of ongoing research at the centre. More than 30 posters were presented. The best poster and oral presentations were awarded presentation prizes. The program also included workshops and ample time for social interaction and leisure activities. The organising committee consisted of Marta Baranowska, Anna Bujko, Asbjørn Christophersen, Stian Foss, Gerbrand Koster and Anders Sandvik. CIR will organise smaller research retreats in 2014 and 2016, and plan larger events in 2015 and 2017.
KICK-OFF SEMINAR - WORK PACKAGE ORGANIZATION

In conjunction with the successful midterm evaluation of CIR as a Centre of Excellence, the research plan for 2013-2017 was updated and restructured. Projects are now grouped in a matrix of work packages (WP) that bridge disease models and cross lab-boundaries:

WP1 - Function of APCs in autoimmunity and allergy.
WP2 - T-cell repertoire in autoimmunity and allergy.
WP3 - Pathogenic T-B collaboration.
WP4 - Pathogenic and regulatory antibodies.

With this organisation we aim to advance synergy and promote discovery through enhanced scientific interaction. WP coordinators have been appointed to facilitate scientific interaction within CIR. To launch this program and raise awareness about the research plan among CIR scientist, we organised a kick-off seminar in August. The seminar was followed by a summer party and fjord cruise.

CONTRIBUTORS AND TITLES:

• Inger Sandlie - “Presentation of the work package organisation and coordinators”.

A taste of WP2 - T-cell repertoire in autoimmunity and allergy

• Shuo-Wang Qiao - “Studying T cells in the new sequencing era”.
• Asbjørn Christophersen - “The CD4+ T cell response to gluten in peripheral blood”.

A taste of WP3 - Pathogenic T-B cooperation

• Johanne Jacobsen - “Naïve Idiotype-specific B and T cells collaborate efficiently in the absence of dendritic cells”.
• Simone Bürgler - “T-bet mediates upregulation of the CLL risk marker CD38 in response to T cell-derived IFN-γ”.

•
Education and career development

PHD

Education of scientists is a major activity at CIR. CIR has the ambition to educate 35 new PhDs during the 10-year period as a Centre of Excellence. Since CIR commenced operations in December 2007, 31 students at the centre have successfully defended their thesis, and we are in good condition to reach the production milestone. In 2013, 5 PhD students defended their thesis:

**OLE AUDUN W. HAABETH**, “Inflammation driven by tumor-specific Th1 cells protects against cancer”. Supervisors: Alexandre Corthay and Bjarne Bogen.

**GUNNVEIG GRØDELAND**, “APC-targeted DNA vaccines against influenza”. Supervisor: Bjarne Bogen.

**PIER ADELCHI RUFFINI**, “Translational Development of targeted DNA vaccines for idiotypes of B cell malignancies”. Supervisor: Bjarne Bogen.

**KRISTINA BERG LORVIK**, “Inflammation mediated by tumor-specific Th1 or Th2 cells protects against B-cell cancer”. Supervisors: Alexandre Corthay and Bjarne Bogen.


MSc/MD

In 2013, seven CIR students graduated from the University of Oslo with a Master of Science degree and one student completed the Medical Student Research Program:

- Malin Bern
- Tor Espen N. Bendvold
- Bergrun Eggertsdottir
- Arnar Gudjonsson
- Benedicte Semb Hagen
- Henriette C. Jodal
- Aram Nikolai Andersen
- Marte Fauskanger

GENDER EQUALITY PROGRAM

At CIR and generally in molecular biomedical research there is a high proportion of female PhD students and postdocs, while the majority of the senior scientists and group leaders are male. CIR and the University of Oslo value gender diversity and aim to increase the number of female researchers in senior scientist positions. Women, more so than men, leave academia during their postdoctoral engagements and transition to independent researchers. CIR acknowledges that the centre, our host institution and other academic institutions nationally and abroad are at risk of losing many talents, possessing valuable and highly specialised competency.

In 2013, in line with the gender diversity strategy of the University of Oslo, CIR has provided two development grants to support the career of female scientists. CIR has obtained earmarked funding from the Research Council of Norway (RCN) to launch this program. Following an evaluation of applicants by the centre’s scientific advisory board, financial support has been granted for two years to two selected talents. The gender equality program will be continued and new career development grants for female scientists will be announced in 2014.

CAREER DEVELOPMENT AND OPPORTUNITIES

CIR continue to support the career development of our talents. Based on competitive selection, CIR will financially support the participation of 3 postdoctoral fellows and researchers at a personal development program - Entering Leadership in Research. The program aims to create awareness of leadership and develop the candidates’ ability to fill a leader role, offer personal development training to enhance the career, and increase self-management skills as a foundation for quality in own research.

The CIR management acknowledge that the lack of permanent academic positions to compete for is a major concern among our young talents. Our host institution has installed a ‘phasing in scheme’ to secure its investments in talent development and the human capital fostered by CIR over the 10 ten-year-period as a CoE. Several permanent academic positions will be made available through this ‘phasing in scheme’. In 2013, the management and Board have worked together with the Institute of Clinical Medicine and Faculty of Medicine at the University of Oslo to advertise a new academic position within the area of autoimmunity or allergy. The ambition has been to fill the position in 2014. Due to space constraints at the Department of Immunology, the CIR Board has decided to postpone the release of the advertisement. The CIR management and Board will actively work to solve the space constraints and to develop career opportunities for CIR talents.
Publications

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Papers in scientific journals


Books and book chapters


Andersen JT and Sandlie I (with Novozymes): Albumin variants (WO2011051489 A2).


Andersen JT and Sandlie I: Modulation of albumin half-life (EP9174698.2).

Andersen JT and Sandlie, I (with Novozymes): Albufuse mutations (EP11164989.3).

Andersen JT and Sandlie, I: Albumin combination mutants (EP12177916.9 and EP12191859.9).

Bogen B and Braathen R: Heterodimeric vaccine molecules (U.S. Provisional Patent Application Serial No. 61/695,639).


Bogen B and Fossum E and Greideland G: Vaccibodies targeted to cross-presenting dendritic cells (US serial no: 61538,186).


Johansen F-E, Sandvik A and Engstad RE: Methods of treating or preventing inflammatory disease of the intestinal tract (PCT/ GB2008/003850).

Løset GÅ and Sandlie I: Multivalent phage display systems and methods (WO2011/036555).

Løset GÅ. Frigstad T, Sandlie I and Bogen B: Disulphide bond-stabilized functional soluble MHC class II heterodimers (WO2011/101681).


Ruffini PA, Fredriksen A and Bogen B: Homodimeric protein constructs (WO2010/61358513, EP10167291.3).

Sandlie I, Andersen JT and Bern M: Albumin variants fused to immunogens (AlbuVax) for improved transcellular delivery (61033-13082-US-P).


Sandlie I, Andersen JT and Sand KMK: Human albumin mutants with decreased binding to FcRn (2132-13083-US-P).


PUBLICATION RECORD

Number of publications per year appearing in international peer-reviewed scientific journals authored or co-authored by CIR scientists.
Dissemination activities

Invited lectures 40
Oral presentations 40
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Invited lectures

Andersen JT: «FcRn-mediated rescue of engineered IgG and albumin variants». MDG 2nd Biologics Symposium, May 14, Basel, Switzerland.

Andersen JT: «FcRn- not just for kids!». MRC Laboratory of Molecular Biology, June 7, Cambridge, UK.


Bogen B: «Enhanced DNA vaccines that encode targeted fusion proteins». World Vaccine Congress and Expo 2013, April 16-18, Washington DC, USA.

Bogen B: «New partnerships for innovation in global health» Research Council of Norway (GLOBVAC) and NORAD seminar, June 4, Oslo, Norway (Moderator).

Brandtzaeg P: «EntVac Report 2013: Salivary SIgA as a non-invasive proxy for intestinal immune responses». Enteric Vaccine Portfolio Holders, Workshop at PATH Office (Program for Appropriate Technology in Health), February 21-22, Washington DC, USA.


Brandtzaeg P: «Why are tonsils and Peyer’s patches so different MALT structures?» International Symposium on Tonsils and Mucosal Barriers (8th ISTMB), July 18, Zürich, Switzerland.


Lundin KEA: «Celiac disease». Columbia University, March 12, New York, USA.

Lundin KEA: «Celiac disease». Box Hill Hospital, June 6, Melbourne, Australia.

Lundin KEA: «Celiac disease». Grand Round, Alfred Hospital, June 6, Melbourne, Australia.


Sandlie I: «Tailoring the lifespan of biopharmaceuticals by targeting the neonatal Fc receptor (FcRn)». University of Cape Town, February 19, Cape Town, South-Africa.

Sollid LM: «Potential celiac disease - A debatable issue». 15th International Celiac Disease Symposium, September 22-25, Chicago, USA.

Sollid LM: «Integrating T cell and B cell immunity in celiac disease». 15th International Celiac Disease Symposium, September 22-25, Chicago, USA.

Sollid LM: «Environmental control of the celiac disease antibody response». ESF-EMBO symposium on B cells from bedside to bench and back again. September 2-7, Pultusk, Poland.

Sollid LM: «On autoimmunity: lessons from celiac disease». Federation of European Biochemical Societies Congress 2013, July 6-11, St. Petersberg, Russia (Keynote speaker).


Sollid LM: «Autoimmunity, mucosal and extra-intestinal inflammation in celiac disease». Clinical Immunology Society Annual Meeting. April 25-28, Miami, USA.

Sollid LM: «On autoimmunity: Lessons from celiac disease». BSI South Wales Immunology group - Seminar series. March 6, Cardiff, UK.


Oral presentations

Baekkevold ES: «Human airway mucosal DCs respond to TSLP and induce Th2 responses». World Immune Regulation Meeting (WIRM VII), March 13-16, Davos, Switzerland.

Bergseng E: «The difference in the endogenous peptide repertoire of the similar HLA-DQ2.5 and DQ2.2 molecules». Norwegian Biochemical Society Contact Meeting, January 31-February 3, Lillehammer, Norway.

Bergseng E: «Different endogenous peptide repertoires of the celiac disease associated HLA molecules DQ2.5, DQ2.2 and DQ7.5». 15th International Celiac Disease Symposium, September 22-25, Chicago, USA.


Gracia IE: «Experimentally-induced early recruitment of CD14+ monocytes in human allergic rhinitis». ISMA (International Symposium on Molecular Allergology), EAACI (European Academy of Allergy and Clinical Immunology), December 5-7, Vienna, Austria.


Mateus D: «SNX Tubes and their Physical Properties in Endosomal Sorting». EMBO conference, System Dynamics in endocytosis, September 27-October 4, Villars, Switzerland.

Müller E: «Using live imaging to investigate the mechanisms underlying tumor cell killing by macrophages». 41st Meeting and Summer School of the Scandinavian Society for Immunology, April 14-17, Copenhagen, Denmark.

Snir O: «Analysis of autoreactive gut-plasma cells and their blood memory compartment in celiac disease». ESF-EMBO symposium on B cells from bedside to bench and back again. September 2-7, Pultusk, Poland.

Stamnaes J: «Determination of in vivo transglutaminase 2 activity in mice». 15th International Celiac Disease Symposium, September 22-25, Chicago, USA.

Steinsbø Ø: «Gluten- specific IgA of plasma cells from celiac disease lesions have restricted VH/VL gene usage and few mutations». FOCIS Annual Meeting 2013, June 27-30, Boston, USA.

Baekkevold ES: «Human airway mucosal DCs respond to TSLP and induce Th2 responses». World Immune Regulation Meeting (WIRM VII), March 13-16, Davos, Switzerland.

Brandtzaeg P: «Salivary IgA as a non-invasive readout for intestinal immune response against experimental enterotoxigenic Escherichia coli (ETEC) infections». Mucosal Vaccines, Adjuvants & Delivery (MUCOVAD 2013), 25-27 September 2013, Copenhagen, Denmark.

Brandtzaeg P: «Salivary IgA as a readout for gut immunity after experimental enterotoxigenic Escherichia coli (ETEC) infection». Implementation Research in Global Health, The 8th Conference on Global Health and Vaccination (GLOBVAC) and the 25th Anniversary of the Centre for International Health, October 16-17, Bergen, Norway.


Foss S: «FcRn regulates the long serum half-life of IgG. In vitro interactions studies reveal that FcRn binds IgG based therapeutics with disparate properties». Norwegian Biochemical Society Contact Meeting, January 31-February 3, Lillehammer, Norway.

Snir O: «Analysis of autoreactive gut-plasma cells and their blood memory compartment in celiac disease». FOCIS Annual Meeting 2013, June 27-30, Boston, USA.

Stamnaes J: «Determination of in vivo transglutaminase 2 activity in mice». 15th International Celiac Disease Symposium, September 22-25, Chicago, USA.

Steinsbø Ø: «Gluten- specific IgA of plasma cells from celiac disease lesions have restricted VH/VL gene usage and few mutations». FOCIS Annual Meeting 2013, June 27-30, Boston, USA.
Andersen JT: «FcRn - not just for kids!». Department of Biosciences seminar, University of Oslo, October 14, Oslo, Norway.

Andersen JT: «Molekylær design gir skreddersydd medisin». Cutting Edge 2013 - Fantastisk forskning, elleivill eksperimentering, sensasjonelle startups, October 17, Oslo, Norway.

Bakke O: «Imaging the dynamics of the endosomal pathway». CMIC seminar, February 14, Trondheim, Norway.

Bakke O: «Cellular Imaging, a Bottleneck in Post genome Research?». BiO/NCMM Retreat, December 5-6, Sundvollen, Norway.

Brandtzaeg P: «B cells in the mucosal immune system». International PhD Course: Immunology of the Skin and Mucosal Surfaces, University of Copenhagen, December 2, Copenhagen, Denmark.

Brandtzaeg P: «T cells in the mucosal immune system». International PhD Course: Immunology of the Skin and Mucosal Surfaces, University of Copenhagen, December 3, Copenhagen, Denmark.

Brandtzaeg P: «Food allergy». International PhD Course: Immunology of the Skin and Mucosal Surfaces, University of Copenhagen, December 3, Copenhagen, Denmark.

Brandtzaeg P: «Mat og helse: Økologisk landbruk og GMO som bakteppe». Landsmøte for distriktslederne i OIKOS (Økologisk Norge), November 16, Oslo, Norway.

Bürgler S: «Studier av betennelsesfremkallende signalmolekyler (cytokiner) og overflatemarkører (CD38) ved KLL». Oslo University Hospital - Rikshospitalet (stabsmøte), August 30, Oslo, Norway.

Media coverage

«Idéprisen 2013 til teknologi for å utvikle vaksine mot HIV og kreft» AN Andersen (Bogen and Bakke) on TTO Inven2’s website. www.inven2.com/no/news/201310/id%C3%A9prisen-2013-til-teknologi-%C3%A5-utvikle-vaksine-mot-hiv-og-kreft


«The immune system and infections» LA Munthe in newspaper Dagbladet and website Klikk Helse, May 1. www.dagbladet.no/2013/05/01/tema/klikk/velvere/helse/forkjolelse/26947562/ www.klikk.no/helse/forkjolelse/article816071.ece

«The immune system and disease» LA Munthe on national radio NRK P1 “Norgesglasset”. May 3.

Wang D: «Role of human CD4+ T cells on malignant plasma cell survival in multiple myeloma patients». Norwegian Society for Immunology Research Retreat, March 8, Geilo, Norway.
About CIR

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About CIR

FACTS AND FIGURES

Centre for Immune Regulation (CIR) was established in December 2007 as a Centre of Excellence appointed by the Research Council of Norway. Following a successful midterm evaluation, CIR will continue to operate as a CoE till the end of 2017. CIR is also a FOCIS (Federation of Clinical Immunology Societies) Centre of Excellence.

Our host institution is the University of Oslo. Oslo University Hospital is an equal consortium partner. The centre is organised directly under the Faculty of Medicine and the centre Director reports to the Dean. CIR comprises research groups from the Faculty of Mathematics and Natural Sciences, the Faculty of Medicine and from Oslo University Hospital. Centre staff is employed at the Department of Biosciences, the Department of Immunology and the Department of Pathology.

Approximately 100 persons, producing 65 person years, are involved in research at CIR. A moderate drop in person year output in 2013 is mainly due to organizational restructuring, where part of Bogen’s group left CIR to establish the K.G. Jebsen Centre for Research on Influenza Vaccines.

CIR actively recruits international talents and currently more than 20 nationalities are represented at the centre. The overall gender balance at CIR is approximately 40/60 with an overweight of female members among postdocs, PhD students, master students and technicians.

RESEARCH GROUPS

CIR consists of five research groups headed by professors, Ludvig M. Sollid, Inger Sandlie, Oddmund Bakke, Bjarne Bogen and Frode L. Jahnsen. Sollid’s group includes the group of Gustavo de Souza, head of the proteomics core facility and projects. Bakke’s group includes the group of Alexandre Corthay. Professor Ludvig A. Munthe joined CIR as a new group leader in January, 2014.

MANAGEMENT

The centre is headed by Director Ludvig M. Sollid and Deputy Director Inger Sandlie. The centre management is supported by an administrative coordinator, Anders Sandvik. The Director has the daily responsibility for project management, administration and delivery.

CIR BOARD

The governing board of CIR has four members; two from the University of Oslo (UiO) and two from Oslo University Hospital (OUS). The board is appointed by UiO.

- Hilde I. Nebb (chair), Dean of Research, Faculty of Medicine, UiO.
• Svein Stølen, Dean of Research, Faculty of Mathematics and Natural Sciences, UiO.
• Erlend B. Smeland, Director of Research, Innovation and Education, OUS.
• John Torgils Vaage, Head of the Department of Immunology, OUS.

The authority of the board is to ensure that the intentions and terms of contract described in the Centre of Excellence agreement are fulfilled. Furthermore, the board approves the annual budget and ensure that centre activities are completed as outlined in the project description and funding plan, within the adopted time frame.

SCIENTIFIC ADVISORY BOARD
CIR has a scientific advisory board (SAB) consisting of European world-class scientists. The SAB’s mandate is to critically evaluate and advice on the centre’s scientific performance and progress.
• Professor Søren Buus, University of Copenhagen, Denmark.
• Professor Rikard Holmdahl, Karolinska Institutet, Stockholm, Sweden.
• Professor Sirpa T. Jalkanen, University of Turku, Finland.

FOCIS CoE CLINICAL ADVISORY BOARD AND LAY ADVISORY BOARD
As a Federation of Clinical Immunology Societies (FOCIS) Centre of Excellence (FCE), CIR has established two advisory boards.

The clinical advisory board is responsible for facilitating translational research at CIR.
• Head physician Knut E. Lundin (chair, gastroenterologist, OUS).
• Professor Il Geir E. Tjønnfjord (haematologist, OUS and UiO).
• Professor Knut Dahl-Jørgensen (paediatrician, OUS and UiO).

The lay advisory board focuses on strategic development, fundraising and community outreach.
• The Director of the Norwegian Celiac Society.
• The Secretary General of the Norwegian Asthma and Allergy Association.
• The Secretary General of the Norwegian Diabetes Association.
CIR staff and students

CENTRE PERSONNEL 2013

CIR STAFF DEVELOPMENT

* Headcount includes unpaid MSc/MD student and staff that left or joined CIR during 2013
Postdocs

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<tr>
<th>NAME</th>
<th>FUNDING*</th>
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<tr>
<td>Jan Terje Andersen</td>
<td>S-EN RHA</td>
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Researchers

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<td>Oddmund Bakke</td>
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PhD Students

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<tr>
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<td>Marta Baranowska 1</td>
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<td>Axel Berg-Larsen</td>
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<td>Malin Bern 3</td>
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<td>Marita J.H. Borg</td>
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<td>Anna Buiko</td>
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<td>Christophersen</td>
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<td>Sian Foss</td>
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<td>Kristina B. Lorvik 4</td>
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<tr>
<td>Anna Lysén 1</td>
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</table>
The list of CIR staff and students include both members that left and joined the Centre during 2013. Several CIR members have changed employer and funding body during 2013. The listed funding body and employer refer to the status per December 2013.

1 K.G. Jebsen Centre for Influenza Vaccine Research from May 2013, following organisational restructuring at CIR.
2 Defended PhD thesis in 2013.
3 Graduated in 2013, continued at CIR as PhD student.
4 Not employed by CIR in 2013, defended PhD thesis in 2013.
5 Graduated in 2013.
6 Graduated in 2013, continued at CIR as technician.
### NATIONAL

<table>
<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Magnar Bjørås</td>
<td>Department of Microbiology</td>
<td>Oslo University Hospital</td>
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<tr>
<td>Heidi Kil Blomhoff</td>
<td>Institute of Basic Medical Sciences</td>
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<td>Rune Blomhoff</td>
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<tr>
<td>Ralph Dollner</td>
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<td>Terje Espevik</td>
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<td>Norwegian University of Science and Technology</td>
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<td>Peter Gaustad</td>
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