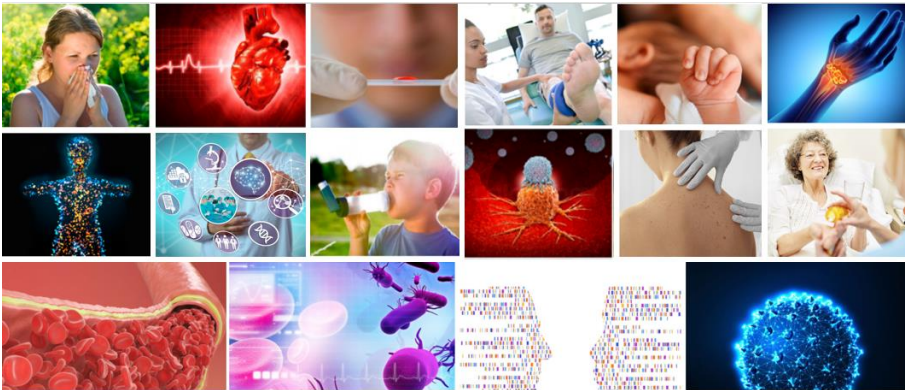


# CLINICAL ACADEMIC GROUPS (CAGs)

University researchers and clinical researchers collaborate and develop new ideas together, resulting both in faster scientific results and better treatment of patients



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## **CAG Allergy**

The purpose of CAG Allergy is to reduce the increasing number of patients suffering from allergic diseases, including eczema, asthma and rhinitis as well as food and drug allergy.

Allergy affects all age groups, and it may be lifelong and have major implications by reducing patients' quality of life and increasing the occurrence of cardiac, psychiatric and autoimmune comorbidities.

Allergy often results in disability and shortened life expectancy, just as the socio-economic cost of allergic diseases are considerable.

The CAG will solve this major challenge by conducting ground-breaking research in early diagnosis, new individualised treatments and by taking a new holistic approach to patient care.

The core of the CAG consists of leading experts from general practice and five specialties involved in treating allergic patients. They work together with high-profile basic research units in immunology and across healthcare sectors.

The strong structure of the CAG provides an optimal environment for pioneering research and will attract international researchers and funding. It will pave the way for transforming clinic practice to meet the needs of future patients at the right level of expertise from the start.

The work will be linked up to new educational initiatives with the specific aim of increasing knowledge and recruiting new scientists and clinicians to develop the field in creative synergy and to enhance our basis for international competitiveness.

CAG chairman Jeanne Duus Johansen

CAG vice chairman Charlotte Menné Bonfeld

## **CAG Host Infections Laboratory Research Drugs (CHILD)**

There is a need for fast and reliable diagnostics and effective prevention of infections. This lack causes 50 per cent of all children to be treated unnecessarily with antibiotics during the first two years of their life and 30 per cent to be hospitalised with an infection during childhood. This has significant socio-economic and human costs and contributes to the antibiotic resistance crisis.

CAG CHILD means to improve prevention and treatment of the large number of children affected by infections each year. The CAG consists of an ambitious group of highly committed basic researchers and clinicians, including all four paediatrics wards in the Capital Region of Denmark. This makes it possible to collect biological material from children suffering from infections and infection-like inflammation and to apply it in basic research.

Infection is the most frequent cause of disease among Danish children and responsible for 10 per cent of all deaths among children below the age of one. Infections include everything from common airway infections not requiring treatment seen in all children to rarer, life-threatening infections such as meningitis.

The CAG will contribute to the implementation of the latest new knowledge on prevention and diagnosing in the healthcare system's handling of infections in children.

CAG chairman Ulrikka Nygaard

CAG vice chairman Søren Buus

## **CAG in Cancer Immunotherapy (CAGci)**

One in every three Danes contracts cancer at some point in their lives, and just below 285,000 Danes live with a cancer diagnosis. In Denmark the one-year survival rate for cancer is 75 per cent for men and 77 per cent for women.

CAGci seeks to improve treatment with immunotherapy for cancer patients to ensure that more cancer patients survive the disease.

Immunotherapy represents a significant breakthrough in cancer treatment, and new forms of immunotherapy are rapidly being approved for treatment of still more forms of cancer. The new treatment options indicate that far more patients, even patients where the disease has spread, can become survivors of cancer.

Immunotherapy is based on the immune system's ability to detect and kill cancer cells and will lead to changes in most, if not all, forms of cancer treatment over the next few years.

However, the implementation of new forms of immunotherapy has been so rapid that many clinicians face pressing questions and challenges with regard to treatment. The overall aim of CAGci is to develop evidence-based clinical solutions to these challenges and to offer evidence-based training of health staff in cancer immunotherapy.

By strengthening the cross-institutional and cross-disciplinary knowledge exchange between clinicians and researchers within cancer immunotherapy, CAGci will be able to explore the potential of immunotherapy for the benefit of patients, their relatives, and society.

CAG chairman Inge Marie Svane

CAG vice chairman Anders Woetmann Andersen

## **CAG Modulating the Infant Microbiome for Disease Prevention**

In the Western world the prevalence of asthma and other chronic inflammatory diseases has more than doubled over the last 50 years. Between 250,000 and 300,000 adult Danes have been diagnosed with asthma, and a total of 7-10 per cent of all schoolchildren in Denmark suffer from asthma.

CAG Modulating the Infant Microbiome for Disease Prevention will therefore seek to improve prevention of chronic inflammatory diseases and treatment of paediatric asthma.

The CAG will strengthen existing knowledge of the role of intestinal bacteria in the development of chronic inflammatory diseases among children. Imbalance in the bacterial composition and maturation of the intestines and airways can affect children's risk of developing asthma later in life. The overall aim of the CAG is therefore to understand the connection between the infant microbiome and the development of chronic inflammatory diseases.

The studies of the CAG will be based on a large amount of unique data collected from a mother-child group within the COPSAC2010 project. Over the last eight years, the project has followed children with an imbalance in the bacterial composition and thus increased risk of developing diseases. The mother-child group data offers a unique opportunity to outline the mechanisms that link the infant microbiome – before the emergence of disease – to the development of common chronic inflammatory diseases.

The CAG will seek to develop new strategies for prevention and effective intervention targeted at the microbiome to protect the child from diseases.

CAG chairman Hans Bisgaard

CAG vice chairman Søren Johannes Sørensen

## **CAG Physical Activity and Sport in Clinical Medicine (imPAct)**

Physical inactivity and sedentary behaviour is the new public health challenge. It is considered responsible for 40 million deaths worldwide each year and includes four major disease types (cardiovascular, cancers, respiratory and diabetes).

CAG Physical Activity and Sport in Clinical Medicine aims to initiate translational research activities to directly couple laboratory and clinical research groups within physical activity. Our activities and collaboration will lead to the cross-fertilisation of disciplines across hospitals and university faculties/institutes. In addition, it will increase the synergy between research, clinical activity and education within the area of physical activity in prevention, disease treatment and rehabilitation.

Regular physical activity has beneficial effects within prevention and treatment of chronic diseases. Further, physical activity can improve the treatment and rehabilitation of patients after trauma and injury, and prevent future musculoskeletal disorders. Yet, the use of physical activity in daily clinical medical practice is very limited.

The CAG will seek to connect theoretical researchers directly with clinical departments. It will create a better formalised academic coupling of research-active clinicians to the experimental milieus.

The role of physical activity in complex diseases is not fully elucidated, and the interplay between physical activity and pharmacological treatment is poorly understood. The curriculum of the Danish study programme in medicine only contains very sporadic information about the effect of physical activity on the sick body. However, this should be integrated into the programme.

The CAG will involve co-supervision of PhD students between experimental and clinical research groups and introduce physical activity into the curriculum of the study programme in medicine.

CAG chairman Michael Kjær  
CAG vice chairman Flemming Dela

## **CAG Precision Diagnostics in Cardiology**

The field of cardiology is characterised by many patients who, even with treatment, suffer from significant morbidity and mortality due to their heart disease. Almost half a million Danes suffer from heart diseases, and one in four across the population die from a cardiac cause.

With CAG Precision Diagnostics in Cardiology we have created a unique research collaboration which strives to ensure more efficient and accurate diagnostics and individualised treatment of cardiac patients.

Leading researchers and clinicians from the University of Copenhagen and the highly specialised cardiac units in the Capital Region of Denmark have joined forces to reduce morbidity and mortality of heart diseases.

Precision diagnostics is a prerequisite for offering precision therapy and eventually personalised medicine. Gradually, several ‘omics’ technologies (genomics, proteomics, metabolomics etc.) will be combined with clinical and registry data on most cardiac patients in the region.

Presently applied work-up strategies in cardiology generally lead to rather unspecific diagnoses, and correspondingly we provide imprecise ‘one-size-fits-all’ therapies. This applies to ischemic heart disease, myocardial diseases, arrhythmia and congenital heart diseases and for acute management in emergency rooms.

There has been a tremendous – and rapid – increase in our understanding of cardiac diseases at the molecular and cellular levels, not least achieved through advances in genetics. This actionable knowledge has not yet been translated into clinical practice.

The CAG Precision Diagnostics in Cardiology will ensure the transfer and implementation of the rapidly increasing knowledge of cardiovascular disease.

CAG chairman Henning Bundgaard

CAG vice chairman Søren Brunak

## **CAG Research Osteoarthritis Denmark – Prevention and Treatment Through the Lifespan of Patients (ROAD)**

CAG ROAD means to improve the quality of life of persons with osteoarthritis (OA), which is the second most widespread condition in Denmark next to allergies. Around 900,000 Danes suffer from osteoarthritis (OA), and the costs of the condition with regard to both treatment and loss of production are substantial.

The CAG will increase focus on prevention and develop better treatment for patients.

Based on the latest new research-based knowledge it will shed light on the risk factors and disease mechanisms affecting the development of OA.

In light of the demographic development with increased life expectancy and an expected increase in the number of persons with obesity, the number of persons suffering from OA is likely to grow, possibly leading to great human and social costs.

In addition, OA has significant socio-economic consequences in the form of treatment costs, handicap, reduced quality of life and lost earnings.

CAG ROAD is a strengthened cross-disciplinary partnership between researchers and clinicians and other professionals within the field of OA. Together they will translate basic and clinical research into improved quality of life for persons with OA.

CAG chairman Anders Troelsen

CAG vice chairman Stine Jacobsen



## **CAG Translational Hematology**

The vision of CAG Translational Hematology is to improve the treatment, quality of life and survival of patients with blood cancer.

The focus is on acute myeloid leukaemia (AML), myeloid dysplastic syndrome (MDS) and premalignant conditions i.e. clonal cytopenia of undetermined significance (CCUS) and clonal hematopoiesis of indeterminate potential (CHIP).

The CAG collaboration includes the hematological departments and associated laboratories in all the Danish regions. The national collaboration is anchored in the Danish Research Center for Precision Medicine in Blood Cancers.

Our main aim is to identify and target blood cancer stem cells. To do this, we have established a platform which enables comprehensive drug screening, which is an important tool for identifying the best available treatment for the individual patient, also called precision medicine or personal medicine. In addition, we are working on establishing pre-clinical models (PDX and other mouse models) that may serve for identifying new stem cell targeting treatments.

The CAG is conducting two investigator initiated clinical trials, and several more are in the pipeline. We are working on integrating molecular and clinical diagnostics, patient reported outcomes and treatment opportunities to develop algorithms that may all help stratifying patients for individualized clinical management.

The CAG will work on improving the translational medicine and on further education of the next generation and present clinicians and scientists in the field of blood cancers.

CAG chairman Kirsten Grønbæk

CAG vice chairman Krister Wennerberg

## **CAG Personalised Oncological Surgery (POS)**

CAG POS intends to reduce morbidity and increase survival for patients diagnosed with colorectal cancer. The CAG vision is to implement a generic research approach by combining clinical and basic research through Personalised Medicine (PM) treatment of patients undergoing oncological surgery.

Each year 5,000 patients are diagnosed with colorectal cancer in Denmark. The financial burden is substantial as major complications after colorectal cancer surgery increase costs up to three times. Only one in three patients with complications returns to work within three months compared to one in two patients without complications. The proportion of patients who never return to work is also doubled after postoperative complications. Preventing recurrence after surgery will result in a dramatic reduction in overall costs.

Current oncological and surgical treatment of patients with cancer is performed according to standardised pathways. Even with high adherence to these pathways and with state-of-the-art oncological, perioperative and surgical treatment, one in four patients suffers from complications within 30 days after colorectal cancer surgery and one in three patients will develop disease recurrence. With current treatment strategies, too many patients either do not get the right surgical or oncological therapy or experience complications without benefitting from the treatment.

There is compelling evidence that a tailored approach delivering the right treatment at the right time will have dramatic effects on the prevention of complications and recurrence after surgery.

The CAG will provide a state-of-the-art clinical research platform for PM in surgery through a collaboration between basic scientists specialised in big data, experts in translational techniques in the laboratory and a multidisciplinary team of experts from each phase of the entire patient care pathway.

CAG chairman Ismail Gögenur

CAG vice chairman Ali Salanti

## **CAG GREATER COPENHAGEN RESEARCH CENTRE FOR SYSTEMIC LOW-GRADE INFLAMMATION (LOGINFLAM)**

The CAG LOGINFLAM aims to improve treatment for patients with diseases associated with low-grade inflammation (LGI). The CAG vision is to establish an internationally recognised centre of LGI research with a track record of excellent scientific results, education and innovation that has improved understanding of LGI-associated pathologies and contributed to a reduction of their individual and societal burden.

LGI is implicated in most noncommunicable diseases, e.g. type 2 diabetes, cardiovascular disease, periodontitis, neurodegenerative diseases and cancer. These diseases account for massive direct and indirect health costs; thus, LGI represents a substantial societal burden.

Also, traditional chronic inflammatory diseases, e.g. periodontitis, rheumatoid arthritis, primary Sjögren's syndrome and systemic lupus erythematosus, as well as adverse effects of therapeutic interventions, e.g. transfusions or surgery, are linked with LGI. These diseases frequently share inflammatory pathways and coexist in individual patients, suggesting that treatment of one LGI-dependent disease may favourably affect another comorbidity.

While LGI research has attracted interest, clinical implementation of results has been limited. This is partly due to a predominant interest in conventional 'disease-specific' mechanisms and interventions, e.g. antidiabetic or lipid-lowering drugs, and a belief that inflammatory mechanisms often are epiphenomena and not primary pathogenic drivers of disease. However, there is increasing realisation that even after optimal conventional treatment, persistent LGI represents a residual 'inflammatory' risk, and that inflammation is a maker and not merely a marker of disease.

By joining the forces of researches of proven excellence, the CAG creates synergies that promote high-quality LGI research, teaching, innovation and clinical implementation.

CAG chairman Peter Riis Hansen

CAG vice chairman Palle Holmstrup

## **CAG SKIN CANCER INNOVATION CLINICAL ACADEMIC GROUP (SCIN CAG)**

The vision of SCIN CAG is to reduce skin cancer (SC) incidence, morbidity and socioeconomic costs related to SC. It will improve the quality and equality of care for patients and substantially benefit research, education and society through a consolidated interdisciplinary collaboration focussing on Individual Risk Assessment, SC prevention, Precision Diagnostics and Individualised Treatments.

Collaborating on this interdisciplinary effort, SCIN CAG will unite all dermatology departments across the Capital Region of Denmark and Region Zealand and, furthermore, consolidate the multidisciplinary collaboration with transplantation units, plastic surgery and oncology to secure equal care for SC patients.

The collaboration also includes the Technical University of Denmark (DTU), focusing several CAG activities on artificial intelligence (AI).

Skin cancer is the most common cancer globally, with an increasing incidence that is currently higher than for all other cancers combined. Daily, approximately 100 Danes receive a SC diagnosis, and 40 per cent of these will eventually develop additional tumours. Representing approximately 3 per cent of the Danish population, about 150,000 persons are currently affected by the disease nationally, classifying SC as an endemic disease. The costs of SC are consequently substantial, reflected by notable patient morbidity, heavy socioeconomic burdens and significant mortality in immunosuppressed populations.

CAG chairman Merete Haedersdal

CAG vice chairman Lars Kai Hansen

## **CAG Prognostication of Acute Recovery Capacity – in an Aging Population (ACUTE-CAG)**

The ACUTE-CAG vision is to improve acute healthcare for older and frail multimorbid patients with chronic diseases and polypharmacy.

Approximately 50 per cent of elders above the age of 65 suffer from health conditions that limit their ability to function and work full-time.

More than 1 million in 1.3 million hospital admissions per year in Denmark are acute, and 70 per cent concern elders, making emergency departments (EDs) a hub for opportunistic risk screening and interventions.

The onset of acute illness in the multimorbid elderly population is often complicated by competing acute and chronic conditions and polypharmacy, resulting in an increased risk of adverse reactions to pharmaceuticals and other therapeutic choices.

Only a few mechanistic or interventional studies are initiated from the onset of acute illness due to logistical difficulties at busy EDs with 24-hour patient flow. Consequently, despite recommendations and political ambitions, acute multimorbid elders are rarely treated and investigated as a group.

ACUTE CAG aims to solve this societal and healthcare challenge to benefit education and the development of viable solutions.

ACUTE CAG investigates non-disease-specific measures and the implementation of multimorbid treatment strategies from a translational approach. This includes multiple clinical disciplines and collaboration with e.g. social-political-economics researchers.

CAG chairman Ove Andersen

CAG vice chairman Lene Juel Rasmussen

## **CAG Center for Endotheliomics**

The CAG Center for Endotheliomics seeks to improve survival rates of critically ill patients via precision diagnostics and treatment by uncovering how the individual patient's endothelium contributes to multi-organ failure or, at worst, death.

In Europe, more than one million critically ill patients die of multi-organ failure each year, and in Denmark alone more than 7,500 intensive-care patients die from multi-organ failure each year. Multi-organ failure develops secondary to shock caused by trauma, sepsis or after resuscitated cardiac arrest. This process critically involves the type and severity of endothelial damage developed by the individual patient which, at worst, leads to reduced oxygen in the vital organs and death. The core function of the CAG is therefore to decipher the processes related to the endothelial cell which contributes to multi-organ failure.

The CAG brings clinical experts in trauma, sepsis and cardiac arrest treatment together with experts in systems biology, bioengineering and bioinformatics. Together they will – using omics technologies and mathematical modelling of the metabolism of the endothelial cell – provide new knowledge of its role in critical illness and multi-organ failure, identify diagnostic markers of the individual patient's endothelial phenotype and thus open up new possibilities for targeted precision treatment.

The CAG introduces genome-scale metabolic models as the scaffold for multi-omics data integration and computational modelling as tools to decipher the pathophysiology of the endothelial cell responsible for multi-organ failure and progression clinically. Additionally, supervised machine learning algorithms will be applied to data from electronic patient records, Danish registries and clinical databases in order to characterise the clinical disease trajectories resulting from the individual patient's endothelial cell response.

CAG Chairman Pär Ingemar Johansson

CAG Vice Chairman Bernard O. Palsson

## **CAG The Zealand Inflammation Research Initiative (ZIRI)**

CAG ZIRI strives to increase the quality of life and survival rates of patients with chronic MPN blood cancers through early-stage diagnostics and improved treatment for MPNs and comorbidities.

MPNs (Philadelphia-negative myeloproliferative neoplasms) are a group of chronic blood cancers – essential thrombocytosis, polycythemia vera and primary myelofibrosis. MPNs are often preceded by a long pre-diagnostic phase of up to 5-10 (or even 20) years of repeated disabling or life-threatening blood clots in e.g. the brain, heart or lungs.

MPNs are typically grouped among the rare diseases. However, a Danish study that screened 20,000 citizens for MPN gene mutations has shown that 3.2 per cent have a mutation that is either a precursor to an MPN blood cancer or an undiagnosed blood cancer. In Denmark, approx. 10,000 citizens live with an undiagnosed MPN blood cancer and constantly increased risk of blood clots in e.g. the brain, heart or lungs. Patients with MPN blood cancer also have an increased risk of getting other types of cancer. Therefore, MPN blood cancers should be diagnosed at a much earlier stage than is the case today.

Many MPN patients also suffer from comorbidities, including brain disease (dementia), drusen, age-related macular degeneration (AMD), cardiovascular disease, lung disease, osteoporosis with increased risk of bone fractures, chronic kidney disease and increased risk of other types of cancer. The MPNs and associated comorbidities contribute to a significantly reduced quality of life and ability to work.

CAG chairman Hans Carl Hasselbalch  
CAG vice chairman Lars Rønn Olsen

## **CAG Novel Strategies to Diagnose and Treat Bacterial Infections (BACINFECT)**

CAG BACINFECT will improve the treatment outcome for patients with infectious diseases through better diagnostics and development of new therapeutic strategies.

Bacterial infections become more and more difficult to treat with antibiotics, and according to the WHO, infectious diseases will constitute a greater health risk than cancer in a few decades. This is the result, among other things, of effective spread of pathogenic bacteria due to extensive use of antibiotics leading to the emergence of antibiotic-resistant bacteria. On the host site we see increasing numbers of senior citizens and patients with weak immune systems as well as increasing numbers of persons worldwide suffering from lifestyle diseases such as diabetes, obesity and smoking.

Vital to successful suppression of many infections is detection at an early stage, fast diagnostics and optimised treatment. This CAG collaboration will shed light on the underlying causes of unsuccessful diagnostics and therapy leading to continued infection, and it will identify infection markers capable of predicting outcomes of various types of bacterial infections. For these purposes, the CAG will develop improved infection models, imitating the organs and tissues which frequently harbour infections.

CAG BACINFECT research is conducted by clinicians and researchers together across universities and hospitals. Clinical problems are converted into biological questions, which are addressed and answered and finally translated into clinical solutions, improving both diagnostics and therapy. The members of this strong interdisciplinary consortium have expertise within clinical and molecular microbiology, cell biology, bioinformatics and, in particular, relevant types of bacterial infections.

The research is supported by newly established biobanks comprising clinical isolates from infected patients and affiliated databases containing genomic, phenotypical and clinical data.

CAG Chairman Helle Krogh Johansen  
CAG Vice Chairman Søren Molin



## **CAG Imaging-Guided Cancer Surgery (IGCS)**

CAG IGCS strives to increase the life expectancy and quality of life of cancer patients undergoing surgical treatment by improving the methods for complete removal of cancer tissue.

Each year, more than 1,700 patients are diagnosed with head and neck cancer in Denmark. When suitable, surgery is the first priority for treatment.

The fundamental challenge in cancer surgery is distinguishing between cancer tissue and normal tissue, and small microscopic pieces of the tumour are often overlooked and left in the area to cause recurrences of the illness. If the surgeon fails to remove the entire tumour, the patient is subjected to chemotherapy or radiation, but such supplementary treatment is a significant burden to the patient, which may subsequently affect their quality of life and functional capacity.

Focussing on the main challenge in cancer surgery, improved methods for complete removal of cancer tissue may lower the postoperative and financial consequences significantly, benefitting both the patients and society.

There is a great need for new technology allowing for precise intraoperative visualisation of cancer to guide resections with tumour-free margins. Optical imaging represents a promising development within the area, where fluorescent molecules are attached to the molecules that attach to cancer tissue. Using unique camera systems, optic imaging can potentially enable intraoperative visualisation of tumours and metastases and thus help the surgeon remove all cancer in the patient.

Successful translation and implementation of optical imaging and 3D navigation may revolutionise surgical cancer treatment and have a significant positive effect on the life expectancy and quality of life of cancer patients.

CAG chairman Christian Buchwald

CAG vice chairman Andreas Kjær