

FACULTY OF HEALTH AND MEDICAL SCIENCES
UNIVERSITY OF COPENHAGEN



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Center for Healthy Aging

Key persons in CEHA



Professor
Lene Juel Rasmussen
Managing Director,
Molecular Aging



Assoc. Professor
Lene Otto
Health in
Everyday Life



Assoc. Professor
Astrid Jespersen
Health in
Everyday Life



Professor
Thomas Söderqvist
Health in
Everyday Life



Professor
Allan Krasnik
Society, Culture and
Health Care Policy



Professor
Kirsten Avlund
Body and Life



Professor
Erik Lykke Mortensen
Body and Life



Professor
Flemming Dela
Muscle and Matrix



Professor
Michael Kjær
Muscle and Matrix



Professor
Martin Lauritzen
Neuroscience



Professor
Ian D. Hickson
Molecular Aging



Professor
Vilhelm Bohr
Molecular Aging



Head of
Administration
Tina Gottlieb

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Life research

What is age – but a number? This saying says much about age being what we make of it: age is not only a matter of the body but very much of the mind because we do not all age equally. In other words, aging is something that is highly individual. This approach to aging is more than just a manner of speaking but also a driver for the research being done at the Center for Healthy Aging (CEHA). Individual aging means that in order to be able to give any answers as to how we can achieve healthy aging, we researchers need to look at a whole range of factors and mechanisms in human lives: From DNA, molecules and cells, via body and brain, to the lives we live with our social relations and physical activities. From electron microscope to cultural history helicopter, these days aging research is broader and much more multifaceted than it used to be when it mainly consisted of research into disease in the narrow sense. Nowadays, we understand that we have to look at all aspects of life to be able to understand aging processes. Current aging research could actually be called life research.

At CEHA, our overall framework embraces all areas of research and we call it – “Energy for life”. Irrespective

of whether we are investigating the significance of molecular energy centres in the aging process or researching into the level of activity of the elderly or social relations, some of the issues we are investigating are centred on energy levels. At many levels and in many situations, energy is one of the keys to the many mysteries in aging research.

Successful interdisciplinary research

In the first five years of research at CEHA, we worked on the basis of our wish to understand the biological mechanisms in aging and their role in the lives of individuals and society. Our ambition was, and still is, for scientific insights to be translated into new, better types of prevention. This we have done and will continue to do by way of the interdisciplinary research being pursued at CEHA over the past five years. The interdisciplinary approach has provided gains but also challenges because it is very demanding. The Center’s highly qualified specialists have been highly successful in taking a holistic approach to research without at any time losing focus on their own special fields of research. This has meant that the Center has been able



Professor Lene Juel Rasmussen, Managing Director

to produce breakthrough results in its research. At the same time, this interdisciplinary way of working has in itself raised the profile of CEHA among the general public and in the international and national world of research.

Valuable involvement

CEHA is involved in several intervention projects that establish direct dialogue between Danish citizens, government representatives and medical/scientific professionals interested in healthy aging. There is tremendous demand for research in this field, suggesting that aging research is valued by the elderly and Danish politicians alike, addressing major societal issues and concerns. Knowledge about how to maintain activity into old age will help improve quality of life for the elderly and the entire human population, in Denmark and beyond.

New knowledge of social activity

Quality of life may have a different meaning, or be achieved in a different manner, for different individuals. CEHA researchers believe that social activities are important for healthy aging. Several CEHA projects recognize

the importance of the fundamental human need for supportive, healthy social networks.

New targets in aging research

CEHA's initial 5-year funding allocation from Nordea-fonden, which generously supported a critical phase in our growth, ended in 2013; however, Nordea-fonden has granted to CEHA II, our second phase, an award of DKK 150 million, which we hope will allow CEHA to meet our research goals through 2018. Thus, the Center will remain an active player in the field of aging research. Demographic forecasts project that the elderly population will continue to grow disproportionately throughout the world, which will only increase demand for improved quality and quantity of health services. CEHA hopes to be at the forefront of the effort to meet this need at home and elsewhere. In aging research, new questions are constantly arising and CEHA is looking forward to being part of the answer.

A handwritten signature in blue ink that reads "Lene Juel Rasmussen".

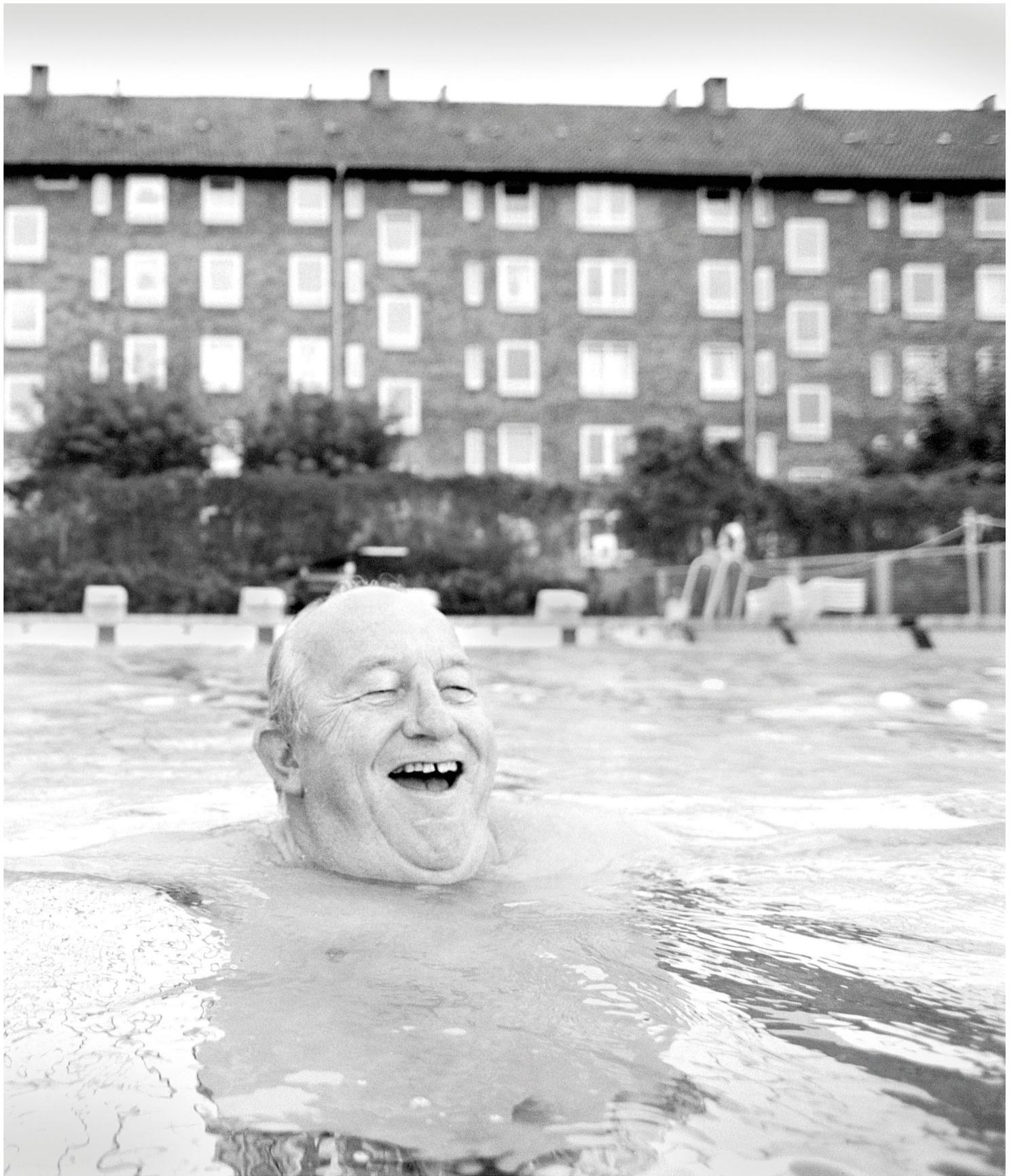
Professor Lene Juel Rasmussen, Managing Director

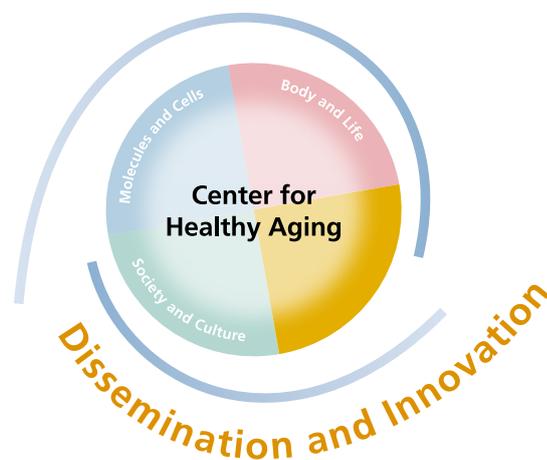


Eliora Z. Ron, PhD
Chair of BAM (Bacteriology & Applied Microbiology) of
IUMS (International Union of Microbiological Societies)
Scientific Director of MIGAL
Professor of Microbiology
Tel Aviv University
Tel Aviv, Israel

I would like to express my gratitude to the Center for Healthy Aging and to its Managing Director Professor Lene Juel Rasmussen for providing an excellent example for us in the Galilee, Israel. I am the scientific director of a small research institute – MIGAL – situated in the most northern part of Israel. MIGAL was awarded an EC grant under the FP7 REGPOT program, aimed at developing existing or emerging excellence in the EU's convergence and outermost regions. The grant was given for the development of CEREHA – Center of Excellence in Research on Environment, Health and Aging. To develop such a center in a region that is far from the European core of research and industrial development is both a challenge and opportunity. Having been impressed with the scientific structure and academic achievements of CEHA we requested CEHA to join us as partners in the project and also invited Prof. Rasmussen to join our Scientific Advisory Committee. We consider ourselves lucky to be guided by the expertise of CEHA and are pleased to watch the building of nice collaborative research projects. We are even more pleased to see that the contacts between our two institutes were broadened and also include our younger scientists.

I wish to congratulate CEHA for their excellence and thank them for helping younger institutes developing research in this highly important and often neglected area of our life – aging.





Program 5

Health in everyday life

Group leaders

Astrid Jespersen, Associate Professor

Lene Otto, Associate Professor

Thomas Söderqvist, Professor

Late life is often thought of as a life phase characterized by deterioration, frailty, disease and increased dependence. This way of describing and thinking of late life is undoubtedly true to some extent, but it gives a negative view on what it means to age and of late life. Aging is also life experience and it involves a range of stimulating social and cultural changes. In Program 5, aging is investigated as more than biological and functional decline. The main focus of the research in Program 5 (Health in everyday life) is therefore on how people deal with aging in their everyday lives to maintain or increase their quality of life. Program 5 research can be grouped under two interrelated themes: 1. Aging and Health in Everyday Life at the Department of Ethnology, SAXO-Institute and 2. Aging Science Communication Studies at Medicinsk Museion. A unifying concept in Program 5 is health promotion, and Program 5 researchers study health promotion theoretically and engage in health promotion in a practical manner. In Aging and Health in Everyday Life, the research projects seek to understand how health-promoting knowledge, health practices and products are implemented and integrated in everyday life during the life course. Hence, one guiding premise in this theme is that in order

to understand and improve the effect of health promotion, it is crucial to acquire knowledge of the processes and rationales of people's everyday life, and how a specific perception of "the good life" shape very different health practices. Research projects under this theme study the use of health technology in everyday practice, how older adults use and appreciate health promotion initiatives, as well as the role of physical activity in health practice and lifestyle change. The second theme, Aging Science Communication Studies, takes its point of departure in the fact that health promotion activities and health practices requires active participation as well as the development of new platforms for communication. Medicinsk Museion hosts the Aging Science Communication Studies research group. The long-term goal of the group is to develop new methodologies for communicating aging research to the general public, focusing on museum exhibitions/events and new media. The group is engaged in three research projects: 1) using art to communicate the experience of aging and health practices; 2) understanding recent central theoretical concepts in ageing; and 3) analyzing patterns of social media communication among individuals or families affected by type 2-diabetes.

Researchers in Program 5 perform extensive ethnographic fieldwork, such as observations, interviews, visual ethnography, archive studies and auto-ethnography. The focus has been on different aspects and different understand-

ings of aging and processes of aging in everyday life. Fieldwork is conducted in activity centers, out-patient clinics, lifestyle and fitness centers, and in the home environment. Although fieldwork is time-consuming, it produces a unique collection of qualitative data that are being analyzed. The results of these studies will be published in dissertations and scientific papers, as appropriate.

Program 5 is addressing the following questions:

- How is the concept of active aging used in health practice and what are the consequences? How could we reframe the concept in order to produce better active aging policy and practice?
- How is fatigue understood and experienced as a symptom and a problematic side-effect of stroke?
- How is the aging body used and experienced? (i.e., what is meant by the embodiment of aging?)
- What typifies aging among immigrants in Denmark and how does their use of healthcare services differ in Denmark and in their home countries?
- What is the relationship between local health promotion activities and everyday health practice? What will promote healthier lifestyles in everyday life?
- Can we develop and use welfare technologies and new communication platforms?
- What is the history of the concept of successful aging?
- Can we document experiences with qualitative community-based interventions?

Program 5 will contribute to an understanding of:

- Transformation in our cultural understanding of aging; for example, how aging is less associated with dependency, and more associated with activity, independence and healthy life.
- Changing collective and individual experiences in an aging society, leading to new roles and identities.
- How health knowledge, technologies and practice are part of everyday life, and how knowledge shapes roles and identities as well as the perception of body, health and self.
- How our concept of old age is constructed, and how age, as a primary element of identity, can lead to social inequality.

Program performance

In 2013, two Ph.D. dissertation projects were completed, to be defended in spring 2014. Five dissertations by Ph.D. students in Program 5 are scheduled for completion in 2014.

Researchers held a seminar to discuss the results of a review of community-based health interventions worldwide. The project found that many health-promotion initiatives do not yield insight into everyday life among the elderly, and do not appreciate how different communities form and function. We suggest that successful community-based initiatives for the elderly should adopt a multi-faceted, qualitative approach, and should be customized to account for local conditions in a specific community. This information will be incorporated into future studies by Program 5.

Program 5 has given priority to outreach activities, including presentations, seminars, research applications, networking (nationally and internationally), educational activities in different contexts, publication and media activities. Program 5 is involved in a range of promising network and stakeholder activities and has succeeded in attracting additional funding in 2013. Astrid Jespersen is PI in two large research projects funded by the UCPH excellence program: 1. Governing Obesity will provide novel means for managing obesity and its consequences at early and late stages of the disease, via effective interventions at the societal and individual level, while avoiding unintended negative effects. The initiative was granted a total of 31.7 million DKK (4.2 million Euros). 2. Counteracting Age-Related Loss of Skeletal Muscle Mass: an Interdisciplinary Innovation Project on Making Lifestyle Changes through Exercise and Diet aims to prevent loss of skeletal muscle mass in the elderly. The project will examine the effects of exercise and protein intake, and identify the individual and social barriers that prevent the elderly from making lifestyle changes. The project is a collaboration between researchers from Programs 5 and 2 and was granted a total of 19.6 million DKK (2.6 million Euros).

A major objective of Program 5 is to (re)establish humanistic aging research and to pursue promising interdisciplinary and international research collaborations to support this objective. A highlight of this effort was the successful organization of a Symposium on the Biopolitics of Aging, hosted by Program 5 researchers in 2013.

Results

- Significant progress was made towards establishing humanistic aging research as an important and central field of study.
- We collected a large amount of qualitative data on aging, health-promotion initiatives and practices in everyday life.
- We established empirical and theoretical humanistic aging research as a significant field and agenda item within a number of influential and interdisciplinary humanistic research networks.
- We produced a museum exhibition on aging.
- We submitted the concept of “successful aging” to a critical historical and philosophical analysis.
- We developed a queer-theoretical approach to understanding vulnerability and frailty.
- We developed digital methods for analyzing online communities for individuals affected by type 2 diabetes.
- The international network and collaborations among Danish humanistic aging researchers were strengthened via the visiting professor program, the PhD exchange program, conference participation and research proposals.
- We hosted Dr. Alex Faulkner, University of Sussex (UK), Professor Sarah Nettleton, University of York (UK), Dr. Tiago Moreira, Durham University (UK), and Dr. Suzan Yazici, Akdeniz University (Turkey) for short term interactions with Program 5.
- We organized and hosted the international symposium, The Biopolitics of Aging.
- We obtained additional funding for Program 5.
- We contributed to public awareness and debate about aging and health issues through dissemination and outreach.
- We contributed to the National and EU research-policy debate on interdisciplinary research.
- Elderly were encouraged to practice and analyze

drawing, as a new and unconventional method for engaging elderly in reflection on the experience of aging.

The concept of active aging is a tool often used to set the agenda for policies that target the elderly in Europe. In a Danish context, “active aging” is primarily promoted as physical activity, an approach that risks overlooking other activities, such as participating in social networks.

Many research-based health-promotion initiatives fail to include insights about elderly people’s everyday lives, and often do not reflect an understanding of how different communities may form and then function in practice. Thus, implementing “successful” community-based initiatives for the elderly will require a multi-faceted, qualitative approach that is adaptable to local conditions.

The widespread use of small, easily accessible health technologies in relation to exercise practices in people’s everyday lives is likely to motivate and enable them to change their lifestyle habits.

Initiatives that promote lifestyle changes among moderately overweight but otherwise healthy men often help them succeed in making temporary lifestyle changes, but tend to be inadequate in encouraging them to maintain a healthier lifestyle.

Elderly Turkish immigrants tend to engage in highly complex cross-border health practices, which are often unrecognized by Danish health authorities.

Current rehabilitation practices are based on the idea of “a return to everyday life one had before the incident”. But this approach fails to recognize the possibility that incidents in late life may mark the threshold of a new life phase, possibly characterized by increased frailty.

Conclusions

Program 5 has been working for the past five years to (re)establish humanistic aging research in Denmark. This has involved recruiting young talented researchers trained in ethnological, philosophical, anthropological and folkloristic studies to work together in Program 5

and in CEHA. The program has made significant progress towards establishing humanistic aging research and cultural gerontology as an important and central field of study in Denmark. Through extensive ethnographic fieldwork, a large body of qualitative data on aging, health-promotion initiatives and practices of everyday life has been gathered and analyzed. Program 5 is studying the transformation in our cultural understanding of aging, as a result of which aging is less associated with dependency and more associated with activity, independence and a healthy life. Program 5 also studies the impact of an aging society changes on cultural forms, and how the collective and individual experience of aging shapes new roles and identities.



Photo: Liv Carlé Mortensen, Property of Medical Museion, University of Copenhagen.

Program 4

Society, Culture and Healthcare Policy

Group leaders

Allan Krasnik, Professor

Carsten Hendriksen, Associate Professor

Susan Whyte, Professor

Introduction

Drugs constitute a major intervention technology for preventing, postponing and curing frailty and chronic diseases in the elderly. In Denmark, approximately 85% of the population aged 75 years or older consumes at least one prescription drug daily, and 60% consume more than three prescription drugs daily. As longevity and its concomitant frailties and chronic conditions increase, long-term use of prescription medication for prevention and health promotion becomes an ever more urgent problem for policy makers, health care providers, caretakers, and the elderly themselves. The current level of prescription drug use is associated with huge costs, ethical dilemmas, as well as risk of serious adverse drug reactions and/or interactions. The benefits of preventive treatment are often not clear, should be balanced against potential complications, and considered in the context of sustainability, timeframe of effects, possible alternative approaches such as increased physical activity and dietary changes, and people's own understanding and care of their health.

Background and hypotheses

The research is based on a cross-disciplinary approach to the role of preventive medication as a major intervention

with strong implications for society, health services and the health of an aging population. The studies combine public health and social sciences taking advantage of the unique opportunities in Denmark for research on issues of healthy aging related to society, policy and health services. These include the vast amount of Danish registry data on health and social determinants of healthy aging, as well as the easy access to informants from different social and ethnic population groups, community organisations, and from the national health care system. A series of qualitative and quantitative studies are in progress, which are grouped by three sub-themes. The three sub-themes represent key issues related to actors, processes and effects of policies and health services relevant to preventive medication, as follows: a) decision-making by diverse health professionals and consumers regarding use of preventive medication; b) social and ethnic inequalities in prescription and use of preventive medication; and c) development, use and effects of coordinating tools relevant to preventive medication. Thereby, the program aims to improve healthy aging by contributing to better understanding of the role of long-term preventive medication in healthy aging; better decision-making and coordination regarding choice of preventive interventions by health care providers and consumers; and more equitable and fair policy and practice related to preventive drug interventions with an impact on healthy aging.





Example of assistive technology; scene from the CEHA television series “Fauli, fat and finised?”, DR2.

Program performance

The community study focusing on the young old (50-75 years) living in Vordingborg documented how bodily perceptions are changing through a public emphasis on active aging and the urge to take up new fitness and exercise practices, focus on healthy diets, use of measuring devices, and emergent large-scale use of prescription drugs to lower blood pressure or blood cholesterol. The data collection included ethnographic interviews, participant observation, and analysis of policy documents, drug sales statistics and media coverage relevant to aging and longevity.

A healthy adherer effect has been documented among individuals with high blood pressure and high total cholesterol. The study examined whether long-term changes in dietary habits and physical activity are associated with primary intervention using lipid-lowering and antihypertensive medications. The results indicate that preventive drugs and behavioral changes are not substitutes for one another, but are useful as a combined intervention.

Special attention is needed to support those who are not adhering to any components of the intervention.

A study on elderly receiving home nursing care has identified perspectives on social relations, prevention and medicine through participant observations and interviews. The recipients of home nursing were fully compliant during administration of medication, but they did not always agree (i.e., were not compliant) with diagnostic tests for disease. Still most of the care recipients in this study worked on healthy habits in relation to food and exercise, and wanted to participate in physical rehabilitation, if on their own terms.

Sub-studies have been finalized on decision-making processes in Danish general practice in regards to prescription of blood pressure medications and dilemmas in and conditions of possibility for testing blood pressure lowering drugs in Danish private and public hospitals. The studies are based on interviews and participant observations, and they focus on the role of general practition-

ers and patients in the development of new drugs, and attempts to regulate prescriptions through the promotion of rational drugs. The study examines how general practitioners make decisions regarding discontinuing use of cholesterol-lowering drugs. A qualitative methodology was used that draws on participant observations, focus group discussions and interviews. The analysis has been developed into a process and structure story. The process is divided into three sections: cues, considerations and actions. The structural aspects are identified by analyzing the role of clinical guidelines and by focusing on traits in general practitioners that are most relevant to their discontinuing medication.

Studies of social and ethnic inequalities in prescription and use of preventive medication utilized a database established through linkage to several national registries. Utilization of cholesterol-lowering drugs was analyzed according to age, indication, gender, migration history and socio-economic gradient. Drug utilization in multi-ethnic societies is the theme of several sub-studies. For example, use of preventive statin therapy was compared in non-Western immigrants and Danish-born residents with diabetes. Use of healthcare services in Turkey by Turkish immigrants in Denmark is also being studied, using quantitative data from a nationwide survey, interview data, and registry data on health and health behavior among ethnic Danes and Turkish immigrant families and their descendents.

The key elements of a tool for improved prescription by general practitioners were developed based on the frailty concept and focusing on mobility and cognitive measures. Studies on care-coordination interventions have been carried out in the context of care-coordination, policy implementation and governance. The focus has been on three cases involving care-coordination interventions, which represent different strategies to improve coordination: Information technology involving a shared medication record; financial incentives involving a fee improved quality and coordination of care for patients with diabetes; and regulation at the administrative level involving healthcare agreements. These studies suggest that better care coordination is possible, even though significant challenges remain in designing and implementing effective policies.

A study carried out jointly by the Veterans Health Administration (VA) and the Danish healthcare system (DHS) is examining organizational frames for improving care paths and coordination of preventive drug medication. Despite VAs substantial number of vulnerable patients with multiple chronic illnesses, the large public healthcare system has succeeded in implementing initiatives that support coordinated care and have a positive impact on chronic patient care, use of medication and early interventions. Qualitative interviews have been conducted with key individuals at the VA, with additional interviews planned at DHS, as well as surveys at the VA and at DHA.

Results

- Community studies have provided new understanding of differences in perceptions and experiences of aging related to gender and to having children or not. More attention should be given to identifying individuals and groups, who are less health conscious and thereby less likely to use preventive medication or change health behavior.
- Some patients who participate in the testing of new medications report only symptoms they believe are of “relevance” to the trial potentially leading to an underreporting of adverse events.
- Attempts to regulate general practitioners prescriptions via the promotion of “rational” drug use can have unanticipated consequences. Because regulation builds on knowledge that can be in discord with practical realities, general practitioners sometimes turn to industry sales representatives for pharmaceutical information despite endorsing the regulatory ideal.
- Research-active physicians feel they need to collaborate with pharmaceutical companies to maintain research productivity in public hospitals. As a consequence, physicians sometimes accept participation in and spend research resources on drug trials that may not generate clinical or scientific value.
- The increasing use of statins during 1996-2009 represents a gradual shift towards preventive statin therapy in individuals aged 75+ without cardiovascular disease (CVD) or diabetes. Our study has revealed marked gender differences in statin therapy with lower incidence in younger women with MI and

higher incidence in women without CVD, diabetes or primary hypertension, which may be a consequence of focusing on cholesterol as a risk factor independent of gender.

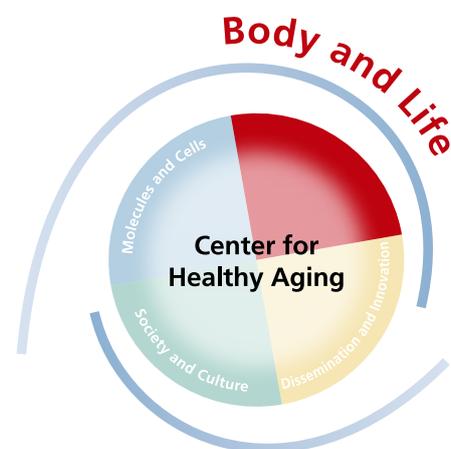
- The high-risk strategy to prevent CVD by initiating statin therapy seems to be inequitable, reaching primarily high-risk subjects in lower risk SEP-groups. Lower income groups (especially men aged 40-64) are more likely than higher income groups to discontinue lifelong preventive statin therapy.
- Immigrants are less likely to be treated with recommended drug therapy than native Danes. This holds for both statin therapy in subjects with diabetes and antidepressant therapy after hospitalization with depression. Immigrants from Turkey more often use health care and drugs from foreign sources than Danish-born. The differences are especially dramatic among migrant women and the elderly.
- Discontinuation of statins is not routinely considered by GPs to the same extent as diagnosis and treatment. A consultation to question current medical treatment can be routine, rather than in response to a patient decision. The professional culture can act as a barrier; for example, many GPs were reluctant to discontinue a hospital physician's prescription because of their "expertise".
- Health care agreements are considered a useful tool for strengthening coordination between the regions and municipalities and are more positively assessed as a tool for service coordination than the previous health plans. The adoption of a fee for better quality and coordination of care for patients with diabetes has been very slow; implementation of a shared medication record has been difficult, due to technical issues.
- The organizational frames at the Veterans Health Administration (VA) support the coordination of care to a high extent. In particular, VA implemented an IT-system that includes clinical reminders, overview of outliers, accessibility of providers, patient outreach, agreement of responsibility, quality assurance measures, checking for drug interactions, and close linkage between clinical information and practice and health services research.

Conclusions

Preventive medication is a powerful and widely-used intervention with strong potential impact on healthy aging. There are excellent research opportunities in Denmark for studies on health care decision-making, social and ethnic inequalities and care coordination within the universal, but fragmented health system, and additional documentation and data are available through well developed health-related registries. CEHAs Program 4 is carried out by a strong team of researchers, with competencies and expertise in qualitative as well as quantitative methodologies in several complementary disciplines. The skills and knowledge of these researchers equip them well for research on healthy aging, from a community and population-based perspective. The research team is addressing complex issues related to the development and use of preventive medication as well as other preventive strategies, the moral imperatives related to compliance with or discontinuation of prescribed preventive drugs, and social inequalities in the availability of or access to prescription drugs, which does not reflect patterns of need. Tools have been developed for functional monitoring to support decision-making in general health care practice, and study results identified and analyzed successes and failures of different initiatives for better coordination of care. International comparative studies have been initiated to study health organizations using integrated and comprehensive mechanisms for achieving better continuity and quality in preventive care for aging populations. Such populations are at risk for multiple chronic diseases, for which new therapeutic and/or preventive care options may be available. If they receive well coordinated high quality care, the aging population could experience both a better quality of health along with increased life span.



Photo: Liv Carlé Mortensen, Property of Medical Museion, University of Copenhagen.



Program 3

Body and life

Group leaders

Erik Lykke Mortensen, Professor
Kirsten Avlund, Professor
Rikke Lund, Associate Professor

Introduction

The focus of CEHA Program 3 is to identify biomarkers of early aging and life course influences on aging. Program 3 scientists are using epidemiologic methods to analyze large data sets on midlife- and old age cohorts as well as data from national registries. Findings from these studies may contribute to developing and refining interventions which can delay aging-related disability and loss of independence.

A crucial research aim in relation to healthy aging is to identify markers which may indicate accelerated aging processes. Such markers may be biological and physiological indicators of decline in cognitive and physical functioning which could be early indicators of frailty and disability. We are focusing on several biological markers (e.g. low-grade inflammation, telomere length, mitochondrial function), physiological indicators (e.g. muscle strength, balance), cognitive decline and self-reported indicators of aging (e.g. disability, fatigue). We analyze associations between different aging markers and examine whether they follow the same patterns or act independently of each other.

Program 3 addresses the influence of life course processes on frailty and specific signs of early aging. Our focus is on the biological, psychological and social factors that influence aging processes over the entire life course, and we analyze 1) whether it is possible to explore strain factors over the life span, i.e., when and how long they typically influence the individual; 2) whether there are certain vulnerable periods in life, and 3) if the duration of strain is of special importance. We also aim to understand the variety of health outcomes that are potentially influenced by negative aspects of social relations, low socioeconomic position and stress. This has not previously been investigated in detail in longitudinal designs.

Background and hypothesis

An important aim of Program 3 is to identify early signs of aging which may reflect aging processes that have not yet become manifest as pathological conditions, but appear as biological, psychological or social dysfunction. We hypothesized that knowledge about such early signs of aging in midlife is important to identify vulnerable individuals and prevent that frailty, disability and comorbidity become manifest. Signs of early aging may include molecular markers (e.g. inflammation and DNA-damage) and markers at the individual level (e.g. cognitive decline, sarcopenia, impaired oral health, unexplained fatigue), which have been associated with later chronic disease, frailty and mortality in old age. Consequently, the following hypotheses are explored:

- Cognitive decline, sarcopenia, chronic inflammation, oral health, unexplained fatigue, oxidative DNA damage and mitochondrial dysfunction may be biomarkers of early aging and can be used to identify at risk individuals.
- Functional and biological markers, such as IL-6, IL-15, hsCRP, TNF-alpha, oxidative DNA, RNA and protein modifications, mitochondrial functions, sarcopenia, oral health, cognitive decline, and unexplained fatigue may be associated with frailty, disability, and comorbidity in midlife.
- Some of these biomarkers may reflect one common underlying biological aging process, while others may be independent markers of different pathways.
- Functional decline and disease risk in late life may be predicted, based on functional biomarkers as well as biological and behavioural risk factors in midlife.

The life course approach assumes that various biological, social and psychological factors over the life course independently or interactively influence health and disease from early life and into old age. There is some evidence that early biological, social and psychological factors influence the incidence of chronic disease in adulthood and that such early factors (e.g. growth, early cognitive ability, social environment) may influence the aging process decades later. To further investigate the life course approach we explore the following hypotheses:

- Biological, psychological and social factors in childhood and adolescence influence early aging in midlife and functional decline and development of neurodegenerative and cardiovascular disorders in late life.
- Some specific biological, psychological and social factors in childhood/young adulthood and midlife physical and psychosocial exposures influence early aging processes independently, and other factors interact during the life course.
- It is possible to identify “windows of susceptibility” over the life course where the effects of some exposures act more strongly.
- Early life intelligence and health contribute to social mobility and social differences in early aging when genetic and family environmental factors are taken into account.

- Medical registers on hospital care and prescriptions can be used as outcome measures for different neurodegenerative and cardiovascular disorders.

Program performance

The largest project and the most significant accomplishment of Program 3 in the area of life course research has been the Copenhagen Aging and Midlife Biobank (CAMB). CAMB currently includes data collected during 2009-2011 on participants from the Metropolit Study, the Copenhagen Perinatal Cohort and The Danish Longitudinal Study on Work, Unemployment and Health. With a participation rate of 40%, 7,241 of the invited persons answered a questionnaire on health, use of medicine, early signs of disability, fatigue, socioeconomic status, work-ability, work life history, social relations, social capital, health behaviour, sleep, life events, indoor climate and mental health. In total, 5,578 (31%) of the invited participants answered the questionnaire and completed a series of exams and tests, yielding data on height, weight, waist measurement, body fat percentage, blood pressure, spirometry, muscle strength, maximal muscle force, flexibility in lower back, balance and chair rise speed. Periodontitis and aerobic capacity were also measured in two subpopulations of CAMB participants. Non-fasting blood samples were obtained and analyzed immediately for hemoglobin, blood sugar, HbA1c, total cholesterol, fractionated lipid profile, and hsCRP. Additional tests relevant to aging-associated conditions have been conducted on the complete set of samples: these include genetic tests for putative “biomarkers” of aging, blood cytokine levels, acute phase and other blood proteins, and genetic tests for polymorphisms in inflammatory genes. Markers for low-grade inflammation were also measured, including TNF-alpha, IL-1beta, IL-18, IL-6, IFN-gamma, IL-10, BDNF and IL-1 autoantibodies. Unused blood was stored in a research biobank for future studies. Questionnaire data were scored and verified twice and coded for social class. Derived variables were established, data “cleaned” and documented/annotated, and other quality control measures are being implemented on the entire database.

Planned future life course studies include analyses on 1) the influence of life course socioeconomic position on

low-grade inflammation in late midlife, 2) the effects of cognitive function and SES in childhood on physical performance in midlife, 3) the impact of work history on functional limitations in late midlife, 4) the relationship between changes in cohabitation status in early or midlife on low-grade inflammation in late midlife, 5) associations between cardiovascular risk factors throughout life and cognitive decline, and 6) the influence of occupational status and social relationships during the life course on cognitive decline in old age.

An important life course study explores the relationship between socioeconomic position (SEP) early in life and use of prescribed preventive medicine in middle-aged men as possible markers of early aging, and will examine whether any associations are mediated by cognitive function in young adulthood. This will be examined by analyzing whether father's social class at participants' birth is associated with use of prescribed preventive medications, and whether the association differs between the specific types of preventive medicine when cognitive function, educational status, BMI and comorbidity in early adulthood are taken into account. The analyses are based on data from the Metropolit birth cohort. A recent publication shows that low SEP in childhood predicts initiation of statin use, but also a higher probability of discontinuation of statin treatment. High IQ in young adulthood is associated with a lower probability of discontinuation of treatment with antihypertensives. Future analyses, awaiting further funding, will focus on the use of anxiolytics, hypnotics, sedatives, and antidepressants.

An important focus of Program 3 is the role of perceived fatigue in aging-related functional decline. Our research has shown that biological, physiological, and psychosocial factors, including depressive mood, are involved in fatigue. The evidence suggests that similar factors cause fatigue in late midlife, early old age and advanced old age, and that these factors are modifiable. Therefore, symptoms of fatigue should be considered when planning interventions to promote independent functioning and well-being. A separate series of analyses have been conducted to optimize the Avlund Mob-T Scale which is one of the most widely-used scales/instruments for quantifying fatigue. Program 3 researchers are optimiz-

ing, refining and revalidating this instrument by item response models to make it more sensitive to change, and thus more useful for detecting the quantitative change in response to an intervention. To improve our understanding of specific biological factors underlying fatigue, we plan to explore possible relationships between fatigue and mitochondrial function/dysfunction or increased expression of inflammatory markers. Preliminary analyses show that IL-6 expression changes in fatigued 85-year-old individuals, and that the ratio of mitochondrial ROS to dNTP in isolated peripheral blood mononuclear cells is associated with fatigue in middle-aged men. In the future, we will analyze the relationship between fatigue in healthy older adults and incipient functional decline and mortality at a more advanced age. We also plan to study the role of bioenergetics in the etiology or onset of fatigue and/or functional decline, to develop new tools for quantifying fatigue, and to develop interventions for treating unexplained fatigue in older individuals.

Another early marker of aging may be periodontal inflammation. Periodontal inflammation in early old age tends to be associated with cognitive decline and mortality. This suggests that periodontitis may be a marker of chronic inflammation or a weak host defence system. In future studies, we will analyze whether allostatic load, as a cumulative biological measure of lifetime chronic stress, is associated with higher susceptibility to periodontitis. These findings could contribute to our understanding of the impact of stress and inflammation on age-related decline and/or dysfunction and identify appropriate targets or methods for novel and more effective interventions.

Our studies on psychosocial factors have focused on the importance of socioeconomic position, social relations and perceived stress in relation to early signs of aging. Socioeconomic position and social relations are predictors of functional limitation, ischemic heart disease, metabolic syndrome and poor health behaviours. Thus, interventions to improve people's social network could potentially reduce and/or mitigate adverse health effects caused by or related to dysfunctional or inadequate social networks.

Individual differences in perceived stress may contribute to individual differences in aging trajectories. Preliminary results show that stress related to demands, worries and, to a lesser degree, conflicts with close social relations is associated with lower heart rate variability (i.e. lowers the parasympathetic response) to a greater extent in men than in women.

Results

- Establishment of the CAMB database and completion of several papers describing the database.
- Socioeconomic position in childhood and later in life is associated with cognitive function at ages 12, 18 and 57 years, as well as with changes in cognition between young adulthood and middle age. Birth characteristics seem to be of minor importance.
- Low level of education, few intellectual activities and many social leisure activities in childhood predict decline in cognitive function during adult life.
- Low socioeconomic position in childhood predicts initiation as well as discontinuation of statin use.
- High IQ in young adulthood is associated with a lower probability of discontinuation of treatment with anti-hypertensives.
- Higher intelligence in late adolescence is associated with less mortality in midlife (50-60 years old) both for internal (all diseases) and external causes (suicide, accident, homicide).
- Occupational social class shows a significant social gradient in physical performance, allostatic load, personality and cognitive ability in late midlife.
- Increased leisure activity from age 50 to 80 is consistently associated with the level of cognitive ability, but not with age-related cognitive decline.
- Increased physical activity at age 60 or 70 shows a weak association with less cognitive decline in old age.
- Personality traits related to higher stress levels are associated with the level of cognitive function, but do not predict cognitive decline from 50 to 70.
- In 75 to 80 year-old persons, perceived fatigue is associated with onset of walking limitation; muscle strength was one of the explanatory factors.
- In healthy middle-aged men, fatigue was significantly associated with onset of cardiovascular disease and mortality.
- The total number of leukocytes, lymphocytes and neutrophils is associated with fatigue in young and old individuals, and length of telomeres in leukocytes from fatigued older individuals appears to be shorter than telomeres from non-fatigued older individuals.
- Depressive symptoms are closely related to fatigue, even though a substantial number of older adults with fatigue do not report depressive symptoms.
- Strain and worry in social relationships are related to fatigue in men in aged 50-60.
- Socioeconomic position shows a strong social gradient in mobility limitations and poor dynamic balance in middle-aged and older individuals.
- Poor social relations (lack of support as well as stressful interactions with close social relations) and lack of access to a social network increase the risk of functional limitation, ischemic heart disease, metabolic syndrome and poor health behaviours.
- Strain and worry in social relationships are risk factors for fatigue, functional limitations, heart disease, metabolic syndrome, heart rate variability, poor health behaviours and mortality.
- Periodontitis in older adults is related to poor cognitive performance and higher mortality.
- Smoking and alcohol consumption are associated with missing teeth in late midlife.
- Low-grade inflammation is associated with disease and lifestyle factors (alcohol consumption, smoking, and sedentary activity) in late midlife.
- High allostatic load in old age is associated with low socioeconomic position and sedentary behaviour throughout life.

Conclusions

Program 3 researchers use other cohorts such as the Glostrup 1914 cohort and register data to identify important determinants of age-related changes across the lifespan. Nevertheless, the completion of the CAMB database must be considered a milestone not only for Program 3 researchers, but for CEHA and Danish aging research in general. The CAMB biobank and database have several strengths: 1) the use of several measures of

age-related changes: biological measures (e.g. markers of low-grade inflammation), results from a wide range of physical tests, cognitive tests, clinical data and self-reported data (e.g. on fatigue), 2) the large variety of social, mental and health variables at different points in life, which enable numerous analyses of the complex interactions between these factors and early aging indicators in midlife, 3) the possibility of analyzing the effects of different types of determinants on early aging indicators (biomedical variables, data on oral and physical health, psychosocial factors, data on health behavior and on living conditions), 4) the possibility of obtaining comparable information both for all CAMB participants and all non-participants from the Danish health and social registers from 1968 until now, and 5) the CAMB may provide unique possibilities for understanding “The Scandinavian Welfare Paradox of Health”, i. e. the substantial social inequalities in health in spite of redistribution of income and social benefits.

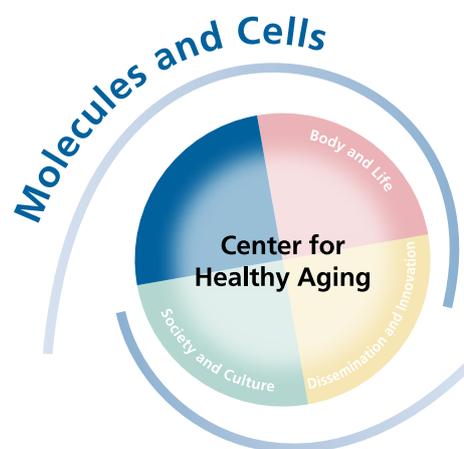
CAMB will also provide unique possibilities for the proposed CEHA analyses of how multiple exposures and adversities across the lifespan influence aging processes and age-related changes in health and in physical, social, and cognitive function across the lifespan. In the planning and design of these studies we will make optimal use of the important knowledge gained during the first five years and reflected in the main results listed above.



Scene from the CEHA television series, "Fauli, fat and finished?", DR2.



Foto: Scampix.



Program 2

Muscle and matrix

Group leaders

Flemming Dela, Professor

Michael Kjær, Professor

Introduction

Aging of the musculo-skeletal system is associated with gradual loss of muscle mass and function, impaired recovery of function after disease or inactivity, and degenerative changes in connective tissue. Aging is also associated with life-style related diseases, particularly due to decreased daily physical activity. Over the last 5 years (2009-13), Program 2 researchers have been studying the mechanisms that underlie these and other age-associated changes in metabolism and the musculo-skeletal system.

Background and hypothesis

Observational studies demonstrate that physical training and short-term immobilization alter function of muscle and the dynamic properties of human matrix and muscle in human subjects. This prompted us to explore directly the impact of long-term physical training on muscle mass and connective tissue elasticity in aging human subjects. One possible explanation for poor recovery from acute muscle loss in elderly is lost regenerative capacity of the muscle stem cells (satellite cells) and diminished activation of muscle anabolic pathways. There is overwhelming evidence that physical inactivity and low fitness levels are directly linked to increased morbidity and mortality.

Physical inactivity is directly linked to increased incidence of chronic diseases including cardiovascular disease and type 2 diabetes. Therefore, it is highly relevant to investigate the mechanisms underlying the effects of physical activity or inactivity on muscle metabolism. Such knowledge will allow medical professionals to customize training programs or other therapies for each individual, selecting a therapy that accounts for health status, gender, age and recent life style or training history.

Program performance

Adaptability and maintenance of skeletal muscle in elderly individuals – role of inflammation and hormones

Life-long physical activity limits the extent of low-grade inflammation in older individuals and is associated with better maintenance of muscle mass. Master athletes – elderly individuals who have trained all their lives – have low levels of inflammatory mediators. A similar pattern is seen in young trained individuals, and trained master athletes demonstrated the same inflammatory level in circulating blood as young untrained counterparts, indicating a “rejuvenating” effect in individuals more than 50 years old. Interestingly higher expression of inflammatory markers is observed in individuals with lower muscle mass (i.e., inflammation and muscle mass are inversely correlated) independent of the number of satellite cells, age or training. Although inflammation tends to increase

the number of muscle stem cells in young individuals, this is not observed in elderly individuals, in whom inflammation is not linked to exercise-induced increase in muscle protein mass.

Countermeasures during and slower recovery after immobilization in aging human skeletal muscle

Muscle mass and force is lost rapidly when physical activity decreases in young and old individuals. Lower limb immobilization caused impairment in single muscle fiber force independent of age. Early in a given period of immobilization/inactivity, muscle mass loss is similar and very pronounced in young and elderly; however, during 14 days of inactivity, greater loss of muscle was observed in young than in older individuals. This likely reflects decreased protein breakdown and increased protein synthesis in the elderly. This suggests that it is especially important to take steps to prevent muscle loss in the very first days of bed rest or inactivity in elderly individuals. Muscle mass and force increased more slowly during the 4-6 weeks after return to activity in older than in young individuals.

The connective tissue and its adaptation to physical activity in old individuals – dynamic or non-dynamic?

Connective tissue undergoes renewal to a greater extent during childhood and adolescence than in adults and the elderly. Despite the relatively “static” state of tendon tissue in adults, isolated fibroblasts form tendon-like structures in vitro in the presence of serum from young and old individuals. In addition, estrogen has an anabolic effect skeletal muscle, bone and tendon in post-menopausal women. Insulin-like growth factor 1 (IGF-I) also stabilizes connective tissue in immobilized limbs in young and old individuals, and stimulates synthesis of collagen in tendons in older individuals. Elderly individuals have less collagen but a higher number of cross-links in tendons, allowing their mechanical properties to be conserved independent of age. Master athletes had low levels of non-enzymatic advanced glycation end products (AGEs) in tendons, which could indicate that the tissue is more compliant in elderly individuals who train as master athletes.

Metabolic consequences of inactivity

Comprehensive, invasive clinical studies in young and elderly humans showed that one week bedrest or two weeks in a cast on one leg has detrimental effects including altered metabolism, decreased blood flow, insulin resistance and endothelial dysfunction, with normal functions being restored only after several weeks physical rehabilitation.

Mitochondrial role in insulin resistance and physical activity

Mitochondria play a pivotal role in metabolism and energy production, and are thought to play a major role in insulin resistance. However, we have obtained a large body of experimental evidence that mitochondrial dysfunction in type 2 diabetes due to lack of mitochondrial mass, as a reflection of a physically inactive lifestyle. In addition, there may be qualitative changes as the dynamics (fission, fusion and networks) of the mitochondria with exercise training. This possibility is being explored using newly developed confocal 3D imaging of mitochondria in human tissues.

Muscle bioactive lipids

It has been proposed that ceramides, diacylglycerols and fatty acids and their breakdown products attenuate insulin signaling leading to insulin resistance. However, we demonstrated that ceramide is higher in type I muscle fibers in normal individuals as well as obese individuals and type 2 diabetics, which is counterintuitive to ceramide having a major influence on muscle insulin resistance. In addition we have not seen changes in muscle ceramide content despite of improved glucose tolerance in morbidly obese. These results are not consistent with the idea that ceramide is a major mediator of insulin resistance in muscle.

Results

- Lifelong endurance-exercise in trained athletes is associated with lower levels of inflammatory markers and greater thigh muscle area than in untrained individuals.
- The number of satellite cells in skeletal muscle is not correlated with level of training; in contrast, differential satellite cell content in different types of muscle fibers



Scene from the CEHA television series, "Fauli, fat and finished?", DR2.

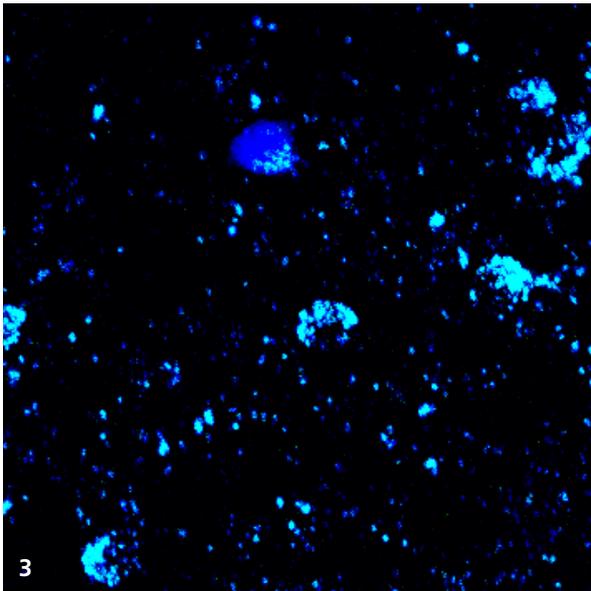
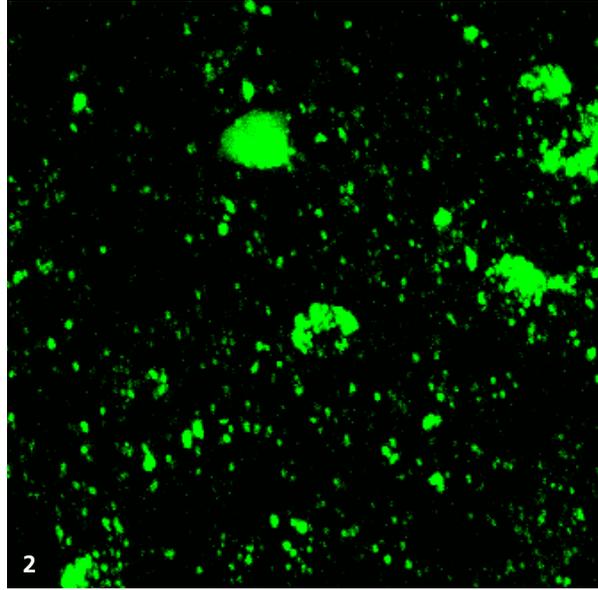
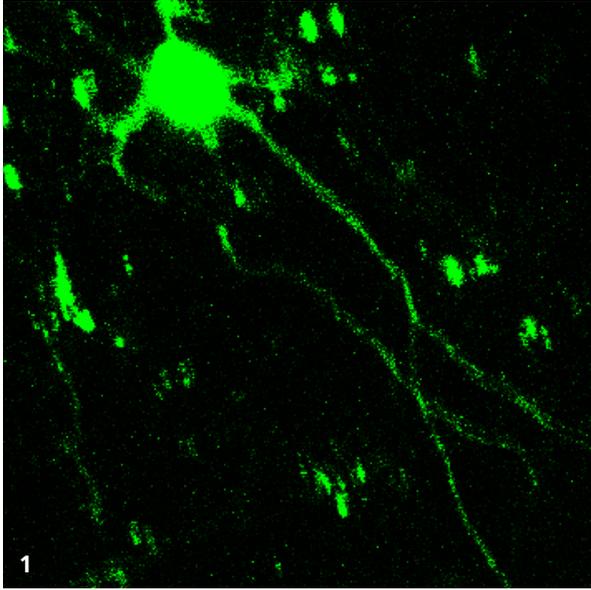
- correlates with level of training, independent of age.
- Young and old subjects experience immediate loss of muscle after inactivity, while older subjects are protected against delayed muscle loss, due to less proteolysis and stronger anabolic signalling than younger individuals.
- Diminished muscle re-growth after immobilization in elderly humans was associated with less response in satellite cell proliferation, rather than any difference in local growth factor signaling.
- In elderly individuals, growth hormone stabilizes muscle matrix during muscle inactivity and rehabilitation.
- Life-long physical activity can reduce the accumulation of non-enzymatic cross-linking and thus preserve elasticity in matrix tissues like tendon.
- Simvastatin-treated patients have a lower maximal mitochondrial respiratory capacity in muscle than untreated controls.
- Mitochondria from patients with type 2 diabetes demonstrate higher substrate specificity than non-diabetic controls.
- Metformin lowers blood glucose but it does not inhibit complex I in the electron transport chain, as previously thought.
- Whole body fat oxidation is not impaired in patients with type 2 diabetes.
- Greenlandic Inuit children have a different metabolic health profile than Danish children.
- Insulin resistance is not due to a mitochondrial dysfunction in the muscle.
- Ceramides in skeletal muscle are not major regulators of insulin signaling or insulin resistance in humans; however, ceramides are more abundant in type I muscle fibers than other skeletal muscle fiber types.
- Fat oxidation at rest predicts peak fat oxidation during exercise and metabolic phenotype in overweight males.
- Obese humans have similar mitochondrial function

but higher capacity for fat oxidation in leg and arm muscles than non-obese controls.

- Morbidly obese subjects can demonstrate improved glucose tolerance after intensive life style intervention while the abundance of muscle ceramide and triacylglycerol remain unchanged.
- Consumption of a fat rich diet does not influence muscle ceramide content.
- IL-6 release is higher across the arm than the leg during whole body exercise.
- Bariatric surgery in morbidly obese patients improves insulin secretion via an effect on the incretin hormones, but intrinsic β -cell function is unaltered.
- High intensity interval training promotes reversal of insulin resistance in patients with type 2 diabetes.
- Glycogen synthase is targeted to different intracellular glycogen pools by phosphorylation at sites 1b or 2+2a.
- Contraction-induced lipolysis is not impaired by inhibition of hormone-sensitive lipase in skeletal muscle.
- Skeletal muscle vascular endothelial growth factor (VEGF) is found in intracellular vesicles and secreted in response to muscle contraction.
- FAT/CD36 does not localize to mitochondria, but localizes to small vesicles found primarily in the subsarcolemmal region.

Conclusions

Regular physical activity improves your inflammatory status, and maintains muscle mass and function. In old age, muscle loss with inactivity occurs extremely fast, and the regain of muscle is impaired. Connective tissue can retain its elasticity and can be stabilized by regular physical activity throughout life; local growth factors (i.e., estrogen and growth hormone) also improve matrix function in the elderly. Cholesterol-lowering drugs (statins) interfere with skeletal muscle performance and mitochondrial respiration, a fact to be considered when statins are prescribed to prevent cardiovascular disease. Skeletal muscle contains bioactive lipids such as ceramides, but in contrast to previous beliefs, their abundance does not correlate with improved insulin sensitivity. Intrinsic mitochondrial respiratory function is normal in muscle characterized by insulin resistance; however, muscle mitochondrial capacity may be impaired in insulin resistant muscle due to inactivity.



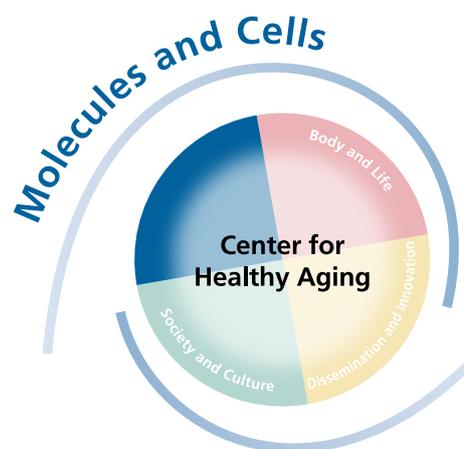
Visualization of interneurons in the brain

Two-photon images of the somatosensory cortex of a genemodified mouse, expressing fluorescent protein in a subset of neurons, termed basket cells or parvalbumin positive interneurons.

One image (picture 1) shows a single parvalbumin positive interneuron, with cell soma and long projections towards other neurons in the brain (bottom).

The other two (picture 2 and 3) images show the same field of view – 2 parvalbumin positive interneuronal somas and their projections to other cells in the brain, obtained using different excitation wavelength, which is why one image is purely green and the other is blue. In the blue image, the dark blue color shows cell bodies and the light blue color shows their projections forming onto other cells.

These neurons specialize in synchronizing activity of other neurons, primarily the so-called pyramidal neurons, in the brain. These interneurons have obtained their name due to the basket-like appearance their projections form onto other neurons. Via these projections they control activity of a large fraction of neurons. A single parvalbumin positive interneuron project to hundreds of pyramidal neurons, and 1 pyramidal neuron receive inputs from multiple parvalbumin positive interneurons forming a highly complex neuronal network. These interneurons and their ability to synchronize activity are vital for maintaining normal brain functions, higher cognitive functions and are also selectively vulnerable towards aging and age-related brain disease, such as Alzheimers disease.



Program 1b

Neuroscience

Group leaders

Martin Lauritzen, Professor

Poul Jennum, Professor

Linda Bergersen, Professor

Egill Rostrup, Associate Professor

Introduction

Program 1b is exploring how aging influences brain function in the context of animal model systems and a cohort of Danish men born in 1953. One research goal is to identify factors that influence or predict changes in cognitive function, especially cognitive decline in middle or late life leading to dementia. To this end, we are exploring markers of brain function in persons with mild to moderate cognitive decline. State-of-the-art methods are being used to image brain function and activity, including patterns of activity during sleep. The methods will identify brain activity and function involved in perception, attention and problem-solving, and, novel tools were developed to identify altered sleep patterns in men with mild cognitive impairment, Alzheimer's or Parkinson's disease. In animal model systems, we have identified unique features of brain repair mechanisms and brain information processing linked to aging.

Background and hypothesis

Information processing is the basis for cognitive function and coding of signals determines the energy requirements for mental activity. We hypothesized that pre-

clinical cognitive decline might be reflected as a disrupted sleep pattern, and disrupted activation in functional neuroimaging signals. We further hypothesized that in animals, aging would have an impact on cognition by altering the function of brain astrocytes and electrophysiological variables.

Our research program explores the following hypotheses:

- 1 Sleep disturbances influence cognitive performance and may coincide with and cause cognitive decline.
- 2 Disrupted functional neuroimaging signals predict cognitive decline and unhealthy aging.
- 3 Deregulation of intracellular calcium homeostasis characterizes brain aging in mice in vivo.
- 4 Electrophysiological signals that normally accompany cognition are disturbed in aging.

Our objective is to predict and prevent cognitive decline in unhealthy aging.

Program performance

Clinical studies: Ongoing clinical studies include an interdisciplinary project that is analyzing cognitive performance and biomarkers of brain function in 200 males born in 1953 (a subset of the Copenhagen Metropolis Cohort). The study participants were cognitively assessed when they appeared before the draft board as young adults and as part of CAMB (Copenhagen Age and Midlife Biobank) in 2009. The inclusion criteria for

the study specified 100 males that performed better in IQ tests in 2009 than at draft (Group 1) and 100 males that obtained substantially lower than expected scores in 2009 than at draft (Group 2, negative change in cognitive performance). Consequently, this is a true longitudinal study.

Out of 553 invited individuals, 207 males agreed to participate in cognitive testing, sleep, MR scans (neuroimaging), and odontological examination. Blood samples were analyzed for mitochondrial function, telomere length, ApoE genotype, and genome scanning as well as individual SNP analysis.

- The two groups did not differ with respect to their baseline cognitive function, but they did differ significantly on most (but not all) tests performed at age 58. Therefore differences in baseline capability did not explain the differences in cognitive performance in 2009.
- Structural MR images of 193 subjects did not reveal serious abnormalities, but 43 males showed slight white matter changes, or evidence of previous but unnoticed infarcts. These findings suggested an abundance of sub-clinical structural brain changes that may affect brain performance, in middle-aged non-diseased males.
- Brain activation patterns were significantly different in the two groups, such that men whose IQ tested lower in 2009 demonstrated less spontaneous activity during focused brain activation, a distinct pattern of spontaneous neural network activation when in a resting condition, and localized decrease in perfusion in a central brain region. Similar patterns are observed as early signs of neurodegenerative disease, but they have not previously been documented in clinically healthy subjects.
- Markers for dysfunctional sleep-wake patterns were also investigated, because sleep dysfunction is common in patients with neurodegenerative disorders including synucleinopathies like Parkinson's disease. Here, specific changes in micro-RNA expression were observed in Parkinson's patients with hypersomnia.
- We identified specific electrophysiological changes and early markers for Parkinsonism (REM sleep

disorders=RBD). Because RBD patients frequently develop Parkinson's disease, RBD patients are candidates for intervention studies to prevent disease progression.

- Undiagnosed sleep apnea is common in study participants whose IQ tested lower in 2009; however, weak or no correlation was observed between sleep measures and cognitive performance. However, cognitively impaired males reported significantly lower subjective sleep quality, even though cognitive decline was not explained by objectively measured sleep disturbances. Subjective bad sleep quality accompanying cognitive decline is a warning sign and may be used clinically.

Brain power/Preclinical

We have worked to define unique markers for brain aging, analyzing the interaction between nerve cells and astroglial cells, as well as brain blood flow and brain energy metabolism under normal and pathological conditions.

- We have focused on: (1) the spatiotemporal development and kinetics of Ca^{2+} changes in neurons and astrocytes in response to sensory input; (2) developing methods to analyze astrocyte Ca^{2+} waves in the cerebellum, and 3) the mechanisms and consequences of Ca^{2+} waves.
- Our data suggest a direct correlation between cerebral metabolic rate of oxygen ($CMRO_2$) and summed excitatory postsynaptic currents in response to synaptic excitation. We also found that stimulation-induced increases in cytosolic Ca^{2+} do not stimulate oxygen use, as hypothesized by us and other research groups. The use of oxygen is governed solely by "demand", i.e. ATP consumption.
- Ca^{2+} signals in astrocytes are linked to brain pathology. We have reported that the occurrence of spontaneous Ca^{2+} waves is 20 times more frequent in the cerebellar cortex of old mice than in younger adult mice, which correlated with lower resting brain oxygen tension. Spontaneous Purkinje cell activity was not associated with increased glia wave activity, but spontaneous glial waves did affect intracellular Ca^{2+} activity in Purkinje cells, suggesting that aging may also affect Purkinje cells.

- Information processing was assessed in aged mice, revealing that aging was associated with a decline in synaptic activity. Specifically, the cells that underlie perception and cognition signaled more weakly in old than in young mice, while the cells were otherwise normal. This suggests that specific cell types may contribute critically to healthy brain aging.
- We have proposed that lactate is a “volume transmitter” in brain. We now show – for the first time – that the G-protein coupled lactate receptor, GPR81 (aka HCA1), which promotes lipid storage in adipocytes, is also active in the mammalian brain, including the cerebral neocortex and hippocampus. In the brain, GPR81 is stimulated by physiological concentrations of lactate and by the agonist 3,5-dihydroxybenzoate to reduce cAMP levels. Cerebral GPR81 is concentrated on the synaptic membranes of excitatory synapses, with a postsynaptic predominance. GPR81 is also enriched at the blood-brain-barrier. In synaptic spines, as well as in adipocytes, GPR81 immunoreactivity is located on subplasmalemmal vesicular organelles, suggesting that the protein is trafficked between intracellular stores and the plasma membrane. The results indicate that, through activation of GPR81, lactate can act as a volume transmitter; namely, lactate abundance links neuronal activity, cerebral energy metabolism and energy substrate availability, as well as regulating consumption of neuronal glucose and glycogen.
- Implementation of structural and functional MR techniques, and development of new technique for quantitative assessment of cerebral blood flow and examination of participants.
- Sleep examinations of 207 participants including diurnal salivary variations in melatonin and cortisol concentrations.
- Sampling and analysis of blood from all participants for routine examination, telomere length, GWA and APOE genotyping.
- Creation of clinical database that is made accessible to all scientists in Center for Healthy Aging based on Project Proposal Forms and approval by steering committee.
- Implementation of 2-photon microscopy for use in normal and transgenic mice.
- Development of analytical tools to detect multicellular calcium signals in tissue with a very low signal-to-noise ratio and identification of spontaneous glial calcium waves in aged mice brains.
- Identification of extrasynaptic GABA receptors in generation of cortical gamma EEG activity, and examination in normally aged mice and in selective progeria mice strains, i.e. transgenic mice with Cockayne B syndrome.

Results

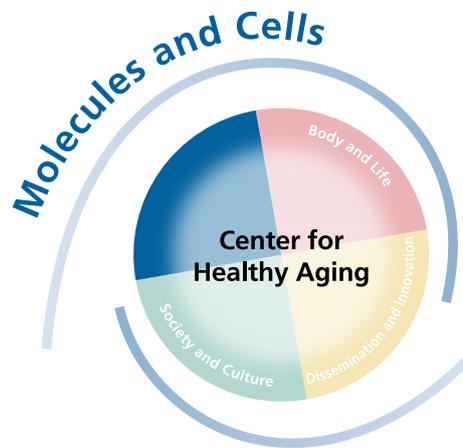
- Case report forms developed and implemented for the subprojects.
- Handbook with Standard Operating Procedures (SOP) prepared including, but not limited to, approved scientific protocols for subprojects, and statements of collaboration.
- Implementation of clinical neurocognitive test battery including CANTAB (Cambridge Neuropsychological Test Automated Battery) and other neurocognitive tests tailored for detection of minimal cognitive impairment.
- Analysis of cognitive function in 207 participants and correlation to previous cognitive test results for the same persons.

Conclusions

The Clinical Neuroscience project has proceeded according to plan. A total of 207 participants completed the study and during the course of the project a number of papers have been published. Our clinical neurocognitive test battery confirmed the validity of the 2 groups of respectively declined and improved intelligence. While none of the participants fulfilled the criteria for mild cognitive impairment, cognitive decline in intelligence had widespread implications for a large number of other neurocognitive domains. The clinical project has indicated that cognitive decline is associated with decreased un-stimulated salivary secretion and a bad subjective sleep experience. Importantly the functional magnetic resonance imaging studies suggested that cognitive decline was associated with a disrupted ability to produce network activity and the default mode network that brain uses when preparing for a task was severely affected – similar to the pattern that is observed

in patients with Alzheimer's disease (AD). This could suggest that our test-persons may be at risk for developing AD and that an intervention should be carried out. The predictive value of this finding will be assessed in the project planned from 2014-2018.

The experimental project established the infrastructure for performing 2-photon microscopy at CEHA. We have identified unique variables relevant to healthy aging, including spontaneous glial calcium waves in cerebellum in vivo that increases the brain's O₂ use without increasing O₂ supply at the same time, which may lead to increased frailty of the aged brain. In addition, our work has pointed to a special category of neurons that is underlying basic elements of perception and cognition as being particularly vulnerable to aging. In addition our studies have indicated that animals with premature aging have defects in energy production in the hippocampus area, the brain region that is responsible for memory formation, providing unique insights into the consequences of early aging mechanisms. Taken together, our experimental work points to new avenues for prevention and intervention in order to change the course of unhealthy brain aging that will be examined further in future studies.



Program 1a

Molecular aging

Group leaders

Lene Juel Rasmussen, Professor

Ian Hickson, Professor

Vilhelm Bohr, Professor

Anne Marie Lynge Pedersen, Associate Professor

Research and results

Program 1a, Molecular aging, aims to define the contribution of genomic instability to the aging process and the role of DNA repair pathways in suppressing genomic instability. DNA repair protects against premature aging by counteracting perpetual damage to the nuclear and mitochondrial genomes from intrinsic and external sources. Although cells efficiently repair multiple types of DNA damage, errors in DNA repair can lead to mutations, and alterations in genome structure or gene expression profiles. The cellular response to perpetual cycles of DNA damage and repair is critical for healthy cellular and tissue physiology, and ultimately for organismal lifespan. By understanding the molecular causes of aging and the molecular basis of DNA repair, we aim ultimately to develop novel strategies to diagnose, prevent and treat age-related pathologies. Our collective research interests, and key findings during the 2009-2013 period, are summarized briefly below:

Mitochondrial dysfunction in aging

The mitochondrion is the “powerhouse” of the cell, and the organelle in which cellular energy (in the form of

ATP) is generated through oxidative phosphorylation and the electron transport chain. A by-product of oxidative phosphorylation is the production of reactive oxygen species (ROS), which can damage DNA and other organelles. Mitochondrial dysfunction is considered a factor contributing to cognitive decline, neurological defects, muscle weakness, and fatigue. We study how DNA repair pathways maintain mitochondrial genome integrity, and prevent mitochondrial dysfunction. In particular, we have developed unique tools to investigate two key DNA repair processes in the mitochondrion: base-excision repair (mtBER) and transcription-coupled DNA repair. We are examining how alterations, or imbalances, in DNA repair contribute to age-related pathologies and mitochondrial dysfunction. Interestingly, we have demonstrated that DNA ligation is the rate-limiting step in mtBER, and that overexpression of DNA ligase in mitochondria increases survival of oxidatively-stressed cells.

We are also investigating how mitochondrial dysfunction directly (and progressively) impacts general cell physiology. For example, mitochondrial dysfunction alters nucleotide biosynthetic pathways, and this causes nucleotide pool imbalances and ensuing nuclear genome instability. Furthermore, a hallmark of Alzheimer’s disease is the formation of intraneuronal neurofibrillary tangles composed of hyperphosphorylated tau protein. Recent results suggest that mitochondrial dysfunction leads to abnormal tau phosphorylation, revealing a potential

mechanistic link between mitochondrial dysfunction and neurodegeneration. Finally, because mitochondria play an essential role in intracellular calcium homeostasis, we are also examining how mitochondrial dysfunction alters Ca²⁺-signalling in different cell types.

Molecular defects in premature aging disorders

Premature aging disorders provide invaluable insights into the aging process. A number of premature aging disorders have been identified in humans, and in some of these disorders, the underlying genetic defects have been successfully identified. All premature aging disorders are characterized by genome instability and/or defective DNA repair; therefore, cells from patients with different premature aging disorders are useful tools for understanding molecular mechanisms of DNA repair.

The RecQ family of DNA helicases are required for the maintenance of chromosome stability in all organisms. In humans, a defect in any one of three RecQ family members (BLM, RECQL4 and WRN) leads to a defined syndrome associated with premature aging. To understand RecQ helicase functions, biochemical studies are conducted using purified RecQ family proteins (and their binding partners), and molecular genetic studies are performed using model organisms or cell-based systems. RecQ helicases process specific DNA structures arising during DNA replication or chromosome segregation. For example, we discovered that unprocessed DNA replication intermediates present at centromeres, telomeres and “fragile sites” normally persist into mitosis (as so-called “ultra-fine bridges”) where they are resolved by BLM and its interacting proteins. We also identified a number of novel interactors of the RECQL4 protein, which remains very poorly characterized. A working hypothesis, based on ongoing studies, is that RECQL4 performs two distinct roles in human cells: one during the early stages of DNA replication, and another in repairing certain types of DNA damage. We aim to determine how these two roles are conducted, regulated and coordinated in human cells.

The role of extrinsic cell stress in aging

Aging is associated with an elevation of circulating inflammatory cytokines. We are exploring salivary gland

function and structure in patients with the systemic, inflammatory disease, Sjögren’s syndrome, as a model for tissue-specific premature aging. In this disease, the salivary gland tissues undergo accelerated aging with progressive inflammation, degeneration and fibrosis leading to glandular dysfunction. Our results indicate that the cytokines TNF- α and IL-20 affect Ca²⁺-signalling and ROS production, leading to an abnormal secretory response in patients with Sjögren’s syndrome. Biopsies are being collected from normal and diseased salivary glands and the blood and saliva samples are being stored in a BioBank for future study. The samples will be utilized to study oxidative DNA damage and its role in tissue-specific premature aging.

We have also examined how DNA lesions are processed in cells infected by *Helicobacter pylori*, a bacterial pathogen associated with high incidence of gastric cancer. Following infection with *H. pylori*, DNA mismatch repair (MMR) is down-regulated, leading to genomic instability in gastric epithelial cells. While it is widely believed that susceptibility to infection is higher in older individuals, these findings suggest that bacterial infections may also promote premature aging by interfering with DNA repair processes.

We have established collaborations within CEHA and elsewhere in Denmark through which we can gain access to clinical biopsy specimens. Such material is essential for the discovery of novel biomarkers, and for understanding the etiology of age-related pathologies. We also aim to build on the expertise of our colleagues within CEHA, for example, in the study of cognitive deficiency or muscle dysfunction during human aging.

Results

- Mitochondria contribute to checkpoint responses in mammalian cells, and also regulate the levels of nucleotide pools. Therefore, mitochondrial dysfunction can promote genome instability within the nucleus.
- DNA ligation is the rate-limiting step in mitochondrial BER. Overexpression of ligase III in mitochondria enhances cell survival after oxidative stress.
- The human premature aging disease, Cockayne syndrome, is associated with elevated levels of mitochondrial stress.

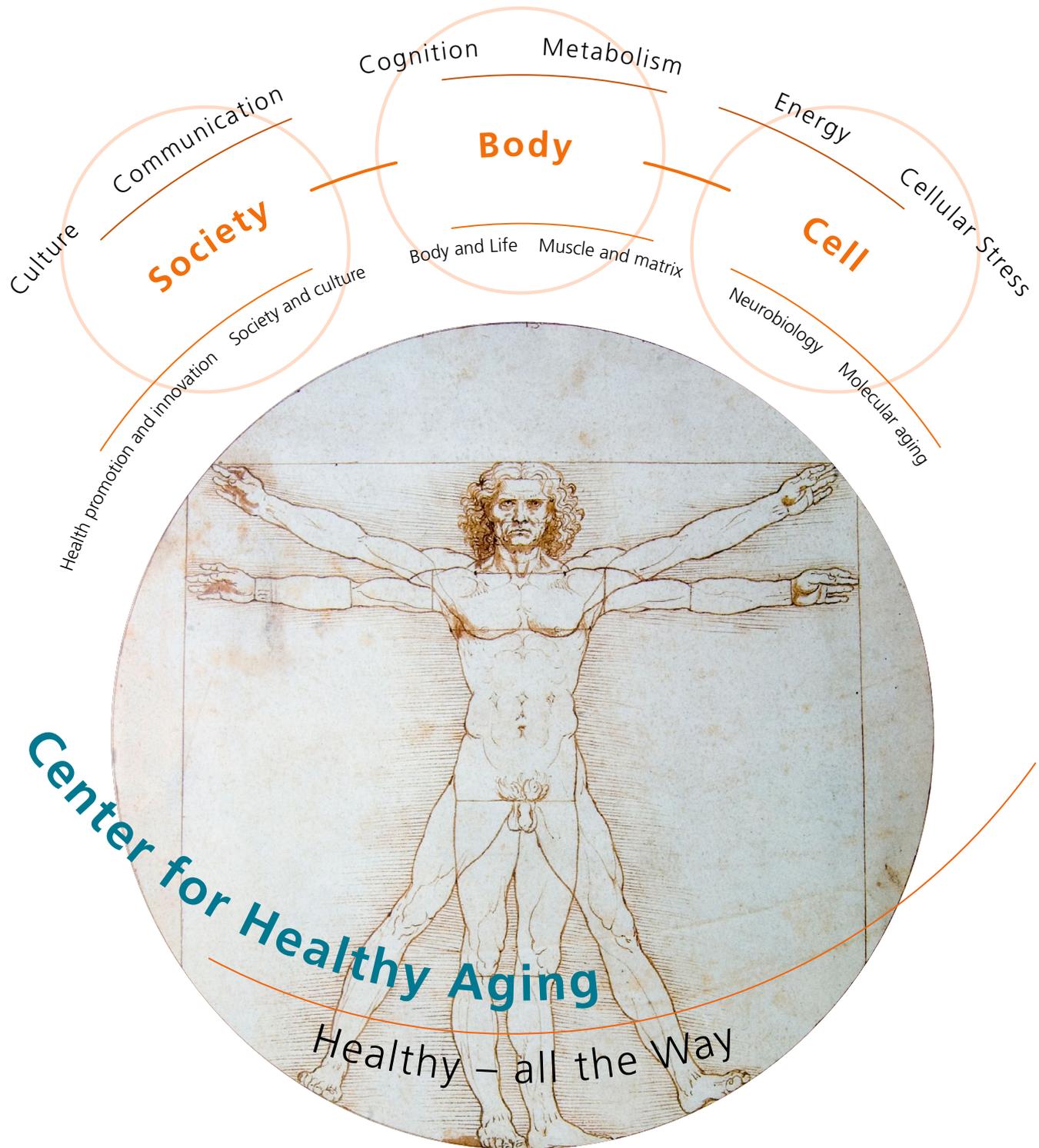




- Nuclear architectural protein lamin A/C, which is mutated in the human premature aging disorder Hutchinson-Gilford progeria, affects base excision DNA repair and mitochondrial bioenergetics by activating PARP-1.
- RecQ helicases perform evolutionarily conserved roles to “dissolve” problematic DNA structures that naturally arise during DNA replication and mitosis.
- Cells frequently enter mitosis with unrepliated, or inadequately processed chromosomes following DNA replication. This is a major potential source of genome instability.
- Common fragile sites, which are detectable as gaps and breaks on metaphase chromosomes, are actively created by a nuclease (MUS81) to prevent chromosome mis-segregation events occurring during mitosis.
- ML216 is a small molecule inhibitor of BLM helicase that could be useful as an anticancer therapy, especially in cancers displaying ALT (“alternative lengthening of telomeres”).
- PICH is a DNA translocase that binds to DNA bridges, and facilitates accurate chromosome segregation during mitosis.
- The human RecQ helicase RECQL4 interacts with BER and MMR proteins. We have functionally characterized a number of disease-causing mutations in human RECQL4.
- Degenerative changes are more prevalent and pronounced in salivary glands from patients with primary Sjögren’s syndrome than in healthy age-matched controls. A number of genes were identified that exhibited altered expression levels in Sjögren’s syndrome patients.
- The cellular responses to TNF- α and IL-20 in salivary gland acinar cells are mediated through the activation of PKC.
- *Helicobacter pylori* infection generates genetic instability in gastric cells. Our results suggest that both APE-1 and YB-1 are involved in mtDNA repair during *H. pylori* infection. Furthermore, multiple DNA repair activities protect mtDNA during *H. pylori* infection.
- Increased hyposalivation, poor dental health, and increased levels of the putative aging biomarker P16ink4a in labial salivary gland tissue samples correlates with lower cognitive performance in late midlife; one or more of these biomarkers may be an early clinical sign of age-related cognitive decline.
- Self-reported persistent low vitality is not associated with altered mitochondrial oxidative phosphorylation capacity in PBMCs; other cellular dysfunctions may contribute to dNTP imbalance and altered ROS production in PBMCs.

Conclusions

The Molecular aging Program is studying the role of DNA repair in conserving genome stability and counteracting aging. DNA repair protects the nuclear and mitochondrial genomes from intrinsic and external DNA damaging agents. We have characterized mitochondrial and nuclear DNA repair pathways, and demonstrated how defects in DNA repair can cause premature aging. A major focus of our research is human RecQ helicases, which are mutated in a number of distinct premature aging disorders. We have shown that RecQ helicases perform an evolutionarily conserved role in “dissolving” problematic DNA structures that naturally arise during DNA replication and chromosome segregation. Surprisingly, aberrant DNA replication intermediates are remarkably prevalent, and cells frequently attempt to segregate incompletely replicated, or inadequately processed chromosomes after DNA replication. This is a major potential source of genome instability. We also demonstrated that mitochondrial dysfunction can lead to an array of physiological changes in cells and tissues that manifest as progressive age-related pathologies. Furthermore, we have investigated how extrinsic sources of cellular stress contribute to cellular and tissue aging. For example, we characterized cellular responses to inflammatory cytokines and pathogenic infections, and demonstrated that they can exacerbate cellular aging. Ultimately, we envision that these analyses will lead to novel strategies or tools for diagnosing, preventing, and treating age-related diseases, thus promoting healthy aging.





Major collaborative projects within CEHA

2009-2013

Coordinator: Astrid Jespersen

Fatigue and everyday life – Experience of fatigue among healthy people and people suffering from apoplexy (Programs 1b and 5).

The Fatigue and everyday Life – Experiences of fatigue among healthy people and people suffering from apoplexy interdisciplinary project spent most of 2013 on finishing the PhD dissertation, which was handed in on September 2nd and subsequently accepted for oral defense the 24th of January 2014. The title of the thesis is “A Question of Location – Life with Fatigue after Stroke” and it deals with the experiences of fatigue after stroke. The thesis is based on a qualitative fieldwork among people who have had a stroke, and explores how a stroke may dislocate and relocate the experience of fatigue and how a new location of fatigue calls for new meaningful contexts in everyday life. The findings have been presented at a number of national and international seminars and conferences. Collaboration between Programs 1b and 5 made it possible to conduct fieldwork at the outpatient clinic at Glostrup Hospital, and facilitated contacts between researcher PhD Fellow Michael Andersen and several informants with stroke. On the 24th of January 2014 the project will be concluded and the findings will feature as a part of the knowledge base of CEHA 2014-2018.

Coordinator: Astrid Jespersen

Cross-border healthcare among Turkish immigrants in Denmark with particular focus on the elderly (Programs 4 and 5).

The aim with a comparative study of respectively Turkish retirees in Denmark and Danish retirees in Turkey was to investigate specifically how health perceptions and health practices are influenced by various migrant situations in later life, and how their health care practices and use are related to homeland and host-land, respectively. The study consist of two different ethnographies in two different settings; one qualitative study among elderly Turkish immigrants in Denmark and one qualitative study among Danish retirees in Turkey. The study among Turkish migrants in Denmark was carried out as part of an interdisciplinary study in CEHA (Programs 4 and 5) in 2011-2012, and the study among Danish migrants in Turkey was carried out in 2013. The first and quantitative part of the study (executed by program 4) showed that there was greater use of all somatic healthcare services in a foreign country among Turkish immigrants compared to ethnic Danes. The qualitative study among the Turkish migrants in Denmark, however, showed that the practice of cross-border healthcare services and medication consumption was not as widespread as indicated in the quantitative study and that the 30 Turkish immigrants interviewed were more authoritative on the Danish medicalization regime and health system than expected. We could not conclude a lack of compliance with the

Danish healthcare system due to cross-border practices. However, the comparative study of Danish migrants living in Turkey showed that they are utilizing all variations of cross-border medicine; in Turkey as well as in Denmark, and that they are very competently able of finding and using the medicine they want, in both countries.

The project has resulted in three articles published in English and one in progress, one anthology in English containing eight chapters about Nordic seniors on the move, two articles in Danish, nine oral presentations in academic settings, one poster (English), the organization of a panel debate at a conference, two oral presentations in a public forum and one popular report about best practices for health promotion targeted at immigrants. Furthermore, regarding dissemination and interaction with public audience and user-involvement two arrangements were held.

- 1 In cooperation with the Senior Council and Local Council of Bispebjerg; an area of Copenhagen, a "theme day" about health promotion for Turkish women was carried out. All presentations were given in Turkish, for instance by the CEHA visiting scholar from Turkey; MD Suzan Yazici, and the wife of the Turkish ambassador in Denmark participated as well.
- 2 A conference for both locally engaged Danish seniors (Ældreråd) and professionals working locally in Denmark in the field of health and migration (Sundhedsarbejdere, forebyggere) was arranged, which successfully resulted in mutual dialogue and inspiration.

Coordinator: Allan Krasnik

Continuity of Care: An international comparative analysis of tools and settings for coordination of preventive drug medication (Program 3, 4, and 5).

A joint comparative study of the organizational frames for and provider perspective on care paths and coordination of care in relation to preventive drug medication in the Veterans Health Administration (VA) and Danish healthcare system (DHS) has been developed. Despite VAs substantial number of vulnerable patient with multiple chronic illnesses, the large public healthcare system has succeeded in implementing initiatives in order to support coordinated care with positive effects on the

chronic patient care, patterns of medication and early interventions. To study the organizational frames for coordinated care path for preventive drug medication, 13 qualitative interviews with key persons has been conducted for VA and a similar number will be conducted in DHS. The key persons have been identified by the national experts in the project group. Content analysis is used for the qualitative data.

The preliminary results showed that the organizational frames at the Veterans Health Administration (VA) support the coordination of care to a high extent. In particular the IT-system with clinical reminders and overview of outliers, the accessibility of providers, the patient outreach, the agreement of responsibility, the culture supporting quality assurance, including the built in double check of drug interactions, and the close link between the clinical world and health services research all contribute to why VA is a successful model of integrated and cost-effective care with high quality services to its patients. There are big potentials for the Danish health care system to learn from VA. The findings may play an important role in promoting policy interventions for preventive drug medication for chronic care that enhance continuity of care – especially among vulnerable patients who have fewer resources themselves for coping with insufficient coordination by the healthcare service.

Outcomes for 2013 were: Preparation of interview guide, study visits to VA in Los Angeles and data collection (interviews and observation at the VA – Los Angeles).

The future plans of the study is to investigate the providers' perspectives on coordinated care path for preventive drug medication by sending out electronic questionnaires to relevant hospital staff and primary care clinicians who are responsible for the daily care of patients with diabetes in VA and DHS. Data will be analyzed using multiple logistic regression models. Furthermore, rooting in the findings from this study, a larger application on comparable studies between VA and DHS, including intervention studies in DHS using tools and practice learnt from VA, will be submitted in 2014.

The project is conducted in close collaboration with Professor Paul Shekelle, University of California, Los Angeles, Director at Quality Assessment and Quality Improvement Program, Rand Health California, and Associate Professor Caroline Goldzweig, VA Los Angeles as well as the MD, PhD Anne Frølich, Capital Region and Bispebjerg Hospital.

Coordinator: Kirsten Avlund and Vilhelm Bohr
Fatigue (low subjective vitality) in middle-aged men correlates with levels of reactive oxygen species, dNTPs, DNA damage, body mass index and physical performance (Program 1a, 2, and 3).

Fatigue in middle-aged and older adults is a complaint that is poorly understood and difficult to diagnose or predict. We are analyzing peripheral blood mononuclear cells (PBMCs) isolated from subjects with a range of fatigue levels, for correlates to fatigue that could potentially serve as fatigue biomarkers. Fatigue level was based on the SF-36 vitality scale, and was assessed in the Metropolit cohort described above. The blood tests entailed measurements of oxygen consumption rate (OCR), dNTP ratios, reactive oxygen species (ROS) levels, DNA damage (strand breaks and estimation of oxidative lesion 8-oxoG) as well as telomere length. OCR was measured using the Seahorse Biosciences XF analyzer. Measurements were taken before (basal), and at points after, addition of electron transport chain (ETC) inhibitors to generate several OCR parameters representative of ETC response. Vitality score was inversely correlated to ROS levels (N = 97) and to dTTP levels (N = 79) and positively correlated to dCTP levels (N = 34). We also found that strand breaks, body mass index (BMI) and several physical performance parameters (such as grip strength) were associated with vitality score. This not only revealed underlying molecular damage with vitality but also that further validated subjective feelings of energy (vitality) as a measure of fatigue and energy since it associated with physical performance. There was no effect of the mitochondrial oxygen consumption parameters (efficiency of mitochondrial ATP production) on vitality scores. These data might lead to further investigation into ROS, dNTP levels or DNA damage as contributing biomarkers for early detection of human fatigue or fatiguing illnesses

(such as chronic fatigue syndrome of fibromyalgia) and may provide insights for therapeutic intervention.

Coordinator: Michael Kjær
Skin and tissue characterization of a patient with apparent dimorphic rates of skin aging (Program 1a and 2)

A 30-year-old female presented with severe wrinkling of the skin on her upper body, which she had developed over the last 5 years. The most affected areas were her face, neck, breast and upper arms, but the lower extremities were completely unaffected. The skin changes were a major cosmetic problem to the patient. She had prior to the skin changes an intentional weight loss of 20 kg (BMI at the time of examination was 30). We analyzed two skin biopsies, one taken from the patient's affected upper body (neck) and another from her unaffected lower body (thigh), with transmission electron microscopy (TEM) and real-time RT-PCR, and from cell cultures of both biopsies we analyzed proliferation rates, cell senescence and response to UVB and oxidative stress.

We found that the patient had a lack of elastic fibers in the upper body (affected region) biopsy as well as increased cell proliferation rate and higher mRNA expression levels of elastin from the affected skin area. This data fit with the diagnosis of acquired, localized cutis laxa and adds more information, specifically that the fibroblasts from the affected area surprisingly have enhanced proliferation and stress resistance and have no alteration in senescence. This leads us to the hypothesis that lack of elastic fibers in the affected area may allow for enhanced local skin cells proliferation.

Coordinator: Martin Lauritzen
The interdisciplinary neuroscience project (Program 1a, 1b and 3).

Cognitive test scores in midlife reflect not only individual differences in age-related decline, but also individual differences in cognitive ability characterizing young adults. Using the Metropolit Cohort and CAMB data (described above 22), we have demonstrated that there are substantial correlations between draft board intelligence scores and cognitive ability in late midlife, and 207



individuals with unusual large changes in cognitive ability from young adulthood to late midlife have been selected for detailed clinical evaluations such as comprehensive neuropsychological assessment, functional magnetic resonance imaging (fMRI), assessment of sleep patterns and oral health.

The Clinical Neuroscience project has proceeded according to plan and spent most of 2013 on finishing results from the clinical evaluations to be included in several PhD-projects, Master project and manuscripts for publication. The projects include seven PhD-projects that have been handed in or defended in 2013 or will be in 2014. Five of the PhD-titles are (1) "Late midlife sleep pattern and sleep structure and the association to age-related changes in cognition. The Metropolit Birth 1953 Cohort", (2) "Clinical, neurophysiological and molecular biological aspects of salivary gland function in relation to age-associated changes in cognitive function", (3) "The dynamic brain – Activity patterns in cognitive aging and during cerebral blood flow modulation", (4) "Motor pattern in REM sleep behavior disorder and Parkinsonian disorders" and (5) "Inhibition in Parkinson's disease: A focus on prepulse inhibition and Rapid eye movement sleep Behavior Disorder (RBD)". The main conclusions of some of these PhD-projects are: (1) Subjective measurements of sleep in middle-aged males show an association between self rated sleep quality and cognition (2) Results of examinations of hyposalivation, poorer dental health and increased expression of the molecular aging biomarker P16ink4a indicate that these may constitute potential peripheral correlates of cognitive decline in men in late midlife and (3) using MRI, distinct alterations in functional brain organization related to cognitive decline have been found. Importantly, the fMRI studies suggest that cognitive decline is associated with a disrupted ability to produce network activity, and the default mode

network that brain uses when preparing for a task is severely affected – similar to the pattern that is observed in patients with Alzheimer's disease (AD).

The interdisciplinary sub-project "Altered level of deoxythymidine triphosphate is associated with cognitive impairment", aims to evaluate mitochondrial ROS production and whole-cell levels of deoxyribonucleotides triphosphates including dTTP as early biomarkers of dementia. The project shows no association between mitochondrial production of ROS and changes in cognitive ability in men in late midlife, whereas a significant correlation between whole-cell levels of dTTP and cognitive decline has been found. Moreover, a sub-project has established the infrastructure for performing 2-photon microscopy at CEHA. We have identified unique variables relevant to healthy aging, including spontaneous glial calcium waves in vivo that increase the brain's O₂ use without increasing O₂ supply at the same time, which may lead to increased frailty of the aged brain. Our work has also pointed to a special category of neurons that underlies basic elements of perception and cognition as being particularly vulnerable to aging. Finally, our studies have indicated that animals with premature aging have defects in energy production in the hippocampus area, the brain region that is responsible for memory formation, providing unique insights into the consequences of early aging mechanisms.

Therefore, several novel potential biomarkers of cognitive decline and/or risk for developing AD have been found in based on the inclusion of approximately 200 participants and points to new avenues for prevention and intervention in order to change the course of unhealthy brain aging. The value of these findings will be assessed in the project planned from 2014-2018 and further participants and new examinations will be included as part of our future work.





In memory of Professor Kirsten Avlund

Kirsten Avlund was the university's first professor of gerontology, and she played a crucial role in the establishment and development of CEHA. She was a talented person of unusual integrity and a unique combination of qualities; she was intelligent, energetic, enthusiastic, persistent, generous, gregarious, optimistic, and had a wonderful sense of humor.

With a background as an occupational therapist she became an interviewer on the 70-year follow-up of the Glostrup 1914 cohort in 1984. This was the start of her lifelong interest in aging. She continued to follow and study the 1914 cohort, on which she worked until her death. Kirsten's international reputation was built on the measures of mobility and fatigue that she developed and which have been widely adopted in the international aging research community.

Kirsten Avlund's energy, enthusiasm, and optimism were not hampered by her serious fight with cancer. During the years after her first treatment in 2006, she established the Copenhagen Aging and Midlife Biobank

(CAMB), a large biobank based on three cohorts and now one of CEHA's central research resources. At the same time, she was the head of the CEHA life course program (Program 3), established important Danish and international collaborations, and supervised young researchers and PhD Students with dedication and enthusiasm. Throughout her long research career, Kirsten Avlund made many important contributions to gerontology and related fields. Her work on CAMB will probably be her most important contribution, and it is tragic that she died just before publications appeared in the literature.

People will remember Kirsten Avlund as a well-balanced person whose enthusiasm, optimism, generosity, humor, and warm laugh could overcome all tensions and help avert any sense of impending crisis. Danish aging research and CEHA have lost a driving force and a central figure who will be sorely missed for a long time.

Professor Erik Lykke Mortensen is now the interim leader of CEHA Program 3.



Staff

2013

Complete staff list

- Paid by CEHA¹
- ◐ Partly paid by CEHA²
- Not paid by CEHA

Total

Paid or partly paid by CEHA: 94 persons

Not paid by CEHA: 117 persons

Definitions:

- 1 ● represents 1 person paid 1 full work year (37/hours per week in 12 months).
- 2 ◐ represents 1 person paid part time in 1-12 months or full time in less than 12 month.

Senior researchers

- Program 5
- Astrid Pernille Jespersen, Associate Professor
 - Lene Otto, Associate Professor
 - Thomas Söderqvist, Professor
- Program 4
- ◐ Allan Krasnik, Professor
 - ◐ Susan Reynolds Whyte, Professor
 - Carsten Hendriksen, Associate Professor
 - ◐ John Sahl Andersen, Associate Professor
 - Signe Smith Nielsen, Assistant Professor
 - Helle Wallach Kildemoes, Assistant Professor
 - Annegrete Juul Nielsen, Assistant Professor

- Program 3
- Kirsten Avlund, Professor
 - Erik Lykke Mortensen, Professor
 - Rikke Lund, Associate Professor
 - Finn Diderichsen, Professor
 - Merete Osler, Professor
 - ◐ Charlotte Nilsson, Assistant Professor
 - Kaare Christensen, Professor
 - Ulla Christensen, Associate Professor
 - ◐ Henrik Brønnum-Hansen, Associate Professor
- Program 2
- ◐ Flemming Dela, Professor
 - Michael Kjær, Professor
 - Peter Magnusson, Professor
 - Jørn Wulff Helge, Associate Professor
 - Clara Prats, Associate Professor
 - Nina Beyer, Associate Professor
 - Lars Holm, Associate Professor
 - Abigail Mackey-Sennels, Associate Professor
 - Jesper Løvind Andersen, Senior Researcher
 - Peter Schjerling, Senior Researcher
- Program 1b
- Martin Lauritzen, Professor
 - Poul Jennum, Professor
 - Linda Hildegard Bergersen, Professor
 - Egill Rostrup, Chief Physician
 - Anne Marie Lyng Pedersen, Associate Professor

- Birgitte Fagerlund, Senior Researcher
- Krisztina Benedek, Chief Physician
- Merete Osler, Clinical Professor
- Steen Gammeltoft, Chief Physician
- Program 1a Ian Hickson, Professor
- Lene Juel Rasmussen, Professor
- Steen Dissing, Professor
- Anne Marie Lynge Pedersen, Associate Professor
- Katerina Tritsarlis Jondahl, Associate Professor
- Jytte Overgaard Larsen, Associate Professor
- Hocine Mankouri, Research Associate Professor
- Ying Liu, Associate Professor
- Claus Desler, Assistant Professor
- Sasha Liberti, Assistant Professor
- Scott Maynard, Assistant Professor
- Mansour Akbari, Assistant Professor

Guest researchers

- Program 3 Carlos Mendes de Leon, Professor
- Ivan Bautmans, Professor
- Doug Morse, Associate Professor
- Alan Gow, Post doc
- Robert Fieo, Post doc

Postdoc

- Program 5 Anne Leonora Blaakilde
- Program 4 Bjarke Oxlund
- Mikkel Wass
- Margit Kriegbaum
- Program 3 Minna Mänty
- Margit Kriegbaum
- Nadia Dich
- Program 2 Takashi Yokota
- Steen Larsen
- Amelia Gaudalupe Grau
- Monika L. Bayer
- Rene B Svensson
- Mette Hansen
- Katja Heinemeier
- Pernilla Eliasson

- Søren Reitelseder
- Ulla Ramer Mikkelsen
- Christian Couppe
- Anders Fabricius Nedergaard
- Program 1b Claus Mathiesen
- Lene Rask
- Louise Juhl Boni
- Program 1a Sheroy Minocherhomji
- Yao Qi
- Anna Bizard
- Kata Sarlos
- Susanne Germann
- Maciej Kliszczak
- Diana Huttner
- Marianne Smedegaard Hede
- Jesper Strickertsson

PhD students

- Program 5 Adrian Bertoli
- Louise Scheel Thomassen
- Aske Juul Lassen
- Michael Andersen
- Hanne Hellerup Eriksen
- Maja Schøler
- Program 4 Bodil Ludvigsen
- Sarah Wadmann
- Andreas Rudkjøbing
- Michael Nixon
- Program 3 Rikke Hodal Meincke
- Jolene Masters Pedersen
- Anette Ekmann
- Anne Møller
- Gunhild T. Christensen
- Kristine Harsen Bachkati
- Program 2 Michael Taulo Lund
- Martin Gram Jensen
- Andreas Vigelsø Hansen
- Merethe Hansen
- Liselotte Bruun Christiansen
- Malene Kristensen Maag
- Stinna Skaaby
- Marianne Kristensen
- Ditte Søgaaard
- Sune Dandanell Jørgensen

- Jakob Agergaard
- Mette Flindt Heisterberg
- Anders Ploug Boesen
- Andreas Herchenhan
- Rie Harboe Nielsen
- Kasper Dideriksen
- Cecilie Jæger Leidesdorff
- Rasmus Bechshøft
- Program 1b ● Naja Liv Hansen
- Katja Linda Waller
- Christiane Elisabeth Sørensen
- Sanne Barsballe Jessen
- Anna Horwitz
- Laura Gertrud Sørensen
- Laura Graves Ponsaing
- Otto Henriksen
- Jacob Kempfner
- Program 1a ○ Guido Keijzers
- Martin Borch Jensen
- Sara Bursomanno
- Christian Nielsen
- Nicolai Larsen
- Aiste Aleliunaite
- Özgun Ozer
- Victoria Bjerregaard
- Christiane Elisabeth Sørensen
- Jon Durhuus
- Dekang Liu
- Maria Angleys
- Thomas Lau Hansen
- Nima Fankouri

Research assistants

- Program 5 ● Amy Beth Clotworthy
- Louise Scheel Thomasen
- Morten Hillgaard Bülow
- Michael Andersen
- Program 3 ● Maria Hach
- Program 2 ○ Thor Munch Andersen
- Rannvá Dahl
- Tine Dohlmann
- Annesofie Thorup Olesen
- Program 1b ● Kristian Klinkby

- Kjeld Andersen
- Program 1a ● Kim Daugaard

Bachelor/Master students

- Program 5 ○ Liv Grønnow
- Camilla Søgaard
- Program 2 ○ Peter Riis Andersen
- Caroline Wiuff
- Julie Hagstrøm Danielsen
- Rie Dybboe
- Stine Dam Søndergaard
- Program 1b ○ Liva Spindler Mørk
- Niloofer Sherazi
- Kiyana Zarnani
- Program 1a ○ Tran Thuan Son Dinh
- Esther Saxild
- Jane Hübertz Frederiksen

Pregraduate research students

- Program 3 ● Signe Hovmand Nørgaard
- Program 2 ● Nynne Bjerre Andersen
- Sina Dalby
- Jesper Nørregaard
- Ida Jørgensen
- Morten Hindsø
- Nana Lassenius Kramp
- Cathrine Scheuer
- Anne Line Jørgensen
- Arthur Ingersen
- Jacob Bülow
- Nikolaj Mølkjær Malmgaard-Clausen
- Mathias Bech Møller

Lab technicians

- Program 2 ● Katrine Qvist
- Regitze Kraunsøe
- Jeppe Bach
- Lise Rask
- Thomas Beck
- Ann-Marie Sedstrøm
- Ann-Christina Ronnie Reimann
- Camilla Brink Sørensen
- Anja Sisko Jokipii-Utton

-
- 
- Caroline Bøjstrup
 - Ida Trondhjem-Haakonsson
 - Program 1b Micael Lønstrup
 - Program 1a Theresa Wass
 - Malgorzeta Clausen
 - Louise Rosgaard Duus
 - Anne Marie Bundgaard

Secretaries

- Program 5 Jonas Møller Pedersen
- Program 3 Annegrethe Hansen
- Program 2 Jacqueline van Hall
- Else Pedersen
- Birgitte Kjær
- Program 1a Elin Erichsen

Other

- Program 4 Janne Sørensen, Coordinator
- Julie Bay, Student Assistant
- Program 3 Drude Molbo, Data Coordinator
- Eva Jepsen, Project Coordinator
- Program 2 Christina Neigaard Hansen,
Molecular Biologist

CEHA administration

- Tina Gottlieb, Head of Administration
- Line Damberg, Academic Officer
- Mikael Kjærsgaard Møller,
Communication Officer



Selected publications

2009-2013

Program 1a

Biebricher A, Hirano S, [Enzlin JH](#), Wiechens N, Streicher WW, Wang LHC, Nigg EA, Owen-Hughes T, [Liu Y](#), Peterman E, Wuite GJL, [Hickson ID](#). PICH: a DNA translocase specially adapted for processing anaphase bridge DNA. *Molecular Cell* 51, 691-701, 2013.

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Internationalization and networking

IARU – International research cooperation

The Center for Healthy Aging has from the outset been closely associated with the International Alliance of Research Universities (IARU), a prestigious alliance that includes the University of Copenhagen. The other IARU members are Yale University, University of California at Berkeley, Swiss Federal Institute of Technology in Zurich (ETH), University of Cambridge, University of Oxford, National University of Singapore, Australian National University, Peking University and the University of Tokyo. The Alliance is a valuable networking opportunity for members of CEHA, who arrange meetings and workshops and utilise IARU as a mechanism for enhancing collaboration and future research activities. The close association between CEHA and IARU is a cornerstone in the efforts to internationalize CEHA. Detailed information on IARU/CEHA can be found at www.iaruni.org/research-initiatives/aging. The effort from the Center has been spearheaded by Professors Vilhelm Bohr, National Institute on Aging, NIH, USA, and Albert Gjedde, University of Copenhagen, both associates of the Center.

IARU – International congress

CEHA also actively participates in the IARU Aging, Longevity and Health project. In October 2010, an IARU Congress was held under this umbrella. The Congress was hosted by Rector Ralf Hemmingsen, University of Copenhagen and Dean Ulla Wewer, Faculty of Health and Medical Sciences, University of Copenhagen and

organized by Center for Healthy Aging under the leadership of Managing Director Lene Juel Rasmussen and Professor Vilhelm Bohr. The purpose of the Congress was to provide an opportunity for researchers from the IARU Aging, Longevity and Health Network and others to exchange data and ideas, and to plan, initiate or extend collaborative research projects.

At the 2010 IARU Congress, 123 delegates from IARU countries/universities discussed their ongoing research. The presentations at the Congress were very diverse, including molecular and cellular studies as well as population-based and sociological studies. A report covering the topics of the many presentations from the congress delegates is published in *Mechanisms of Aging and Development* (Rasmussen LJ, Sander M, Wewer UM, Bohr VA., Aging, longevity and health. *Mech Aging Dev.* 2011, Oct;132(10):522-32. Epub 2011 Jul 23).

IARU Installation – An Aging World

An exciting public installation, which lies on the “art-science” interface, was inaugurated by Director of Medical Museion Thomas Söderqvist at the Faculty of Health and Medical Sciences, during the opening session of the IARU Congress in October, 2010. The purpose was to raise awareness of the IARU collaboration, CEHA and aging research at the University as well as to add an aesthetic / artistic component to the IARU Congress.



IARU Presidents and Senior Officers from IARU universities visited CEHA and the Faculty of Health and Medical Sciences in 2012.

Back row, from left: SO Don Filer, Director of International Affairs, Yale University; Ian Young, Vice-Chancellor, Australian National University; Leszek Borysiewicz, Vice-Chancellor, University of Cambridge; Andre Hamilton, Vice-Chancellor, University of Oxford.

Front row, from left: Yoichiro Matsumoto, Executive Vice President, University of Tokyo, SO Pradeep Chhibber, Director of Institute of International Studies, University of California, Berkeley; Ralf Hemmingsen, President, University of Copenhagen; Tan Chorch Chuan, President National University of Singapore; Ralph Eichler, President ETH; ZHOU Qifeng, President, University of Peking.

The installation was produced by Medical Museion, the Faculty's science communication research and museum unit, headed by Professor Thomas Söderqvist, director of the Medical Museion. It showed patterns of demographical change over time and the persistent large differences in population age structure in rich and poor countries around the world. The physical diagrams were constructed from acrylic plastic and illuminated by fibre optics, and the map of the world was presented quite unconventionally as a disc, with China, Japan and Papua New Guinea in the center of the earth.

This fascinating installation, which is currently exhibited in an auditorium at the University of Copenhagen, became a focal point for researchers, staff, students and visitors to the University during the IARU Congress.

IARU – Presidents annual meeting in Copenhagen

Each year, the IARU Presidents hold a meeting at one of the ten IARU universities. In 2012, the University of Copenhagen hosted the Presidents Meeting, which included a visit to the Faculty of Health and Medical Sciences and the Center for Healthy Aging. Dean Ulla Wewer, Faculty of Health and Medical Sciences, and Managing Director Lene Juel Rasmussen, CEHA, received the visiting Presidents at the Faculty of Health and Medical Sciences and chaired the visit, giving presentations on CEHA and on the Faculty's IARU activities.

IARU – Empowerment of the aging network

At the IARU Presidents meeting in 2013, the University of Copenhagen suggested that a Steering Committee of the Aging Longevity and Health network should be



Students and teachers at the Global IARU Summer School.



Summer school coordinator
Associate Professor Ying Liu.

formed to promote engagement at all IARU campuses in collaborative activities, including workshops, exchange programs and jointly-funded research projects. All present at the President's meeting expressed their support for the proposal. At present, eight out of ten universities have appointed representatives to the IARU Steering Committee

As a first activity along these lines, the University of Copenhagen contributed DKK 1.3m (235.000 USD) to support a joint IARU program in June 2014, to include three IARU Congresses, (17-22 June, 2014) and a first meeting of the IARU Aging Longevity and Health Steering Committee (20 June, 2014). In spring 2014, scientific organizing committees are coordinating this initiative under the leadership of CEHA Managing Director Lene Juel Rasmussen. The organizers are expecting approximately 200 IARU researchers and others individuals interested in the field of aging to attend. The conference themes will include:

- Molecular Aging
- Neurodegeneration and Aging
- Cultures of Aging
- Social Interventions and Aging
- Life Course Issues and Aging
- Aging in a National and International Perspective
- Scientific careers for young scholars

Further information on these activities is available at www.iaru-conferences-2014.dk.

The conferences will coincide with Euroscience Open Forum in 2014 (ESOF2014). ESOF2014 will be held in Copenhagen. See esof2014.org/info.

IARU – Summer school

Since 2011, CEHA has hosted a three-week international summer school in July as part of the University of Copenhagen's role in the IARU Global Summer Program (GSP). CEHA offers the course Interdisciplinary Aspects of Healthy Aging on an annual basis, and CEHA investigators and invited speakers from other universities give lectures at this international summer school. The summer school is coordinated by Associate Professor Ying Liu.

The GSP is an intercultural and interdisciplinary experience for a diverse group of students from IARU universities. The CEHA course is aimed at students who are interested in all aspects of aging research. It represents all CEHA research projects and promotes the interdisciplinary nature of CEHA. The course combines lectures and hands-on work interdisciplinary projects. The lectures provide students with basic research concepts and principles in the field of aging research in the humanities, social sciences, epidemiology, neurology, physiology, and molecular biology. At the end of the course, students present their work and write essays about their research. See healthyaging.ku.dk/education/iaru-summer-school.

IARU – Graduate Student Conference in Singapore

In 2012, the National University of Singapore (NUS), Singapore held an Inaugural IARU Graduate Student Conference titled The Challenge of Aging. The purpose was to facilitate interaction between IARU PhD students involved in aging research. The graduate students were presented studies on translating research to policy, social demography and gerontology in Asian cultures. The Graduate Student Conference coincided with the larger Global Asia Initiative (GAI) Conference, a forum to discuss multidisciplinary aging research relevant to Asian populations. The GAI presentations described studies in medicine, engineering, sociology, policy design and technology development, highlighting the need for multidisciplinary and holistic approaches in aging research. CEHA participants included PhD students from Programs 1a, 2, 3 and 5, Managing Director Lene Juel Rasmussen and the Head of CEHA Administration Tina Gottlieb. The conference afforded a unique opportunity to network with international aging researchers and administrators at the IARU Secretariat and laid the foundation for future collaborations within IARU.

Inspired by this event, CEHA is planning to host the next IARU Graduate Student Conference as part of the IARU Conference Program of June 2014 (see p. 67).

iHAN – International Healthy Aging Network

The International Healthy Aging Network (iHAN) is a group of researchers affiliated with IARU who collaborate in studying molecular and cognitive markers of healthy and unhealthy brain aging. The collaboration is working towards collecting and understanding PET imaging from diseased and normal human brains, and in identifying molecular markers of Alzheimer's disease. iHAN members are from Monash and Queensland universities in Australia, Yale, Johns Hopkins, and University of California, Berkeley in the US, Aarhus and Copenhagen Universities in Denmark, and Oslo University in Norway.

iHan promoted a series of seminars in November and December 2013, entitled Beyond the Amyloid Cascade, given by Albert Gjedde at the Lawrence Berkeley Labora-

tory of the University of California in Berkeley, where iHAN-trainee Adjmal Nahimi MD was hosted by Director William Jagust MD, and at the Center of Advanced Imaging at the University of Queensland in Brisbane, where iHAN-analyst Anders Rodell PhD and iHAN-trainee Michael Gejl MD currently are hosted by Director David Reutens MD, as well as at the BRAINlab at the Panum Institute's Department of Neuroscience and Pharmacology of the University of Copenhagen. Also in November 2013, the BRAINlab of the Department of Neuroscience and Pharmacology and the CEHA hosted Professor Fahmeed Hyder PhD of Yale University, who spoke on Changes of Brain Energy Metabolism with Aging.

Mitochondria accumulate at the necks of dendritic spines, where they have the potential to interact with amyloid-beta and phosphorylated tau and to influence neurotransmission, and/or neuromodulation. It is possible that stress-induced change in the mitochondria contributes to healthy aging (Rodell et. al 2013). *In vivo* approaches are being developed to test whether mitochondrial stress ultimately increases respiratory capacity. Other questions include: 1) how do divergent metabolic pathways optimize metabolism? 2) does the balance between oxygen and glucose consumption and fatty acid metabolism influence mitochondrial membrane potential?

Publications of the Danish arm of iHAN in 2013:

Darusman HS, Call J, Sajuthi D, Schapiro SJ, Gjedde A, Kalliokoski O, Hau J. Delayed response task performance as a function of age in cynomolgus monkeys (*Macaca fascicularis*). *Primates*. 2013. [Epub ahead of print]

Darusman HS, Sajuthi D, Kalliokoski O, Jacobsen KR, Call J, Schapiro SJ, Gjedde A, Abelson KS, Hau J. Correlations between serum levels of beta amyloid, cerebrospinal levels of tau and phospho tau, and delayed response tasks in young and aged cynomolgus monkeys (*Macaca fascicularis*). *J Med Primatol*. 2013. Jun;42(3):137-46. doi: 10.1111/jmp.12044. Epub 2013 Mar 26.

Fast R, Rodell A, Gjedde A, Mouridsen K, Alstrup AK, Bjarkam CR, West MJ, Berendt M, Møller A. PiB Fails to Map Amyloid Deposits in Cerebral Cortex of Aged Dogs with Canine Cognitive Dysfunction. *Front Aging Neurosci*. 30;5:99, 2013 doi: 10.3389/fnagi.2013.00099. eCollection 2013.

Gjedde A, Aanerud J, Braendgaard H, Rodell AB. Blood-brain transfer of Pittsburgh compound B in humans. *Front Aging Neurosci*. 7;5:70, 2013. doi: 10.3389/fnagi.2013.00070. eCollection 2013.

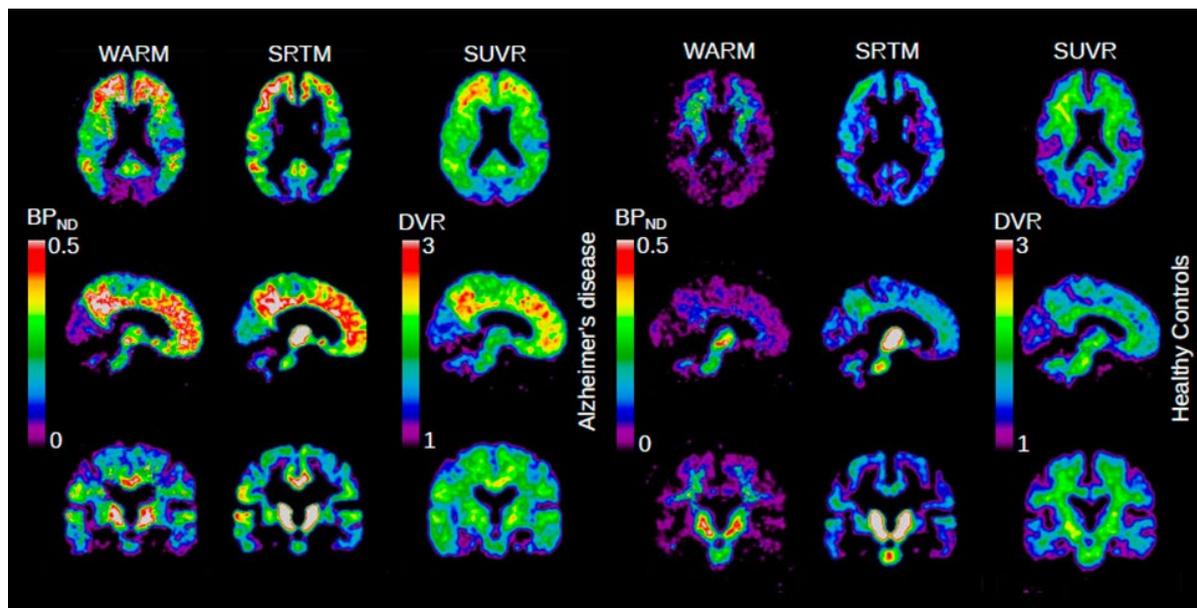


Image of brain maps of amyloid-beta accumulation in brain of patients with Alzheimer's disease, analyzed by three different methods (WARM, SRTM, SUVR). Left panels: Patients. Right panels: Healthy age-matched volunteers. Note the greater differentiation observed with WARM (from Rodell et al. 2013, see list of references).

Kumakura Y, Gjedde A, Caprioli D, Kienast T, Beck A, Plotkin M, Schlangenhaus F, Vernaleken I, Gründer G, Bartenstein P, Heinz A, Cumming P. Increased turnover of dopamine in caudate nucleus of detoxified alcoholic patients. *PLoS One*. 11;8(9), 2013. e73903. doi: 10.1371/journal.pone.0073903. eCollection 2013.

Lauritzen KH, Morland C, Puchades M, Holm-Hansen S, Hagelin EM, Lauritzen F, Attramadal H, Storm-Mathisen J, Gjedde A, Bergersen LH. Lactate Receptor Sites Link Neurotransmission, Neurovascular Coupling, and Brain Energy Metabolism. *Cereb Cortex*. 2013 [Epub ahead of print]

Rodell A, Aanerud J, Braendgaard H, Gjedde A. Washout allometric reference method (WARM) for parametric analysis of [(11)C]PIB in human brains. *Front Aging Neurosci*. 27;5:45, 2013. doi: 10.3389/fnagi.2013.00045. eCollection 2013.

Rodell A, Rasmussen LJ, Bergersen LH, Singh KK, Gjedde A. Natural selection of mitochondria during somatic lifetime promotes healthy aging. *Front Neuroenergetics*. 12;5:7, 2013. doi: 0.3389/fnene.2013.00007. eCollection 2013.

Other international events and networking GDN4 and GDN5

The fourth Genome Dynamics in Neuroscience Meeting (GDN4) was coorganized by the Centre for Molecular Biology and Neuroscience (CMBN) and CEHA. The conference was held in Oslo, Norway on September 19th to 22nd 2012. It was the fourth in a series of international meetings addressing genome instability and DNA repair in the context of neuroscience and aging.

The objective of the meeting was to highlight key aspects of DNA damage and repair in aging, neurodegeneration and the pathogenesis of neurological disease, and to improve our understanding of how nerve cells communicate in the healthy and diseased brain. Topics included genome dynamics and maintenance, epigenetics, bioenergetics, stem cell biology, brain development, microbial model systems and synaptic communication. The conference brought together world-leading scientists to discuss the state-of-the-science in understanding normal brain

aging and in the pathogenesis of neurodegenerative diseases. A special issue in the journal *Mechanisms of Aging and Development* titled "Genome Dynamics Shaping Neuroscience" is a by-product of the meeting:

Rasmussen LJ, Shiloh Y, Bergersen LH, Sander M, Bohr VA, Tønjum T. DNA damage response, bioenergetics, and neurological disease: the challenge of maintaining brain health in an aging human population. *Mech Ageing Dev.* 2013 Oct;134(10):427-33. doi: 10.1016/j.mad.2013.05.001. Epub 2013 May 10.

The fifth Genome Dynamics in Neuroscience Meeting (GDN5) will be held in collaboration with the IARU Conferences in Copenhagen on 17-20 June, 2014 (described above). See also www.iaru-conferences-2014.dk/Genome-Dynamics-in-Neuroscience-and-Aging.aspx.

International Symposium on the Biopolitics of Aging

In December 2013, Program 5 organized an international symposium on the biopolitics of aging. The symposium consisted of four public keynote lectures by internationally renowned researchers and five workshops. The symposium was a great success with more than 50 invited participants. Possible future collaborations involving CEHA and non-CEHA scientists were discussed. See also (see p. 11).

CEREHA

CEHA also recently became a partner in the newly funded Israeli Centre of Excellence for Research on Environment, Health and Aging (CEREHA). CEREHA is the most important aging research initiative in the Galilee region of Northern Israel.

MARRIAGE

CEHA is a member of the EU funded Initial Training Network MARRIAGE. The overall objective of this Network is to provide state-of-the-art training in study of the biology of aging. The network includes European Aging Centers and the Training Network will create a pan-European Network focused on ageing research.

ABRAHAM

CEHA is also active in the establishment of the network ABRAHAM, which include researchers, companies, governmental institutions and patients/citizen. ABRAHAM aims to create a transatlantic network with partners from the EU, the USA and Canada. This network will build on several existing projects, some of which involve transatlantic partnerships that focus on aging-related issues, such as genome stability and metabolism and systems biology. The founding partners of ABRAHAM are the University Medical Center Groningen (The Netherlands, EU), University of Copenhagen (Denmark, EU), University of Newcastle upon Tyne (United Kingdom, EU), Mayo Clinic (Minnesota, USA) and McGill University (Montreal, Canada) and all have extensive collaborations with industries in the food, pharmaceutical and medical technology sectors. ABRAHAM aims to enhance integration in the field of biobanking and basic aging research in order to contribute to the goal set by the European Commission, namely adding two extra healthy years to life in 2020.

KIC

The European Institute of Innovation and Technology (EIT) based in Budapest, Hungary has recently launched a call for Knowledge and Innovation Communities (KICs) to provide innovative solutions to societal problems as part of Horizon 2020, the European Unions's framework programme. A KIC is a highly integrated, creative and excellence-driven partnership which brings together the fields of education, technology, research, business and entrepreneurship. The KIC tackles grand-challenges of the European Community to ensure economic growth along with sustainable solutions in the 21st century. CEHA intends to apply for funding under this initiative.



Visiting professor program

In 2010, CEHA established a visiting professor program, which has been expanded and strengthened since its inception. The program facilitates cross-disciplinary interactions in the international aging research community, and has attracted wide participation from scientists at several well respected universities. Among others, the following individuals participated in this program during the period of 2010-2013:



Professor Carlos Mendes de Leon

Carlos Mendes de Leon, University of Michigan, School of Public Health, spent two periods of several months each in residence at CEHA during 2010-2011 and three shorter periods in 2012-13. Professor de Leon's main research focus is the effects of social relations, socioeconomic position and ethnic status on aging. Professor de Leon has been an inspiring supervisor for postdoctoral fellows and PhD students in CEHA. He collaborates in ongoing CEHA research activities, is a co-author on publications with CEHA faculty and is planning to continue to collaborate with CEHA in the future.

Publication:

Mänty M, Mendes de Leon C, Rantanen T, Era P, Pedersen AN, Ekman A, Schroll M, Avlund K. Mobility-related fatigue, walking speed and muscle strength in older people. *J Gerontol Med Sci.* 67A: 523-9, 2012.



Professor Linda Hildegard Bergersen

During 2011, Visiting Professor Linda Hildegard Bergersen and one of her PhD students, Christine Regnell, initiated an interdisciplinary research project with CEHA researchers. Professor Bergersen and Christine Regnell are permanently affiliated with the Brain and Muscle Energy Group in CMBN at the University of Oslo, Norway. Professor Bergersen stayed at CEHA for six months in 2011 and continued as a Visiting Professor of Neurobiology for the academic year 2012, and since October 2013 as CEHA Professor at the University of Copenhagen. The main focus of Professor Bergersen's research is energy failure in the brain and its impact on synaptic plasticity. One ongoing project is a collaboration with CEHA Managing Director Professor Lene Juel Rasmussen, which will measure morphological and/or chemical changes at synapses in a DNA repair-deficient transgenic mouse model for the premature aging disease Cockayne syndrome. In 2012, Professor Bergersen recruited PhD student, Signe Holm-Hansen, and provided her with a three-year PhD student fellowship from the Danish Lundbeck Foundation for a project on Energy Failure in the schizophrenic brain, a collaboration involving the Universities of Copenhagen, Oslo and Sydney. Professor Bergersen and Miriam Kolko are also using funding from Veluxfonden to support postdoctoral fellow Dorte Skytt on a project concerning mitochondrial dysfunction in the Müller cells in the retina. Professor Bergersen participated as co-organizer of the GDN4 conference, described above.

Professor Bergersen works closely with Professors Lene Juel Rasmussen (Program 1a), Martin Lauritzen (Program 1b) and CEHA associates Vilhelm Bohr and Albert Gjedde. In 2013 Bergersen, Albert Gjedde, Signe Holm-

Hansen and their co-workers discovered a G-protein coupled lactate receptor in the brain (Lauritzen et al., *Cerebral Cortex* 2013).

Publications:

Bergersen LH, Bramham CR, Hugdahl K, Sander M, Storm-Mathisen J. The changing brain—insights into the mechanisms of neural and behavioral adaptation to the environment. *Neuroscience* 5;247:412-22, 2013.

Cheng C, Edin NF, Lauritzen KH, Aspmodal I, Christoffersen S, Jian L, Rasmussen LJ, Pettersen EO, Xiaoqun G, Bergersen LH. Alterations of monocarboxylate transporter densities during hypoxia in brain and breast tumour cells. *Cell Oncol (Dordr)*. 35(3):217-27, 2012.

Lauritzen F, Eid T, Bergersen LH. Monocarboxylate transporters in temporal lobe epilepsy: roles of lactate and ketogenic diet. *Brain Struct Funct*. 2013. [Epub ahead of print]

Lauritzen F, Heuser K, de Lanerolle NC, Lee TS, Spencer DD, Kim JH, Gjedde A, Eid T, Bergersen LH. Redistribution of monocarboxylate transporter 2 on the surface of astrocytes in the human epileptogenic hippocampus. *Glia* 60(7):1172-81, 2012.

Medin T, Rinholm JE, Owe SG, Sagvolden T, Gjedde A, Storm-Mathisen J, Bergersen LH. Low dopamine D5 receptor density in hippocampus in an animal model of attention-deficit/hyperactivity disorder (ADHD). *Neuroscience* 9;242:11-20, 2013.

Puchades M, Sogn CJ, Maehlen J, Bergersen LH, Gundersen V. Unaltered lactate and glucose transporter levels in the MPTP mouse model of Parkinson's disease. *J Parkinsons Dis*. 1;3(3):371-85, 2013.

Rasmussen LJ, Shiloh Y, Bergersen LH, Sander M, Bohr VA, Tønjum T. DNA damage response, bioenergetics, and neurological disease: the challenge of maintaining brain health in an aging human population. *Mech Aging Dev*. 134(10):427-33, 2013.

Regnell CE, Hildrestrand GA, Sejersted Y, Medin T, Moldestad O, Rolseth V, Krokeide SZ, Suganthan R, Luna L, Bjørås M, Bergersen LH. Hippocampal adult neurogenesis is maintained by Neil3-dependent repair of oxidative DNA lesions in neural progenitor cells. *Cell Rep*. 27;2(3):503-10, 2012.

Rinholm JE, Bergersen LH. Neuroscience: The wrap that feeds neurons. *Nature*. 25;487(7408):435-6, 2012.

Rinholm JE, Bergersen LH. White matter lactate – Does it matter? *Neuroscience*. 2013. pii: S0306-4522(13)00846-4.

Vafaee MS, Vang K, Bergersen LH, Gjedde A. Oxygen consumption and blood flow coupling in human motor cortex during intense finger tapping: implication for a role of lactate. *J Cereb Blood Flow Metab*. 32(10):1859-68, 2012.



Senior Research Fellow Alan Gow

Alan Gow, Centre for Cognitive Ageing and Cognitive Epidemiology and Psychology, University of Edinburgh, spent three months at CEHA in the summer of 2011, two months in 2012, and three months in 2013. His main research interest is the influence of leisure time activity and occupation on cognitive aging using prospective longitudinal data from the Glostrup 1914 cohort. The results demonstrate that increased activity (leisure or physical) was consistently associated with the level of cognitive ability; however, the association was attenuated when adjusted for baseline cognitive ability suggesting that the observation reflects preserved differentiation and not an influence of activity on cognitive decline. A small association remained for increased physical activity and less cognitive decline in individuals tested at age 60 or 70. Intellectually challenging occupations were associated with a higher level of cognitive ability, controlled for age, sex, education and social class. However, when an earlier measure of cognitive ability was accounted for (assessed at age 50), the association was reversed; thus, of two individuals with the same baseline level of cognitive ability, the one in the more intellectually challenging occupation had lower subsequent cognitive ability. These results have been published in two international articles in 2012. The results have also been presented at conferences in Denmark and abroad.

Publications

Gow A, Avlund K, Mortensen EL. Occupational characteristics and cognitive aging in the Glostrup 1914 Cohort. *J Gerontol: Series B. Psychological Science*. In press, 2014.

Gow AJ, Mortensen EL, Avlund K. Activity participation and cognitive ageing in the Glostrup 1914 cohort from age 50 to 85. *J Am Geriatr Soc*. 60:1831-8, 2012.



Postdoctoral Fellow Robert Fieo

Robert Fieo, Centre for Cognitive Ageing and Cognitive Epidemiology and Psychology, University of Edinburgh, spent six months at CEHA in 2011, one month in 2012, and one month in 2013 investigating the validity of self-reported measures of fatigue, in particular, construct validity of the Avlund Mob-T Scale. Fieo established a formal hierarchy of scale items across time for the measure, which made it possible to gauge an individual's "distance" from the high risk zone and minimize measurement error. Robert Fieo's further work includes development of a sensitive activity scale among older adults and validation of the widely used MFI-20 fatigue measure using updated item response models. In collaboration with Columbia University, the salient characteristics that increase the risk of death in the depressed elderly with frailty will be investigated. To date, this collaboration has led to publication or submission of three articles.

Publications

Brown PJ, Liu X, Fieo R, Rantanen T, Sned JR, Rutherford R, Devanand DP, Roose SP, Avlund K. Frailty and depression in older adults: A high-risk clinical population. *Am J Geriatr Psychiatry*, In press, 2014.

Fieo R, Mortensen EL, Rantanen T, Avlund K. Improving a measure of mobility-related fatigue (the Mob-T Scale) by establishing item intensity. *J Am Geriatr Soc*. 61:429-433, 2013.

Fieo RA, Mortensen EL, Lund R, Avlund K. Expanding the interpretive power of the Multiple Fatigue Inventory-20. *Assessment*. Submitted, 2014.



Associate Professor Doug Morse

Doug Morse, Department of Epidemiology and Health Promotion, New York University College of Dentistry, spent a one-year sabbatical (2011-12) at CEHA. He has studied associations of cognitive function and lifestyle variables with oral health in late midlife and old age. The main results during his stay were: 1) Significant associations were found between periodontal disease and cognitive function in an older cohort after adjusting for other important covariates. 2) Smoking and alcohol consumption are associated with missing teeth in late midlife. 3) Allostatic load in early old age influences the course of periodontal disease at advanced old age.

Publications

Kamer AR, Morse DE, Holm-Pedersen P, Mortensen EL, Ellefsen B, Avlund K. Periodontal inflammation in relation to cognitive function in an older Danish population. *Journal of Alzheimer's Disease* 28: 613-24, 2012.

Morse DE, Avlund K, Christensen LB, Fiehn NE, Molbo D, Holmstrup P, Kongstad J, Mortensen EL, Holm-Pedersen P. Smoking and drinking as risk indicators for tooth loss in middle-aged Danes. *J Aging Health*, In press, 2013.

Salazar CR, Factor-Litvak P, Morse DE, Holm-Pedersen P, Pedersen AN, Bruunsgaard H, Krabbe KS, Avlund K. Social and behavioral determinants of allostatic load in a cohort of older Danish adults. *American Journal of Public Health*. Submitted, 2013.



Senior Lecturer Tiago Moreira

Tiago Moreira, School of Applied Social Sciences and Fellow of Wolfson Research Institute, visited CEHA three times during 2011-12; in 2012, for three months in residence. He is an internationally recognized sociologist, STS and aging researcher. His research explores the complex interactions between knowledge and health-care, paying particular attention to the role of technology in medical settings, the use of health technology in residential settings (i.e. patients in their home environment), the collective design and evolution of healthcare standards, and political issues relating to clinical trials. He is also interested in ethnographic studies relevant to neurosurgery. During his stay at CEHA, he completed a book, held master-classes for PhD students, took part in internal meetings and seminars, started a pilot study and developed and submitted a research proposal on Public Engagement in Aging research (PEAR). He co-supervises two PhD students at CEHA and serves on PhD thesis review committee. In 2013, Moreira was a keynote speaker at the international symposium Biopolitics of Aging.

Publication:

Moreira T. *The Transformation of Contemporary Health Care The Market, The Laboratory, and the Forum*. Routledge, 2012.

O'Donovan O, Moreira T, Howlett E. Tracking Transformations in Health Movement Organisations: Alzheimer's Disease Organisations and their Changing "Cause Regimes". *Social Movement Studies*, 2013.

Selected shorter stays:

Senior Lecturer Sarah Nettleton

In 2010, Sarah Nettleton, Senior Lecturer in Social Policy in the Department of Sociology, University of York, UK, came to CEHA as a visiting scientist to carry out empirical research on the sociology of the body, to explore “body projects”, “body techniques”, “reflexive body techniques”, and “changing bodies”. Ms Nettleton led a Master Class and held discussions with CEHA PhD students.

Senior Research Fellow Alex Faulkner

Alex Faulkner, Centre for Biomedicine and Society, King's College London, visited CEHA in 2010. Dr. Faulkner's research focuses on the influence of medical technology on healthcare practice and society, with special focus on technology that impacts or might have future impact on aging and degeneration/regeneration. Dr. Faulkner presented a lecture, led a Master Class and held discussions with CEHA PhD students.

Assistant Professor Suzan Yazici

Suzan Yazici, Assistant Professor, Akdeniz University, Department of Gerontology is a medical doctor, family physician, and gerontologist whose main interests are health and migration, health promotion and successful aging. Suzan Yazici participated in a collaborative project in CEHA which examined health issues among elderly Turkish migrants in CPH. She is currently studying perception of aging among Turkish academics and non-academics and anti-aging practices among women stratified by socioeconomic factors.

Professor Jeremy A. Greene

Jeremy Greene, Harvard University and Harvard Medical School, visited CEHA in June 2011 and August 2013. His first book: “Prescribing by Numbers: Drugs and the Definition of Disease” (2007, Johns Hopkins University Press) documents the efforts of drug manufacturers to market risk-reducing pharmaceuticals to individuals afflicted by chronic disease, which is also the main research focus of CEHA Program 4. Dr. Greene presented lectures to CEHA on Political Representations of the American Elderly as Pharmaceutical Consumers and on the policies and

processes involved in development of drugs. Dr. Greene also presented master classes and met with CEHA researchers. In 2013, Jeremy Green was appointed to the Scientific Advisory Board for LIFESTAT (“Living with Statins”, lifestat.dk/dk).

Senior Research Fellows George Leeson and Kenneth Howse

Two core members of the Oxford Institute of Ageing in Great Britain (OIA), George Leeson and Kenneth Howse, visited CEHA in December 2012 and George Leeson also visited in July 2013. George Leeson, who is co-director of OIA, was formerly responsible for the Longitudinal Danish Future Study and served as an advisor to the Danish Government Programme on Ageing Workers, and Older People and Technology. He is the author of *New Horizons*, *New Elderly* and Editor of the *Journal of Population Ageing*. His colleague Kenneth Howse researches healthcare and intergenerational justice in aging societies. He is the founding Editor of *Ageing Horizons* and serves as Oxford coordinator of the IARU Aging, Longevity and Health project. Leeson and Howse held an informal publication workshop and master classes for PhD students, presented two seminars on healthy aging, healthcare services and the demography of death, met with CEHA researchers, and made plans for future collaboration between CEHA and OIA.

Professor Paul Shekelle

The large public Veterans Administration (VA) in USA has succeeded in implementing initiatives in order to support coordinated care with interesting effects on prevention of chronic diseases, patterns of medication and early interventions. Paul Shekelle, University of California, Los Angeles, Director at Quality Assessment and Quality Improvement Program, Rand Health California visited CEHA in October 2011 in order to discuss and plan a joint comparative study of tools and outcomes for integrated care related to healthy aging. A project outline has afterwards been developed through virtual meetings between Paul Shekelle and other researchers at the VA, CEHA researchers and researchers from Bispebjerg Hospital. Data collection started in autumn 2013 after joint identification of existing comparable data related to diabetes care.



Collaboration between Centre for Human Movement and Healthy Ageing, University Medical Center, Groningen and Center for Healthy Aging, University of Copenhagen

In 2012, CEHA hosted visiting postdoctoral fellow Han Boter, and visiting Professor Tibor Hortobagyi, Centre for Human Movement and Healthy Ageing, University Medical Center, Groningen, Han Boter stayed at CEHA for three months in 2012 to analyze the correlation between self-reported fatigue using the MFI-20 and fatigue deduced by measuring chair-rise and hand grip strength, in a joint effort by CEHA Programs 2 and 3. The project will enhance our understanding of the role of fatigue in aging process and whether fatigue causes physical inactivity, whether an exercise intervention can decrease fatigue, and whether voluntary reduction of physical activity leads to perceived-fatigue and/or fatigability.

Publication:

Boter H, Mänty M, Hansen ÅM, Hortobágyi T, Avlund K. Self-reported fatigue and physical function in late midlife. *Journal of Rehabilitation Medicine*. In press, 2014.

Collaboration between Boston University and Center for Healthy Aging

Postdoctoral Fellow Nadya Dich, Boston University, stayed at CEHA for four months in 2012, to study the "Positive work environment as a protective factor against the negative impact of life stress on physiological functioning in midlife," a CAMB Stress & Health sub-study using data on 203 men and women aged 49-51. Unfortunately, the analyses turned out to be under-powered. As a result, Nadya is studying the association between major life events in childhood and adult life and cumulative physiological dysregulation in the ~5.500 participants in CAMB. A research protocol and collaborative agreement has been approved and a paper has been submitted based on the results.

Publication:

Dich N, Hansen ÅM, Avlund KA, Lund R, Mortensen EL, Brunsgaard H, Rod NH. Early life adversity potentiates the effects of later life stress on cumulative physiological dysregulation. *Psychosomatic Medicine*, Submitted, 2014.

Collaboration between Vrije Universiteit Brussels and Center for Healthy Aging

In 2013, professor Ivan Bautmans participated at CEHA in a collaboration on the relationship between self-perceived fatigue, muscle endurance, and inflammation. The collaboration aimed to validate the fatigue resistance test data in CAMB and to determine the relationship between handgrip strength and self-perceived fatigue. An abstract based on the findings was prepared and submitted for presentation at the Nordic Gerontological Congress 2014.

Publication in preparation

Bautmans I, Beyer I, Avlund K, Bruunsgaard H, Molbo D, Mortensen EL, Lund R. The relationship between self-perceived fatigue, muscle endurance, and circulating markers of inflammation in participants of the Copenhagen Aging and Midlife Biobank (CAMB)





Educational activities in 2009-2013

An important goal for CEHA is to educate the next generation of aging researchers. To this end, CEHA scientists make a concerted effort to provide high quality educational resources to CEHA students/trainees, and to recruit junior and senior scientists with appropriate research interests and/or expertise to the CEHA faculty. CEHA's educational programs include undergraduate and graduate level courses on aging-related topics as well as opportunities for postdoctoral studies under the mentorship of CEHA faculty. Educational activities have increased on all levels during the 2009-2013 time period, as described below.

Faculty-supported PhD projects

The Faculty of Health and Medical Sciences, University of Copenhagen, funds 23 CEHA PhD scholarships at the 33% level (DKK 500,000), and 2 PhD scholarship at the 100% level. Additional PhD projects are funded by CEHA or by other sources.

PhD courses

In 2010, CEHA researchers taught or contributed to 7 PhD level courses, increasing to 40 in 2013.

PhD level courses included:

- *Life course influences on health changes in adult life*, organized by Professor Kirsten Avlund and Associate Professor Rikke Lund, 2010 (Program 3)
- *Brain aging*, organized by Professor Martin Lauritzen, 2010 (Program 1b)
- *Mitochondrial Summer School*, organized by Assistant Professor Claus Desler, 2011 (Program 1a)
- *Exercise physiology in basic and applied research*, organized by Associate Professor Lars Holm, 2012 (Program 2)
- *Localising and managing uncertainties course organizers and lecturers*, organized by Professor Susan Whyte and post doc Bjarke Oxlund, 2011 (Program 4)
- *Interdisciplinary communication*, offered by the Network for Young Scholars, 2012 (NYS)
- *Aging muscle: size, signalling and satellite cells*, organized by Associate Professor Abigail Mackey, Senior Researcher Jesper L Andersen and Senior Researcher Peter Schjerling, 2013 (P2).

Master level

CEHA Faculty also teach masters level courses, including 2, 33, 27 and 54 courses in 2010, 2011, 2012 and 2013, respectively.

Master level courses included:

- *Gerontology*, Course leader and lectures Assistant Professor Charlotte Nilsson, 2013 (Program 3)
- *DNA repair, mitochondria and aging*, Assistant Professor Scott Maynard, 2013 (Program 1a)
- *Living condition and health of older people*, lecturer and group instructor Postdoc Helle Wallach Kilde-moes, 2012 (Program 4)
- *Interdisciplinary aspects of healthy aging*, CEHA

- researchers, 2011-2013 (All CEHA Programs)
- *Training and rehabilitation*, Associate Professor Nina Beyer, 2011 (Program 2)
 - *Cultural health studies*, Associate Professor Lene Otto and Associate Professor Astrid Jespersen, 2010 (Program 5)

Undergraduate level

CEHA offered 5 undergraduate level courses in 2010 and 41 undergraduate level courses in 2013.

Undergraduate level courses included:

- *Molecular aging*, multiple lectures, Associate Professor Hocine Mankouri, 2013 (Program 1a)
- *Medical physiology and pathophysiology*, multiple lectures, Associate Professor Abigail Mackey-Sennels, 2013 (Program 2)
- *Structure and function of the Danish healthcare system*, PhD Student Sarah Wadmann, 22 lectures, 2012 (Program 4)
- *Medical science and technology studies*, PhD student Morten Bülow, 2011 (Program 5)
- *Prevention in adults and older people – the role of the social- and health care system*, course organizers Associate Professor Carsten Hendriksen and Professor Kirsten Avlund, 2010 (Program 3)

Postgraduate and miscellaneous

CEHA researchers participate in lectures at university and non-university affiliated venues, including public and private hospitals, increasing from 40 in 2011 to 148 in 2013.

Selected examples:

- *Social relations and the importance for the elderly*, Aarhus DaneAge Association, Associate Professor Rikke Lund, 2013 (Program 3)
- *Age-related decline in functional ability and the risk of falling*, The Danish Building Research Institute, Aalborg University, Associate Professor Nina Beyer, 2013 (Program 2)

- *Rehabilitation of frail elderly*, The Local Government Denmark, Dept. for Social and Health Policy, PhD Student Louise Scheel Thomassen, 2012 (Program 5)
- *Expectations, Conceptions and Challenges – Aging in 2012*, DJØF Senior, Danish Union for Social Scientists in Denmark, Postdoc Anne Leonora Blaakilde, 2012 (Program 5)
- *Prevention for maintenance of age-appropriate functional ability among older adults*, lecture for members of an expert group appointed by the National Board of Social Services, Postdoc Charlotte Nilsson and professor Kirsten Avlund, 2012 (Program 3)
- *Physical activity and health*, Upperup Danish Folk High School (Upperup Højskole), Associate Professor Jørn W. Helge, 2012 (Program 2)
- *Chronic pain and sleep disorders*, Joint Annual Meeting of the Scandinavian Association for the Study of Pain and the Danish Pain Society, Professor Poul Jensen, 2012 (Program 1b)
- *Nutrition and physical activity in relation to weight loss – Recommendations to elderly*, Course for General Practitioners, Postdoc Mette Hansen, 2011 (Program 2)
- *Aging and driving safety*, Theme days for Central Denmark Region and the Danish Road Directorate, Postdoc Mikkel Vass, 2011 (Program 4)
- *Medicalised old age – A double-edged sword*, The Danish Gerontological Association's Annual Meeting and Leader Forum's Senior Days (Ældredage), Associate Professor Carsten Hendriksen, 2009 (Program 4)



Selected joint activities, awards and events

CEHA site visit and retreats

CEHA site visit in 2012

An external review committee performed a site visit and review of CEHA on 21-23 May 2012. During the site visit, six experts representing CEHA's main areas of research assessed progress and the quality of CEHA research and activities during its first three and a half years. A very positive site visit report was submitted to Nordea-fonden and CEHA in June 2012. The review panel included:

- Professor Hans Einar Krokan (Chair)
Institutt for kreftforskning og molekylær -medisin, NTNU Norwegian University of Science and -Technology, Norway
- Professor Jaber Gubrium (Vice-Chair)
Department of Sociology, University of Missouri, USA
- Professor George M. Martin
Department of Pathology, University of Washington / Institute of Molecular Biology, UCLA, USA
- Professor Elena Volpi
Division of Geriatric Medicine, University of Texas, Medical Branch, USA
- Professor Dorly Deeg
VU University Medical Center, EMGO Institute – LASA, Amsterdam, the Netherlands
- Professor Sarah Lamb
Anthropology, Brandeis University, USA

Retreats and SAB meetings

CEHA holds a retreat approximately 1-2 times per year, so that CEHA scientists can share data from ongoing projects, accomplishments, concerns and to identify areas of shared interest and opportunities for collaboration. The fall retreat usually coincides with the annual meeting of the CEHA Scientific Advisory Board (SAB; see below).

The latest retreat was held at the Danish National Museum in Copenhagen in November 2013. The retreat was attended by SAB members and included a keynote speech by Assoc. Dean for Ageing Thomas Kirkwood, Newcastle Initiative on Changing Age, Newcastle University, UK.

CEHA research seminars

The CEHA research seminar series promotes interaction between CEHA research groups and opportunity to establish collaborations among Center members and other interested researchers. The series included 5 seminars in 2009, 15 in 2010, 11 in 2011 and 7 in 2012. [I 2013 erstattet af med internal visits]

Network for Young Scholars

Network for Young Scholars (NYS) was established in 2010 by CEHA undergraduate and postdoctoral fellows to promote interdisciplinary research training, educational activities, and improve social interactions among



young CEHA researchers. The Network is coordinated by CEHA PhD and postdoctoral volunteers, who form a Steering Group.

The NYS Steering Group members are:

- Claus Desler, Associate Professor
Program 1a (2010, 2011, 2012, 2013)
- Sanne Jessen, PhD student
Program 1b (2010, 2011, 2012, 2013)
- Andreas Vigelsø Hansen, PhD student
Program 2 (2011, 2012, 2013)
- Michael Simon Nixon, PhD student
Program 4 (2011, 2012, 2013)
- Hanne Eriksen, PhD student
Program 5 (2010)
- Maja Schøler, PhD student
Program 5, (2010, 2011, 2012, 2013)
- Morten Bülow, PhD student
Program 5 (2010, 2011, 2012, 2013)
- Line Damberg, Academic Officer
CEHA Administration (2010, 2011, 2012, 2013)

Since the network emerged, 10 events have been held, with selected events described below:

Conferences on aging

In 2011 and 2012, NYS conducted two interdisciplinary conferences on aging. The first was entitled Forever Young? and the second Active Aging. The latter was



arranged within the framework of the EU Year for Active Aging (p. 98). Both conferences were open to participants outside CEHA and were very successful with nearly 100 participants each

PhD courses and workshops

NYS has offered courses and workshops including a PhD course on Interdisciplinary Communication (described below), a course on Power Point presentations, a poster workshop, a workshop on communication skills, an afternoon session on how to handle the press and a session on external funding.

Interdisciplinary Communication

During four months in 2012, ten young researchers from different CEHA programs participated in a six day practical PhD course on Interdisciplinary Communication. The initiative to the course came from NYS, and the course was designed in collaboration with communication consultant Lars Mathiasen from Swift & Gelinde APS, who also led the course.

The goal was to strengthen the scientists' written and oral skills presenting scientific projects and data in the most efficient way – both in an interdisciplinary environment and in public outreach. The participants learned how to approach scientists from other academic backgrounds, as well as the general public, the press, health politicians and institutions, etc.

The course included a mix of oral and written science communication exercises. Participants were asked to write a popular scientific article about their own research project targeting the science sections of Danish newspapers. The articles have been used in various settings, including in the Danish Gerontological Association's newsletter, which is directed at health professionals, researchers and others interested in aging research. Participants also composed two oral presentations: One targeting the first year level of high school and another aimed at researchers from different academic backgrounds than their own. All three assignments were reviewed by the instructor and the course participants. Participating PhD students were rewarded with 6.9 ECTS Points.

Internal visits

In 2013, the Network for Young Scholars (NYS) organized three full day seminars for CEHA researchers, as listed below:

- 1 *Doing qualitative research: Working with the qualitative interview, qualitative methods, qualitative empirical data and analytical coding hereof.*
Seminar arranged by Program 5 at the Saxo Dept., Faculty of Humanities, University of Copenhagen, 27 September 2013.
- 2 *Doing qualitative and quantitative research: Working with life course studies and questionnaire surveys. Working with preventive medication and focus groups.*
Seminar arranged by Program 3 and 4 at the Center for Society and Health, Faculty of Health and Medical Sciences, University of Copenhagen, 11 October 2013.
3. *Doing quantitative research in a health science lab: Working in a molecular lab – How to use cells for research. Working in a biomedical lab – How to measure fitness level and body composition.*
Seminar arranged by Program 1 and 2 at the Panum Institute, Faculty of Health and Medical Sciences, University of Copenhagen, 9 December 2013.

Selected awards and events



Professor Ian D. Hickson: Fellow of Royal Society and member of EMBO

Professor Ian Hickson (Program 1a), who joined CEHA in 2010 received the prestigious Fellow of Royal Society (FRS) award in 2010. The Royal Society acts as the UK government's chief scientific advisory group. Candidates for election to the Fellowship must have made "a substantial contribution to the improvement of natural knowledge".

Election to EMBO membership

In 2011, Ian Hickson was awarded life-long membership to the European Molecular Biology Organization (EMBO). EMBO is an organization of leading life scientists, which supports exceptionally talented scientists and promotes scientific exchange and policies in order to strengthen European research. Membership in EMBO recognizes commitment to research excellence and exceptional achievement in life science research from molecular biology and plant sciences, to neuroscience, computational neurobiology and cellular immunology.

Major grant to Professor Ian D. Hickson

Professor Hickson received a grant from the European Research Council (ERC) of DKK 18 million over five years commencing in April, 2013. The ERC Advanced Grants allow exceptional established research leaders of any nationality and any age to pursue ground-breaking, high-risk projects that open new directions in their respective research fields or other domains.



Professor Kirsten Avlund received the Andrus Viidik Prize in Gerontology

Professor Kirsten Avlund (Program 3) received the Andrus Viidik Prize at the 20 Nordic Congress in Gerontology held in Reykjavik in 2010. The prize is given every other year to an outstanding researcher in Gerontology in the Nordic countries. In relation to the prize, Kirsten Avlund published an overview article on her main research area (Fatigue in Older adults. An Early indicator of the Aging Process?, Aging Clinical and Experimental Research 2010; 22: 100-115).



Professor Michael Kjær received the Global Excellence Award and Queen Ingrid's Research Award

In 2011, Professor Michael Kjær (Program 2) and the Institute of Sports Medicine at Bispebjerg Hospital were among Copenhagen hospitals and university units awarded the Capital Region's coveted Global Excellence Award. The award came with a grant of 1.5 Million DKK. The funds are intended for teamwork and outreach activities.

Michael Kjær received the Dronning Ingrid's Forskerpris (Queen Ingrid's Research Award) in 2010. The award is given once a year to a person who provides a focused and active contribution to the Danish arthritis research and through this research advance the possibilities for preventing and treating arthritis. The award included 100,000 DKK.



Professor Albert Gjedde received the Global Excellence Award in Health

Professor Albert Gjedde from the Molecular Neurobiology of Aging Unit of CEHA (Program 1b) was among ten Copenhagen hospital and university units awarded the Capital Region's coveted Global Excellence Award in 2010. Albert Gjedde received the award because of his research in age-related brain diseases such as Alzheimer's and Parkinson's. The award included a grant of 1.5 Million DDK.



PhD Student Martin Borch Jensen received the EliteForsk Travel Grant

In 2011, HRH crown prince Frederik and Minister of Science Charlotte Sahl-Madsen awarded a number of EliteForsk Travel Grant grants to some of Denmark's most talented researchers. Among these was Martin Borch Jensen, PhD student at CEHA, who received an EliteForsk travel scholarship for 300.000 DKK. The scholarship is awarded to sixteen PhD students for travel to leading research institutions around the globe. Martin Jensen used the scholarship to perform work at the National Institute on Aging in Baltimore, USA.



Professor Kaare Christensen

CEHA appointed Professor Kaare Christensen as Honorary Professor at CEHA in late 2011. Kaare Christensen's research focuses on the genetic and environmental determinants of health and survival with a special focus on nonagenarians and centenarians. Kaare Christensen collaborated with CEHA prior to 2011, but Christensen's formal affiliation with CEHA will strengthen this relationship and promote ongoing collaborations involving CAMB and Danish Twin Studies.



Illustration: www.mir.no

Molecular aging lab – and the future Mærsk Building

The CEHA Molecular Aging Unit in the Department of Cellular and Molecular Medicine opened its renovated laboratories in the Panum building in December 2009. This event gathered CEHA researchers at a central physical location for the first time. The Faculty of Health and Medical Sciences, University of Copenhagen, supported the renovation, and the new facilities attract students, young researchers, guest professors and collaborators to CEHA. Additional renovation of the Panum Building is underway, and will be completed in 2015, at which time CEHA will occupy the first two floors of a 14 floor new research building.

Management

CEHA's management structure includes the Managing Director, Steering Committee, Strategic Advisory Committee, International Scientific Advisory Board and Administrative staff. All subordinate management report on CEHA activities and progress to the Dean of the Faculty of Health and Medical Sciences, Ulla Wewer, who is ultimately responsible for managing CEHA.

Steering Committee

The role of the Steering Committee is to discuss and ensure the progress of research, financial issues and recruitment, as well as research planning and outreach. The Chair of the Steering Committee is the Director, Lene Juel Rasmussen (Program 1a), and the members are program leaders of the six research programs. The Committee meets four to eight times a year.

Steering Group members:

- Managing Director – Professor Lene Juel Rasmussen (Chair)
- Professor Ian Hickson (Program 1a)
- Professor Martin Lauritzen (Program 1b)
- Professor Flemming Dela (Program 2)
- Professor Kirsten Avlund (Program 3); replaced by Professor Erik Lykke Mortensen in 2013
- Professor Allan Krasnik (Program 4)
- Associate Professor Lene Otto (Program 5); replaced by Associate Professor Astrid Pernille Jespersen in 2013

Meetings in 2013: 5 March, 2 April, 2 September, 22 October.

Strategic Advisory Committee

The role of the Strategy Advisory Committee (STAC) is to strengthen the strategic work of the Center. It advises on and supports the Center's prospective strategic development (e.g. mission, vision, strategy, advice on recruitment, funding, outreach, progress and results) to maximize performance. The members of STAC are: Dean (Chair), Managing Director (Vice Chair), two principal investigators representing Programs 1+2 and Programs 3+4+5, respectively, as well as an international principal investigator. STAC holds meetings ad hoc.

STAC members:

- Dean – Professor Ulla Wewer (Chair)
- Managing Director – Professor Lene Juel Rasmussen (Vice Chair)
- Professor Vilhelm Bohr (International Principal Investigator)
- Professor Michael Kjær (Principal Investigator; Program 1+2)
- Professor Erik Lykke Mortensen (Principal Investigator; Program 3+4+5)



Steering Group

From left to right: Professor Flemming Dela, Professor Lene Juel Rasmussen (Chair and Managing Director), Professor Martin Lauritzen, Professor Ian Hickson, Professor Allan Krasnik, Associate Professor Lene Otto, and Professor Kirsten Avlund.



Strategy Advisory Committee

From left to right: Professor Vilhelm Bohr, Professor Michael Kjær, Professor Ulla Wewer (Dean and Chair), Professor Lene Juel Rasmussen (Managing Director and Vice Chair), and Professor Erik Lykke Mortensen.



International Scientific Advisory Board

From left to right: The International Scientific Advisory Board members Professor Jan Vijg, Professor Sara Arber, Professor David G. Nicholls, Professor Steve Iliffe, Professor Rudi Westendorp, Professor Tone Tonjum (Chair), and Professor Diana Kuh.

Joint meetings

During the autumn 2012, the STAC meetings were held as joint meetings with selected members of the Steering Committee. The focus of these meetings was to draw up an extension application to Nordea-fonden for CEHA (2014-2018).

Participants:

- Managing Director Professor Lene Juel Rasmussen (Program 1a)
- Professor Michael Kjær (Program 2; coordinator for Program 1+3)
- Professor Erik Lykke Mortensen (Program 3; coordinator for Program 1+2)
- Professor Vilhelm Bohr (on Skype, as well as coordinator for Program 1a+1b)
- Professor Martin Lauritzen (Program 1b)
- Professor Flemming Dela (Program 2)
- Associate Professor Lene Otto and Associate Professor Astrid Pernille Jespersen (coordinators for Program 4+5)
- Professor Albert Gjedde (CEHA associate and coordinator for Program 1b)

Joint meetings in 2012: 24 July, 31 August, 1 October.

International Scientific Advisory Board

The role of the International Scientific Advisory Board (SAB) is to provide advice about strategic planning, recruitment, feasibility, progress and development of the Scientific Program. The Board proposes criteria for evaluating scientific progress and success, assists in establishing suitable external domestic and international collaborations, and advises on scientific goals. Finally, SAB helps CEHA leadership ensure that its research programs meet the highest international standards and achieve optimal scientific impact.

The International Scientific Advisory Board (SAB) includes nine distinguished scientists, representing broad scientific expertise relevant to CEHA research. The Board meets once a year,

The SAB members are:

- Professor Tone Tonjum, Head of the Board, Oslo University
- Professor Rudi Westendorp, Leiden University Medical Center
- Professor Jan Vijn, Albert Einstein College of Medicine
- Professor Leona Samson, Massachusetts Institute of Technology
- Professor Diana Kuh, MRC Unit for Lifelong Health and Aging and MRC National Survey of Health and Development
- Professor Steve Iliffe, University College of London
- Professor Sara Arber, University of Surrey, Guildford
- Professor David G. Nicholls, Buck Institute for Age Research

In 2013, the SAB meeting took place on 13-14 November 2013.

CEHA Administration

Administrative staff manage the logistics of Center activities and help coordinate research activities and programs. The secretariat is centrally located in the Panum Building, Faculty of Health and Medical Sciences. In 2013, it includes two full-time and one part-time employees: Tina Gottlieb, Head of Administration (full-time); Line Damberg, Academic Officer (full-time); Mikael Kjærsgaard Møller, Communication Officer (part-time).





Communication, outreach and media

CEHA devotes resources to promote its research activities in the international scientific community and the non-scientific community in Denmark and beyond

A selection of these activities during 2009-2013 is described below:

Website

CEHA's website, in Danish and English, provides general information about CEHA's organization, research, staff and collaborations. It also includes a calendar, announcements, newsletters and press releases. The web address is sundaldring.ku.dk (Danish version) and healthyaging.ku.dk (English version). CEHA also maintains a Facebook page.

IARU newsletters

Approximately once a year, the Faculty of Health and Medical Sciences, University of Copenhagen, publishes IARU News, a newsletter that provides information on the IARU Aging, longevity and health project/network and other relevant IARU activities. IARU News is a platform for dissemination of information on CEHA and its activities. The latest issue of IARU News was released in 2012 (healthyaging.ku.dk/international/iarunews) and the next is planned for March 2014.

Internal newsletter

The CEHA Newsletter provides a mechanism for internal communication in CEHA. Its purpose is to keep CEHA researchers, staff and close collaboration partners aware of meetings, seminars, media and administrative issues. The newsletter also describes ongoing research and promotes networking within and outside of the Center. From 2012, CEHA News was issued online, as part of the CEHA website. The newsletter is published approx. six times a year. In 2013: February, April, June, September and December (healthyaging.ku.dk/ceha-news).

Best Age and press conference

Coinciding with the IARU Congress in 2010, a press conference and round table discussion entitled "Living longer and stronger – A new approach to age" were held. More than 100 individuals attended this event, which provided high visibility coverage in the media including print publications and Danish National Radio.

A panel of invited distinguished international researchers and panellists shared views on aging, its problems, challenges and opportunities. Some discussion focused on current and future demographic change in Danish society. The Danish Minister for the Interior and Health participated in the event. The press conference solidified a collaboration between the Danish magazine Monday Morning, the University of Copenhagen and CEHA. The



Front page of the Monday Morning Supplement
The force of the elderly (Ældrestyrken).

aim of this collaboration entitled “Best Age” (Alderbedst) was to give a more varied picture of the elderly and the aging world. An online forum associated with the event provided opportunity for discussion with a panel of researchers, politicians, representatives of professional organizations and prominent public figures. The conclusions and outcomes of “Best Age” were published in the Monday Morning Supplement “The force of the elderly” (Ældrestyrken; healthyaging.ku.dk/press/alderbedsteng).

Exhibitions on Healthy Aging and CEHA Panum Building, Faculty of Health and Medical Sciences

In 2010, the exhibition “Healthy aging: A lifespan approach” opened in the Panum Building, Faculty of Health and Medical Sciences. The Medical Museion in collaboration with CEHA produced the exhibition, which ran until the closing of the IARU Congress in October 2010, enabling national and international audience participation.

The exhibition focused on healthy aging research and CEHA. It also included photos and interviews of Danish centenarians by the photographer Liv Carlé Mortensen (“100 Light Years”).

Medical Museion

During 2012, the Medical Museion, a combined museum and research unit at the Faculty of Health and Medical Sciences, University of Copenhagen, hosted a number of events with CEHA postdoctoral fellow Lucy Lyons (Program 5). Lucy Lyons’s research examines the activity of drawing as a method of communicating experiences of medical healthcare, focusing on aspects of aging. The events included an exhibition opening, a workshop and a seminar. All three events involved an artistic approach to the subject of aging. Before the exhibition opening, Lucy Lyons gave a seminar titled “Artistic research: Interventions with Medical Museion”, where she explained how she uses art in her research, and how this art became an exhibition at Medical Museion. Further, Lucy Lyons, Danish photographer Mette Bersang, and UK sculptor Joanna Sperry Jones gave a hands-on workshop at which they and the participants examined everyday medical objects through drawing, photography and much more. See www.museion.ku.dk/whats-on/events/look-again-exploring-medical-objects-through-art.

YouTube: www.youtube.com/watch?v=H0Wd9K_OEM8&feature=relmfu and www.youtube.com/watch?v=2jlvhOLnlo4&feature=relmfu.



EU Year for Active Aging, 2012

“Aging”, “healthy aging” and “aging research” is increasingly becoming part of the public agenda in Denmark as well as internationally, and EU declared 2012 as the European year for active aging and solidarity between generations. The intention was to raise awareness of the contribution that older people make to society, as well as to encourage policymakers and relevant stakeholders at all levels to take action with the aim of creating better opportunities for active aging and



Dentures from different time periods. From the Exhibition on Healthy Aging and CEHA, 2010.



Lecturer Aske Juul Lassen (Program 5) at a public meeting.

strengthening solidarity between generations. The EU Year promoted active aging in the three main areas of: Employment, Participation in society and Independent living. The Year for Active Aging formed an excellent outreach platform for CEHA, which played an active role in conferences and activities during the year (see selected activities below):

The opening conference

Denmark, which held the Presidency of the Council of the EU in the first half of 2012, opened the EU Year with an international conference on Active Aging in January. It focused on how innovation can lead to solutions for the challenges of aging related to work life, social conditions and health. CEHA Researchers Professor Kirsten Avlund and Assoc. Prof. Carsten Hendriksen (both Program 3) participated with the presentations "What do we know about the significance of physical activity" and "Good practice example: Preventive house calls", respectively.

The conference was co-arranged by the Ministries of Employment, Health and Social Affairs and Integration.

The CEHA conference on Active Aging: NYS's annual conference

Also NYS arranged a conference within the framework of the EU Year for Active Aging. It was entitled "Active aging" and took place in September. The conference attracted nearly 100 participants, including such stakeholders as representatives from Danish municipalities, the DaneAge Association, the Senior Citizen Council Aarhus municipality, Ministry of Social Affairs and Integration, and the Danish Medical Association.

Conference: Solidarity between Generations

Another conference of the EU Year was held in September in Middelfart, Denmark: "Solidarity between Generations". It focused on the qualities of developing positive relations between children, young people

and the elderly. The target group was young and older citizens with an interest in bridging the generational gap, staff from the health and care sector as well as relevant organizations and institutions. CEHA Postdoc Anne Leonora Blaakilde (Program 5) participated with the presentation "Generation gap or generational cultures?".

Lectures: Active aging – the last youth!

The Danish Nurses Organization celebrated the EU Year with the event "Active aging – the last youth!" at the Danish Nursing History Museum in Kolding, Denmark. CEHA Postdoc Anne Leonora Blaakilde (Program 5) and Professor Kaare Christensen, Danish Aging Research Center, University of Southern Denmark (CEHA associate) lectured on "Active aging" and debated with the audience. (www.dsr.dk/dshm/Sider/Nyheder/Foredragom-aktiv-aldring-.aspx).

Lectures: Active aging – Is it really necessary?

CEHA co-organized a seminar together with the Danish Society of Gerontology targeted at gerontologists, staff of the Sector for the Elderly in Municipalities, healthcare practitioners and educators, etc. The seminar was entitled "Active aging – Is it really necessary?". It focused on active aging from different scientific and practical perspectives and on how we conceptualize and use the notion of "active aging", as scientists or as practitioners working with the elderly. From CEHA, Assoc. Prof. Rikke Lund (Program 3) and PhD Student Aske Juul Lassen (Program 5) lectured with presentations on "Aging in a life course perspective" and "A critical view on "active aging"", respectively. The presentations were followed by discussions with the audience.

Radio: The immortals

During 2012, three CEHA researchers featured in a radio broadcast in the series on "The immortals" (De udødelige) on the radio channel Den2Radio. In June, Professor Kirsten Avlund (Program 3) performed in a program titled "How do we manage our daily life when we get older?" which focused on correlations between how we live and how we age, as well as on the importance of physical activity. In December, Associate Professor Claus Desler (Program 1a) and PhD Student Anette Ekmann (Program 3) participated in the Mitochondria and fatigue

program on the themes of "energy", "fatigue" and new research within these fields. See den2radio.dk/udsendelser/de-uddelige-5-hvordan-klarere-vi-vores-dagligliv-nar-vi-bliver-gamle and den2radio.dk/udsendelser/de-uddelige-23-mitochondrier-og-fatigue.

Closing conference and the Danish Academy

In December, the national closing conference focused on the brain, active work life, future focus on "active aging" as well as on local initiatives for creating social interaction between generations. As part of the agenda, a series of three television documentaries on active aging titled "Still going strong" were presented. They dealt with some of the choices seniors face when it comes to work, voluntary work and a healthy and active life. The documentaries were supported by a series of television lectures for the television series the Danish Academy (Danskernes Akademi), broadcast by the national television DR2. Professor Kirsten Avlund (Program 3) and Postdoc Bjarke Oxlund (Program 4) lectured at the Danish Academy with the presentations "Active aging. Is that what we want?" and "Life measured in numbers", respectively. These lectures are available at: www.dr.dk/DR2/Danskernes+akademi/Sundhed_Sygdom/Aktiv_aldring_Vil_vi_det.htm and at www.dr.dk/DR2/Danskernes+akademi/Sundhed_Sygdom/Livet_maalt_i_tal.htm.

Health promotion day for Turkish migrant women

In March 2012, Turkish migrant women from the Copenhagen area were invited to learn about health and healthy aging at the Bispebjerg Community Center. The aim was to inspire Turkish women to live healthier lives and to provide information about private and public health offers. At the same time, the event served as fieldwork for the CEHA research project "Cross border healthcare among Turkish immigrants in Denmark", an cross-disciplinary project between Program 4 and 5. The themed day was a great success and the women stated that they had received valuable new information about health issues. It was also concluded that there is a great unmet need among the Turkish women and, most probably among all immigrant groups, for more information about health issues. The event was arranged by Signe Gronwald Petersen, Suzan Yazici (Program 4),



Departure: "Tour de North Cap".



Scene from the CEHA television series, "Fauli, fat and finished?", DR2.

Anne Leonora Blaakilde (Program 5) and Tove Auda from the Local Committee of Bispebjerg. The collaboration with the Local Committee not only facilitated access to immigrant citizens and data collection, it also turned out to be an excellent opportunity to get an understanding of the possibilities and potential barriers for future health promotion in a local area.

Health promotion report – citizens with other ethnic background

In November 2012, CEHA published the report "Health promotion for vulnerable citizens with other ethnic origin than Danish. Experiences from ten successful organisations in the Copenhagen Area". The purpose was to disseminate positive experiences and activities recounted by leaders or volunteers working at Copenhagen NGOs aiming to help people of various ethnic origins, especially in order to promote their physical, mental and social health, and to provide inspiration and encouragement to organizations and municipalities. The intention was also to provide in-depth understandings and practical use for others wishing to help and improve the health of vulnerable citizens of non-Danish ethnicity, especially the elderly (sundaldring.ku.dk/formidling/rapport-sundhedsfremme).

CEHA on television

CEHA has been featured several times on Danish national television. Selected programs are described below:

"Tour to North Cape" at TV2

Researchers from Program 2 followed a group of men aged 46-71 years, who traveled on their own initiative from Copenhagen to North Cape, Norway (2770 km) by bicycle in 14 days. Program 2 scientists conducted tests on the athletes muscle function during and after the trip. They scientists quantified muscle energy expenditure in the cyclists using a doubly labelled water technique at 30 Mj per day, probably the highest ever measured in this age group. The scientists estimated that the cyclists performed at the limit of their capacity.

TV2 aired five documentary episodes on the "Tour de North Cape", featuring the work of CEHA researchers. The episodes were broadcasted nation-wide during primetime, along with coverage of the 2011 Tour de France. Similar coverage of the event aired on other Danish media platforms.

CEHA health promotion on national TV DR2

In 2012, CEHA started a major communication project on healthy aging in a collaboration with the production Company DocEye and the national Danish Television DR. The project was funded by Nordea-fonden. The project included five 30 minute documentaries and was entitled

“Fauli, fat and finished?” as well as material for school children and short web movies for YouTube.

The themes of the five TV documentaries were:

- Signs of aging
- The body
- The brain
- Social relations
- Welfare technologies.

As a leading thread through the documentaries, we follow the main character Søren Fauli and his own health and aging, as well as his struggle towards a healthier life. Søren Fauli is a Danish actor and film director with a humorous approach to his work. He added a funny dimension to the communication of themes of health, aging and what you can do yourself to get a healthier life with higher quality of life in the long run. The series was very well received with approx. 825,000 viewers all together during the broadcasting period in May and June, 2013. Moreover, three out of the five documentaries appeared at the top ten list of the most viewed programs. In addition, the documentaries and CEHA received extensive press coverage in both radio, TV and Newspapers, which has enhanced the health promoting effects as well as CEHA's visibility considerable in the non-scientific world.

See also sundaldring.ku.dk/formidling/fauli-fed-faerdig (in Danish).

The documentary series will be repeated for Danish viewers on DR2 during January and February 2014, and will be shared with Swedish and Norwegian national television stations SVT and NRK.

CEHA health promotion for school pupils

As part of the health promotion project described above, the national Danish Television DR also developed online teaching material for school children, available since August 2013 at the DR online educational website: www.dr.dk/skole/Samfundsfag/N%C3%A5r+jeg+bliver+gammel/N%C3%A5r+jeg+bliver+gammel.htm. The material includes articles, statistics, movies, to enhance study of biology, history and social studies by young students.



Leaflet to participants, series of CEHA lectures.

CEHA lectures on the TV channel DK4

In fall 2013, a series of five independent double lectures with CEHA researchers entitled “Healthy Aging – too little or too much of a good thing?” took place as part of the Open University of Denmark’s program (Folkeuniversitetet). Each lecture focused on a specific area of CEHA’s research in a popular science communication style. Additionally, good advice were given on how to take positive steps to a healthier aging. The lectures are listed below:

- Professor Poul Jennum (Program 1b): “The importance of sleep to a healthy aging”
- Postdoc Bjarke Oxlund (Program 4): “(Hyper)active aging: How new technology and other initiatives change life as a senior”
- Professor Michael Kjær (Program 2): “Physical activity – healthy and never too late!”
- Associate Professor Rikke Lund: “Are social relations able to create a healthier old age?”
- Professor Martin Lauritzen: “The brain and aging”

The five double lectures were recorded by the Danish television channel DK4 and were broadcasted as single lectures in ten separate programs, each program three times during the winter of 2013.



Dialoguing with citizens

In 2013, CEHA also introduced the use of social media to the general public via its Danish language Facebook page, a forum for advice, awareness and debate about healthy aging.

The main goals for the page are:

- To increase awareness about health in all life stages
- To create dialogue with researchers
- To disseminate CEHA research results and knowledge on healthy aging
- CEHA branding

The CEHA Secretariat, the communication department at the Faculty and eight CEHA researchers participates in the project, forming an editorial team. A similar project has not previously been made at the university, and it has been a pilot project to try a different approach to communicate with the general public. In the first 9 months, more than 10.000 individuals have chosen to receive updates from CEHA's Facebook page. On average, each update has actively engaged more than 50 people.

CEHA public meetings

Since November 2011, CEHA has held public meetings on issues concerning aging for the benefit of Danish citizens and all other interested parties. These meetings advertise CEHA's interdisciplinary research activities to health care professionals, politicians, health care organizations and the general public. The first meeting was entitled *Statins – only for the sick?* The target group was Danish general practitioners and other relevant professionals. Five speakers were invited, three of them from CEHA (Program 2 and 4). The meeting was attended by approximately 75 persons.

Another example took place in October 2013, where CEHA hosted a symposium and an "unconference" (event open for the public), which also included a panel debate. The event was entitled *"Career and life course – Does creativity have an expiration date?"* The target group was all interested persons in the working age. Seven speakers were invited, three of whom from CEHA (Program 3, 4 and 5). This public meeting attracted an audience of approximately 50 persons.

CEHA researchers inspire high school teachers

In 2013, the Faculty of Nature- and Bioscience and Faculty of Health and Medical Sciences hosted an "Inspiration Day" with the theme "Energy to life" for high school teachers, teaching science. Novel research within different areas was presented at workshops with 40 participants. CEHA researchers Professor Martin Lauritzen, PhD student Naja L. Hansen, Associate Professor Egill Rostrup and Professor Poul Jennum (all Program 1b) contributed with presentations on the human brain and aging, covering themes such as: processes in the aging brain; blood flow changes and energy metabolism; the

aging brain and sleep; MR scans and neurodegenerative diseases; cognition and aging.

Copenhagen Culture Night

The Copenhagen Culture Night (Kulturnatten) is one of the biggest cultural events of the city. Here, the city opens its doors to its citizens and invites them in to a plethora of cultural experiences as well as the opportunity to get a closer look at the inner workings of different segments of Danish society. In 2011, CEHA participated in this event, presenting results and research projects to a broad audience. CEHA researchers from Programs 1a, 1b and 4, presented 3 lectures on the theme "Health, disease and the good life".

In 2012, CEHA participated in the event "Unhealthy aging – stop the clock!" focused on the positive effects of exercise on health. Participants were instructed in the use of heart rate monitors and were sent out on a walk or run according to their capabilities. A leaflet was distributed with explanations and guidance on heart rate training, exercise methods and advice on healthy aging. The event was arranged by PhD student Andreas Vigelsø Hansen (Program 2) and Professor Henning Langberg (Program 3), assisted by PhD student Martin Gram Jensen and medical student Jesper Nørregaard (both Program 2).

Science theatre

In 2011, CEHA researcher Flemming Dela (Program 2) participated in the Science Theatre's performance Café Perspective. In this venue, 120 health care workers, nurses and dieticians viewed the education program developed by Professor Dela. The play focused on type 2-diabetes and life style-related diseases. The Science Theatre is conceived as a project that reveals scientific lessons in real human stories. The performances are known for their intimacy and close proximity to the audience. The scientist is on stage in his/her role as researcher, together with actors and musicians. During the intermission, there is opportunity for dialogue between audience and the Science theatre cast (including researchers).

The Science Theatre also invited selected foundations, government ministries, etc. to participate in an event at



Leaflet to participants, Copenhagen Culture Night.

the Faculty of Health and Medical Sciences. The purpose was to present the play and – afterwards – to discuss how science theater can inform citizens about health.

Presentations, conference papers and posters

CEHA researchers participate regularly in conferences, seminars and symposia in Denmark and abroad. During the years 2010-2013, CEHA researchers' presentations, papers and/or posters totalled 147, 301, 298, and 305, respectively.

Press activities

CEHAs visibility in the press continues to increase, with 87, 100, 149, 158 and 175 article appearing in the years 2009, 2010, 2011, 2012 and 2013, respectively.

UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES
CENTER FOR HEALTHY AGING

BLEGDAMSVEJ 3B
DK-2200 COPENHAGEN N

TEL +45 35 32 79 00
WWW.SUND.KU.DK
WWW.HEALTHYAGING.KU.DK