UNIVERSITY OF COPENHAGEN CENTER FOR HEALTHY AGING



CENTER FOR HEALTHY AGING Report 2009–2018

CEHA facts in brief	
External grants	>DKK 500m (EUR 67m) in addition to the Nordea-fonden grant
Publications	791 (CEHA 2009–2013); 897 (CEHA 2014–2018)
PhD projects	81 (CEHA 2019–2013) and 91 (CEHA 2014–2018)
Post-doctoral projects	54 (CEHA 2009–2013) and 48 (CEHA 2014–2018)
Visiting professors	Five (2010); nine (2011); nine (2012); eight (2013); seven (2014); six (2015); six (2016); six (2017); and five (2018)
Recruitment	Seven nationally and internationally recognized senior researchers and six new group leaders
International summer schools	• IARU Summer School Interdisciplinary Aspects of Healthy Aging (2011-2018)
	 Innovating Solutions for Aging Populations – innovative solutions to aging related challenges, including Massive Online Open Course (MOOC) (2016-2018)
International networks (selected)	IARU, EIT Health, and ABRAHAM
Communication and outreach (selected)	Keep Your Brain Healthy, People's Political Festival in 2016– 2018, Science Slams, Life on the Line game, Culture Night at SUND (2017–2018)
Awards	Center of Excellence Grant (Danish Research Council/ Grundforskningsfonden); four University of Copenhagen Excellence projects; two Global Excellence Awards; an ERC Advanced Grant; and a Novo Nordisk Foundation Challenge Grant

EDITING AND GRAPHIC DESIGN Elevate Scientific PHOTOGRAPHY Mikal Schlosser and Skipper Photography © Center for Healthy Aging, Copenhagen 2019



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EXECUTIVE SUMMARY

On 1 January 2009, the Faculty of Health and Medical Sciences in collaboration with the Faculty of Humanities and the Faculty of Social Sciences, University of Copenhagen, established the Center for Healthy Aging (CEHA) to undertake cutting-edge interdisciplinary research on aging. By 2018, the Danish foundation Nordeafonden had invested a total of DKK 300m (EUR 40m) in the Center: in June 2018, the foundation awarded an additional DKK 78m (EUR 10.4m) to fund the Center for 5 more years to enable continued research on one of today's most pressing societal challenges. The first phase of the Center (2009–2013) built up the core relational network and systems, and six research programs emerged from smaller pre-existing research groups that were transferred to our Center. During the second phase (2014–2018) the six programs were merged into three themes, and a Communication and Outreach Platform was established. The incremental integration of different types of expertise - biological, psycho-social, cultural, public health policy, and clinical – at CEHA encourages a productive exchange of knowledge and promotes synergy between the participating

groups. This cohesive and holistic approach leads to a more profound understanding of the mechanisms that underlie human aging. It also stimulates the design of experiments that upon positive evaluation will ensure practical and effective interventions to extend healthy lifespan and quality of life.

In this report we highlight CEHA's development by summarizing the aging-related research, activities, and achievements from the last decade: these will serve as the platform from which we will establish the next phase of CEHA.

The complexity of aging

The ongoing increase in life expectancy has radically changed the lifecourse of individuals and the demographic structure of our populations. This development raises key questions including how to live longer in better health and how to be active in society despite the aging process taking its toll. Research on aging must therefore consider and account for diverse biological, social, and economic factors, as well as accounting for lifestyle choices, all of which influence the lifespan, healthspan, and the well-being of an individual's life. There is a widespread misconception that human aging only leads to decrepitude and is not amenable to intervention, which has led to ageism and has arrested innovation. CEHA takes a positive attitude to growing older

and strives to translate aging research into action. Our unique conceptual framework and cross-disciplinary approach allow us to explore aging as a complex and multidimensional issue. The more perspectives we have on aging, the better we can improve individual health and prepare our healthcare system to cope with the changing demographics. Understanding aging at a cellular, individual, and societal level, together with translating this knowledge into effective interventions that enable healthy aging, are of paramount importance. CEHA aims to be at the forefront of this effort by performing state-of-the-art research, applying innovative approaches, and building sophisticated multidisciplinary networks.

Research within CEHA is of a very high international standing, reflected in an impressive scientific output (almost 1700 articles in peer-reviewed journals). Our research findings exemplify the various approaches we use to address the common societal challenge. For example, in one project, researchers collaborated with a municipality, citizens, and local organizations to investigate how the well-being and sense of social belonging among vulnerable groups could be improved. They found that a local framework that offers resources and networking opportunities enhances the sense of well-being among seniors of ethnic minorities. In another project, a large intervention study on physical activity among seniors, researchers found heavy strength-training to be the most effective type of exercise for seniors to maintain muscle mass. This finding has implications for the ability of seniors to stay independent for a longer period, because muscle mass is crucial for maintaining a high quality of life in old age. At the cellular level, one of our studies showed that cellular aging occurs when mitochondria are damaged and our repair system is weakened to the extent that it cannot fully perform its function. Researchers also found that the molecule NAD+ (formed from vitamin B3) is crucial for maintaining the repair system and that it can slow aging processes and repair damage in mice brains.

The quality of our research is also reflected in the funding we have received. This includes a Center of Excellence Grant (Danish Research Council/Grundforskningsfonden), four University of Copenhagen Excellence projects, two Global Excellence Awards, an ERC Advanced Grant, and a Novo Nordisk Challenge Grant. Besides the strategic investment made by the Nordea-fonden



Professor Lene Juel Rasmussen, Executive Director.

Danish Gymnastics and Sports Associations (DGI).

(DKK 378m, EUR 51m), we have successfully obtained external funds to the tune of DKK 586m (EUR 78.5m). We have also been able to attract several internationally recognized experts in aging such as Ian Hickson (Oxford University), Rudi Westendorp (Leiden University), and Ken Arnold of the Wellcome Trust (London), as well as a number of talented young group leaders, who will also play a key role in the further development of CEHA.

Our leadership ensures a common vision and focus on priorities and has made the Center a significant player in the international research community. CEHA occupies key positions in collaborative ventures, such as Aging, Longevity and Health – the aging initiative of the International Alliance of Research Universities (IARU) – and the European EIT Health consortium. Furthermore, CEHA has close partnerships with the National Institutes of Health (NIH) and the National Institute on Aging (NIA), which are among the world's leading research centers.

Impact and outreach: enabling change in society

A defining feature of CEHA is our citizen-centric and impactoriented approach. Much of CEHA's research is done in dialog with key stakeholders, including citizens themselves, and professionals who are working to create a good framework for citizens' healthy aging. Therefore, CEHA has, embarked on a series of collaborative projects in local communities promoting health at old age. An illustrative example of active engagement with citizens and other stakeholders is the successful outreach project "Keep Your Brain Healthy", developed in close collaboration with the Agency for Culture and Palaces and the Educating the next generation of aging researchers and health sector professionals is a priority for CEHA. The Center was instrumental in building the educational campus within the EIT Health initiative of healthy living and active aging, and our researchers actively participate in developing new educational activities in collaboration with the EIT Health partners. CEHA has built up a rich portfolio of educational offerings, which include graduate programs, PhD schools, international summer schools, and Massive Open Online Courses offered on the Coursera platform. In addition, bachelor's and master's theses and PhD projects are an integrated part of the research portfolio of the CEHA research groups. Our Network for Young Scholars (NYS) organizes career seminars and networking events that bring together students and young researchers across the Center.

Looking to the future: CEHA's next phase

The Center has made its mark on the global landscape of research and innovation into human aging, as evidenced by the progress described in this report. But there is more to be done. We will continue to undertake ground-breaking research, strengthen our relationships with stakeholders, and advance our outreach activities.

We have achieved much so far; the experience we have harvested since establishing CEHA in 2009 has been invaluable, and, importantly, practicable.

We look forward to building on these strong foundations in the years to come, working toward the goal of healthy aging for our society and making a real difference to the lives of older citizens.



CEHA: TACKLING CHALLENGES IN AGING RESEARCH

Major demographic changes across the globe are causing a rapid increase of elderly people in virtually all societies: by 2050, 20 percent of the global population will be older than 60 years of age and the number of people over the age of 80 will have tripled¹. The developed countries of the world have seen an unprecedented doubling of average lifespan over the 20th century, and it is estimated that average life expectancy of newborns will gradually increase to about 100 years during the 21st century. These trends impose economic, cultural, medical, social, and public-health challenges that will affect individuals, communities, and economies, and whose full implications are only just beginning to be fully understood and appreciated.

Aging is a leading risk factor for nearly all major chronic diseases, which increase morbidity and significantly drive healthcare costs². In Denmark, the latest population projection predicts that the proportion of those over the age of 65 will increase from 18 percent in 2018 to 24 percent in 2042, after which it will decline slightly (source: Statistics Denmark; Fig. 1). Consequently, aging is one of the most broadly recognized societal challenges that we will face in the coming decades, and the goal of 'healthy aging' is thus an urgent priority³.

Active and healthy aging has been proposed as a keystone for a

sustainable Europe. Danish policies and priorities reflect this approach to aging. Danish welfare policies outline a range of intersectoral strategies focusing on individual and structural factors affecting the ability to maintain health and live actively and independently into old age. This includes, for example, the law on preventive home visits that is now targeted on groups of elderly at risk of functional decline; reablement to help people regain the ability to look after themselves; increased focus on elderly patients in coordinated care policies across primary care, hospitals, and municipal services; housing developments; and the so-called 'dignity policy' with associated funding seeking to ensure improved innovative and holistic care for elderly at the local community level.

From an individual perspective a longer life can be seen as progress. Especially, if there is an increase in the high-quality years of life. Therefore, the growing number of elderly people will not necessarily become the burden that many fear. Rather, a growing number of functional elderlies will become a new resource, both regarding general labor as well as civil society.

Challenges in aging research

There are several overarching issues that need addressing in order to achieve healthy aging:



Figure 1. Historical and forecasted demographic changes in Denmark and globally.

- Despite the critical relevance of human aging to European society, we have limited understanding of the basic biological mechanisms that contribute to and influence it, and how these mechanisms relate to disease development.
- 2. We do not fully understand how the environment contributes to human aging and, more importantly, how the biological and environmental factors interact. This knowledge is essential to defining strategies that extend 'healthspan' – the period of years lived without disabilities, during which people can live active lives.
- The effect of genetic and lifestyle factors on health parameters must be analyzed extensively in population studies. This knowledge will be fundamental to addressing the unsustainable burden of the aging population on healthcare systems, where a dramatic shift in approach is needed.
- 4. Drugs and other interventions that target basic aging processes have been discovered that, in the laboratory setting, not only enhance healthy lifespans but also delay age-related chronic diseases and disabilities. Furthermore, a number of biomarkers for early detection of age-related pathologies have been identified. Translation of these and other emerging interventions into clinical applications will transform healthcare and, consequently, society as we know it.
- 5. The community our neighborhood plays a major role in our health; therefore, it is crucial to understand how the heterogeneity of local communities influences the promotion of health and energy of aging citizens. Thus the active collaboration and dialog with partner municipalities will constitute interventions based on research activities and generate insights into the organization and implementation of care for the elderly.

Clearly, aging is a complex process that can be understood fully only by using multiple perspectives – biological, social, psychological, and cultural. It is thus crucial to employ a multidisciplinary, holistic, cell-to-society research approach when developing interventions and policies aimed at promoting the healthy aging of individuals and societies. With this in mind, CEHA was set up in 2009.

CEHA's vision and mission

Since its inception, CEHA has consistently improved our understanding of aging at the cellular, individual and societal level, brought together researchers with diverse disciplinary backgrounds, trained many doctoral and post-doctoral students, and promoted healthy aging by engaging with a wide range of stakeholders. Extensive epidemiological, imaging, and physical exercise studies have made it possible for researchers at CEHA to identify health-promoting interventions. Furthermore, through communication studies we have shown how people can be engaged in and made aware of healthy lifestyles.

CEHA is embedded within the University of Copenhagen, an arrangement that brings numerous mutual benefits. The

CEHA'S VISION AND MISSION

The Center's vision is to take a leading role in discovering biological, social, psychological, and cultural mechanisms in aging and learning how these can be translated into preventive action.

Our mission is to produce research to a high international standard on major aspects of aging, to contribute substantially to training young researchers interested in aging and related fields, and to investigate how research findings can be used in health promotion efforts aimed at preventing unnecessary age-related decline and disease and at improving the conditions of the middle-aged and the elderly.

university provides substantial financial support including salaries of senior faculty and staff, co-financing of PhD scholarships, and state-of-the-art research facilities and environment for the Center's interdisciplinary research at the Faculty of Health and Medical Sciences.

CEHA's strategic goals are:

- to undertake cutting-edge, multidisciplinary research to better understand the aging process;
- to devise a new understanding of aging that encompasses both the individual and societal levels;
- to challenge the negative discourse of aging, frailty, and dependency by focusing instead on energy, resilience, intrinsic capacities, and (psychosocial) functional abilities;
- to communicate policy-relevant research and concrete recommendations to the relevant stakeholders in government and other sectors in Denmark and beyond;
- to contribute to the public discourse on aging by undertaking innovative outreach activities.

Furthermore, the location of the Center within the University of Copenhagen enables exploitation of the synergies between units of the faculties of Health and Medical Sciences, Humanities, and Social Sciences. Examples include the Novo Nordisk Foundation Center for Protein Research (http://www. cpr.ku.dk/) and the Novo Nordisk Foundation Center for Basic Metabolic Research (http://metabol.ku.dk/); the Copenhagen Center for Health Research in the Humanities (https://core. ku.dk/); the Center for Health Economics and Policy (https:// chep.ku.dk/); and the Center for Chromosome Stability (https:// ccs.ku.dk). Furthermore, CEHA contributes to the University with educational and training activities within the fields of aging research (e.g. innovative master's level summer schools, PhD courses, and postdoctoral projects; see "Research training"). There are thus continuous multiple synergies between the Center and larger research and strategic initiatives at the University of Copenhagen.

- 2. Global status report on non-communicable diseases 2010, WHO: http://www.who.int/nmh/publications/ncd_report_full_en.pdf
- 3. Horizon 2020 Societal Challenge 1: Health, Demographic Change and Wellbeing and Strategic Foresight which acknowledges the demographic trend of aging is reiterated as putting increased pressure on health systems

^{1.} Population Division, DESA, United Nations: http://www.un.org/esa/population/publications/worldaging19502050/pdf/81chapteriii.pdf

CEHA'S UNIQUE APPROACH

The following characteristics (see Fig. 2) highlight the uniqueness of this Center:

Multiple disciplines

We are committed to an interdisciplinary research approach to understand aging: our researchers are drawn from multiple disciplines, encompassing biology; health, medical, and social sciences; and humanities from universities around the world. The vibrant infrastructure of CEHA embedded in the University of Copenhagen, together with a strong leadership team and many established international collaborations, ensures that the multidisciplinary approach is effective and synergistic.



Stakeholders

Figure 2. CEHA's approach is interdisciplinary and holistic, and focuses on engaging with multiple stakeholders through impactful communications and outreach.

Holistic approach

We seek to understand all dimensions of aging – biological, social, psychological, and cultural – and at all scales, ranging from the cell through individuals to society. This approach to understanding aging is quite unique and only a few institutions around the world take this type of approach.

Scientific excellence

We promote rigorous and innovative research on aging by bringing together top international scientists to address important questions from multiple perspectives. A common conceptual framework for all researchers at the Center, regardless of discipline, ensures that we stay focused on our main priorities and remain successful in translating our findings into innovative health-promotion interventions to aid healthy aging.

Capacity building

We train the next generation of aging researchers via our highquality educational programs, with an emphasis on the holistic approach and ensuring excellent communication skills when interacting with the media, citizens, and stakeholders.

Outreach

We engage with a wide range of stakeholders including the Danish public, policymakers, municipalities, and businesses to communicate our research so as to inform concrete interventions and policies to promote healthy aging.

Constant evolution and challenging stereotypes

We are a dynamic center that tunes our research and adapts our engagement to respond to changing scientific and social issues. We are committed to contributing to the education of citizens by challenging ageism in our society and the habitual thinking about lifecourse that postulates that becoming dependent and disabled is inevitable with aging.

CEHA is emphasizing multidisciplinary collaborations among CEHA scientists and between CEHA scientists and their national and international colleagues, because we understand that collaboration stimulates creativity and growth, leading to synergy between the participating groups. We hope that this approach





Figure 3. Development of CEHA 2009–2018.

will hasten progress and allow each researcher to accomplish more than he or she could accomplish working independently.

CEHA coming of age

Since its emergence in 2009 by a generous donation from Nordea-fonden, CEHA has championed interdisciplinary research on aging that has often had a medical and scientific interest in disease and frailty. In the second grant period (2014-2018), CEHA research also focused on prevention and health promotion. Simultaneously, CEHA has consistently addressed the societal and cultural dimensions of aging, which has developed into collaborative projects in Danish municipalities to improve health and well-being.

Since its launch, CEHA has gone from consisting of highlevel monodisciplinary researchers primarily from the University of Copenhagen to consisting of high-level multidisciplinary aging researchers from the University of Copenhagen as well as international colleges. The Center, which began with 110 employees in 2009, now boasts 235 employees in 2018. This has resulted in a steadily growing number of individual research collaborations (see publications: www.healthyaging.ku.dk/ publications/) and participation in prestigious international collaborations and networks such as IARU, the Alliance for Biology of ageing Research And Healthy Ageing Multidisciplinary biobanking approaches (ABRAHAM), and EIT Health.

CEHA (2009–2013)

CEHA was set up to promote leading-edge research on human health and aging, with an emphasis on understanding how human behavior and lifestyle choices modulate life trajectories and health outcomes from a cell-individual-society perspective. During this initial period, the Center established a solid research platform that has provided new knowledge and insights into the mechanisms of aging at the societal and individual levels. For example, our research showed that endogenous (cellular/ biological) stress and exogenous (social, interpersonal) stress influence both lifespan and healthspan.

Furthermore, while early life experiences can have delayed negative consequences in later life, the converse is also true. Conditions in adult life can (at least partially) compensate for damaging early life experiences, and genetic and social factors in early life can protect against strains and stress in late life. Knowledge about such early signs of aging in midlife is important to identify vulnerable individuals and prevent frailty, disability, and comorbidity becoming manifest. This was carried out by a set of jointly programmed projects that emerged from various disciplines within the field of aging (Fig. 3).

CEHA (2014–2018)

The second phase of CEHA (Fig. 3) was launched to contribute to basic knowledge of aging and to lay critical and valuable ground for promoting healthy aging in the Danish population through intervention and social innovation projects. Research during this period built on knowledge gained from CEHA (2009–2013) and the large number of interdisciplinary collaborations that have been facilitated by the establishment of the Center.

A unifying theme in CEHA (2014–2018) has proved to be the strong significance of 'energy' in aging. One of the key findings is that people's ability to maintain active lifestyles (active aging) promotes a specific version of good old age based on a strong body and an active physical and social existence to improve the quality of life of older people. By the end of 2018, CEHA had delivered a series of multidisciplinarily devised, and collaboratively executed, interventions on how people can age more healthily (see later sections). These interventions form the basis for new outreach projects in the coming funding period.

Developing an engagement strategy

Outreach and stakeholder engagement have grown in importance as CEHA has evolved. In 2014, CEHA strengthened this area to expand the focus beyond citizens. We developed a stakeholder strategy for the 2014–2018 period that targeted decision-makers, organizations for the elderly, healthcare professionals, and selected patient organizations. The Center now regularly undertakes joint events with organizations, arranges stakeholder meetings for selected stakeholders, and contributes with columns in municipal healthcare newsletters and Danish newspapers. In 2017 we initiated the "Keep Your Brain Healthy" project in collaboration with DGI and the Agency for Culture and Palaces. These initiatives and our experiences from the past 5 years have paved the way for the ambitious outreach program to be implemented in the next period (2019–2023). CEHA will further transform itself toward an integrated group of researchers and innovators that will use their unique skills to implement intervention and outreach projects in collaboration with key stakeholders.

ORGANIZATION, MANAGEMENT, AND RECRUITMENT

Organization

CEHA is organized as a network of research units: by the end of 2018 it spanned seven different departments within three University of Copenhagen Faculties (Humanities, Social Sciences as well as Health and Medical Sciences) and in three hospitals in the Greater Copenhagen Area (Hvidovre, Glostrup, Bispebjerg). From 2014–2018, the research units were organized in three multidisciplinary research themes (I-III), (Fig. 4).

Since August 2017, a majority of CEHA researchers, including the management and secretariat, have been 'centralized' on the 2nd and 3rd floors of the Mærsk Tower. This 15-storey building with state-of-the-art facilities and laboratories is designed for interdisciplinary research, and it provides unique opportunities for interaction and collaboration among CEHA researchers. It is also a place for interaction with non-CEHA faculty and staff working in aging-related fields, such as biology, applied physiology, neuroscience, behavior, anthropology, economics, and ethnography. Highly popular guided tours are opening the Mærsk Tower to the public: since its opening, more than 27,000 visitors have been able to have a closer look at the building's architecture, art, and research facilities, including CEHA.

Management and advisory boards

The administrative duties of the Center are carried out by the Executive Director, a Steering Group, an International Scientific Advisory Board, and Administrative Staff. The Executive Director Lene Juel Rasmussen and Deputy Director Rudi Westendorp (appointed in October 2016) report to the Dean of the Faculty of Health and Medical Sciences, Dr Ulla Wewer, who is ultimately responsible for all CEHA activities. CEHA management staff are located within the Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences.

Operational tasks at CEHA, including strategic planning and development, and coordination between themes, are agreed upon by the directors and executed by the Executive Director. The administrative staff manage logistics and help coordinate research activities and programs, working closely together with the Communication and Outreach Platform. The Secretariat is centrally located in the Faculty of Health and Medical Sciences and consists of an Administrative Team and Communications Team. The main oversight committee for CEHA is the Steering Group. The group members include leaders of each of the three CEHA themes (Fig. 4), as well as the leader of the Communication and Outreach Platform (see Appendix A.1 for the list of members). The Steering Group provides oversight for research activities, financial issues, recruitment, strategic planning, and outreach. The Chair of the Steering Group is the Executive Director and the Co-Chair is the Deputy Director.

CEHA is supported by an International Scientific Advisory Board (SAB), which reports to the Dean. It includes eight distinguished scientists, representing broad scientific expertise relevant to CEHA research.

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

Internally, CEHA is supported by an Internal Advisory Committee, which includes the Dean, the Deputy Director, the Executive Director, and two internationally renowned researchers, Professor Vilhelm Bohr (NIH) and Professor Carlos Mendes de Leon (University of Michigan School of Public Health, USA). The heads of departments and Deans of the Faculties of Humanities and Social Sciences are also involved through coordinated meetings. The Executive Director meets the Dean twice every month. The Steering Group meets approximately eight times a year, while CEHA management and staff meet with the SAB once a year in connection with the annual SAB meetings. Support from the Internal Advisory Committee is requested on an ad hoc basis.

Staff

As of 31 December 2018, CEHA had 73 full and part-time employees (funded by the Nordea-fonden grant) plus 162 employees paid by external funding (non-Nordea-fonden funding), including staff paid by the University of Copenhagen. Of these staff, there are 54 senior researchers; 31 postdocs; 10 guest researchers; 55 PhD students; 23 research assistants;



Figure 4. CEHA's organization. Departments associated with a theme are listed below the respective theme.

30 bachelor/master/pregraduate research students; and 13 lab technicians. 91 PhD projects were completed in CEHA (2014–2018). Among the research and research support staff (PhD students apart), 20 are from Theme I, 74 are from Theme II, and 77 are from Theme III. Figure 5 shows how the staff composition has changed through time.

CEHA has a strong Visiting Professor Program, which has led to CEHA hosting many guest professors for stays of a few weeks to several years. For each year the number of guest professors at the CEHA were: five (2010); nine (2011); nine (2012); eight (2013); seven (2014); six (2015); six (2016); six (2017); and five (2018).

Recruitment and researcher support

CEHA's recruitment strategy 2014–2018 was to 1) recruit at least one or two internationally recognized researchers, and 2) create career opportunities for top young scientists by appointing a number of junior group leaders. The Visiting Professor Program is one of the tools we have used to achieve these goals. We consider this ambition achieved, having recruited seven nationally and internationally recognized senior researchers and six new group leaders (named and described below).

Top recruits

In 2010, Ian Hickson (Oxford University, UK), a leading expert

in genome maintenance systems, was recruited as Professor in Genome Stability and Aging in CEHA's Molecular Aging Unit (Theme III). The same year, he received the Fellow of The Royal Society award. In 2013, Professor Hickson received an ERC Advanced Grant, and in 2015 he obtained a Center of Excellence Grant to establish the Center for Chromosome Stability.

Karsten Vrangbæk started as Theme I leader in 2015. He is Professor at the Political Science and Public Health Department and Director of Center for Health Economics and Policy, University of Copenhagen. Professor Vrangbæk is involved in international research and educational activities focusing on health policy, health systems analysis, economic consequences of aging populations, and public–private collaboration in health- and elderly care.

In 2015, Rudi Westendorp, Leiden University Centre, Netherlands, joined CEHA's Theme II as Professor of Medicine at Old Age. At CEHA, he is investigating innovative solutions for promoting the length and the quality of life of older people. Professor Westendorp has since 2016 been responsible for CEHA summer schools, and he also played a key role in the joint proposal for a Knowledge and Innovation Community (KIC; a European Union (EU) Horizon 2020 initiative; see "Research collaborations and networking"). In 2018, Professor Westendorp received an NNF Challenge Programme Grant with Lene Juel Rasmussen and Tom



Figure 5. Staff composition over time.

Kirkwood as co-applicants.

In 2016, Tom Kirkwood was employed as Professor of Biogerontology (Theme III) in a strategic role in interdisciplinarity and development of the research and training environment. Over the last 12 years, he led the growth of the Newcastle University Institute for Aging, UK, to become one of the leading centers for aging research worldwide. He has made notable contributions in the fields of evolutionary genetics of aging and longevity, molecular mechanisms of cellular aging, and in the relationship between intrinsic aging and age-related diseases and frailty.

Ken Arnold was appointed Creative Director of Medical Museion and Professor at Copenhagen University in June 2016. He also holds a position as Creative Director at the Wellcome Trust, London, where he focuses on developing international opportunities for cultural collaboration and exchange. He holds a PhD in the History of Science from Princeton University and a BA in Natural Sciences from Cambridge University. He regularly speaks and writes on museums and the relations between the arts and sciences.

As a result of the Visiting Professor Program, Professor Linda Bergersen and Dr Tiago Moreira were recruited on a part-time basis to CEHA. After her visiting professorship Bergersen (Professor of Physiology at the University of Oslo, Norway) started as part-time Professor of Neurobiology of Aging at CEHA in 2013. Her main research area is brain energy production and neurotransmission. Dr Tiago Moreira (Durham University, UK) also joined CEHA during 2016–2017 as an Adjunct Professor following several years as a guest professor in Theme I. His research explores the interaction between knowledge and healthcare, especially the role and use of health technology.

Young group leaders

In 2014, Associate Professors Maria Kristiansen (Department of Public Health) and Bjarke Oxlund (Department of Anthropology) from the University of Copenhagen were recruited as group leaders in Theme I, which focuses on community-based interventions. Associate Professor Nete Schwennesen replaced Bjarke Oxlund when the latter moved to a new position at the Danish Institute for Human Rights in 2017. Associate Professor Maria Kristiansen is involved in health services research, social and ethnic inequality in health, and access to healthcare among older people. In 2018, she was among 24 young researchers selected to join "UCPH Forward", a talent program for excellence in research. Associate Professor Schwennesen's research is based on medical anthropology, sociology, and science and technology studies, using ethnographic fieldwork to explore healthcare technologies in the context of rehabilitation and promotion of active aging. CEHA has been successful in retaining talented young researchers who started their career at the Center as PhD students and postdocs, and who were recruited as associate professors by 2018. Examples include Steen Larsen, Abigail Mackey, Mansour Akbari, and Claus Desler.

At a junior level (assistant professors), CEHA has recruited: Javier Peña-Diaz from the Federal Institute of Technology in Zurich, Switzerland, in 2016 (Theme III; focus on DNA repair in aging-related disease); Andrés López-Contreras from the Spanish National Cancer Center, Spain, in 2014 (Theme III; focus on impact of genomic instability on aging); Morten Scheibye-Knudsen from the NIH in 2015 (Theme III; focus on aging interventions, DNA damage, mitochondria, metabolism, neurodegeneration); and Simon Bekker-Jensen from the Center for Protein Research, Denmark in 2016 (Theme III; focus on cell biology, cell stress, aging).

All young group leaders will continue their work and research for the coming period 2019–2023.

Support from the Communication and Outreach Platform

CEHA is giving high priority to communicating its research and knowledge – not only within the scientific community, but also to a wide range of stakeholders and the general public. The Communication and Outreach Platform was established to support and train the researchers to communicate via mass media, social media, and events to disseminate results and knowledge efficiently. In addition to scientific journals as a means of publishing findings, CEHA uses a broad cross-media form of communication and reaches its target audience via many channels of communication. The Platform is also prepared to blaze new trails (see "Societal impact: engagement, outreach, and communication" for details).



RESEARCH COLLABORATIONS AND NETWORKING

CEHA collaborates actively with several institutions and networks, both within Denmark and around the world (see Fig. 6). Apart from scientific and outreach advantages, these collaborations enforce the mobility of researchers and students and play a key role in CEHA's recruitment strategies at all levels. Below we describe some of these collaborations.

Selected international collaborations

CEHA and the University of Copenhagen participate in and interact regularly with the 10 other leading research universities in the International Alliance of Research Universities (IARU, http://www.iaruni.org/). IARU's Aging, Longevity and Health (ALH) initiative is an important network within the international aging research community, and its goals – including promoting institutional joint working – align well with CEHA's research goals. The 11 international research-intensive universities involved have a shared global vision and a commitment to educating future world leaders and to examining aging as a 21st-century issue with a multidisciplinary approach.

IARU network

CEHA has from the beginning been the driving force within the ALH network. This work has led to permanent activities such as the annual international IARU Summer School Interdisciplinary Aspects of Healthy Aging and the IARU Graduate Student Conference (on rotation between IARU partners since 2012). In 2014, CEHA further empowered the IARU network by forming the ALH Steering Committee. Professor Lene Juel Rasmussen was the first chair (2014-2016), followed by Professor Hiroko Akiyama, University of Tokyo (2016-2018), and the current chair Professor Sarah Harper, University of Oxford. This structure gave new energy to the network and increased the focus on research and funding. In 2016, four common research focus areas were defined: Biology of Aging; Cohorts, Cognition and the Brain; Changing Demographic, Economic, Social, Physical Environments and Healthy Aging; and Technology and Aging. At the Steering Committee meeting in Singapore in October 2018, a new joint research framework – developed by Associate Professors Maria Kristiansen (CEHA/University of Copenhagen) and Louise Lafortune (Cambridge University) - was presented with the ambition to implement a shared strategy for new projects and

applications.

CEHA has also hosted highly successful events, conferences, and workshops for IARU members and other interested scientists such as: the international congress on ALH, which included a press conference, in 2010; and two international congresses (*Cultures of Health and Aging?* and *Biology of Aging*) as well as an IARU Graduate Student Conference in 2014 (*Aging Research and Scientific Careers*). These activities have attracted attention to CEHA and strengthened relations between researchers and their students.

The close association between CEHA and IARU is a cornerstone in the efforts to internationalize CEHA.

Network on basic and translational aging research

In 2011, CEHA joined forces with major research centers in Groningen (The Netherlands), Cologne (Germany), and Newcastle (UK) to form a research network for basic and translational science in healthy aging. CEHA also has an active collaboration with the NIH/NIA via Professor Vilhelm Bohr, who is associated with CEHA as a group leader in Theme III. Professor Bohr has been instrumental in the establishment of CEHA. The close collaboration with Professor Bohr has been fundamental in securing excellent recruitments to CEHA such as the professors lan Hickson and Linda Bergersen and Associate Professor Morten Scheibye-Knudsen and in the sharing of infrastructure with the NIH/NIA.

EIT Health

In 2014, the European Institute of Innovation and Technology (EIT) launched a call for Knowledge and Innovation Communities (KICs), as part of the larger EU initiative, Horizon 2020. The KICs aim to encourage stakeholders in education, technology, research, business, and entrepreneurship to establish excellencedriven partnerships and provide innovative solutions to tackle the grand challenges (health, climate, bio-economy, etc.) facing the EU. The winning consortium – EIT Health – today consists of more than 50 core partners (and their 90 associate organizations). These include leading businesses, public partners, research centers, and universities from nine EU countries (including the University of Copenhagen).

Global		
IARU	AU, CH, CN, DK, GB, JP, SG, US, ZA	
ABRAHAM	CA, DK, GB, NL, US	
RUBICON	AU, DK, GB, IN, IT, NL, USA, ZA	Nordic (DK ELIS NO SE)
InterAge	DK, US	NormaCare
COPS	AI, BE, DK, EE, ES, GB, NL, NO, SE, US	SIA - Social
EU		Inequalities in Aging
EIT Health	BE, CH, DE, DK, EE, ES, FR, GB, HU, IE, NL, PO, PT, SE	
ECRIN Nutrition hub	AT, BE, CH, CZ, DE, DK, EE, ES, FI, FR,	Denmark
	GR, HU, IE, IS, IT, NL, NO, PO, PT, SE, UK	SMK - Health, Human and Culture
TENSINaC	DK, GB, SE	Techno-Anthropology Lab
Activity- and Health-enhancing	DK, FI, IT	Aalborg University
MouseAge	AT, BE, CH, CY, DE, DK, EE, ES, FR, GR, HR, HU, IE, IL, IT, LT, LV, NL, NO, PT, RO, RS, SL, TR, UK	Danish Aging Research Center (DARC)

Figure 6. Overview of CEHA's collaborations.

The goal of EIT Health is to promote entrepreneurship and develop innovations in healthy living and active aging, providing Europe with new opportunities and resources to improve quality of life and healthcare. EIT health revolves around three programs: 1) Accelerator for business development, 2) Campus for educational activities, and 3) Innovation Projects. EIT Health provides opportunities for new and strengthened collaborations between CEHA, the University of Copenhagen, IARU universities, and beyond. Since the launch of EIT Health, CEHA has been involved in several activities in the campus program. Examples include: 1) the Innovating Solutions for Aging Population summer course, developed in collaboration with the Copenhagen Business School, Novo Nordisk A/S, and the innovation and entrepreneurship hub SUND Vækst (2016); 2) BRIDGE – a network involving the University of Copenhagen, Copenhagen Business School, Uppsala University, and Erasmus University Rotterdam to share and implement pedagogic and digital didactic practices in connection with a summer school at each campus (2017); 3) Healthy Aging in 6 steps, a MOOC on healthy environments and citizen involvement, in collaboration with the Leyden Academy on Vitality and Ageing and Delft University of Technology (2017); and 4) EpiDEMprev, a European PhD program on Epidemiology of aging and Dementia Prevention in partnership with Universidad de Coimbra and Imperial College London (2018).

ABRAHAM network

CEHA is also active in (ABRAHAM, which was created in 2010 and includes researchers, companies, governmental institutions, and patients/citizens. ABRAHAM aims to create a transatlantic network with partners from the EU, the USA, and Canada to enhance integration in the field of biobanking and basic aging research in order to contribute to the goal set by the European Commission to add two extra healthy years to life by 2020. This collaborative effort harmonizes, standardizes and exchanges data and materials from biobank and cohort studies, facilitates shared use of infrastructures, facilities and expertise, and enables exchange visits of personnel to participating institutes exploring options for new projects and/or pilot studies.

This network builds 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 are: the University Medical Center Groningen (The Netherlands), University of Copenhagen (Denmark), University of Newcastle upon Tyne (UK), Mayo Clinic (Minnesota, USA), and McGill University (Montreal, Canada), all of which have extensive collaborations with industries in the food, pharmaceutical, and medical technology sectors as well as experience in human clinical trials. Since 2013 CEHA has, together with the ABRAHAM network, participated in the Annual Alliance for Healthy Aging Conference series, the EU Marie Curie ITN MARRIAGE, as well as several EU research and infrastructure applications.

MouseAge

A key prerequisite for developing new interventions for agerelated conditions and promoting healthier aging is the availability and use of mouse models for preclinical research studies. There is currently a lack of such models and a need for standardized methodologies to test and evaluate interventions. Therefore, to improve the quality of European aging research, coordinated interdisciplinary action is needed to standardize methodologies and guidelines for animal welfare, and to define endpoints. A centralized model for storing and disseminating information about these models and technologies is also needed. Accordingly, *MouseAge* – in which CEHA participates – was launched in 2014 as a European COST Action network for preclinical testing of interventions in mouse models of age and age-related diseases. This Action proposes to set-up a highly interactive and flexible European network, which will create a critical mass of cross-disciplinary scientists, clinicians, and industrial partners to reach consensus on ways to test preclinical interventions in aging mice. It will consolidate current best practices across leading European institutions and researchers, maximize resource efficiency, and provide a platform to help train the next generation of scientists. More information: https:// www.mouseage.eu/

National collaborations

Within Denmark, Themes II and III in CEHA actively collaborate with the Danish Aging Research Center (DARC) at the University of Southern Denmark. This collaboration has resulted in several scientific publications, as well as education of PhD students that have been co-supervised by CEHA and DARC researchers.

Theme III CEHA researchers also collaborate closely with research groups at the Novo Nordisk Foundation Center for Protein Research, University of Copenhagen. These collaborations have also resulted in high-level scientific publications as well as in the recruitment of Assistant Professor Simon Bekker-Jensen to Theme III. CEHA Theme I-III researchers have multiple ongoing collaborations with clinical departments at several Danish hospitals in the Greater Copenhagen area that are crucial for several successful CEHA projects such as LISA, COLOSMA, and LIFESTAT. See "CEHA (2014–2018) overview" for details.

Collaborating with municipalities

Much of CEHA's research is done in dialog with citizens as well as all the professionals who are working to create a good framework for citizens' healthy aging. Municipalities are one of the natural collaborative partners for our research because they have political responsibility for many of the areas that affect healthy aging.

The *Transferring healthy aging* is an umbrella study in Theme I exploring implementation of diverse interventions and the tension between context-dependency and efficacy on the one hand, and transferability of healthy aging interventions on the other. The study includes:

- community-based loneliness intervention targeting elderly community-dwelling adults to be followed longitudinally and compared with loneliness interventions in other municipalities;
- transferability of healthy aging interventions across contexts, target groups, and organizational settings;
- community-based intervention for ethnic minority elderly women conducted in a private-public partnership;
- register-based study focusing on healthcare utilization across diverse ethnic and socioeconomic groups adding further to the focus on healthy aging, and in particular inequalities in health and disease in older age;
- series of user-involvement activities with the participation of experts, health professionals, interest organizations, private business, and elderly people focusing on diet, physical activity, and social relations.

Stakeholder strategy

The stakeholder strategy (further described in "Societal impact: engagement, outreach, and communication") has provided a framework for engagement and external collaborations in the past 5 years. The primary target groups are elderly organizations,



municipal decision-makers, healthcare professionals, and selected patient organizations. The aim is to highlight and discuss healthy aging with stakeholders through events, workshops, seminars, and lectures organized by CEHA and by engagement during joints projects and events. A successful example of this

Mærsk Tower, 2018.

is CEHAs participation at the People's Political Festival in 2016, 2017, and 2018. More importantly, our strong communication efforts and work with stakeholders has paved the way for new types of collaborations that integrate research, communication, and implementation.

RESEARCH THEMES AND PROGRAMS CEHA (2009–2013): A brief retrospective

From 2009 to 2013, the goal of CEHA was to conduct leadingedge research on human health and aging, with an emphasis on understanding how human behavior and lifestyle choices modulate life trajectories and health outcomes. We also aimed to identify mechanisms to develop and implement diagnostic and/or preventive interventions that minimize health burdens associated with normal and accelerated aging and aging-related chronic disease. The common thread running through this research period was 'frailty' and the research was centered on five research programs. Below is a brief description of each program, followed by a description of the major cross-disciplinary projects conducted during this phase – more details in Appendix A.2.

Programs

1A. MOLECULAR AGING – focus on oxidative stress, lactate signaling, calcium homeostasis, neuroenergetics, mitochondrial dysfunction, and neurodegenerative diseases. **Program leader**: lan Hickson

The Molecular Aging Program studied the role of DNA repair in conserving genome instability and counteracting aging. We demonstrated how defects in DNA repair can cause premature aging. 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 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.

1B. NEUROSCIENCE – focus on oxidative stress, genomic instability, calcium homeostasis, neuroenergetics, mitochondrial dysfunction, and neurodegenerative diseases. **Program leader**: Martin Lauritzen

The Neuroscience Program explored how aging influences brain function in the context of animal model systems and a cohort of Danish men born in 1953. We showed 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 the 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 suggests that our test-persons may be at risk of developing AD and that an intervention should be carried out. The predictive value of this finding is being assessed in the project carried out in CEHA from 2014 to 2018.

2. MUSCLE AND MATRIX – focus on understanding metabolic, genetic, and lifestyle factors that influence skeletal muscle function throughout the lifecourse.
 Program leaders: Michael Kjær and Flemming Dela

The Muscle and Matrix Program studied how regular physical activity improves inflammatory status, and maintains muscle mass and function especially in old age. We showed that morbidly obese subjects can demonstrate improved glucose tolerance after an intensive lifestyle intervention, while the abundance of muscle ceramide and triacylglycerol remain unchanged. We also demonstrated that consumption of a fatrich diet does not influence muscle ceramide content. In addition, we showed that high-intensity interval training promotes reversal of insulin resistance in patients with type-2 diabetes.

3. BODY AND LIFE – focus on lifecourse perspective on aging. **Program leaders**: Kirsten Avlund and Erik Lykke Mortensen

In the Body and Life Program we studied the influence of lifecourse processes on frailty and specific signs of early aging. The largest project and the most significant accomplishment of the Program was the Copenhagen Aging and Midlife Biobank (CAMB). The completion of the CAMB database is a milestone not only for Program 3 researchers, but for CEHA and Danish aging research in general. CAMB has provided unique possibilities for collaborations among CEHA researchers on 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. Program 3 researchers also used other cohorts such



Figure 7. Overview of multidisciplinary projects in CEHA 2009–2013.

as the Glostrup 1914 cohort and register data to identify important determinants of age-related changes across the lifespan.

4. SOCIETY, CULTURE AND HEALTHCARE POLICY – focus on preventive medication, health services, and health of an aging population.

Program leader: Allan Krasnik

The research in Program 4 applied 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. We developed tools for functional monitoring to support decision-making in general healthcare practice, and study results identified and analyzed successes and failures of different initiatives for better coordination of care. Aging populations are at risk of multiple chronic diseases, for which new therapeutic and/or preventive care options may be available. International comparative studies were initiated to study the continuity and quality in preventive care for aging populations in health organizations using integrated and comprehensive mechanisms. If they receive well-coordinated high-quality care, the aging population could experience both a better quality of health along with increased lifespan.

5. HEALTH IN EVERYDAY LIFE – focus on how people deal with aging in their everyday lives to maintain or increase their quality of life.

Program leaders: Lene Otto, Astrid Jespersen, and Thomas Söderqvist

Program 5 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.

Multidisciplinary projects

In addition to the main focus of each Program described above, several multidisciplinary projects were conducted across the programs (Fig. 7).

FATIGUE AND EVERYDAY LIFE – experiences of fatigue among healthy people and people suffering from apoplexy (Programs 1b and 5).

Coordinator: Lene Otto (Astrid Jespersen)

Combining the expertise of ethnological/qualitative approaches (M Andersen from Program 5) and healthcare professionals from the outpatient clinic and neurological department at Glostrup Hospital (Paul Jennum and Hysse Birgitte Forchammer, Program 1b), we analyzed the experiences of fatigue among healthy people and people with apoplexy. We found among other things that current rehabilitation practices are based on the idea of "a return to the everyday life one had before the incident." However, this ideal fails to recognize that incidents in late life mark a threshold of a new life phase, often characterized by increased frailty (PhD Thesis A question of location – life with fatigue after stroke; Andersen M, 2013).

CROSS-BORDER HEALTHCARE – among Turkish immigrants in Denmark with particular focus on the elderly (Programs 4 and 5). **Coordinator**: Lene Otto (Astrid Jespersen)

A joint project between ethnology and public health combining a quantitative study on the use of healthcare services among Turkish immigrants with a qualitative study⁴ among 30 Turkish immigrants investigating the concrete health practices such as the practice of utilizing crossborder healthcare services and medication consumption. Among other things the project found that elderly Turkish immigrants engage in highly complex cross-border health practices, which are often unrecognized by the Danish health authorities.

4. Nielsen SS, Yazici S, Petersen SG, Blaakilde AL, Krasnik A. Use of cross-border healthcare services among ethnic Danes, Turkish immigrants and Turkish descendants in Denmark: a combined survey and registry study. BMC Health Services Research 13 (12, 1): 390, 2012.

CONTINUITY OF CARE – an international comparative analysis of tools and settings for coordination of preventive drug medication (Programs 3, 4, and 5). **Coordinator**: Allan Krasnik

This cross-national study was done in collaboration between public health and medical researchers in Denmark and the USA. By conducting qualitative interviews with providers and health managers in the Veterans Health Administration and in the Danish Healthcare System, we identified elements of importance for the provision of care to vulnerable people with type-2 diabetes and ways to improve the quality of care to vulnerable type-2 diabetes patients in Denmark.

FATIGUE (LOW SUBJECTIVE VITALITY) in middle-aged men correlates with levels of reactive oxygen species, dNTPs, DNA damage, body mass index, and physical performance (Programs 1a, 2, and 3).

Coordinators: Kirsten Avlund and Vilhelm Bohr

By combining the experience in DNA metabolism in program 1 with the epidemiological experience of program 3 we detected novel biomarkers in a human cohort with individuals with fatigue⁵. This insight may help us in future to provide earlier indications of signs of fatigue and therefore provide earlier intervention.

SKIN AND TISSUE CHARACTERIZATION of a patient with apparent dimorphic rates of skin aging (Programs 1a and 2). **Coordinator**: Michael Kjær

By combining the molecular expertise within DNA, the imaging experience within electron microscopy, the physiological knowledge within connective tissue, and the clinical approach

KEY OUTCOMES OF CEHA (2009–2013)

- Science 791 publications
- Capacity-building

81 individual PhD students/employed-enrolled and 54 individual postdocs/employed during the five years of CEHA (2009–2013)

- Funding from external grants more than DKK 223m (approximately EUR 30m) in addition to the Nordea-fonden grant
- Awareness 672 media mentions (of which 47 on radio; 41 on TV)

to dermatology, it was possible across disciplines to carry out this study that supported the idea that lack of elastic fibers in skin allowed for enhanced local skin proliferation⁶.

THE INTERDISCIPLINARY NEUROSCIENCE PROJECT (Programs 1a, 1b, and 3). **Coordinator**: Martin Lauritzen

This project was initiated as a collaboration between the Research Centre for Prevention and Health, The Capital Region of Denmark, the Department of Public Health at the University of Copenhagen, and diagnostic departments at Rigshopitalet Glostrup and Panumbased research groups at the Center for Healthy Aging. The overall purpose has been to identify early indicators of cognitive decline in a Danish birth cohort of males born in 1953, as indicated by repeated follow-up examinations of cognitive function since childhood. The study^{7.8} has already now provided important information of potential biomarkers of cognitive decline.

- 5. Maynard S, Keijzers G, Gram M, Desler C, Bendix L, Budtz-Jørgensen E, Molbo D, Croteau DL, Osler M, Stevnsner T, Rasmussen LJ, Dela F, Avlund K, Bohr VA. Aging (Albany NY) 5(11): 850–64, 2013.
- 6. Nygaard RH, Maynard S, Schjerling P, Kjaer M, Qvortrup K, Bohr VA, Rasmussen LJ, Jemec GB, Heidenheim M. Acquired cutis laxa localized to the upper body in an adult female. Case Reports in Dermatology 8: 42–51, 2016.
- 7. Hansen NL, Lauritzen M, Mortensen EL, Osler M, Avlund K, Fagerlund B, Rostrup E. Subclinical cognitive decline in middle-age is associated with reduced task-induced deactivation of the brain's default mode network. *Human Brain Mapping* 35: 4488–4498, 2014.
- 8. Desler C, Frederiksen JH, Angleys M, Maynard S, Keijzers G, Fagerlund B, Mortensen EL, Osler M, Lauritzen M, Bohr VA, Rasmussen LJ. Increased deoxythymidine triphosphate levels is a feature of relative cognitive decline. *Mitochondrion* 25: 34-37, 2015.



CEHA (2014–2018) overview

During the first phase of CEHA, the Center established a solid research platform that has provided new knowledge and insights into the mechanisms of aging at the societal and individual levels. An important common theme at the time was 'frailty' and the retention of vitality in its broadest sense, for healthy aging and for society. In CEHA's second phase (2014–2018) our research specifically focused on the significance of 'energy' in aging processes, not only as it relates to individual bodies and processes at the cellular level, but also as it relates to psychological and social dimensions, including interest in one's surroundings and engagement with other people. This reorganization was a natural development from disciplinary and multidisciplinary approaches in CEHA (2009–2013) to a growing tendency toward interdisciplinarity.

Building on knowledge gained from CEHA's first phase (see Appendix A.2 for achievement overview), and the large number of successful interdisciplinary collaborations that have been facilitated by the establishment of the Center, we reorganized the Center around three research themes, which were chosen to enhance the multidisciplinary collaborations at CEHA (see Fig. 8). We also established a Communication and Outreach Platform.

CFHA themes

I. COMMUNITY INNOVATION FOR HEALTHY AGING CEHA researchers investigate the significance of the local community and opportunities for promoting the health and

KEY OUTCOMES OF CEHA 2014–2018

Science 897 publications

Capacity-building

91 individual PhD students/employed-enrolled and 48 individual postdocs/employed during the five years of CEHA (2009-2013)

- Funding from external grants more than DKK 339.7m (approximately EUR 45.5m) in addition to the Nordea-fonden grant
- Awareness

1,581 media mentions (of which 32 on radio/podcast; 41 on TV and 194 on Keep Your Brain Healthy (2017–2018)

energy of the elderly in the last stage of life. Much of this work is being done in collaboration with four Danish municipalities. Our researchers are also engaged in studying how historical and social changes have influenced relations between people and between generations.

II. LIFECOURSE AGING PROCESSES: LIFESPAN EXPOSURES AND HEALTHY AGING

This is an area in which CEHA's researchers investigate the



Figure 8. Overview of multidisciplinary projects during CEHA (2014–2018).



- Public Health
- Cellular and Molecular Medicine Clinical Medicine (Bispebjerg Hospital)
- Anthropology
- **Biomedical Sciences**
- Communication
 - Clinical Neurophysiology (Rigshospitalet and Hvidovre Hospital)



different factors that influence aging processes throughout life, how citizens could be motivated into active lifestyles and what happens to cells, muscles, and the brain as we get older. Researchers are also carrying out an intervention project focusing on physical activity to protect against age-related changes in musculature and the brain.

III. ENERGY BALANCE IN HUMANS: what are the mechanisms underlying reduced energy? In this theme researchers focus on the cellular and physiological mechanisms that cause energy levels to dwindle as we age.

See Appendix A.3 for achievement overview.

Key multidisciplinary projects

CALM (THEMES I AND III)

The Counteracting Age-Related Loss of Skeletal Muscle Mass project is an interdisciplinary research collaboration focusing on age-related loss of skeletal muscle mass and the effect of dietary protein and physical activity in achieving a healthier and more active lifestyle among older people. A systems approach that is both qualitative and quantitative is being used, and addresses the roles of biological, sensory, clinical, physiological, and cultural factors. CALM aims to generate scientific evidence, recommendations, and innovative solutions to counteract agerelated loss of skeletal muscle mass in elderly Danes.

LIFESTAT

Living with statins (Themes I–III): is an interdisciplinary project that leverages approaches and knowledge from medicine, the humanities, and the social sciences to analyze the impact of statin use on health, lifestyle, and well-being among Danes who are 4–60 years old.

CALM and LIFESTAT were both launched in 2013 with grants from the University of Copenhagen Excellence Programme for Interdisciplinary Research (www.research.ku.dk/strengths/ excellence-programmes).

LISA (THEMES II-III)

The Live active - Successful Aging project is investigating the influence of different training types on muscle function over a prolonged period. Interventions are being performed over the course of a year both in healthy people and in those with chronic disease and the participants will be followed for 10 years after the intervention to assess the ability to adhere to training long term and to potentially change behavior and attitude to exercise. Recruitment is ongoing, and the included subjects are studied at years 2, 3, 5, 7, and 10 after inclusion. Preliminary results suggest that heavy resistance training improved muscle mass and strength, whereas medium-intensity training had a lower effect on muscle mass and strength. The control group participated actively in social activities (e.g. visits to art exhibitions, lectures on brain health, wine tastings) and small-group activities (e.g. card playing, literature reading). Preliminary conclusions suggest that strength training stimulates the release of anti-inflammatory cytokines such as IL-6. The observations will be compared to the results of similar studies in animal model systems.

COLOSMA (THEMES II-III)

This ongoing clinical neuroproject (since 2009), the Copenhagen Longitudinal Study of Male Cognitive Aging, has provided important information on associations between cognitive functioning and biological and brain parameters. The COLOSMA study indicates that cognitive decline can be predicted with high sensitivity by recording changes in cerebral rhythmic activities evoked by complex visual stimuli.

Theme I Community innovation for healthy aging

GROUP LEADERS

Astrid Jespersen, Ethnology, Saxo Institute, Faculty of Humanities

Discipline: Cultural analysis, health in everyday life, qualitative methods, innovation studies

Karsten Vrangbæk, Health Economics and Policy, Department of Public Health, Faculty of Health and Medical Sciences and Department of political Science, Faculty of Social Sciences

Discipline: Health policy and economics, comparative health policy, health services research

Nete Schwennesen, Anthropology, Department of Anthropology, Faculty of Social Sciences

Discipline: Anthropology of life and health, aging, gender, technologies, community studies

Maria Kristiansen, Public Health Sciences, Department of Public Health, Faculty of Health and Medical Sciences *Discipline*: Health services research, mixed-methods, intervention studies, person-centered care, inequality

Rationale, focus, and aims

Perceptions of a meaningful and fulfilling life, and the ability to achieve this, are shaped by individual experiences and values across the lifespan. Local communities are important settings to study, as they incorporate the many facets of everyday life that shape health behaviors and quality of life for diverse groups of elderly people. Such community factors include the availability and relevance of health promotion initiatives, spaces for interaction with others, leisure activities for diverse groups of elderly people, the built environment and social capital/networks within elderly populations and across generations. There are also important social and structural differences within communities that affect people's ability and interest in health interventions, including differences in services (level and types), health status, functional capacity, gender, education, (former) occupation, ethnicity, and familial situation. The rationale of Theme I is rooted in this recognition of the importance of focusing not only on individual knowledge and skills in health promotion initiatives, but rather contextualizing health in the life-course (time) and context (space) of people. An important contextual change is the 2007 Danish municipal reform, which enhanced the responsibility of municipalities for health promotion and challenged them to focus on citizenoriented health promotion aiming at creating, shaping, and facilitating ways of aging healthily. We made use of this development to examine the impact of new policies and health technologies as applied in selected municipalities in promoting health and well-being.

Health-promoting interventions to address healthy aging within heterogeneous populations need to engage local communities directly and hence require cross-disciplinary research and close collaboration between a variety of stakeholders such as civic organizations, municipalities, general practitioners, hospitals, and aging citizens themselves.

Our studies have focused on achieving an understanding of the actual doing of health – that is, the ongoing everyday practices, meanings and negotiations of health – rather than a normative assessment of health knowledge and behavior, as the foundation for promoting health successfully among aging citizens, which is a central theme in CEHA (2014–2018).

The activities in Theme I have reflected the overall aim of conducting high-quality research on aging practices and perceptions as well as local contexts and policies that influence such practices. The second main ambition was to engage in collaboration with societal partners, primarily at the local community (municipal) level and including NGOs and informal citizen groups. The research approaches reflect several complementary academic disciplines, such as ethnology, health services research, and anthropology.

To support the overall aim, we have focused on:

 developing sustainable interdisciplinary academic networks to explore how new understanding of aging and the heterogeneity of local communities influences the ways in which health and energy are promoted in aging citizens;

THEME IN NUMBERS

Number of publications: 132 + book chapters 17 2014: 15 + book chapter 1 2015: 13 + book chapters 3 2016 : 43 2017: 22 + book chapters 8 2018: 39 + book chapters 5

PhD students (completed): 13 2014: 7

2015: 0 2016: 1 2017: 3 2018: 2

- exploring the various opportunities and barriers to healthy aging and lifelong energy at the community level, and applying this knowledge in collaboration with societal partners;
- identifying innovative approaches to private-public collaboration in health and aging and devising new modalities for the active participation of aging individuals in shaping policies and services.

Organizational developments

In 2015, Professor Allan Krasnik left the management group of Theme I due to other research obligations and was replaced by Professor Karsten Vrangbæk (theme leader together with Associate Professor Astrid Jespersen) and Associate Professor Maria Kristiansen. In 2017, Associate Professor Bjarke Oxlund left the management group of Theme I to pursue a career outside the University of Copenhagen. He was replaced by Associate Professor Nete Schwennesen.

Key achievements

Continued interaction with selected municipalities and the publication of results from a variety of research projects are key achievements of Theme I. The projects and the interactive collaboration with municipalities has fostered a broad and comprehensive understanding of complexities, challenges, and opportunities of promoting healthy aging in local settings. The projects and publications have provided insights into a diverse range of aging-related topics including the role of networks, social relations, and volunteering. Other research achievements include the provision of detailed knowledge about aging experiences and practices among vulnerable and socioeconomically challenged citizens. A number of projects have investigated aging-related issues among ethnic minorities and loneliness. Other projects have investigated the role of specific types of interventions or technologies for aging practices and the promotion of healthy aging.

The sub-projects in Theme 1 have, among other things, provided insight into policies for addressing issues such as loneliness among the elderly; coordination of care through municipal/regional health centers (co-location of health- and social-care actors); Media mentions: 241 (national) + 13 (international) 2014: 70 (national) + 13 (international) 2015: 38 (national) + 0 (international) 2016: 32 (national) + 0 (international) 2017: 40 (national) + 0 (international) 2018: 61 (national) + 0 (international)

External funding (excluding the Nordea-fonden grant) (total amount DKK): 53,547,630 2014: 17,600,000

2014: 17,000,000 2015: 1,032,550 2016: 190,000 2017: 28,049,204 2018: 6,675,876

engaging citizens and the voluntary sector in developing health and elderly care; and the implementation of welfare technologies in municipal and clinical contexts. Ethnographic studies have been conducted looking into the relations between the everyday life of the elderly, civil society, and municipalities. This work has centered on initiatives such as Cycling without Age, lunch cafés, local exercise associations, and social housing areas, and asks how the professional and voluntary boundaries, continuity in community initiatives, and citizen involvement is challenged and developed through co-creation. Theme I has also developed a deeper insight into the challenges of providing healthcare to aging immigrants and ethnic minorities in Denmark. We are currently involved in several intervention studies that explore ways of providing diversity-sensitive health care and rehabilitation in collaboration with municipalities and other stakeholders. The diversity of topics and the extensive research activities are reflected in a large number of publications in a diverse range of international peer-reviewed journals (see Appendix A.4: selected publications and www. healthyaging.ku.dk/publications).

Theme I has been successful in obtaining external research funding for a number of projects dealing with issues such as coordination of care between municipalities and regions; aging in the Arctic; digital rehabilitation in the context of dementia; guality of life and social relations among older LGBT people; documenting effects of large-scale structural community changes and developing participatory interventions in ethnically diverse housing communities; identifying the effects of diet interventions that build on cultural backgrounds and social networks among older migrant women in deprived communities; documenting effects of targeted programs to upgrade municipal rehabilitation of patients with Parkinson's disease; and exploring social inequality in cancer care programs for older adults with colorectal cancer. Some of these add-on projects are short term, while others will continue in the coming years. The success in obtaining external funding underscores the sustainability of the Theme I. We have also successfully engaged with a range of stakeholders to develop project proposals and secure funding, and have collaborated with e.g. Høje-Taastrup municipality, Copenhagen municipality, the Alzheimer Association, the Parkinson Association, the Danish Heart Association, all five municipalities in Greenland, and Ishøj municipality.

Theme II

Lifecourse aging processes

GROUP LEADERS

Erik Lykke-Mortensen, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Psychology, behavioral science, public health and lifecourse

Martin Lauritzen, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences and Department of Clinical Neurophysiology, Rigshospitalet, Glostrup, Denmark

Discipline: Aging, human brain function and neurodegenerative disorders

Rikke Lund, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Social epidemiology, public health and lifecourse **Flemming Dela**, Department of Biomedical Sciences, Faculty of Health and Medical Sciences

Discipline: Diabetes, metabolism, physical activity, exercise, cardio-vascular diseases, mitochondrial physiology

Rudi Westendorp, Department of Public Health, Faculty of Health and Medical Sciences

Discipline: Geriatric medicine and all disciplines related to aging research

Rationale, focus, and aims

The lifecourse perspective on aging assumes that aging processes are ongoing over most of the lifespan and that behavior, exposures, and morbidity during any life period will affect functioning, health, and morbidity during later life. It is further assumed that there are cumulative and combined effects on individual aging trajectories of exposure to different adversities and exposure to risk factors throughout the lifespan. Thus, our rationale is that it should be possible to characterize individuals by their lifetime exposures and their associated risk for early aging and dysfunction. In addition, we suggest that it should be possible to stimulate an energetic and active lifestyle in aging individuals by implementing physical training and other interventions to promote higher energy levels and a physically active and energetic lifestyle throughout old age.

The theme's principal aims are:

- to analyze the influence of lifecourse exposures on aging trajectories and individual differences in aging;
- to characterize early cognitive decline and identify early predictors of age-related cognitive decline;
- to evaluate the effects of physical activity interventions and to evaluate adherence to high and low intensity interventions;
- to establish a cohort of statin users and to conduct interdisciplinary research to describe the complexity of a medical issue from biological, humanistic, and anthropological points of view.

Since aging processes are ongoing over most of the lifespan, lifecourse studies are essential to understand individual differences in aging and to design interventions which optimally stimulate an active lifestyle and promote healthy aging. Thus, lifecourse studies are essential for working toward the vision and mission of CEHA to identify and create innovations that enable individuals and the population to age more successfully. Because many lifecourse issues relate to biological, behavioral, and social sciences, lifecourse research is inherently interdisciplinary. Within CEHA, lifecourse researchers have initiated and contributed to several interdisciplinary projects, thus furthering CEHA's aspiration to work across disciplines.

Organizational developments

This theme was substantially strengthened by the recruitment of Professor Rudi Westendorp in 2015 from Leiden University Medical Centre, Netherlands, and recruitment of an Associate Professor in Gerontology, Charlotte Juul Nilsson. The close collaboration between CEHA lifecourse researchers and the

THEME IN NUMBERS

Number of publications: 434 + book chapters 3 2014: 51 2015: 90 2016: 95 2017: 99 + book chapters 2 2018: 99 + book chapters 1

PhD students (completed): 53

2014: 7 2015: 10 2016: 12 2017: 10 2018: 14 **Media mentions**: 640 (national) + 257 (international) 2014: 117 (national) + 0 (international) 2015: 149 (national) + 251 (international) 2016: 143 (national) + 6 (international) 2017: 104 (national) + 0 (international) 2018: 127 (national) + 0 (international)

External funding (excluding the Nordea-fonden grant) (total amount DKK): 45,753,484

2014: 5,282,547 2015: 5,685,500 2016: 10,936,069 2017: 5,023,368 2018: 18,826,000

Danish Aging Research Center (Kaare Christensen) has been further developed with collaborative PhD and postdoc projects and the initiation of a large Nordic collaboration (NordForsk funded project: Social Inequalities in Aging). The collaboration between lifecourse researchers and Michael Kjaer's physical intervention group at Bispebjerg Hospital (Theme III) has also been further developed and so has the close project collaboration with the Danish Research Centre for Magnetic Resonance at Hvidovre Hospital (Hartwig Siebner). Additionally, the lifecourse group and Associate Professor Maria Kristiansen (Theme I) collaborate closely on a large intervention project in a socially disadvantaged neighborhood led by Rikke Lund. Over the years, national and international research collaboration has been expanding, and this process will continue in the coming years.

Key achievements

During CEHA (2014–2018), data collection has been an important effort for Theme II researchers: several databases have been completed, including the CAMB database, the Danish Conscript Database, and the registry based Folkesundhedsdatabasen. There are by now about 70 individual projects based on the CAMB database and several projects based on the conscript database or on Folkesundhedsdatabasen. The CAMB database has been described by R Lund et al. in International Journal of Epidemiology, 2015.

Two CEHA projects: COLOSMA and LifeMabs combine cognitive assessment and MRI scanning. The clinical neuroproject COLOSMA is one of the oldest and most successful multidisciplinary CEHA projects. It has provided important information on associations between cognitive functioning and biological and brain parameters, while an epidemiological study suggests an association between social resources and cognitive decline (A Gow et al., 2016, *Age and Ageing*). COLOSMA is one of the first studies to use draft board IQ results as a basis for evaluating midlife cognitive performance. The results suggest a neurobiological basis for subclinical cognitive decline in late midlife, which includes task-induced deactivation alterations similar to the pattern seen in patients with AD and mild cognitive impairment (NL Hansen et al., 2014, Human Brain Mapping). Data collection continues to date, and by December 2018 the sample consisted of 383 men born in 1953. Data collection has been completed for the LifeMabs project, which includes about 300 men and women born in 1959–1961, with comprehensive assessment of young adults and follow-up. More than 2,500 men participated in the LIKO-15 study, which is the first ever cognitive follow-up study based on the Danish Draft Board Intelligence test. The generated database provides unique possibilities for analyzing effects of lifestyle factors on agerelated cognitive decline. In addition, the physical intervention project Live active – Successful Aging (LISA) has been very successful in recruiting participants for both the initial assessment and the 1- and 2-year follow-ups. About 450 men and women were enrolled, with a very low drop-out rate of 6% over the 1-year intervention and nearly 400 participating in the 2-year follow-up. Preliminary data indicate a positive training effect over the one-year intervention. The LIFESTAT project relates to the use of statins as cholesterol-lowering therapy in primary prevention of cardiovascular disease. This is an interdisciplinary project that leverages approaches and knowledge from medicine, the humanities, and the social sciences to analyze the impact of statin use on health, life-style, and well-being in a cohort of Danish citizens.

Theme II lifecourse researchers have demonstrated how early life exposures, including stress and individual characteristics in young adulthood (e.g. intelligence), predict physical functioning, morbidity, and mortality across the lifespan (M Osler et al., 2015, *World Psychiatry* and GL Petersen et al., 2018, *PLoS ONE*). These studies demonstrate substantial continuity across the lifespan, and individual differences in aging must be identified and interpreted with this perspective.

Theme III Energy balance in humans

GROUP LEADERS

Lene Juel Rasmussen, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences *Discipline*: Aging, human molecular biology, mitochondrial biology, DNA repair and genomic stability, nucleotide metabolism **Ian Hickson**, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences

Discipline: Aging, chromosome stability, DNA repair, ageassociated disease

Michael Kjær, Department of Clinical Medicine, Faculty of Health and Medical Sciences

Discipline: Skeletal muscle and tendon tissue, aging, physical activity, injury

Abigail Mackey-Sennels, Department of Biomedical Sciences, Faculty of Health and Medical Sciences *Discipline*: Skeletal muscle, regeneration, exercise, aging Jørn Helge, Department of Biomedical Sciences, Faculty of Health and Medical Sciences

Discipline: Aging, training, insulin resistance, metabolism, inactivity **Linda Bergersen**, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences *Discipline*: Aging, mitochondrial DNA repair, brain energy failure, exercise

Rationale, focus, and aims

Aging is associated with a general decline in energy levels or 'vitality'. At the cellular and tissue levels, this reduction in vitality correlates with an inability to adequately replace or repair 'worn-out' or damaged components. Theme III aims to better understand the molecular and physiological mechanisms that cause age-associated impairment in physical function. This knowledge will ultimately lead to the development of novel strategies to diagnose and counteract age-associated functional decline, and hence allow individuals to attain a better quality of life as they age.

The theme's principal aims are:

 to study the effect of age-related changes in mitochondrial dynamics and network organization on neuronal integrity and performance; Vilhelm Bohr, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences *Discipline*: Aging, DNA repair, neuroscience, metabolism, neurodegeneration

Tom Kirkwood, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences *Discipline*: Aging, evolution and genetics, mitochondrial mutation, systems biology

Andres Lopez-Contreras, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences *Discipline*: DNA damage, replication stress, mouse models, cancer Simon Holst Bekker-Jensen, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences *Discipline*: Cell stress responses, signal transduction, MAP kinases, DNA damage response, aging

Morten Scheibye-Knudsen, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences *Discipline*: Aging, accelerated aging, aging interventions Javier Pena-Diaz, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences *Discipline*: Molecular aging, DNA repair, neurodegenerative disorders

- to study the molecular mechanisms of NAD+ supplementation on improving age-related decline in mitochondrial function and neuronal integrity in cell lines, in mice, and in *C. elegans* (nematode worms);
- to better understand how nuclear and mitochondrial dysfunction affects specific tissues and organs and leads to loss of vitality during aging;
- to investigate the molecular and cellular basis for agerelated pathologies such as cognitive decline and muscle dysfunction;
- to study human premature aging disorders, as a model for rapid/extreme aging;

THEME IN NUMBERS

Number of publications: 299 + book chapters: 12 2014: 101 + book chapters 7 2015: 44 + book chapters 5 2016: 61 2017: 51 2018: 42

PhD students (completed): 26 + 1 dissertation

2014: 7 + 1 doctoral dissertation 2015: 4 2016: 3 2017: 6 2018: 6

- to better understand how inherently unstable regions of the genome are maintained during our lifespans, and how they contribute to age-related diseases;
- to identify novel 'early warning' biomarkers and prognostic markers for age-related pathologies;
- to establish mouse models for studying organ- and tissue specific functions during aging;
- to examine how physical training induces physiological changes in muscle tissue, and how this knowledge could be exploited to improve vitality during aging;
- to determine molecular causes of, and novel strategies for, effective interventions that can promote healthy aging.

By studying the molecular and cellular mechanisms of aging, Theme III researchers aim to better understand the principal causes of various age-related pathologies. Further characterization, as well as an improved understanding, of reliable 'early warning' biomarkers associated with various pathologies will allow individuals to make informed lifestyle changes to counteract age-related diseases. Theme III therefore integrates biomedical research with human physiology and psychology, and utilizes CEHA's unique links with local municipalities to engage the general public with aging research.

Organizational developments

In CEHA (2014–2018), Theme III expanded to recruit a number of internationally renowned young scientists. These have included Javier Pena-Diaz (2014), Andrés López-Contreras (2014), Morten Scheibye-Knudsen (2015) and Simon Holst Bekker-Jensen (2016). Each of these brings key expertise, and their established international network, to CEHA.

In 2015, a Danish National Research Foundation (DNRF) Center of Excellence, the Center for Chromosome Stability, was established with funding for up to 10 years. This Center is directed by Professor Ian Hickson and also involves Associate Professor Andrés López-Contreras as a PI and Steering Committee member.

In 2016, Professor Tom Kirkwood, a prominent scientist in the field of aging research with a strong international profile, joined CEHA on a part-time basis. Professor Kirkwood has been a leading scientist in the field of aging research for many years, and also has extensive experience in managing a competitive multidisciplinary aging Media mentions: 120 (national) + 79 (international) 2014: 29 (national) + 65 (international) 2015: 27 (national) + 12 (international) 2016: 24 (national) + 0 (international) 2017: 21 (national) + 2 (international) 2018: 19 (national) + 0 (international)

External funding (excluding the Nordea-fonden grant) (total amount DKK): 140,681,416

2014: 80,458,744 2015: 31,407,091 2016: 22,897,011 2017: 19,464,104 2018: 86,454,466

research institute. In 2017, he took on a mentoring role for CEHAs Network of Young Scholars (NYS), advising on new initiatives and the structure for the network and its relaunch in 2018.

In 2018, one of Theme III Pls, Hocine Mankouri, left the University of Copenhagen to take up a position as a Scientific Officer with the Novo Nordisk Foundation.

Key achievements

Certain regions of the human genome are inherently unstable, and difficult to maintain throughout our lifespans. The Hickson Group identified some detrimental consequences of unstable genomic regions and showed how they generate mutations that can be inherited by subsequent cell generations; such mutations are a proposed driver of tissue aging. More specifically, we characterized a new DNA repair process that is required to maintain chromosomal 'fragile sites'. This landmark study was published in *Nature* in 2015, and gained widespread international media attention.

NAD+ is a key co-factor and co-substrate in many cellular processes. Professor Vilhelm Bohr's lab showed that NAD+ supplementation can improve many features of human age-related diseases, such as Alzheimer's disease, in various animal models. These results were published in *Proceedings of the National Academy of Sciences of the United States of America* (2018) and *Nature Neuroscience* (2019). Bohr's lab also identified a novel DNA polymerase in mitochondria (*Molecular and Cellular Biology*, 2017).

Mitochondrial dysfunction can lead to altered bioenergetics, as well as a number of secondary cellular changes, that contribute to age-related pathologies. These include increased DNA damage and altered nucleotide metabolism, which we have demonstrated to be associated with cognitive decline and reduced subjective vitality. These studies, involving many researchers across CEHA (2014–2018), were published in *Aging* (2013 & 2015), *Cell* (2014), *Cell Metabolism* (2014), *Mitochondrion* (2015), and *Acta Physiologica* (2015).

CEHA also studies mouse models of human pathologies or premature aging, which provide unique insights into the physiological mechanisms of aging and permit experimental determination of how age-associated impairment can be counteracted.

In addition, we have demonstrated in human volunteers that muscle mass and function deterioration (e.g. during periods of inactivity) can be counteracted by exogenous growth hormone and/ or anti-inflammatory medication. The loss of skeletal muscle occurs very fast (over a few days) and is initially age-independent and related to proteolytic activity. This discovery will be useful for counteracting permanent muscle loss in both surgical patients and acutely ill patients that are bedridden for short periods.

RESEARCH OUTPUT, MULTIDISCIPLINARITY, AND DISSEMINATION

Research output

CEHA researchers have published almost 1700 scientific publications in the period 2009–2018 (see Appendix A.4 for a list of selected publications). A significant number of these were published in high-ranking international journals within the humanities, social sciences, and biomedicine. These publications have contributed to the understanding that with increasing longevity and the medicalization of the lifecourse, measurements have become more important for managing aging bodies.

Several databases have been fully or partly completed, including the CAMB database, the Danish Conscript Database, COLOSMA, and the registry-based Folkesundhedsdatabasen (Public Health Database), and results from these cohort studies have been reported in several scientific publications during the period 2009–2018.

The LISA and COLOSMA studies have demonstrated how early life exposures, including stress, and individual characteristics in young adulthood (e.g. intelligence), predict physical functioning, morbidity, and mortality across the lifespan. They have provided important information on associations between cognitive functioning and biological and brain parameters while an epidemiological study suggests an association between social resources and cognitive decline.

CEHA researchers have published ground-breaking new knowledge on how basic biological mechanisms determine human physiology. These include how DNA repair and mitochondrial function are hallmarks of human aging. Also, the inclusion of mouse models of human pathologies or premature aging have provided a unique insight into physiological mechanisms of aging, and permit experimental determination of how age-associated impairment can be counteracted.

Multidisciplinarity

The output of CEHA researchers represents a multidisciplinary endeavor to understand the highly complex process of aging using sophisticated and powerful techniques and approaches. CEHA projects appreciate that aging reflects the influences of biological, socio-cultural, and socio-economic factors, as well as individual lifestyle choices, all of which modulate the quantity (lifespan) and quality (healthspan) of an individual's life. Our published work shows that endogenous (cellular/biological) and exogenous (social, interpersonal) stress can adversely influence both lifespan and healthspan.

CEHA has contributed to defining how genetic factors, social class, lifestyle, and education influence aging, not only as individual factors but also in combination with each other. Our growing number of publications authored by CEHA researchers from different scientific fields, as well as between CEHA scientists and their national and international colleagues, show that collaboration stimulates creativity and growth, leading to synergy between the participating groups. This trend will continue in the next phase (2019–2023), and hopefully further develop, to allow each researcher to accomplish more than he or she could accomplish working independently.

Dissemination of research results

CEHA focuses strongly on the dissemination of research results to the scientific community around the world. Each researcher has a busy program participating in conferences, seminars, workshops, etc. worldwide. For example, in 2018, Professor Karsten Vrangbæk was keynote speaker at the Gerontological Society of Israel; Professor Ian Hickson was invited speaker at the EMBO Conference on DNA replication, Heidelberg, Germany; Professor Lene Juel Rasmussen was invited speaker at the conference on Targeting Mitochondria in Health and Disease in Lucknow, India; and Assistant Professor Morten Scheibye-Knudsen organized the Fifth Annual Aging and Drug Discovery conference, Basel, Switzerland.

Seminars and academic events

CEHA hosts or co-hosts academic events to facilitate dissemination of data and promote discussion. Since 2014, CEHA and the Biotech Research & Innovation Centre (BRIC), University of Copenhagen, have organized frequent research seminars on important topics in biological sciences. This seminar series features international speakers, who are at the forefront of their respective fields, and who present seminars on research and/ or technologies that are having a major impact on biological and biomedical sciences. In 2018, the list of speakers included Staffan Eriksson from Department of Anatomy, Physiology and Biochemistry, Sweden; Guillermo de Carcer, Centro Nacional de Investigaciones Oncológicas, Spain; David Sherratt, Department of Biochemistry University of Oxford, UK; Matthias Gaestel, Institute for Physiological Chemistry, Hannover Medical School, Germany; and Tom Kirkwood, Institute for Ageing, Newcastle University, UK.

These seminars are usually attended by 50-100 participants and, in connection with the seminars, discussions are arranged between the international guest speakers and CEHA PhD students and postdocs. The seminars will continue in 2019, with the first to be delivered by Brian Kennedy, National University of Singapore (www.healthyaging.ku.dk/calendar).

IARU conferences

Further, the IARU network is an important dissemination platform and CEHA has hosted scientific international IARU conferences on multiple topics related to the Aging, Longevity and Health project in 2010, as well as two international conferences Cultures of Health and Biology of Aging and an IARU Graduate Student Conference – Aging Research and Scientific Careers – in 2014. In 2018, CEHA hosted a symposium on aging with invited IARU speakers.

At the 2010 conference, 123 participants attended and a report was published in the American journal *Mechanisms of Ageing and Development* (132 (10): 522-32. Epub 2011).

The Biology of Aging conference (2014) was organized by Theme III researchers Lene Juel Rasmussen and Vilhelm Bohr together with external partners Professors Yosef Shiloh, Tel Aviv University, and Tone Tønjum, Oslo University. It included 32 scientific presentations and 10 posters by young researchers. The conference Cultures of Health (2014) covered 29 scientific presentations. It was organized by CEHA researchers from Themes I and II (Allan Krasnik, Astrid Jespersen, Bjarke Oxlund, and Erik Lykke Mortensen) and had 60 participants. An outcome of the latter is the article "The challenges of human population ageing" (Age and Ageing 44:185-187, 2015; doi: 10.1093/ ageing/afu189). Since 2012, the ALH partners have taken turns in organizing the graduate student conferences, which were held in Singapore (2012), Copenhagen (2014), Tokyo (2016), Oxford (2017), and again in Singapore (2018). CEHA PhD students are nominated from each theme to attend and present at these conferences, providing them with a unique opportunity for networking with other young researchers in an interdisciplinary environment and with top international researchers in the field of aging. In 2019, the conference will be hosted by the Australian National University, Canberra.

Network of Young Scholars

NYS is aimed at young researchers affiliated with CEHA. The founding vision was to build a platform for young researchers to promote research training, educational activities, and social networking in an interdisciplinary setting. Since its establishment in 2010, NYS has coordinated and organized different kinds of activities, including Academic Fridays, conferences, and PhD courses. In the wake of the CEHA SAB meeting in March 2018, NYS relaunched itself as a network concentrating on interdisciplinarity, networking, and career development. The revised aim is to strengthen the shared identity and community among the young CEHA researchers, bring them together through academic events, and enlighten them about a career in interdisciplinary aging research. Following its relaunch, NYS has introduced lunch gatherings during which research assistants, PhD students, and postdocs gain insight into the career paths of different principal investigators (PIs) in CEHA. In 2018, NYS organized three such PI Lunches with Professor Michael Kjær, Professor Rudi Westendorp, and Professor Karsten Vrangbæk, respectively. The lunches have been a great success, with between 12 and 23 participants. NYS plans to have three PI Lunches in the spring of 2019 (www.healthyaging.ku.dk/ education/network-for-young-scholars).

Workshops

In December 2018, researchers from Theme I held the workshop "Innovation in practice" to mark the conclusion of 5 years' collaboration with the municipalities of Ishøj, Copenhagen, Vordingborg, and Gentofte, and present key findings from selected Theme I projects. The focus was to discuss the potential of key findings to inform future work and strategies for health promotion and innovation for healthy aging. Additionally, to talk about outreach and new collaborative opportunities in the years to come. The workshop was one of a series of annual workshops that focused on research results and practice-based knowledge collaboration with societal partners.

Symposium on Genome Instability and Neurodegeneration

In 2016, CEHA Professors Lene Juel Rasmussen and Ian Hickson (Theme III) organized and hosted an international Benzon Symposium on Genome Instability and Neurodegeneration (70 participants from more than 10 countries). The format was a combination of state-of-the art lectures by leading experts, and selected oral poster presentations by young scientists. From CEHA, results on, for example, how defects in mitochondrial respiration influence aging phenotypes, and how problems arising during the replication of cellular DNA underlie premature aging syndromes in humans, were presented. CEHA researchers Lene Juel Rasmussen, Ian Hickson, Vilhelm Bohr, Tom Kirkwood, Rudi Westendorp, Claus Desler, and Morten Scheibye-Knudsen gave presentations, whereas Linda Bergersen, Javier Peña Diaz, Thomas Lau Hansen, and Nima Fakouri presented posters.

Engagement and dissemination activities for stakeholders outside academic settings are discussed in "Societal impact: engagement, outreach, and communication".

RESEARCH TRAINING

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 and trainees, and to recruit junior and senior scientists with appropriate research interests and/or expertise to the CEHA faculty (Table 1). CEHA's educational programs include undergraduate- and graduate-level courses on aging as well as opportunities for postdoctoral studies under the mentorship of the CEHA faculty.

In CEHA (2014–2018), educational activities increased every year, and CEHA now offers summer schools, PhD courses, and a MOOC (Massive Online Open Course) focusing on aspects of healthy aging, interdisciplinarity, and innovation. Additionally, CEHA researchers teach and organize various BA, MA, and PhD courses (See annual reports for details: https://healthyaging. ku.dk/publications/annual-reports/). By 2018, 91 PhD students had completed their thesis at CEHA. A selection of the major educational activities undertaken by CEHA is described below

CEHA Summer Courses

As part of the educational activities at the undergraduate level, CEHA offers two summer courses to master's students, described below.

Interdisciplinary Aspects of Healthy Aging

This annual course, which was held for the first time in 2011, is part of the IARU Courses initiative (previously known as the IARU Global Summer Program) and takes place at the University of Copenhagen over three weeks in July. It focuses on exploring the phenomenon of aging through an interdisciplinary lens: by developing project proposals, students get hands-on experience with research methods from a variety of disciplines.

Being part of the exclusive IARU Courses initiative means that the course attracts students from a range of research-intensive universities across the world. From 2011 and 2018, a total number of 132 students (a minimum of 8 and a maximum of 22 students per year) have attended the course, and all of the 11 IARU universities have been represented at least once.

In 2018, CEHA hosted the 8th of the courses. Over the years, highly skilled CEHA researchers have developed, participated in, and improved the summer course. In 2017 and 2018, CEHA postdoc Jolene Lee Masters Pedersen and Assistant Professor Maarten Pieter Rozing have organized the course. The course mainly involves lecturers from CEHA, but it also benefited from inspiring lectures from Professor George Leeson, University of Oxford, from the IARU network.

Innovating Solutions for Aging Populations

This is CEHA's other summer course, an outcome of CEHA's participation in EIT Health. Since it was first held in 2016, the aim of the course has been to contribute to the education of professional health innovators and entrepreneurs at an international level. It includes flipped classroom techniques and consists of two parts: a series of online lectures on the Coursera platform (4,113 learners from June 2016-December 2018), followed by a two-weeks-long, on-campus course at the University of Copenhagen in August.

The course was originally developed in collaboration with the Copenhagen Business School (CBS), the pharmaceutical company Novo Nordisk A/S, and the innovation and

Table 1. Number of individuals from various categories that were trained by CEHA since its launch										
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Postdocs	15	24	29	27	31	25	38	38	35	31
PhD students	9	32	43	43	57	51	59	64	58	55
MA/BA students	2	4	0	15	13	14	20	14	26	25
Pregraduate research students	0	0	13	17	13	18	17	8	11	5



entrepreneurship hub SUND Vækst, but a variety of partners have been contributing since then. These include the Steno Diabetes Center and the start-ups DigiRehab, Injurymap, and KhoraCare. Professor Rudi Westendorp has coordinated the course, and together with representatives from CBS, he taught and supervised both online and on campus.

In 2017, the course was also part of the BRIDGE initiative. BRIDGE is a shared EIT campus initiative involving the University of Copenhagen, CBS, Uppsala University, Erasmus University Rotterdam, Management Center Innsbruck, and public and private partners. The aim was to share and implement best pedagogic and digital-didactic practices and organize sustainable networks within health and innovation. Each campus (Copenhagen, Uppsala, and Rotterdam) hosted a summer course. In 2018, the course was included in the course catalogue at the Faculty of Health and Medical Sciences.

MARRIAGE training network

Since 2012, CEHA has been a member of the EU-funded Initial Training Network MARRIAGE. The overall objective is to provide state-of-the-art training in the study of the biology of aging. The network includes European Aging Centers, and the Training Network will create a pan-European Network focused on aging research. CEHA Professors Lene Juel Rasmussen, Vilhelm Bohr, and Ian Hickson are involved, and CEHA has two PhD projects connected to the program. Multiple complementary training schemes have been implemented in the Network (research projects, courses organized by the Network academic partners, and training organized by the industrial partners). The ABRAHAM groups are part of this Network.

PhD Academy for Interdisciplinary Aging Research (PAIAR)

This academy was established by a group of young researchers to organize PhD courses – an activity that was previously carried out by NYS. CEHA has focused on developing PhD courses at the University of Copenhagen since 2015, and from 2017 PAIAR has developed high-level PhD courses within the field of aging and interdisciplinarity. The courses are open to all students at the University of Copenhagen and to students from other Danish universities and abroad. Among the courses that have been organized are: Interdisciplinary Research: Aging as a field of study (2015); Giving a Good Scientific Presentation (2016); Aging from a Cross Disciplinary Perspective (2017), and How to conduct interdisciplinary research (2018). Additionally, PAIAR has produced a course catalogue of self-sustainable and highquality PhD courses, which will support the continuing process of arranging PhD courses in the future (www.healthyaging.ku.dk/ education/phd-academy-paiar).

CEHA has a long tradition of engaging in dissemination activities outside the university by giving lectures and presentations at public and private hospitals, societies, associations, and organizations, as well as for the general public via, for example, the Danish Open Universities. See the section "Societal impact: engagement, outreach, and communication" for details on outreach to stakeholders and the general public.

SOCIETAL IMPACT: ENGAGEMENT, OUTREACH, AND COMMUNICATION

The basic and applied research carried out at CEHA is directed toward moving into a world where people live longer, healthier, and more meaningful lives. The Center thus engages with a wide range of stakeholders and the wider public to ensure that its research helps inform actions aimed at fostering healthy aging. Over the years, CEHA has worked ever more closely with stakeholders, and has a stated ambition to work together with stakeholders to ensure that research and knowledge is properly implemented. This work is supported by the Communication and Outreach Platform. Through the work of Medical Museion at the University of Copenhagen, our engagement efforts also seek to encourage a critical awareness of issues related to healthy aging and ongoing research that addresses these issues. CEHA also uses its insight into factors that can predict healthy aging to perform intervention studies; this aspect of engagement is covered in "Research themes and programs".

Activity during CEHA (2009–2013)

During the first 5 years of CEHA we focused on using different communication channels to convey aging and health-related information to a broad audience. General information on the Center was provided on the CEHA website in both Danish and English. During the EU Year for Active Aging in 2012, healthy aging was part of the public agenda both in Denmark and internationally. This provided an excellent outreach platform for CEHA, which played an active role in conferences, public meetings, lectures, exhibitions, and Science Theater during the year. Moreover, CEHA featured several times on the Danish National Television channel, DR2. For example, the production company DocEye and CEHA developed a TV documentary series, Fauli, Fat and Finished?, where the audience followed a Danish actor (Fauli) and his health in the context of aging. The CEHA researchers designed and supervised the physiological and clinical experiments and were interviewed during the six episodes. The series had approximately 825,000 viewers (about 15 percent of the Danish population).

In 2013, CEHA launched a Facebook page in Danish, as a forum for advice, awareness, and debate about healthy aging and for branding of CEHA. By the end of 2018, the page had 17,000 followers.

Research undertaken within the Communication and Outreach Platform resulted in two PhDs during this phase – Adrian Bertoli's work on social-media-based disease management and Morten Bülow's work on the history of the 'successful aging' concept. In addition, artist Lucy Lyons' postdoctoral project Drawing Aging culminated in an exhibition called Experiences of Aging in 2012.

Engagement strategy during CEHA (2014–2018)

As part of CEHAs second phase, we acknowledged that engaging and innovative science communication is a prerequisite for research to be useful to society and thereby invested more resources into outreach and communication. The Communication and Outreach Platform works strategically to put knowledge about healthy aging on the agenda and ensure that our research forms the basis for recommendations to both decision-makers and citizens. The activities undertaken in Medical Museion also exploit more dialog-based methodologies, adding a slower but deeper way for audiences to think through some of the complex aging-associated issues. Director of the Medical Museion, Professor Ken Arnold, heads the platform. The employees of the platform are situated at the Medical Museion, the CEHA Secretariat, and at the Communication Department at the Faculty of Health and Medical Sciences.

We work across multiple media and seek to be engaging, innovative, and collaborative. Our methods are adjusted to specific settings, target groups, media platforms, and messages. We develop our formats continuously to adapt to the changing media landscape. Our work operates on three levels: 1) assistance with, and innovation around, direct communications; 2) provision of a platform (e.g. the Medical Museion's auditorium and other public spaces) for interdisciplinary stakeholder dialog and engagement; and 3) experimental public programming including exhibitions, live events, games, and other activities.

The communication platform collaborates closely with the researchers, with a special focus on supporting young researchers to become skilled communicators with outreach as an integral part of their work.

Communicating research to the wider public using mass media

The Danish version of the CEHA website is primarily targeted at stakeholders like employees in elderly organizations, health

Table 2. Social media activities						
FACEBOOK	Followers (growth)	Posts year/month	Reach year/month/post	Engagement rate		
May 2013–Jan 2014	10,119	-	-	-		
2015	10,405	/11	517,179/43,098/4,009	9%		
2016	12,155	/11	1,691,415/140,951/13,423	7%		
2017	15,565	/11	809,881/67,490/7,713	6%		
2018	17,381	/8	416,222/34,685/4,574	6%		
TWITTER	Followers (growth)	Tweets year	Reach year/month	Engagement		
2014	44	-	8,100/2,700	1.1%		
2015	173	26	64,200/4,586	0.8%		
2016	214	101	18,492/1,541	0.6%		
2017	-	54	21,064/1,755	0.7%		
2018	323	37	24,561/2,046	1.2%		
INSTAGRAM	Followers	Post	Likes			
2016	321	99	917			
2017	409	31	441			
2018	431	14	309			

professionals, and politicians, while the primary target groups on the English site are researchers, students, and international partners. The web traffic has increased from 2,520 visitors in 2012 to 41,088 in 2018, an increase of 1,530 percent. In December 2018, the website was relaunched to match the new structure of CEHA with the research tracks, outreach and educational activities (www.healthyaging.ku.dk).

The communication team are facilitators and build bridges between researchers and journalists. The team help researchers find the right angle and the right media for the story, then help sell the story to journalists and assist the journalists with pinpointing the relevant experts. One example of creating content that sets an agenda is a large project to increase awareness of how we age. This was undertaken in association with the popular Danish People's Political Festival in 2016. The festival is a platform for open debate and informal dialog between politicians, citizens, business people, and organizations (113,000 visitors in 2018). Among the communications efforts in 2016 was a string of interviews with Danish celebrities and researchers in two video campaigns produced in collaboration with the communication department at the Faculty of Health and Medical Sciences. Following the festival, one of the video campaigns was used by the Danish national newspaper Kristeligt Dagblad on their website and Facebook page, together with interviews with CEHA researchers.

The press coverage of CEHA research and activities has expanded from 87 articles in 2009 to 340 in 2018. During the past few years, journalists have frequently turned to our researchers as experts in healthy aging, and our research results have been covered from local Danish newspapers to international newspapers, such as *The Times* in the UK.

Using social media for communicating research

We have experimented with various social media, which are important channels for engagement and dialog (Table 2). These experiments have led us to focus on Facebook, Twitter, and Instagram, which are used by 73 percent, 12 percent, and 16 percent of the Danish population, respectively.

In December 2018 we had 17,148 followers on our Facebook page, with a high degree of interaction. The video campaigns launched in association with the Danish People's Political Festival in 2016 were publicized via the Facebook page and had more than 700,000 views. The campaigns increased the numbers of followers and attracted an average of 521 likes, 214 shares, and 54 comments per post. Other campaigns have been launched in close collaboration with DaneAge, Danish Pension Service (PKA), and patient organizations.

The CEHA Twitter account @sundaldring (which translates as healthy aging) was launched in 2014. In December 2018, we had 323 followers. The account is used to live-tweet from events, to promote researchers and events.

In August 2015, the Instagram account @sundaldring was launched. It is used to communicate the research process rather than results, and for events, for example the Political Folk Festivals, The Danish Science Festival (Forskningens Døgn), and Talks on the Top (Talks på Toppen) that involve researchers from the Center. The account has 431 followers as of December 2018.

Events and exhibitions

CEHA is working on innovative dissemination and richer engagement about research findings to the public through dialog-based events, lectures, debates, and exhibitions, where researchers and the Communication and Outreach Platform work together. We investigate the framework for good communication and meaningful, lasting engagement. We learn from our experiments and strive to come up with fresh approaches that enable us to try new ideas as well as stand out in an ever-more-crowded and busy public arena.

In 2018, 42 events were held, ranging from lectures all over Denmark on how to keep your brain healthy to the Copenhagen Culture Night and the People's Political Festival to meetings with health professionals. The events included the CEHA-retreat, which was attended by some of our closest stakeholders, the Rector of University of Copenhagen, and the Minister of Senior Citizens.

Room for aging

Part of Medical Museion's contribution to the societal impact of CEHA has been to devote a specific room to showcasing age related displays and other initiatives. The exhibition *Kintsugi* – *golden body repair*, plays with the Japanese concept for mending porcelain with gold as a metaphor for bodily repair and the aging process. It has formed the background for a wider discussion and the development of a project targeted at the education of future healthcare professionals.

Life on the Line game

We have also produced an innovative group game called "Life on the Line" based on research outcomes from the Center. It looks at the entire process of aging – how the body and life conditions change over a lifetime – in a powerfully informative and fun manner. The game is developed for players in all age groups and has become the centerpiece in the Room for Aging at the Medical Museion. In 2018, a traveling version of the game was made, which has been loaned out for several events. Among others, it has been in use at the science fair "Science Forum 2018", which is targeted at primary school pupils and families, and has been loaned out twice to PKA pension "Pensions day", which targets pension clients aged 55 and above. Finally, the game has been on a 4-month loan to the University of Konstanz, Germany.

Strengthening the communication competence of young scientists

CEHA's young scientists are an increasing focus for the communications team. Because these researchers bear many of the communications responsibilities, participating in public lectures, communication experiments, and events, their competence in communication is of great importance.

In early 2018, the communication team gave three workshops for CEHA's young scientists, giving them a basic understanding of science communication, tools to navigate today's media landscape, and to communicate their research to the public. Many of the participants have since tried out their new skills in events and lectures.

For example, the young scientists have been active at The Danish Science Festival and the Copenhagen Culture Night. The Danish Science Festival takes place every year in April. In 2018, four young CEHA scientists participated by riding city busses and giving the passengers short science lectures – science slams – of just three minutes each. That event resulted in an invitation for participation in the Culture Night in the Ministry of Higher Education and Science. During the Copenhagen Culture Night 2018, 5,300 people visited the Faculty of Health and Medical Sciences, where CEHA was present with fitness, strength and balance tests, science slams, and tours of the laboratories on the 2nd and 3rd floors. Young researchers were the most active communicators during this evening.

Engaging stakeholders

Since 2014, CEHA has worked strategically with stakeholders, with the aim of engaging them in discussions on healthy aging and influencing public agendas through research results and dialog. The primary target groups are elderly organizations, municipal decision-makers, pension companies, government agencies, healthcare professionals, and selected patient organizations. An example of a close relationship with a primary stakeholder is the collaboration with the most influential organization for the elderly in Denmark, DaneAge (750,000 members), with whom we arranged, for example, joint events during the People's Political Festival in 2015, 2016, 2017, and 2018; have published a series of four supplements (entitled "The Good Life") in the Danish newspaper *Politiken*; and are currently developing a joint project to inspire senior citizens to lead active lives.

The following are examples of events and collaborations with stakeholders from 2018:

Keep Your Brain Healthy

During 2017–2018, we have been a partner in a communication project "Keep your Brain Healthy", developed in close collaboration with DGI and the Agency for Culture and Palaces. The activities target seniors between 55 and 75 years of age to encourage them to be active for a longer period of time.

Associate Professor Ellen Garde (Theme II) and Professor Emeritus Albert Gjedde have given 13 lectures around the country in 2018; the lectures collectively attracted an audience of 1,256 people. More than 1,000 participants have joined the local activities organized by libraries and DGI associations. The final evaluation of the pilot project shows that the majority of the participants enjoyed taking part in exercise, social and cultural activities, and in their self-assessments reported improvements in physical and mental well-being. Additionally, in March 2018, the project hosted an inspirational day for interested project participants. Attendees included citizens, libraries, and DGI associations from all over Denmark, who shared experiences and ideas.

Keep Your Brain Healthy has provide a unique platform to disseminate CEHA research to a broad public. The collaboration has provided fruitful experiences and has led to CEHA's maturing as an organization ready to engage in partnerships with stakeholders.

People's Political Festival

Along with the Danish Science Festival (Forskningens Døgn) and Copenhagen Culture Night, the Peoples Political Festival has an important place in the CEHA event calendar. The festival is especially important in relation to stakeholders. The festival provides an opportunity to strengthen CEHA's agenda and boost the dissemination of our research and the profiles of individual researchers. The scientists gain new ideas for research projects, and our participation leads to the strengthening of relationships among the researchers and between the researchers and the communications team.

Every year since 2015, CEHA has brought scientists from all three research themes and from the humanities, social sciences, and health sciences to Bornholm. Our focus has been on sciencecommunication events, often in collaboration with stakeholders, but we have also given high priority to informal coffee meetings and participation in debates. In 2018, CEHA co-organized a debate on dementia care, autonomy and well-being initiated by DaneAge. We also hosted an entertaining quiz and invited our stakeholders to a workshop on conditions for volunteering and co-creation involving professionals and civil-society.

Political hearings

Finally, CEHA participates frequently in political hearings on topics related to the elderly. It happens on average two to three times yearly and these have addressed legislation concerning, for example, social services, quality of homecare standards, preventive homecare, dignity standards in the eldercare, and use of digital communication tools with the elderly.



APPENDICES

A.1 CEHA (2014–2018) management structure

Grant holder (Nordea-fonden Grant)

• Dean Ulla Wewer, Faculty of Health and Medical Sciences

CEHA Steering Group members:

- Executive Director Professor Lene Juel Rasmussen (Chair)
- Associate Professor Astrid Pernille Jespersen (Theme I)
- Professor Karsten Vrangbæk (Theme I)
- Professor Erik Lykke Mortensen (Theme II)
- Professor Martin Lauritzen (Theme II)
- Deputy Director Professor Rudi Westendorp (Theme II)
- Professor Michael Kjær (Theme III)
- Professor Ian Hickson (Theme III)
- Professor Ken Arnold (Communication and outreach)

The SAB members are:

- Professor Boo Johansson, University of Gothenburg, Sweden (Chair)
- Professor Sarah Lamb, Brandeis University, US
- Professor Dr Ulrika Winblad, Uppsala University, Sweden
- Professor Erik Boddeke, University of Groningen, Netherlands
- Professor George Brooks, University of California, Berkeley, US
- Professor Tone Tønjum, Oslo University, Norway
- Professor Jan Vijg, Albert Einstein College of Medicine, US
- Dr Erinma Ochu, University of Manchester, UK.

Deans from:

- Faculty of Humanities, Professor Jesper Kallestrup
- Faculty of Social Sciences, Associate Professor Troels Østergaard Sørensen.

A.2 CEHA (2009–2013): Overview and achievements of the research programs

1A. MOLECULAR AGING

Program leader: lan Hickson

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.

1B. NEUROSCIENCE

Program leader: Martin Lauritzen

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. For this purpose we examined cognitive performance of 207 men, without evidence of differences in IQ when cognitive function was assessed at draftboard examination (baseline), but with important differences when they were 58 years old. We demonstrated significant differences in sleep guality, structural and functional MRI and autonomic function between test-persons with preserved and with decreased cognitive performance. Surprisingly the perturbation of the so-called resting state network activity by functional MRI was disrupted in test-persons with cognitive decline and reminiscent of the patterns observed in patients with Alzheimer's disease. This could suggest that disrupted resting state patterns in functional MRI may accompany cognitive decline. In our current research project we explore this possibility by follow-up examinations of IQ and cognitive tests and fMRI in the same test-persons with five-year intervals. In animal model systems, we have identified unique features of brain repair mechanisms in astrocytes linked to aging. In addition, we have demonstrated that activity of the interneuronal network which underlies cognitive processes and brain information processing are dysregulated during normal aging. The defects in network activity are energy demanding and accompanied by a doubling of the consumption of oxygen, while the supply is reduced. This may explain some of the deficits in cognitive function that accompanies even healthy aging and may

pave the way for an understanding of brain frailty underlying the increased susceptibility of old brains to contract neurodegenerative diseases. Ultimately, we envision that these novel findings will lead to novel strategies or tools for diagnosing and preventing brain frailty, thus promoting healthy aging.

2. MUSCLE AND MATRIX

Program leaders: Michael Kjær and Flemming Dela 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 lifestyle related diseases, particularly due to decreased daily physical activity. In CEHA I, Program 2 researchers have been studying the mechanisms that underlie these and other age-associated changes in metabolism and the musculo-skeletal system. 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. In some types of connective tissue (tendon and cartilage) the growth is only present in childhood and adolescence whereas adult cartilage does not display turnover of the collagen tissue, and the breakdown associated with development of osteoarthritis is not associated with any compensatory tissue replacement.

Aging skeletal muscles contain myonuclei that cover a certain area of cytoplasma (myonuclear domain) and in fibers of similar size neither training nor age had any influence on myonuclear domain, but the fact that older muscle had lower myonuclear domain was simply explained by the presence of a greater proportion of small fibers than in younger counterparts. Regular life-long training is associated with a reduction of the circulating inflammation levels and this is likely to be coupled to maintenance of skeletal muscle mass either directly or via adipose tissue.

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.

3. BODY AND LIFE

Program leaders: Kirsten Avlund and Erik Lykke Mortensen Program 3 addresses the influence of lifecourse 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 lifecourse, and we analyze 1) whether it is possible to explore strain factors over the lifespan, 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.

The focus of CEHA Program 3 was to identify biomarkers of early aging and lifecourse influences on aging. Program 3 scientists used epidemiologic methods to analyze large data sets on midlife and old-age cohorts as well as data from national registries.

Key findings:

• 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.

- Increased leisure activity from age 50 to 80 is consistently associated with the level of cognitive ability, but not with agerelated cognitive decline.
- Mobility-related fatigue is associated with slower walking speed in older adults which suggests that muscle strength is one of the underlying factors explaining the association between mobilityrelated fatigue and walking speed.
- Men who live alone may alleviate their risk of disability onset by being socially active and by having access to satisfactory social relations. Women do not seem to benefit as much from cohabitation as men, although women who live alone and who are not satisfied with their social relations also constitute a significant risk category.

Findings from these studies may contribute to developing and refining interventions, which can delay aging-related disability and loss of independence.

4. SOCIETY, CULTURE, AND HEALTHCARE POLICY Program leader: Allan Krasnik

The research in Program 4 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 organizations, and from the national health-care system. A series of qualitative and quantitative studies 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.

Key findings:

- General practitioners in Denmark seldom take an initiative to discontinue preventive medication once an aging individual has been prescribed anti-hypertensives, cholesterol-lowering drugs or pre-diabetes medication. This leads to a condition of polypharmacy, where a considerable number of individuals end up being hospitalized due to dangerous drug interactions.
- Low-cost measurement technologies such as pedometers, blood pressure meters, and smartphone health apps have become so prevalent that many aging Danes monitor their own health and well-being. While this is in many ways a positive development trend in terms of the overall population health, it simultaneously creates new uncertainties and anxieties as well as a narrow focus on bodily data rather than overall quality of life. Numerical health standards thus have a tendency to become moral standards.

- New treatment guidelines, lower drug prices, and more generous public reimbursement patterns have seriously influenced the uptake of anti-hypertensives and cholesterollowering drugs over the past 15 years. The scientific evidence behind the medical standardization has become stabilized thereby making the encounter between patients and general practitioners in relation to cardiovascular health one in which medicines are prescribed without much further ado. Preventive medication has moved from being controversial to being mundane.
- Home nurses play an important role in the management of the medication of the oldest citizens who receive home nursing assistance. As a kind of state-sponsored, extended family members the home nurses take on the responsibility of providing advice and ensuring compliance in relation to cardiovascular health and other conditions.
- Denmark's health information systems are widely admired, yet barriers to integration of care include organizational fragmentation, unjustified financial incentives, and the absence of a single electronic medical record, which makes rational decisionmaking difficult to bring about.

5. HEALTH IN EVERYDAY LIFE

Program leaders: Lene Otto, Thomas Söderqvist, and Astrid Jespersen

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 understandings 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. Program 5 has made significant progress towards establishing humanistic aging research and cultural gerontology as an important and central field of study in Denmark.

Key findings:

- 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 healthpromoting activities, such as participating in sustainable social networks.
- Many research-based health-promotion initiatives fail to include insights about elderly people's everyday lives and thus end up producing non-relevant and non-appropriate evidence for the target population.
- Implementing 'successful' and relevant initiatives for elderly people requires a multi-faceted, integral approach that is adaptable to the everyday lives of the target group.
- The widespread use of small, easily accessible health technologies in relation to exercise practices is likely to motivate and to help lifestyle changes.

A.3 CEHA (2014–2018): Overview of the key research achievements

Theme I

- We have continued our close relationships with a number of municipalities and have collaborated with them to develop and implement interaction research projects. This has provided insights into the complexities of, and challenges and opportunities for, developing in-depth collaborative health and social care within municipal settings. Dialog on future projects has been initiated with new partner municipalities.
- Our participation in the Counteracting Age-Related Loss of Skeletal Muscle Mass project (CALM) has created an awareness of physical decline among the participants.
 Combined with the knowledge on the importance and effect of muscle training, this awareness is enhancing the propensity to be more physically active.
- Our ethnographic studies of measurements and aging show that the overall trend toward increasing quantification takes different forms for different people and purposes. Numbers can facilitate reflection and communication although they may be interpreted differently by different actors.
- The study of policies for voluntary-sector cooperation revealed a gap between policy formulations in the municipalities and awareness of policies within the community of voluntary associations. This points to a need to rethink the inclusion of stakeholders in policy formulation and implementation.
- The study about municipal/regional health centers as loci for coordination reveals persistent barriers despite co-location of health- and social-care actors. Divergent incentives, cultures, and working conditions create problems in the relationships.
- The research on co-creation in Ishøj shows that user involvement and continuity is both enabled and challenged by the co-creation approach. The project has been presented to the city council and has led to an increased collaboration between the administrative units in the municipality.
- A collaboration with WHO Europe, funded by the European Commission and the EU, has resulted in a comprehensive document detailing the current evidence, best practices, and policy and practice recommendations for ensuring health and well-being of the growing population of older migrants and refugees across the WHO Europe region. The report was launched in November 2018 and will be followed by a series of outreach and research initiatives, with CEHA and WHO Europe as lead partners.
- We have finalized a review (in press) of opportunities and challenges in implementing group-based interventions to enhance social relations in older adults living in nursing homes. Data analysis and write-up of findings from the intervention "Fortæl for livet" conducted in two nursing homes in Copenhagen have also been completed and will be published in 2019. In collaboration with the Danish Heart Association, we evaluated a nation-wide, culturally-sensitive, and

co-created intervention to enhance healthy dietary practices in ethnically diverse older adults through community-based approaches (Hjertevarm mad fra hele verden). The evaluation has been published on the Danish Heart Association webpage in 2018 and a scientific publication was published March 2019.

- In collaboration with the Parkinson Disease Association, we explored opportunities for supporting municipalities in providing person-centered, multimodal rehabilitation for patients and relatives through a new educational program (Parkinsonkoordinator-uddannelsen).
- The STRIT study was initiated, partnerships with citizen groups and other stakeholders established, and staff hired. An office was set up in the community, and qualitative interviews with 31 older adults of Danish and Turkish origin were completed. The questionnaire was developed, translated into seven languages, and the interviewer-administered baseline survey was completed as planned. Co-creation of the first citizen-driven intervention was initiated with a multi-ethnic group of residents driving the process. A range of communication materials were developed, and various forms of communication took place, e.g. through a new website, local media, visual materials distributed in the community, local resource persons/stakeholders, and meetings.
- We conducted an ethnographic study of the implementation of digital technologies in programs of physical rehabilitation for patients who have undergone hip-replacement surgery. The results show that the technology is embedded in a wider constellation of care, which governs whether the technology works as intended or not. Successful implementation requires that patients and health professionals are willing to adjust the technology so that it matches specific body types.
- A qualitative study drew attention to socially isolated older men and added to existing knowledge on the relationship between aging, masculinity, and solitary living. The project concluded that social isolation can be considered to be a mode of social behavior, which is adopted in order to reclaim autonomy.
- An ethnographic study on how older people understand and construct a 'good life' found that social relations, continuity, and an everyday life with work-related or recreational activities was desired. However, this desire was challenged by transitions in old age, such as when the body started to fail and the individuals had to give up meaningful activities. The study concluded that the quality of life depends on how well older people manage to mobilize individual resources as well as resources in their network and surroundings.
- A survey of a sample of Danish adults (N=9154) between the ages of 52-92 years found that loneliness was associated with increased risks of poor self-rated health, limited physical abilities, and multiple diagnoses.
- In a survey investigating Danish medical teachers' perceptions of cultural competence, we found acknowledgement of

the importance of cultural competence and the need to implement cultural competence in the medical curriculum, training of teachers, and strengthening the sensitivity of the organization to diversity.

- An intervention study that explored the involvement of community pharmacists with ethnic minority backgrounds in medication reviews for ethnic minority poly-pharmacy patients highlighted the potential of involving professionals with diverse ethnic backgrounds in such interventions.
- In a review paper, we concluded that there is a need for attention to migration along with other determinants of healthy aging, and for a sensitive and comprehensive approach to policies, practices, and research within the field of healthy aging to accommodate the growing number of aging migrants in Europe.
- The PhD research of Malene Bødker explored how the needs of the aging population are negotiated in the context of 'reablement': a newly emerged form of home care aimed at re-enabling older people to carry out household chores or personal hygiene independently through short-term homebased training programs. The research, compiled in a thesis, took a critical stance to political visions that reablement can simultaneously reduce public eldercare expenditures, improve the lives of older people, and improve the working environment of homecare professionals'. The research explored, by means of an ethnographic approach, how reablement unfolds in the everyday encounters between homecare professionals, older people, and their relatives, as well as the sorts of profound moral implications reablement might have. The findings of this research suggests that researchers, policymakers, and the general public apply a more nuanced approach to aging and eldercare than simply stipulating standardized ways of aging. Such an approach can encompass several versions of what constitutes a good life in old age.

Theme II

• We have characterized the resting connectivity network in subclinical cognitive decline by functional magnetic resonance imaging and demonstrated associations between subclinical cognitive decline and EEG patterns and sleep characteristics. We have also demonstrated how agerelated cognitive decline is influenced by education and socioeconomic position as well as social relations among older people.

- We have demonstrated how early-life exposures, including stress, and individual characteristics in young adulthood (e.g. intelligence) predict physical functioning, morbidity, and mortality across the lifespan.
- We have shown that statin treatment for elevated cholesterol displays a negative effect on skeletal mitochondrial respiratory capacity, which may be explained by the simultaneous finding of decreased Q10 content in the muscle. This is likely to be the mechanism for statin-induced myalgia, a well-known side effect in statin treatment.
- We have designed and collected data for a multi-methods project in a vulnerable group of middle-aged and older people that are otherwise poorly described with respect to aging issues.

Theme III

- We characterized a new DNA repair process that is required to maintain chromosomal 'fragile sites'.
- We have demonstrated mitochondrial dysfunction to be associated with cognitive decline and reduced subjective vitality.
- We have demonstrated that muscle mass and deterioration of function (e.g. during periods of inactivity) can be counteracted by exogenous growth hormone and/or anti-inflammatory medication.
- We have shown that NAD+ supplementation improves key features of neurodegeneration in animal models of Alzheimer's disease.
- We have shown that defects in DNA repair leads to loss of mitochondrial homeostasis and neurodegeneration.
- We have identified and characterized a novel mitochondrial DNA polymerase.
- We have demonstrated that physical training can counteract the degenerative changes in connective tissue, but that at very high age the effect of training on connective tissue and skeletal muscle is very small.
- We have demonstrated a very pronounced, fast, and ageindependent loss in skeletal muscle with inactivity due to proteolytic activation.

A.4 Selected publications (2014–2018)

A complete list of publications is available at www.healthyaging. ku.dk/publications.

For each theme we have listed PhD dissertations from 2018. PhD dissertations by year are available in the annual reports at www. healthyaging.ku.dk/publications/annual-reports.

Theme I

During CEHA (2014–2018), Theme I generated 149 publications.

Lassen AJ, Moreira T. Unmaking old age – political and cognitive formats of active ageing. *Journal of Aging Studies* 30: 33–46, 2014.

Jensen T, Grønnow LC, Jespersen AP. Eating Strategies. An analysis of how frail, home-dwelling older people in Denmark develop strategies to form meaningful eating situations. *Ageing* & *Society*, doi: 10.1017/S0144686X17001076, 2017.

Kristiansen M, Razum O, Tezcan-Güntekin H, Krasnik A. Aging and health among migrants in a European perspective. *Public Health Reviews* 37: 20, 2016.

Mikkelsen ASB, Lund R, Kristiansen M. Social relations and healthcare utilization among middle-aged and older people: a study protocol for an implementation and register-based study in Denmark. *BMC Health Services Research*, 17: 728, 2017.

Schwennesen N. When self-tracking enters physical rehabilitation: From 'pushed' self-tracking to ongoing affective encounters in arrangements of care. *Digital Health* 3, doi: 10.1177/2055207617725231, 2017.

Hillersdal L, Jespersen AP, Oxlund B, Bruun B. Affect and effect of interdisciplinary collaboration. *Science & Technology Studies*. Special issue on Expertise and its tensions (online ahead of press, Oct 2018).

Mikkelsen HH. Idleness: Passive Citizens and Energizing the Danish welfare State. *Anthropology and Ageing* (accepted 2018).

Schwennesen N. Algorithmic Assemblages: Imaginaries and epistemologies in remote monitored physical rehabilitation. *Sociology of Health and Illness*. Special issue on Digital Health (accepted 2018).

Bødker MN, Langstrup H, Christensen U. Home care as reablement or enabling arrangements? Exploring the precarious dependencies of living with functional decline. *Sociology of Health and Illness* (accepted 2018). Vrangbæk K, Scheele CE, Kriegbaum M. Voluntary associations and co-production of health promoting activities for older adults: Experiences and policy lessons from Denmark. *Health Policy* 122(11): 1255–1259, 2018.

PhD dissertations 2018

During CEHA (2014–2018), 13 PhD projects were completed in Theme I.

Anders Møller: De værdige gamle. Om alderdomskonfigurerende praksiser i Danmark omkring år 1900. October 2018.

Malene Bødker: Negotiating needs, negotiating old age. An ethnographic study of reablement in the everyday home care practices of a Danish municipality. Accepted for oral defense in December 2018; defended in February 2019.

Theme II

During CEHA (2014-2018), Theme II published 437 publications.

Asping M, Stride N, Søgaard D, Dohlmann TL, Helge JW, Dela F, Larsen S. The effects of 2 weeks of statin treatment on mitochondrial respiratory capacity in middle-aged males: the LIFESTAT study. *European Journal of Clinical Pharmacology* 73: 679–687, 2017.

Christensen CL, Wulff HJ, Krasnik A, Kriegbaum M, Rasmussen LJ, Hickson ID, Liisberg KB, Oxlund B, Bruun B, Lau SR, Olsen MN, Andersen JS, Heltberg AS, **Kuhlman AB**, **Morville TH**, **Dohlmann TL**, **Larsen S**, **Dela F**. LIFESTAT - Living with statins: An interdisciplinary project on the use of statins as a cholesterollowering treatment and for cardiovascular risk reduction. *Scandinavian Journal of Public Health* 44: 534–539, 2016.

Foverskov E, Glymour MM, **Mortensen EL**, Holm A, Lange T, **Lund R**. Education and Cognitive Aging: Accounting for Selection and Confounding in the Danish Registry-SHARE Data Linkage. *American Journal of Epidemiology* 187(11): 2423–2430, 2018.

Hansen NL, Lauritzen M, Mortensen EL, Osler M, Avlund K, Fagerlund B, Rostrup E. Subclinical cognitive decline in middleage is associated with reduced task-induced deactivation of the brain's default mode network. *Human Brain Mapping* 35: 4488– 4498, 2014.

Kusumastuti S, Gerds TA, Lund R, Mortensen EL,

Westendorp RGJ. Discrimination ability of comorbidity, frailty, and subjective health to predict mortality in community-dwelling older people: Population based prospective cohort study. *European Journal of Internal Medicine* 42: 29–38, 2017.

Morville Th, Dohlmann T, Kuhlman AB, Monberg T, Torp M, Hartmann B, Holst JJ, Larsen S, Helge JW, Dela F. Glucose homeostasis in statin users - the LIFESTAT study. *Diabetes/ Metabolism Research and Reviews*, doi: 10.1002/dmrr.3110, 2018.

Osler M, Rostrup E, Nordentoft M, Mortensen EL, Bruunsgaard H, Fagerlund B. Influence of early life characteristics on psychiatric admissions and impact of psychiatric disease on inflammatory biomarkers and survival: a Danish cohort study. *World Psychiatry* 14: 364–365, 2015.

Osler M, Christensen GT, Garde E, Mortensen EL, Christensen K. Cognitive ability in young adulthood and risk of dementia in a cohort of Danish men, brothers, and twins. *Alzheimer's & Dementia* 13(12): 1355–1363, 2017.

Rask L, Bendix L, Harbo M, Fagerlund B, Mortensen EL, Lauritzen MJ, Osler M. Cognitive Change during the Life Course and Leukocyte Telomere Length in Late Middle-Aged Men. *Frontiers of Aging Neuroscience* 8: 300, 2016.

Wiegand I, Lauritzen MJ, Osler M, Mortensen EL, Rostrup E, Rask L, Richard N, Horwitz A, Benedek K, Vangkilde S, Petersen A. EEG correlates of visual short-term memory in older age vary with adult lifespan cognitive development. *Neurobiology of Aging* 62: 210–220, 2018.

PhD dissertations 2018

In CEHA (2014–2018), 53 PhD projects were completed in Theme II.

Ditte Søgaard: The influence of age and training on human muscle bioactive lipids and coupling to insulin resistance. January 2018.

Sofie Rosenlund Lau: A Matter of Course. An Ethnographic Assemblage of the Routinization of Statins in Denmark. March 2018.

Aja Neergaard Greve: The association between cognition in parents with schizophrenia or bipolar disorder and their offspring. May 2018.

Andreas Søndergaard Heltberg: Social disparity in type 2 diabetes - diagnosis, care, prognosis and effect of structured

personal care. August 2018.

Henriette Elkjær: Efficacy of specialized psychodynamic and systemic group treatment for women with a history of child sexual abuse: 5-year follow-up of a randomized controlled trial. August 2018.

Sasmita Kusumastuti: Prognostication in old age. October 2018.

Agnete Skovlund Dissing: Social Relations, Smartphone Interactions and Well-being in Young Adults. October 2018.

Kasper Bering-Liisberg: Løgn og Statin. October 2018.

Thomas Hoffmann Morville: Glucose homeostasis and physical performance in Danish statin users in primary prevention. November 2018.

Anja Birk Kuhlman: The Influence of statin use, CoQ10 supplementation and exercise on glucose homeostasis. December 2018.

Hanna Birkbak: Social relations and depression among older adults with dual sensory loss in Denmark. December 2018.

Kristine Harrsen Bachkati: Education and Cognitive Ability from midlife to late-life - Epidemiological studies on cognitive trajectories and oral health based on the 1914-cohort. November 2018.

Terese Sara Høj Jørgensen: Social conditions and the course of physical function in old age. December 2018.

Gitte Lindved Petersen: Socioeconomic position across the life course and physical capability in late-middle age. December 2018.

Anne Sophie Weddell-Neergaard: Effects of exercise on visceral fat and inflammation. December 2018.

Theme III

During CEHA (2014–2018), Theme III published 211 publications.

Scheibye-Knudsen M, Mitchell SJ, Fang EF, Iyama T, Ward T, Wang J, Dunn CA, Singh N, Veith S, Hasan-Olive M, Mangerich A, Wilson MA, Mattson MP, Bergersen LH, Cogger VC, Warren A, Le Couteur DG, Moaddel R, Wilson III DM, Croteau DL, de Cabo R, Bohr VA. A high-fat diet and NAD+ activate Sirt1 to rescue premature aging in Cockayne syndrome. *Cell Metabolism* 20: 840–855, 2014. Minocherhomji S, Ying S, Bjerregaard VA, Bursomanno S, Aleliunaite A, Wu W, Mankouri HW, Shen H, Liu Y, Hickson ID. Replication stress activates DNA repair synthesis in mitosis. *Nature* 528: 286–290, 2015.

Desler C, Frederiksen JH, Angleys M, Maynard S, Keijzers G, Fagerlund B, Mortensen EL, Osler M, Lauritzen M, Bohr VA, Rasmussen LJ. Increased deoxythymidine triphosphate levels is a feature of relative cognitive decline. *Mitochondrion* 25: 34–37, 2015.

Hansen RK, Mund A, Poulsen SL, Sandoval M, Klement K,
Tsouroula K, Tollenaere MA, Räschle M, Soria R, Offermanns
S, Worzfeld T, Grosse R, Brandt DT, Rozell B, Mann M, Cole F,
Soutoglou E, Goodarzi AA, Daniel JA, Mailand N, Bekker-Jensen
S. SCAI promotes DNA double-strand break repair in distinct
chromosomal contexts. *Nature Cell Biology* 18(12): 1357–1366,
2016.

Larsen NB, Liberti SE, Vogel I, Jorgensen SW, Hickson ID, Mankouri HW. Stalled replication forks generate a distinct mutational signature in yeast. *Proceedings of the National Academy of Sciences* 114: 9665–9670, 2017.

Mackey AL, Magnan M, Chazaud B, **Kjaer M**. Human skeletal fibroblasts stimulate in vitro myogenesis and in vivo muscle regeneration. *Journal of Physiology* 595(15): 5115–5127, 2017.

Scheibye-Knudsen M, Tseng AHH, Jensen MB, Scheibye-Alsing K, Fang EF, Iyama T, Bharti SK, Marosi K, Froetscher L, Kassahun H, Eckley DM, Maul R, Bastian P, De S, Ghosh S, Nilsen H, Goldberg I, Mattson MP, Wilson III D, Brosh RM, Gorospe M, Bohr VA. CSA and CSB Converge on Transcription-Linked Resolution of Non-B DNA. *Proceedings of the National Academy of Sciences* 113(44): 12502–12507, 2016.

Thomsen K, Yokota T, Hasan-Olive MM, Sherazi N, Fakouri NB, **Desler C**, Regnell CE, **Larsen S**, **Rasmussen LJ**, **Dela F**, **Bergersen LH**, **Lauritzen M**. Initial brain aging: heterogeneity of mitochondrial size is associated with decline in complex I-linked respiration in cortex and hippocampus. *Neurobiology of Aging* 61: 215–224, 2018.

Albers E, Sbroggiò M, Pladevall-Morera D, Bizard AH, Avram A, Gonzalez P, Martin-Gonzalez J, Hickson ID, Lopez-Contreras AJ. Loss of PICH Results in Chromosomal Instability, p53 Activation, and Embryonic Lethality. *Cell Reports* 24: 3274– 3284, 2018.

Keijzers G, Bakula D, **Scheibye-Knudsen M**. Monogenic Diseases of DNA Repair. *The New England Journal of Medicine* 377:1868–1876, 2017.

PhD dissertations 2018

In CEHA 2014–2018, 27 PhD projects were completed in Theme III.

Mette Flindt Heisterberg: Can angiotensin II receptor blockers improve the response to heavy resistance exercise in elderly human muscle? March 2018.

Jane Hübertz Frederiksen: Human DNA mismatch repair; from basic research to diagnosis of Lynch Syndrome. April 2018

Signe Jørgensen: Analysis of DNA replication stress at a telomeric region. June 2018.

Christian Eriksen: Regulation of tendon matrix and mechanical properties in elderly individuals: Influence of physical activity. August 2018.

Anders Karlsen: The maintenance and improvement of skeletal muscle mass and function in healthy elderly individuals and hospitalized patients. November 2018.

Andreas Kraag Ziegler: Effect of exercise training and ageing upon systemic and local inflammation in adipose and muscle tissue. December 2018.

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N O R D E A F O N D E N

Center for Healthy Aging is supported by the Danish foundation Nordea-fonden