

*Strategy document EpiGen and clinical research unit 2014-2017*

**STRATEGIC PLAN 2014-2017 FOR RESEARCH I**  
**MEDICAL DIVISION:**  
**(1) DEPARTMENT OF CLINICAL MOLECULAR BIOLOGY AND**  
**LABORATORY SUBJECTS AND**  
**(2) CLINICAL RESEARCH SUPPORT SECTION**



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## **1.0 FOREWORD**

The 2014-2017 strategic plan for the Department of Clinical Molecular Biology and Laboratory Sciences (EpiGen) and the Section for Research Support (Clinical Research Unit) has been prepared jointly by Professor Hilde L. Nilsen, Head of EpiGen, and Head of Department Helge Røsjø, Department of Research, Medical Division. Nilsen has had primary responsibility for strategy around EpiGen, Røsjø has had primary responsibility for strategy around the Clinical Research Unit and together we have seen the need for closer integration of the two units towards the year 2017.

This document is intended as support for the budget process in the Medical Division for 2014, but also represents strategy for two very central elements in research in the Medical Division towards the year 2017. We believe we have set specific and measurable goals that are ambitious but realistic. The time frame is given by the period 2014-2017. We have also chosen to use some space on background and history to put the work into its proper context and to showcase all the research that takes place at EpiGen and the Clinical Research Unit. On this occasion, we would like to thank all researchers in the Medical Division and other divisions who have contributed information, as well as senior engineer Anna B. Frengen, University of Oslo, who has worked closely with Nilsen on describing the history and status of EpiGen. We have also consulted research leaders at Akershus University Hospital and University of Oslo-Campus Ahus and would like to thank them for their feedback and input.

We believe that the contents of the document may be of interest for the development of research at Akershus University Hospital beyond the Medical Division. However, the document has been drawn up with the Medical Division in mind, but the plan must be included in the further work to develop research at Akershus University Hospital centrally. Finally, we would like to conclude by pointing out that among the key words *to see - to own - to do - to act*, we consider that *acting* is the most important thing now and it is our joint responsibility that this plan is followed up with concrete work towards year 2017.

Lørenskog 07.10.2013

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**2.0 SUMMARY AND VISION Akershus University**

Hospital's aim is to carry out research activities at a high international level that support the company's prioritized medical focus areas. Research at Akershus University Hospital will work in close collaboration with the University of Oslo, which is the company's most important research partner. The Department for Clinical Molecular Biology and Laboratory Sciences (EpiGen) was established in 2001 as a collaborative institute between Akershus University Hospital and the Faculty of Medicine with a mandate to integrate basic research and clinical research. EpiGen today represents a core institution for research in several divisions at Akershus University Hospital and also contributes to clinical operations. EpiGen is located at the university part of Akershus University Hospital and most employees are employed at Campus Ahus. In the hospital line, EpiGen is currently organized under the Research department, Medical division.

The Medical Division has also built up an active clinical research unit, which now carries out larger epidemiological and randomized controlled clinical studies and actively participates in the development of clinical research in Norway. Several trends in international research support the organization of research around combined units for basic research and clinical research. With the University of Oslo's strong focus on life sciences and Akershus University Hospital's large patient base, it makes sense to integrate basic research and clinical research more closely at Akershus University Hospital.

**The medical division wishes by the year 2017, in close collaboration with the Department of Clinical Medicine-Campus Ahus and other divisions in the company, to develop a nationally leading research environment that integrates basic research and high-quality clinical research**

In order to achieve this ambitious but realistic goal, it is important that both basic research and clinical research are developed and strengthened. It is also crucial that such a structure has a clear organization that ensures progress and interaction between basic research and clinical research.

Research at EpiGen and Akershus University Hospital is changing. Employment of new Professionally and organizationally strong manager of EpiGen promises that the section can exploit a potential which for a long period without a leader has not been realised. Furthermore, the ongoing professionalization of clinical research will be able to lift this part of the research activity.

The conditions are thus favorable for further integration and development of basic research and clinical research. The 2014-2017 strategic plan for the Medical Division recommends that this be carried out through an integration of EpiGen and the clinical research unit in the Medical Division and with a joint governing body where Campus Ahus owns EpiGen and Akershus University Hospital owns the clinical research unit.

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**3.0 OBJECTIVES 2014-2017**

Objectives for the period 2014-2017 are the following:

Main goals:

To integrate and develop basic research and clinical research at Akershus University Hospital into a nationally leading research environment

Sub-goals:

- (1) To further develop EpiGen as a sought-after partner for research collaboration by offering a portfolio of front-line molecular, cell biological and experimental animal technologies in an agile project organization structure
- (2) To build up an internationally competitive business within mechanisms for RNA and DNA stability and epigenetics at EpiGen
- (3) To build up a clinical research unit with competence to carry out large epidemiological and randomized controlled clinical trials (4) To carry out a large and internationally innovative clinical trial that includes several divisions in the company

**4.0 BACKGROUND**

Research is a main task for Akershus University Hospital as stated in the assignment document from Health South-East. Research also has a central place in the enterprise

Strategic development plan 2012-2016 and an overall research strategy 2012-2016 has been prepared for Akershus University Hospital. General principles for research at Akershus University Hospital are set out in table 1:

<b>(1)</b> Akershus University Hospital shall aim for research at a leading international level
<b>(2)</b> Akershus University Hospital shall concentrate research on a few areas and build research network nationally and internationally
<b>(3)</b> Akershus University Hospital shall prioritize collaboration with the University of Oslo as the company's most important research partner
<b>(4)</b> Akershus University Hospital shall develop advanced clinical functions via research (strategic investment areas)
<b>(5)</b> Akershus University Hospital shall utilize research to optimize clinical operations

*From the Strategic Development Plan 2012-2016 for Akershus University Hospital*

**Akershus University Hospital wishes to collaborate with  
University of Oslo to conduct research at a high international level  
which supports the company's prioritized medical investment areas**

Clinical research and translational research have been identified as focus areas for the company.

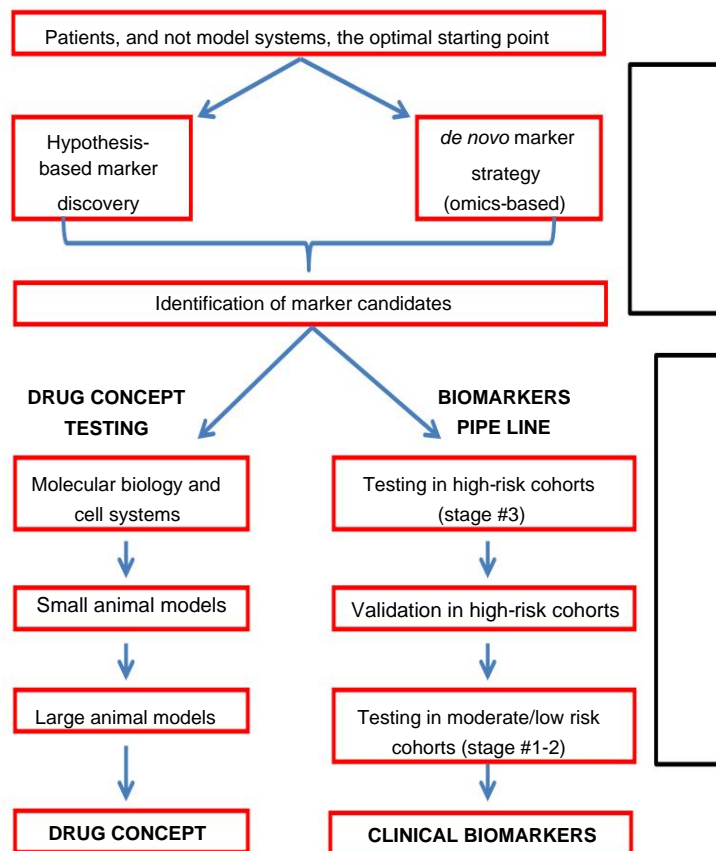
At the same time, the owner, Helse Sør-Øst, has imposed a special responsibility on the university hospitals for basic research and it is expected that Akershus University Hospital has strong groups also in basic research.

**Clinical research** is here defined as all types of research on humans, **basic research** as activities primarily carried out to acquire new knowledge about the underlying basis (mechanisms) for observable facts and **translational research (type 1)** is defined as research that integrates basic research and clinical research.

Akershus University Hospital has several competitive advantages that make it well suited to conducting clinical and translational research at a high level. An important advantage compared to other Norwegian biomedical research institutions is the company's large enrollment area, which includes ~500,000 inhabitants. The company thus has an excellent opportunity to identify phenomena in larger clinical research cohorts that can be further characterized using advanced basic research ("bed-to-bench strategy" as depicted in Fig. 1). In order to succeed in such **front-line research**, which is high-risk research, but which can produce fundamental and fundamentally new knowledge via a multidisciplinary research approach, Akershus University Hospital is dependent on developing environments with leading international expertise in both basic research and clinical research. Frontier research is prioritized by both the EU, the Research Council of Norway and Health South-East. Skilled environments in both basic research and clinical research are also important for Akershus University Hospital to succeed with **research-driven innovation**, defined as knowledge, ideas or inventions that can be launched on the market and provide financial gain. Research-driven innovation is a national initiative from the Ministry of Trade and Industry and the Ministry of Health and Care.

**In order to utilize the hospital's unique patient material, Akershus University Hospital and the  
University of Oslo should jointly develop a research unit that 6  
combines first-class clinical research with advanced basic research**

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**Fig.1.** By using Akershus University Hospital's rich patient material and basic research, DNA, RNA and advanced protein structures in patients' blood (biomarkers) can be identified, among other things, which can provide important information about diagnosis, treatment and the need for follow-up. These substances can also be important pathophysiologically and represent new principles for therapy. Both the invention as a biomarker and therapy can be commercialised.

*Example of a "bed-to-bench strategy" from the Cardiothoracic Research Group v/ Omland and Røsjø. Other research groups associated with EpiGen work according to a similar strategy with target discovery in patient material (blood, biopsies, spinal fluid) and later testing as a biomarker or point of attack for therapy.*

Akershus University Hospital is also an active participant in a European initiative to raise the quality of clinical studies through partnership in the Norwegian Clinical Research Infrastructure Network (NorCRIN). NorCRIN is a large-scale initiative from all Norwegian university hospitals where guidance and standardized templates for, among other things, Good Clinical Practice, Standard Operating Procedures and electronic Clinical Report Forms are offered to raise the quality of clinical research studies. NorCRIN is a national continuation of a European initiative supported by the EU (ECRIN) and an initiative from the Nordic Council of Ministers (Nordic Trial Alliance). However, in order to benefit from the work in NorCRIN, it is crucial that the university hospitals develop robust and professional clinical research units.

**It is important for Akershus University Hospital to develop competent and professional clinical research units in order to achieve the goal of outstanding clinical research**

All of these directions fit well with the research profile and status at Akershus University Hospital and with development trends within the University of Oslo.

Research output at Akershus University Hospital is strongly increasing and Akershus University Hospital and several of the research groups received a positive evaluation in the Norwegian Research Council's national evaluation of biomedical research in 2011. However, a consistent comment from the evaluation panels, both at institutional and group level, was the need for larger units of both researchers and support personnel .

Building a combined unit for basic research and clinical research will be in line with these recommendations and strengthen academic medicine at Akershus University Hospital.

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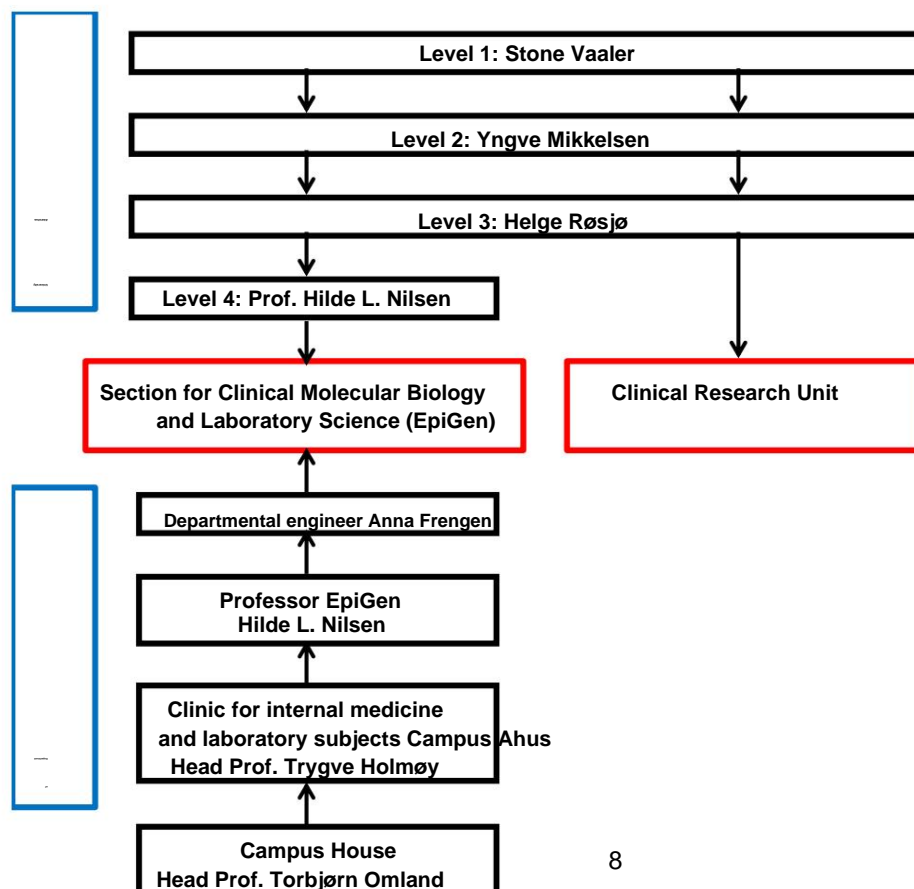
Campus Ahus in the Department of Clinical Medicine, University of Oslo is also growing. The Faculty of Medicine wants to utilize the company's rich patient material for teaching and an increasing number of students will be taught at Akershus University Hospital in the coming years. The University of Oslo is also making plans for and will invest in the field of **life sciences**, defined as all disciplines within science that study the structure, structure and function of living organisms, and are then dependent on collaboration to gain access to patient materials.

**The university's investment in life sciences will increase the need for biological material, which makes Akershus University Hospital an important collaboration partner**

The prerequisites for Akershus University Hospital and Campus Ahus to succeed in their ambitions to further develop the combination of basic research and clinical research are now well in place. Campus Ahus has attracted talented researchers in recent years and Hilde L.

Nilsen has recently been employed as a professor at EpiGen and as head of EpiGen in the Medical Division (level 4). Nilsen will have overall responsibility for strengthening basic research at EpiGen. A clinical research unit has also been established in the Medical Division which runs large epidemiological studies and randomized controlled clinical trials. Helge Røsjø, head of department for Research (level 3), Medical Division leads the research unit and is also Akershus University Hospital's contact person in NorCRIN. Furthermore, EpiGen is integrated into the Department for Research, Medical Division so that the head of the Department for Research, Medical Division now has overall responsibility in the hospital line for both EpiGen and the largest clinical research unit at Akershus University Hospital (Fig. 2). Clinic for internal medicine and laboratory subjects-Campus Ahus is led by professor Trygve Holmøy.

**Fig. 2.** There is now a structure for research at Akershus University Hospital which enables a closer integration of basic research and clinical research with unified management all the way up





## 5.0 HISTORY EPIGEN

The Department for Clinical Molecular Biology (EpiGen) was established in 2001 as a collaborative institute between Akershus University Hospital and the Faculty of Medicine. EpiGen was planned as a central research institute in a new hospital with a clinically oriented research profile and the application of modern molecular biological methods in clinical patient material. An important goal for the institute was to strengthen the hospital as a university clinic and to be accessible to all specialist areas. With the move into a new hospital building in 2008, EpiGen was allocated laboratory areas of ~1,000 m<sup>2</sup> and investments from the Faculty of Medicine of approx. 25 million

NOK for instrument park. The section currently has a large and modern laboratory which is used both for clinical molecular biology research within the major disease groups and for advanced diagnostic examinations of patient samples. Scientific production has been growing steadily and in 2012 there were 4 doctoral degrees (table 2A), there were 6 registered research-driven inventions from researchers connected to EpiGen in recent years (table 2B) and 26 peer-reviewed articles were published in 2012.

**Table 2A.** Doctorates/PhDs from researchers associated with EpiGen in 2012

Candidate's name	Title	Division
Dr. Helge Røsjø	The granin protein family in cardiac disease	Medicine
Dr. Jan Erik Berdal	Airway colonization, pathogenesis and prognosis in mechanically ventilated patients	Medicine
Cand Scientist Lise Aagard Sørby	New insights into markers and mechanisms in colon cancer progression and metastasis	Medicine
Cand. med. Bård Stuen Lundeland	Inflammatory responses in stress and trauma. Impact on Toll-like receptor 4 signaling	Surgery/Medicine (parts of the work were carried out on EpiGen)

**Table 2B.** Research-driven inventions from researchers associated with EpiGen

Inventors	Title	Id	Division
Røsjø/Surroundings (+ others)	Granin proteins as markers of heart disease	PCT/GB0818650.4	Medicine
Røsjø/Surroundings (+ others)	SgII as a prognostic marker in conditions which require critical care	PCT/GB0919901.9	Medicine
Røsjø/Omland/Ottesen (+ others)	Secretoneurin therapy to reduce cardiac arrhythmias	DOFI B-12015 Inside2	Medicine
Ree/Kristensen/Klajic (+ others)	An epigenetic prognostic signature in colorectal cancer	DOFI 13081 Inven2	Medicine
Fladby, Johnsen (+ others)	Alzheimer diagnostics by macrophage function	PCT/EP2009/001210	Medicine
Fladby, Johnsen, Møllergård	Methods and compositions for monitoring phagocytic activity	PCT/US2011/062233	Medicine

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In 2012, the Faculty of Medicine invested a new NOK 22 million in research equipment at Campus Ahus. These funds were used, among other things, to build up the biobank facilities at EpiGen, so that today the department also has a central position in clinical research at Akershus University Hospital. In connection with the reorganization of research in the company, EpiGen was moved from the Research Center to the Medical Division in January 2012. This organization ensures closer integration between clinical environments and the laboratory and was initiated by Vice Adm. director Stein Vaaler. Incorporation of EpiGen in the Department of Research, Medical Division has not come at the expense of offers to research environments at other divisions in Akershus University Hospital (see point #6.4 for research groups using EpiGen in 2013).

**6.0 STATUS OF THE EPIGEN****6.1 General overview**

EpiGen today represents a patient-friendly and high-tech laboratory with a wide range of instruments for modern biotechnological research and clinical analyzes with a total value of ~50 million NOK. Almost all basic research at Akershus University Hospital takes place at EpiGen and the institute also has a central place in clinical research as a center for biobank facilities. For Akershus University Hospital as a young research institution, there is a benefit both academically and financially in the coordination of resources and tasks at EpiGen. Academic medicine at Akershus University Hospital is strengthened by coordinating different environments with complementary expertise and by integrating fellows from different environments

in an open office landscape with fellows and postdocs from other environments and divisions.

Economically, it makes sense to co-locate at EpiGen in that the acquisition of equipment and the acquisition of expertise is for the common benefit of all research environments at the company. As a consequence of this, most of the advanced scientific equipment at Akershus University Hospital is collected and operated by EpiGen. This solution has worked very satisfactorily and is appropriate for operational and financial reasons.

EpiGen is led by a steering group consisting of users and administrative staff from Campus Ahus and Akershus University Hospital (table 3):

Professor Torbjørn Omland	Head of Campus House
Professor Trygve Holmøy	Head of the Clinic for internal medicine and laboratory subjects, Campus Ahus
Head of department Helge	Head of Research, Medical Division
Røsjø Professor Hilde L. Nilsen	Management responsibility EpiGen at Campus Ahus and i Medical Division
Professor Vessela Kristensen	Professor EpiGen
Berit L. Opheim	Head of administration, Campus House
Anna B. Frengen	General manager of the laboratory, Campus Ahus

*Strategy document EpiGen and clinical research unit 2014-2017***6.2 Objectives for EpiGen in 2013**

EpiGen has a three-part objective as shown in table 4:

	<b>Goal</b>
<b>(1)</b>	EpiGen will conduct self-initiated research within the research strategies of Akershus University Hospital and the Faculty of Medicine
<b>(2)</b>	EpiGen will be a core facility that assists clinical research environments with method support
<b>(3)</b>	EpiGen will offer facilities and expertise to carry out clinical investigations based on modern biotechnological methods

A more detailed description of specific projects appears under #6.3 and #6.4.

**6.3 Frontier research at EpiGen**

EpiGen represents an important resource for Akershus University Hospital both quantitatively and qualitatively in research. Researchers and research groups linked to EpiGen lead and participate in large consortia funded both by EU funds and funds from the Research Council of Norway, KG

The Jebsen Foundation and Helse Sør-Øst, as well as carrying out important studies with potential for front-line research (table 5):

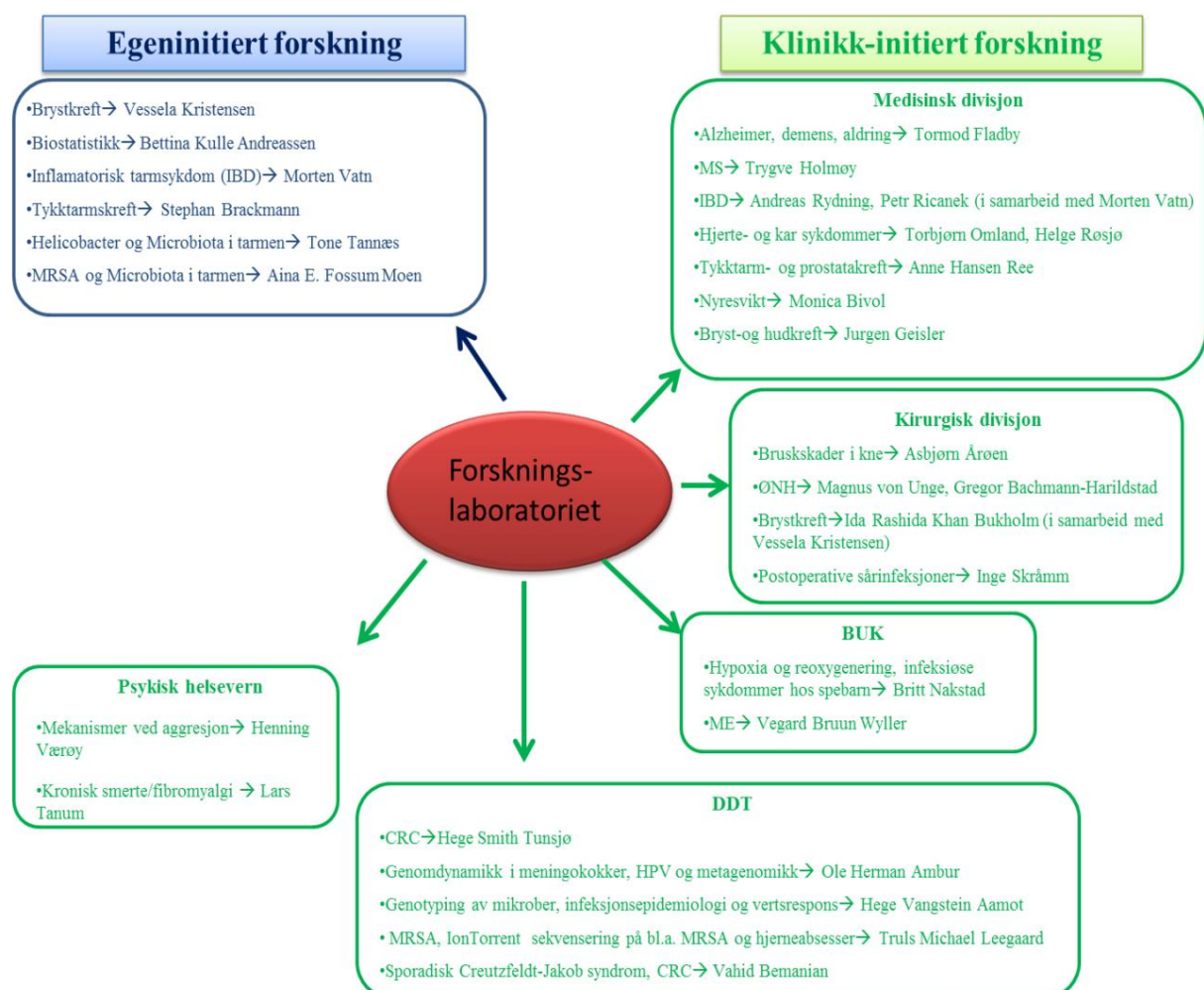
<b>Researchers</b>	<b>Research project KG</b>	<b>Goal setting</b>	<b>Division</b>
surrounding area, Røsjø, Ottesen, Dahl	Jebsen Center for Cardiac Research	Molecular and clinical mechanisms in dyssynchrony and heart failure	Medicine, Campus House (+ others)
surrounding area, Røsjø, Ottesen, Dahl	Secretoneurin: cardiac biomarker and therapy	Secretoneurin as a biomarker and therapy (patented)	Medicine, Campus House (+ others)
Jahnsen, Vatn, Coal Andreassen, Ricanek	"Inflammatory Bowel Disease CHARACTERization by a multi-modal integrated biomarker study"	Development of individualized treatment for inflammatory bowel disease	Medicine, Campus House (+ others)
Nilsen	RNA/DNA quality control and disease mechanism	Molecular mechanisms for RNA and DNA quality control and their significance for aging and disease development	Medicine, Campus House (+ others)
Ree, Røe, The hecto	METOXIA: Metastatic Tumors Facilitated by Hypoxic Tumor Micro-Environments (EU FP7)	Biological role of tumor hypoxia in treatment resistance and metastasis	Medicine, Campus House (+ others)
Ree, Geisler, Roe	MetAction: Actionable Targets in Cancer Metastasis – from Bed to Bench to Byte to Bedside (NFR)	Molecular signaling pathways and treatment of metastatic cancer with biologically targeted drugs	Medicine, Campus House (+ others)
Ree, Røe, chahal, Kristensen	Regional Research Network on Extracellular Vesicles (HSØ)	The role of exosomes in metastasis of hypoxic rectal cancer	Medicine, Campus House (+ others)

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Fladby et al JPND	EU research project APGeM (2014 - 2016)	Genotype-phenotype matching in neurodegenerative disease	Medicine (+ others)
Fladby et al JPND	EU research project BIOMARK ADPD	Biomarkers in AD and Parkinson's	Medicine (+ others)
Fladby et al	Dementia Disease Initiation, (HSØ/RHFene)	Mechanisms in neurodegenerative dementia	Medicine (+ others)

#### 6.4 Research groups using EpiGen in 2013

Researchers from across the company use EpiGen for projects related to basic and translational research and EpiGen also has solid self-initiated research within strategic focus areas as stated in the objectives of the department (Fig. 3):



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### **6.5 Finance at EpiGen 2013**

The operating budget from Akershus University Hospital to EpiGen is NOK 600,000 annually, of which NOK 250,000 is reserved for the Infection Control/Microbiology Department following the cooperation agreement from the reorganization process. EpiGen no longer receives earmarked operating funds from the Faculty of Medicine and a budget of NOK 350,000 is not sufficient to cover annual service agreements on instruments or necessary maintenance of the instrument fleet. Today's operating budget also does not provide room for strategic investments, the phasing in of frontline technologies, the start of pilot trials or the financing of projects in the early phase. This makes it impossible to take care of the role as knee facility in a proper way. It also weakens the possibility of obtaining external funding, as the feasibility of projects is unclear at the time of application. A lack of financial framework can also have an impact on clinical operations as EpiGen is unable to provide service to the departments. Tight financial frameworks are also an obstacle for new technology to be fully utilized in the clinic due to a lack of ICT solutions and a lack of local expertise, particularly in applied bioinformatics.

Today, EpiGen works very well as a host for the part of the research at Ahus that runs large molecular biology projects. But little time is available among the staff to provide method and technology support and provide service to smaller projects and pilot trials. Furthermore, the financial situation for EpiGen represents a threat to the department in that it reduces the possibility of fulfilling the role of core facility in a good way. All these challenges reduce the likelihood that EpiGen and its partners Akershus University Hospital and Campus Ahus will achieve their research goals. Operations at EpiGen are currently mainly based on external project support and publication funds and this is done by the department vulnerable to fluctuations and allows only short-term planning. It is therefore important that EpiGen is secured long-term and predictable funding. This can be solved via funds set aside centrally in Akershus University Hospital for research or possibly by contributions from all divisions that have shares in the laboratory. We believe that user fees will not provide enough predictability for operations, as this will vary from year to year depending on the grant of external funding among the research groups. We still believe that user fees should be included in larger projects and EpiGen will in future require that all larger projects with plans to involve the institute must include costs from EpiGen in their budget according to a template.

## **7.0 STATUS CLINICAL RESEARCH UNIT, MEDICAL DIVISION**

### **7.1 General overview**

A clinical research unit in the Medical Division was established in 2006 with a study nurse and a research bioengineer in a full-time position. This structure has continued and the unit today has the same number of permanent positions. In addition, for the past 4 years, the unit has had a study nurse employed on a contract basis (on leave from a position at the Department of Cardiology) and for the last year has had a doctor on contract as a technical employee. Several fellows are also closely integrated into the work in the clinical research unit, this particularly applies to fellows on the PRADA, ACE 1950 Study and RODEO projects (see #7.3 and #7.4 below for details). Furthermore, the research unit functions as a resource group for clinical research in the Medical Division with the guidance of study personnel employed in other departments: (1) Department of Infectious Medicine (Abvie study), (2) Department of Cardiology (Omemi study) and (3) Clinical and Molecular

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Oncology in Rectal Cancer Group v/ professor AH Ree and postdoctoral fellow K. Røe (MetAction and OxyTarget). Study nurse Vigdis Bakkelund is also a participant in the NorCRIN group that prepares Standard Operating Procedures for clinical research in Norway and head of department Helge Røsjø is the contact person for Akershus University Hospital in NorCRIN and leads the work there on work package #8 (mapping of national research structures).

**7.2 Objectives for the Clinical Research Unit in 2013**

The Clinical Research Unit in the Medical Division aims to promote research in Medicine division and at Akershus University Hospital by offering help with planning and carrying out research projects.

**7.3 Frontline research at the Clinical Research Unit**

Research projects associated with the Clinical Research Unit maintain a high professional standard and in particular projects related to protective treatment against heart damage after chemotherapy and research into the use of highly sensitive troponin measurement have the potential for great scientific impact. These projects have also obtained external funding and have won research awards both internally and externally. The research unit also operates the ACE 1950 Study, which is the company's largest study to date. In this study, researchers at Akershus University Hospital and Campus Ahus, together with the Clinical Research Unit, map all residents of Romerike, Follo and Nesodden born in the year 1950 with regard to cardiovascular disease and related conditions (endocrinological, psychosomatic, cognitive impairment and lung and kidney disease (total 4385 people will be offered participation) [see table 6 for an overview]:

Researchers	Research project	Goal setting	Division
Gulati, Heck, burial mound, Geisler, Røsjø, Steine, Ree, Surroundings	Prevention of cardiac Dysfunction during Adjuvant breast cancer therapy (PRADA)	Randomized controlled study of cardioprotective treatment with chemotherapy and radiation after breast cancer surgery	Medicine, surgery, diagnostics and technology
Pervez, Vigen, Lyngbakken, Hagve, Søyseth, Einvik, Smith, Brynildsen, Thommessen, Rønning, surrounding area, Steine, Røsjø	Akershus Cardiac Examination (ACE) 1950 Study	Epidemiological study of everyone born in 1950 in Romerike, Follo and Nesodden w/ taking pictures of the heart + intracranial vessels, clinical us, spirometry, cognitive testing, anxiety/depression, biobanking (incl. DNA)	Medicine, diagnostics and technology
Jørgensen, Røsjø, Einvik, Høiseith, Søyseth, surrounding area	High-sensitivity troponin measurements across the spectrum of CVD	Use of sensitive troponin assay for personal risk stratification	Medicine

**7.4 Research projects that will use the Clinical Research Unit in 2013**

The Clinical Research Unit in the Medical Division has several ongoing studies and a number of studies that will start in autumn 2013. In addition to these studies, the Clinical Research Unit has provided training to study nurses in the Omemi study (Department of Cardiology) and will support study nurses in the MetAction and OxyTarget studies (table 7):

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Researchers	Research project Objective		Division
Gulati, Heck, burial mound, Geisler, Røsjø, Stone, Ree, <small>Surrounding country</small>	Prevention of cArdiac Dysfunction during Adjuvant breast cancer therapy (PRADA)	Randomized controlled study of cardioprotective treatment with chemotherapy and radiation after breast cancer surgery	Medicine, surgery, diagnostics  and technology
Pervez, Vigen, Lyngbakken, Hagve, Søyseth, Einvik, Smith, Brynildsen, Thommessen, Rønning, surrounding area, Steine, Røsjø	Akershus Cardiac Examination (ACE) 1950 Study	Epidemiological study of everyone born in 1950 in Romerike + Follo with car participation by the heart + intracranial vessels, clinical us, spirometry, cognitive testing, anxiety/depression, biobanking (incl. DNA)	Medicine, diagnostics  and technology
Neukamm, Einvik, Søyseth, surrounding area	The RODEO Study	Randomized controlled study of statin treatment in lung and endothelial function v/ stable COPD	Medicine
Dalgard, Infectious diseases dept	The Abvie study	Randomized-controlled multicenter trial of hepatitis C treatment	Medicine
Winther, Foaling, Beiske, Røsjø, <small>Surrounding country</small>	Thizaid-induced hyponatremia	PhD project on the characteristics, treatment and consequences of hyponatremia	Medicine
Bivol, surrounding area, Røsjø	Inflammation and cardiac function in chronic renal failure	Inflammation and heart damage in chronic kidney failure	Medicine
Smith, Nerdrum, Department of cardiology	The Omemi study	Randomized-controlled trial of omega-3 supplementation in elderly patients with myocardial infarction	Medicine
Kononova, Høiseth, Einvik, Hardang, Hagve, Søyseth	LTOT study at COPD	PhD project on the characteristics, treatment and consequences of LTOT at COPD	Medicine, diagnostics  and technology

**7.5 Finances in the Clinical Research Unit in 2013** The

Clinical Research Unit is financed from the budget of the Medical Division with 2 permanent positions and 1 part-time position. A doctor engaged as a technical employee has been funded by the Cardiothoracic Research Group with the help of external research funds. With increasing activity, there is a need to strengthen staffing and it is likely that one will have to use both internal funds and external research funds to achieve this. The model where the research unit functions as a core facility for clinical studies and where other units are connected via project staff is an interesting model that will increase the number of employees in the short term. We will try this model now in collaboration with Clinical and Molecular Oncology in Rectal Cancer

Group by professor AH Ree and postdoctoral fellow K. Røe where their study nurse will be part of the Research Unit, but will primarily work with their projects. Such collaboration should result in increased professionalism, a better professional environment, increased flexibility in patient inclusion and reduced vulnerability.

*Strategy document EpiGen and clinical research unit 2014-2017***8.0 PLAN FOR THE YEAR 2017****8.1 General**

The University of Oslo, which is the company's most important partner in research, has set academic excellence as the key word for its strategic plan for life sciences. Professional Excellence should thus also be a goal for research at Akershus University Hospital.

Increased investment in life sciences in the Oslo area and integration (convergence) of all disciplines that research living organisms represent a great opportunity for Akershus University Hospital to strengthen its position within the university and academic medicine in Norway.

Akershus University Hospital has patient groups that are complementary to patient groups at Oslo University Hospital. A particular strength is the function as an emergency hospital with unselected patients and our many elderly patients, but we need robust and professional research structures to convert this potential for research into measurable results. It is also important that frontline research requires complete axes from top clinical research to basic research to be successful ("We need all the tools in the toolbox").

**The medical division wishes by 2017, in close collaboration with the Department of Clinical Medicine-Campus Ahus and other divisions in the company, to develop a nationally leading research environment that integrates outstanding basic research and clinical research**

The 2014-2017 strategic plan for the Medical Division recommends that this be carried out through an integration of EpiGen and the clinical research unit in the Medical Division and with a joint governing body where Campus Ahus owns EpiGen and Akershus University Hospital owns the clinical research unit.

**8.2 Strategic goals for EpiGen towards 2017**

EpiGen has two mandates that must be balanced and united in a way that promotes synergies.

EpiGen will conduct self-initiated, internationally competitive basic research. In addition, EpiGen will offer strategic cutting-edge expertise that builds on other clinically relevant research by the company and further develop existing operations. EpiGen also wants to strengthen the basic research component in the strategic investment areas of Akershus University Hospital.

EpiGen will work towards the year 2017 to achieve the following goals:

	<b>Goal</b>
<b>(1)</b>	To build up an internationally competitive business within mechanisms for RNA and DNA stability and their importance for cancer development and treatment, neurodegenerative diseases, including aging, and heart disease
<b>(2)</b>	To expand biobanks in close collaboration with clinical research units
<b>(3)</b>	To develop an agile project organization structure that helps consolidate EpiGen as a sought-after partner for clinical and basic research collaboration
<b>(4)</b>	Acquire status as a core facility in the region for the use of <i>C. elegans</i> as a model system in systems medicine

Molecular medicine and systemic medicine are developing rapidly, largely driven by technological development. There is an expectation among patients, politicians and professionals that medical treatment will become more individualized (personalised treatment).



**A prerequisite for personalized treatment is a better molecular understanding of causal relationships and disease mechanisms as a starting point for knowledge-based diagnostics and treatment strategies**

EpiGen will help ensure that changes in patient material (e.g. mutations) can be identified in biobank material, and that the consequences of the changes are described molecularly, cell biologically and in simple model organisms. The goal for EpiGen is that these findings should lead to knowledge-based development of new diagnostics and treatment regimens. In the coming years, EpiGen, in collaboration with the Clinical Research Unit, will develop complementary expertise in relation to other environments at the University of Oslo and at Oslo University Hospital.

EpiGen today has state-of-the-art premises and advanced technological equipment. Too much focus on technology-driven research entails a risk that the business will not be robust because advanced equipment is expensive to purchase and operate. A technology-driven business will be cost-driving because a lot of advanced equipment will have a short lifespan as technology development takes place at a very high pace. In the coming period, EpiGen will therefore focus on better utilization of the existing equipment park at the same time as we further develop the highly trained staff to expand the portfolio of technologies. This will lower the threshold for the utilization of advanced technologies and therefore contribute to a greater part of the research activity at Akershus University Hospital being lifted up to the forefront of international research. We also believe that a better utilization of strengths will elevate EpiGen to the fore as an attractive partner in network collaboration locally, regionally, nationally and internationally. EpiGen will contribute to projects being developed to a level where local/national/European technology platforms can be used effectively and be a bridge builder for the use of European research infrastructure. It is also a clear choice that EpiGen will seek to complement, not duplicate, existing technology areas at the University of Oslo and Oslo University Hospital. Most of the techniques we need to achieve such an ambitious vision are already present at EpiGen. Work to allocate personnel to complement the technology portfolio with some cell-based techniques has been initiated and funds have been made available from the Medical Division. During 2014, we want to offer the nematode *C. elegans* as a eukaryotic animal model for early phase studies of disease mechanisms (step #1 under Drug Concept Testing in Figure 1). This expertise can only be found in Professor Hilde Nilsen's group, and by being able to offer this, EpiGen will have cutting-edge expertise in Health South-East.

**By 2017, EpiGen wants to position itself as a leading institute for early testing of genetic variations in relevant cell lines and *C. elegans***

We believe there is a need in the region for a core unit for cell lines and *C. elegans* as these model systems are easy to work with, provide a high success rate for genetic modification, are robust and provide information with relevance to cancer and heart disease and the aging process. The costs of keeping these models are low and they do not require an animal facility or new premises. However, there is a need for a research position to set up and operate this model. The Medical Division believes that such an investment should be covered by Akershus University Hospital centrally, either via funds set aside for strategic investments or via funds for research and innovation. It is also need to upgrade microscopes and EpiGen will set aside funds in the budget for 2014-2016 to cover deductibles for upcoming applications for financing new microscopes. The

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there is also a strong need for expertise in applied bioinformatics at EpiGen in order to fully utilize the existing infrastructure and Akershus University Hospital and Campus Ahus must ensure that technologies that must be available locally (e.g. organotypic cell cultures and various image processing technologies) maintain an internationally competitive level.

**In order to assert ourselves at the forefront of research and be able to publish in the best journals, we must master the entire research chain from the identification of epigenetic changes, mutations, or gene expression changes in patients via molecular characterization of changes to functional validation of the changes in suitable model systems (Fig. 1)**

EpiGen will also, together with the Medical Division and Campus Ahus, re-establish the Ahus research forum and other meeting places for the exchange of ideas. EpiGen also wants to stimulate an ongoing dialogue with researchers, clinicians and industry to identify technological bottlenecks for using the large and unselected patient material for innovative patient-oriented research and innovation.

Financially, however, EpiGen is dependent on stronger grants from Akershus University Hospital and the University of Oslo to ensure long-term sustainability and maintain an optimal machine park. In order for EpiGen to be able to contribute to realizing Akershus University Hospital's model of strategic cutting-edge expertise that supports clinical operations and other research at the company, it is essential that the laboratory has sufficient staffing to ensure the continuous establishment of frontline technology. Only through such development can EpiGen (1) increase the relevance, quality and visibility of its own research, (2) increase its attractiveness as a partner and (3) elevate several projects to level 2 publications. It is also important to strive for flexible project organization to ensure agility and good implementation of projects. In order to achieve synergy effects, EpiGen will have a profile that harmonizes with the research profile of both company and university, and integrating the institute closer to the Clinical Research Unit can create stronger ownership from Akershus University Hospital. A possible organizational model is indicated in #8.4 and this is discussed in more detail there.

**Most employees are university employees and EpiGen's premises are part of the university area, but it is crucial for EpiGen that management models are developed that ensure contribution and commitment also from Akershus University Hospital**

*Strategy document EpiGen and clinical research unit 2014-2017***8.3 Strategic goals for the Clinical Research Unit towards 2017**

The clinical research unit in the Medical Division will work towards the year 2017 to achieve the following goals:

	Goal
(1)	To develop a clinical research unit with competence to carry out large epidemiological and randomized controlled clinical trials
(2)	To carry out a large and internationally innovative clinical study that includes several divisions in the company

A core of technical personnel with good expertise in both epidemiological and randomized controlled clinical studies has already been established and these will form the basis of the research unit in the future as well. It is also necessary to increase the number of employees towards 2017 in order to reach objective #2. More employees will ensure an increased breadth of competence and ability to implement. Two possible models for increasing numbers in the environment are (1) connecting other research structures at the research unit via bilateral agreements and (2) increasing access to resources to the research unit so that the unit can employ more people.

The project period 2014-17 should be divided into a short-term part and a long-term part with regard to employment and finances. In the first period, funds for the Research Unit will be based on the Medical Division and possibly external research funds, while in the longer term, grants may come from Akershus University Hospital centrally if it is desired to have a clinical research unit that will serve several divisions in the enterprise. The research strategy for Akershus University Hospital 2012-2016 states that this is to be investigated and it may be natural that the Research Unit in the Medical Division, as the largest research unit in the enterprise, may become involved in a central research unit.

**Regardless of internal organization, it is a goal to develop the Clinical Research Unit into a professional unit that can handle large epidemiological studies and innovative randomized controlled trials**

The process of securing a financial framework for the research unit will thus be, in the short term, to work towards the Medical Division and partners who want bilateral agreements, while in the longer term, clarification will be sought as to whether Akershus University Hospital will create a central clinical research unit. The Medical Division wishes to be a contributor to this work through experience in operating the company's largest clinical research unit and by participating in NorCRIN and thus clinical research development in Norway and Europe.

With increasing experience and expertise in clinical studies, it is natural that the Medical Division and Clinical Research Unit have the objective of conducting large studies of high international quality. Ongoing studies such as PRADA and the ACE 1950 Study represent potential frontier research and provide important experience for new projects. Possible patient groups for a new large study, which the Clinical Research Unit can carry out in collaboration with other divisions in the company, are patients at risk of heart damage after cancer treatment (cardiac oncology) or multimodal risk stratification of patients before and after major surgical interventions. Both of the two indicated studies are well suited to Akershus University Hospital

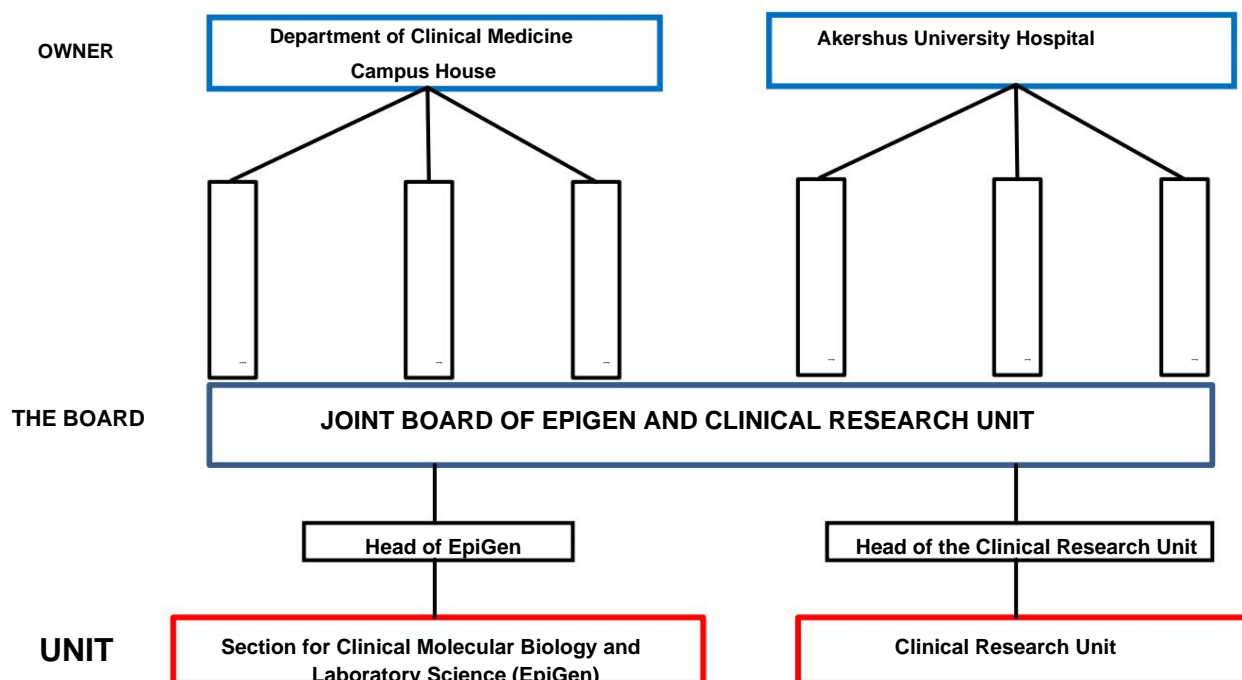
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the company's large and unselected patient material and will involve researchers from, among other things, the Medical Division, the Surgical Division and the Division for Diagnostics and Technology.

**In order to succeed with such a large study, however, it requires a pooling of resources  
Clinical research unit either by bilateral agreements with relevant partners or by Akershus  
University Hospital centrally forming a larger clinical research unit**

**8.4 Integration of EpiGen and the Clinical Research Unit towards the year 2017**

All research at Akershus University Hospital must be based on phenomena observed in patients, as the institution does not have animal facilities ("bed-to-bench strategy"). However, this gives the company has complementary expertise in relation to other university hospitals with stronger focus on discoveries in animal models ("bench-to-bed strategy"). In order to succeed in frontline research and research-based innovation, which is the goal of the University of Oslo with their focus on life sciences, Akershus University Hospital must create the right conditions for the integration of clinical research and basic research. The strategic plan for EpiGen and the Clinical Research Unit in the Medical Division recommends that this be implemented by developing over time a joint superior governing body for EpiGen and the Clinical Research Unit with equal representation from Akershus University Hospital and the Faculty of Medicine. It is natural that ownership of EpiGen lies with the university and that the Clinical Research Unit is owned by Akershus University Hospital. A possible control model is indicated in Fig. 4:



*Strategy document EpiGen and clinical research unit 2014-2017***8.5 Practical work to integrate basic research and clinical research**

In order to succeed in integrating basic research and clinical research, work must be done on several levels. Fellows and researchers are already integrated in a common office environment, but a common research forum must be established that embraces a wide range. During 2014, the Medical Division and Campus Ahus led by Hilde Nilsen at EpiGen will therefore re-establish the Ahus research forum, but in a different form than before. Ahus's research forum will be a weekly presentation of two research projects of 20 min presentation + 10 min discussion with focus on research idea, method and potential for interaction. The meeting will be open to everyone and there will be contributions from all divisions that conduct research at Akershus University Hospital.

Overall, in 2013-2014, the Medical Division will take the initiative for Akershus University Hospital to investigate the possibility of a central clinical research unit at the company and the integration of basic research and clinical research. These processes are owned by Deputy Managing Director Stein Vaaler and Research Manager Hilde Lurås at Akershus University Hospital and the Medical Division will support this work. In order for the goal in this Strategic Plan to be achieved, it is also crucial to have a similar process at the Department of Clinical Medicine-Campus Ahus where Professor Torbjørn Omland and Professor Trygve Holmøy will be responsible. The medical division will also play on a team with the University in this process. The time aspect for the overall process in companies and on Campus Ahus is estimated for 2013-2014 (table 8):

	<b>Goal setting</b>	<b>Milestones for start-up and completion<sup>1</sup></b>	<b>Responsible</b>
(1)	Re-establish Ahus's research forum as a weekly research meeting	Jan 2014/ Evaluation Dec 2014 Nilsen,	Røsjø
(2)	Investigate central clinical research unit at Akershus University Hospital	Fall 2013-Fall 2014	Vaaler, Lurås
(3)	Investigating the integration of basic research and clinical research in a joint structure Akershus University Hospital	Fall 2013-Fall 2014	Vaaler, Lurås
(4)	Investigating the integration of basic research and clinical research in a joint structure Campus House	Fall 2013-Fall 2014	Holmøy, <small>Surrounding country</small>

<sup>1</sup>Responsibility for process in #2-4 lies outside the Medical Division and the timeline here is only an estimate

*Strategy document EpiGen and clinical research unit 2014-2017***9.0 BUDGET 2014-2017****9.1 Generally**

Financial framework for EpiGen and the Clinical Research Unit in the period 2014-2017 will be based on the ownership of the Medical Division for both units in 2014. The budget for 2014 is thus based on the current grant with some growth, to safeguard the mission of EpiGen, and on funding from external sources (other divisions and external research funds for research groups). It may be necessary to change the budget from 2015 if the process at Akershus University Hospital and the Department of Clinical Medicine-Campus Ahus leads to an integration of EpiGen and the Clinical Research Unit from 2015 with financial grants from actors next to the Medical Division. With the University of Oslo's investment in life sciences, it is important that the company and Campus Ahus make clear the benefit of the company's large patient materials and thus ensure increased access to resources also from the Faculty of Medicine

for basic research and clinical research at Akershus University Hospital.

**9.2 Budget EpiGen 2014-2017**

<b>EpiGen budget 2014-2016</b>	<b>2013</b>	<b>2014</b>	<b>2015</b>	<b>2016</b>
Salary and social expenses <sup>1</sup>		4853000	5022855	5198700
Biobank operational position <sup>2</sup>		230000	238050	246400
Biobank operation		20000	20000	20000
Research position <i>C.elegans</i> <sup>3</sup>		700000	700000	700000
Bioinformatics new styling <sup>4</sup>			700000	700000
Operation <sup>5</sup>	350000	600000	600000	600000
Provisions for new purchases <sup>6</sup>		10000	10000	10000
Infrastructure <sup>7</sup>		2000000	2000000	2000000
<b>TOTAL Expenses<sup>8</sup></b>	<b>350000</b>	<b>8413000</b>	<b>9290905</b>	<b>9475100</b>

**Comments on Budget:**

(1)

Of the total budget, the University of Oslo covers most of the salary costs for employees at EpiGen (NOK 3,007,000). Akershus University Hospital currently covers salary costs of NOK 1,846,999 associated with EpiGen. Both the University of Oslo and Akershus University Hospital also covers salaries for professors associated with EpiGen (not included here).

(2)

From a letter dated 22 May 2013 from head of department Karin Vassbakk at the Research and Patient Safety Unit, Research Administration, a sum was granted for the **operation of biobank facilities at Akershus University Hospital, which should cover:**

On-call allowance NOK 160,000 + service agreements NOK 10,000 + 10% position (incl. social costs) NOK 70,000, a total of NOK 250,000 per year. We assume that this is maintained, if necessary we will compensate

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that by means of user funding, and that the biobank activity is also extended to external biobank material against payment.

(3)

We want to create a research position with responsibility for running *C. elegans* as an animal model for studies of disease mechanisms. This expertise can be found in Hilde Nilsen's group. But in order to maintain the competence and have continuity, we must have the opportunity to offer a position to one of her PhD students who will be doing their dissertation during the first half of 2014. We believe this should constitute a strategically important investment for Akershus University Hospital and thus be able to receive funding from Akershus university hospital central (see also #8.2).

(4)

We want to create a new position in applied bioinformatics. This is a function that is not currently offered in the laboratory. This is a paradox because the laboratory is equipped with advanced equipment that is relatively easy to use, but very complicated on the analysis side. Technical personnel or clinicians who wish to run tests on this equipment cannot be expected to familiarize themselves with complicated mathematical and statistically based analyses. Therefore, we need a person who can fill this function. This will increase the applicability of the equipment also for clinicians on a project basis and the position fills a need with regard to translational research close to the patient. We believe this may represent a strategic investment for the company that will benefit all divisions, and in particular the Surgical Division and the Children's and Youth Clinic with their focus on molecular research in patient material, but we will wait for the investment until 2015 as for the year 2014 we prioritize # 3 higher.

(5)

Today's operating budget is an absolute minimum (see appendix specification of operating assets). We are requesting that operating funds be increased by 250,000 to set up cell-based techniques and various chromatin immunoprecipitation techniques. This does not require the purchase of new equipment, but will increase the scope of application for existing infrastructure.

(6)

The microscopes at EpiGen must be equipped and supplemented. In general, the lifetime of instruments can be expected to be shorter than 10 years with today's rapid technological development. We can extend the service life through good service agreements and the development of complementary technologies, but equipment will be ready for replacement in a few years. Most of the funding for new acquisitions will be by application for instrumentation that requires own shares. We will therefore set aside a small sum each year that can cover deductibles in equipment applications.

(7)

A new record for operation of the instrument fleet, including annual service agreements and repairs must be created. This is necessary to maintain the instrument park and maintain the quality of the infrastructure for the benefit of all users, both research environments and the hospital's routine departments that use the laboratory regularly. Today's short-term allocations for the most basic service agreements are not sufficient.

*Strategy document EpiGen and clinical research unit 2014-2017*Summary:

Of the total budget for 2014 of NOK 8,413,000, it is intended that NOK 3,550,000 will be covered by Akershus University Hospital, of which 250,000 from the Unit for Research and Patient Safety, Research Administration and then we believe 700,000 should be covered via strategic funds or funds for research and innovation (C. elegans engagement). In addition, we are asking for NOK 4,117,000 from the Medical Division for 2014 (includes salary funds already in the budget + NOK 2,000,000 for service agreements for equipment that is also used to examine patient samples).

**9.3 Budget Clinical research unit 2014-2017**

Personnel costs make up the majority of the costs of running a clinical research unit. Two employees are permanent employees (Jørgensen, Bakkeland) and one employee has been employed on a contract basis with an annual extension since 2009 (Lorentzen). The main goal of the budget process for 2014 for the Clinical Research Unit in the Medical Division is to convert Lorentzen's position into a permanent position in the Department of Research. In order to run several different studies, including the PRADA and ACE 1950 studies, we will also need to hire two more technical staff. We propose that the costs of these positions be shared between the Medical Division and the Cardiothoracic Research Group in 2014 so that each unit finances one position on commitment each. In the budget, we have also highlighted fellows who work closely at the Clinical Research Unit with their funding source to make clear the total value the Clinical Research Unit has for research in the Medical Division and at Akershus University Hospital.

Funds for operations are on a par with what has previously been handled within the budget for the Department of Research, Medical Division.

The budget for 2015 and 2016 has been continued here only with the view that the Clinical Research Unit will be linked to the Medical Division. At the same time, we have highlighted the costs of a study nurse and bioengineer in the frame on the next page, but to assess the volume research support in other divisions is outside the mandate of this Strategy Document.

<b>Clinical Research Unit</b>	<b>2014</b>	<b>2015</b>	<b>2016</b>
<i>Medical Division</i>			
Med.div., salary and social expenses fixed <sup>1</sup>	1,865,000	1,939,000	2,017,000
Med.div., eng. position <sup>2</sup>	615,000	639,600	665,400
Operation/investment needs equipment <sup>3</sup>	500,000	500,000	500,000
<i>Other sources of funding</i>			
Meadow. position bioengineer CRG <sup>4</sup>	573,000	596,000	619,800
Scholars (UiO) <sup>5</sup>	2,432,000	2,529,300	2,630,300
Scholarship holder (Cancer Association) <sup>6</sup>	615,000	635,000	660,000
<b>SUM Expenses</b>	<b>6 600 000</b>	<b>6 383 900</b>	<b>7 092 500</b>



Template for personnel costs for possible expansion of the Clinical Research Unit to also cover the need for  
research support in other divisions:

A student nurse (salary and social expenses) costs NOK 615,000 per year

Bioengineering (salary and social expenses) costs NOK 567,000 per year

**Comments on Budget:**

(1)

Permanent employees (Vigdis Bakkeland, Marit Jørgensen) + contract position which is desired to be converted to a permanent position (Annika Lorentzen).

(2)

Dedicated nurse (not employed).

(3)

Operating costs and investment needs for equipment are estimated based on assumed operation and needs related only to research in the Medical Division.

(4)

Engagement bioengineer (not employed).

(5)

Scholarship holders funded by the University of Oslo who work closely with the Clinical Research Unit (Jacob A Winther, Magnus Nakrem Lyngbakken, Natalia Kononova, Mohammad Osman Pervez) - salary costs estimated according to the general rate.

(6)

Scholarship holder funded by the Cancer Society who works closely with the Clinical Research Unit (Geeta Gulati) - salary cost estimated according to general rate.