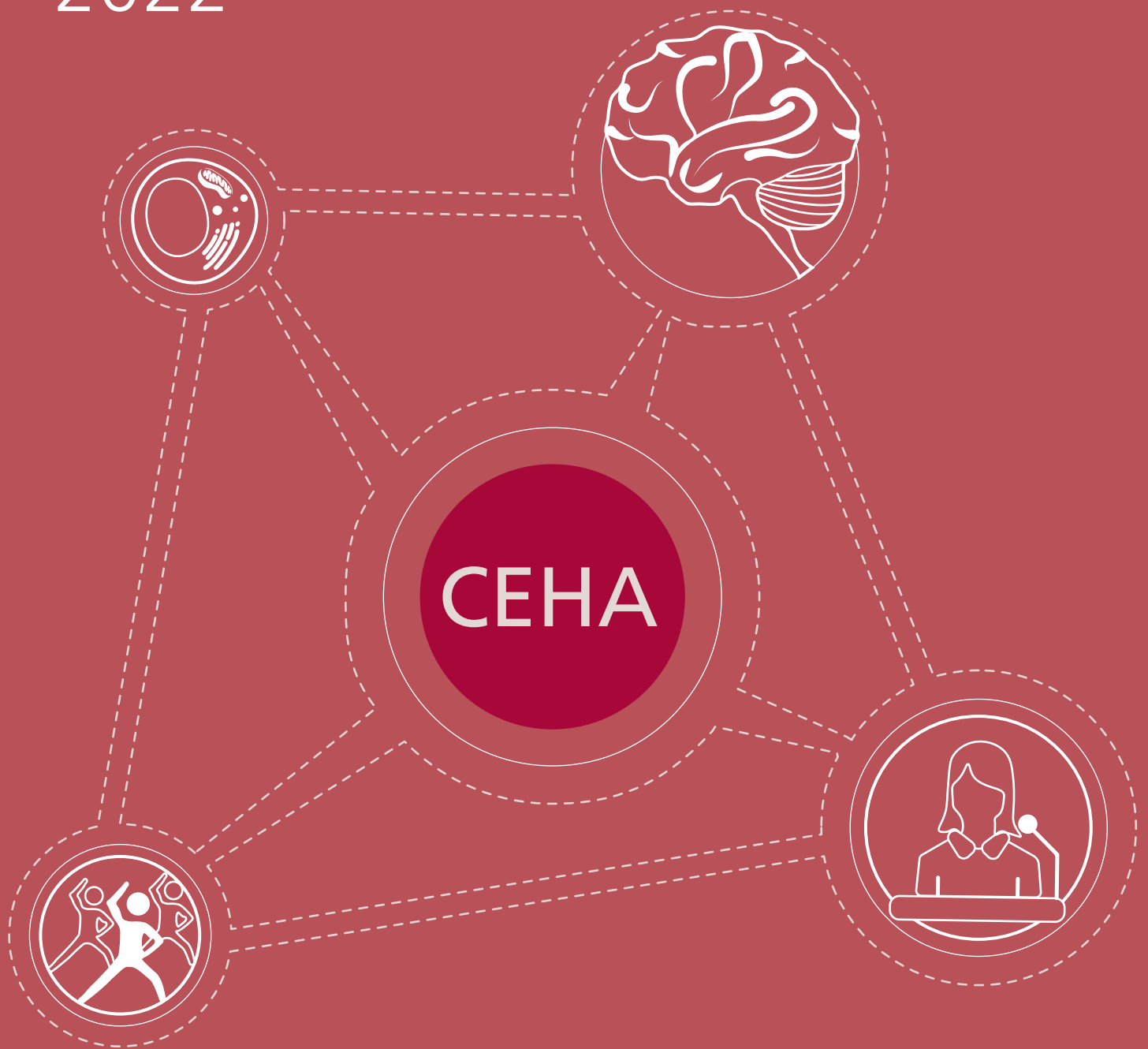


# Center for Healthy Aging

Self-evaluation  
2022



<b>Center for Healthy Aging (CEHA): facts in brief</b>	
External grants	>255 million DKK (34 million EUR) in addition to the Nordea-fonden grant
Publications (January 2018 to August 2021)	505
Completed PhD projects (2018 to August 2021)	44
Postdoctoral projects (2018 to August 2021)	76
Recruitment	Nationally and internationally recognized senior researchers: 9 New Group Leaders: 11
Summer schools (2011–2021)	IARU Summer School on interdisciplinary aspects of healthy aging (The 2020 Summer School was cancelled because of the COVID-19 pandemic)
International networks (selected)	IARU EIT Health Alliance for Healthy Aging Network on Basic and Translational Aging Research, with the University of Groningen Medical Center
Communication and outreach (selected)	2015–2019: People's Political Festival 2017–2021: Culture Night at SUND 2017–2019: Keep Your Brain Healthy 2019: Dissemination Conference: Physical Activity and Aging – From Research to Practice 2020–2021: Outreach project: From Work Life to Retirement Public event with relevant stakeholders: Livssituationer og Overgange i Alderdommen
Awards (selected)	Center of Excellence Grant (Danish National Research Foundation / Danmarks Grundforskningsfond), 2019 ERC Consolidator Grant, 2019 Lundbeckfonden Research Price for Young Scientists, 2019 Novo Nordisk Foundation Challenge Grant, 2019 Bispebjerg Hospital Grand Hagedorn Prize, 2020 EU, Horizon 2020

Editorial direction, editing, and graphic design

Elevate Scientific

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# Executive summary

The baby-boom generation is growing old, and so is the world's population, especially in Western societies and East Asia. In 2020, every fifth Dane was over 65 years old, and by 2030, the proportion of people aged 80+ years in Danish society will have increased by 60 percent compared to today.

Although being over 65 (or even over 80) does not feel or look like it used to, and an increased life expectancy is something to be celebrated, this demographic trend is a challenge that should be taken seriously. Even active, thriving seniors rely on health and care services more than younger people. They are not going to surrender to age-related ailments without a fight—nor should they. Treatment options are constantly improving. However, we are already starting to see our healthcare systems struggle, financially and personnel-wise, to satisfy the demand—not least during the COVID-19 pandemic.

This—and the crucial, long-term support from Nordea-fonden—puts us, at CEHA, in the privileged position of doing something immensely meaningful every day: we are taking a holistic approach to making healthy aging a reality. For 13 years now, CEHA's researchers have been forming a unique hub of knowledge on aging, across research disciplines. Our expertise ranges from the effects of aging on the smallest cellular unit in the human body, through to senior citizens' individual needs, to the macro-movements in our welfare economy. We are also dedicated to outreach and stakeholder engagement, to translating our research into clinical and societal practice, and to nurturing the next generation of researchers in aging.

## Continuing to reach research milestones

Aging is a complex, multidimensional process that can only be understood with the use of a sophisticated interdisciplinary toolbox. As we learn and understand all aspects of human aging—from the cellular level, where it all begins, and up—our ability to develop interventions that promote individual and societal health and well-being will improve, even as population demographics continue to change over time.

Accordingly, CEHA pursues basic and clinical research in diverse disciplines and embraces cross-cutting aging-related interdisciplinary studies, from neurobiology to public health, epidemiology, and the relevant social science disciplines. Our major research discoveries since 2018 include identifying a mitochondrial process in the brain that is likely responsible for Alzheimer's disease, and uncovering the correlation between poverty and physical aging.

The Center is recognized internationally for its high-quality research and its impressive publication record, including more than 2000 articles published in top-tier peer-reviewed journals over the past 13 years.

As an acknowledgement of our excellence, our researchers have received highly prestigious awards for their work. To name just a few, Professor Simon Bekker-Jensen received a European Research Council Consolidator Grant and has been invited to join the exclusive EMBO Young Investigator Programme (which has only 30 members worldwide), and Professor Michael Kjær received the Hagedorn Award and the KFJ Award.

Because of our reputation for groundbreaking high-quality research, the Center's researchers also receive generous external funding. For example, in 2020, Professor Ian Hickson received an award of 45 million DKK (6 million EUR) from the Danish National Research Foundation. Furthermore, between January 2018 and August 2021, CEHA researchers have attracted a total of 255 million DKK (34 million EUR) in external funding in addition to the grant from Nordea-fonden.

## Change through outreach and stakeholder engagement

To make sure that our research reaches the people and organizations that can translate it into clinical and societal practice, CEHA aims to develop and maintain strong relationships with research peers at home and abroad, patient and organizations of interest, municipalities, and private companies. Collaboration and knowledge sharing is something we keep getting better at, and we are giving it high strategic priority.

One example of our citizen-centric and impact-oriented approach in action is the Copenhagen Center for Clinical Age Research (CopenAge) led by Professor Flemming Dela in collaboration with Professor Charlotte Suetta (Department of Clinical Medicine), which combines basic research with clinical interventions to improve the rehabilitation of elderly patients. As another example, since our last self-evaluation in 2017, CEHA researchers formed two clinical academic groups: one investigating the use of physical activity for the prevention and treatment of chronic diseases and prolonged injuries, and one focusing on improving acute treatments for elderly people suffering from multimorbidity.

Furthermore, we have embarked on a series of collaborative projects in local communities. An example is the project “From Work Life to Retirement,” led by Outreach Consultant Barbara Zinckernagel. In the project, we cooperate with three Danish municipalities (Aarhus, Vejle, and Vordingborg) to develop sustainable concepts for helping seniors with little or no education to maintain their health and quality of life as they transition to retirement.

Researchers from CEHA are also diligent participants of various boards and councils aimed at knowledge sharing between relevant stakeholders in our field. These include several groups under the Danish Health Authority, the EU group Science Advice for Policy by European Academies (SAPEA), and the brand new Thinktank for Future Welfare, organized by Tryg Insurance and involving some of Denmark’s most influential patient organizations and unions. Furthermore, in 2019, Associate Professor Maria Kristiansen brought together 200 healthcare stakeholders for a meeting on personalized medicine. Now, with COVID-19 restrictions almost out of the picture, CEHA can once again engage in large in-person events. Indeed, a knowledge festival for stakeholders and seniors is already in the making, in collaboration with Aarhus municipality.

## Change through teaching, networking, and nursing talent

One of the Center’s top priorities is to educate the next generation of basic scientists, clinicians, and health sector professionals, and prepare them for conducting leading-edge interdisciplinary aging-related research. For example, CEHA is a partner in the educational campus component of the European Institute of Innovation and Technology (EIT) Health Initiative, whose focus is healthy living and active aging. Our educational portfolio includes undergraduate, Master’s, and PhD programs, an international summer school, and massive open online courses (MOOCs) on the Coursera platform. The Center also offers courses on innovation and entrepreneurship in the EIT Health PhD Program. Furthermore, we are closely linked with the International Alliance of Research Universities (IARU) Network. Our Network for Young Scholars (NYS) organizes seminars on career development, hosts networking events to bring students and young researchers together, and works with the PhD Academy for Interdisciplinary Aging Research (PAIAR) to develop and organize PhD-level courses.

Center researchers also organize conferences for researchers in aging. For instance, CEHA’s Morten Scheibye-Knudsen and Daniela Bakula, along with Alex Zhavoronkov from Insilico Medicine, organized the 7<sup>th</sup> and 8<sup>th</sup> Annual Aging Research and Drug Discovery Meetings in Copenhagen in September



**Professor Lene Juel Rasmussen,**  
Executive Director



**Dean Ulla Wewer,**  
Faculty of Health and Medical  
Sciences, Nordea-fonden Grant  
Holder

2020 and September 2021. There, leaders in the aging and longevity fields described their latest findings relevant to the molecular, cellular, and organismal basis of aging and aging-related interventions to more than 1000 attendees (some of them participating online).

These are only some highlights of the Center’s many ongoing activities, which are too numerous to describe in this short summary.

## CEHA—in safe hands

CEHA’s activities and the realization of the Center’s ambitions are overseen by CEHA management, who, together with the scientific advisory board, are attuned to the changes in today’s world and guide CEHA’s mission and vision accordingly, to address the most pressing challenges associated with an aging society.

We are proud of what we have achieved to date, with strong overall performance and impact. Furthermore, regular strengths–weaknesses–opportunities–threats (SWOT) exercises allow us to capitalize on our strengths, take advantage of opportunities, and be aware of (and address) weaknesses and threats. We are proud of the concerted action of CEHA researchers, collaborators, and stakeholders.

I would like to end by looking to the future. Just as aging research needs to be interdisciplinary to enable us to really understand the complexity of human aging, so too do societal efforts to adjust to the changing demography need to be multifaceted. At CEHA, we believe that Denmark needs a politically backed national aging initiative that can bring together foundations, relevant organizations, public and private health and welfare providers, and researchers in aging from Danish universities to create a comprehensive aging strategy. Building on our wide-ranging experience, expertise, and genuine passion for healthy aging solutions, we continue to work to make Denmark the best country in the world to grow old in.

*Lene Juel Rasmussen*

*Ulla Wewer*

# 1 Center for Healthy Aging (CEHA): Tackling the aging challenge holistically

## 1.1 Aging: A global societal challenge

We are currently witnessing a rapid increase of the elderly population in virtually all societies. It is predicted that 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 tripled<sup>1</sup>. This situation is driven by major demographic changes across the globe. Specifically, the developed countries have seen an unprecedented doubling of the average lifespan over the 20<sup>th</sup> century, and it is estimated that the average life expectancy of newborns will gradually increase to approximately 100 years during the 21st century. In Denmark, according to the latest population projection, the proportion of those over the age of 65 will increase from 20 percent in 2021 to 24 percent in 2042 (Fig. 1a).

Aging is the leading risk factor for nearly all major chronic diseases, increasing morbidity and significantly driving healthcare costs<sup>2</sup>. Furthermore, the increasing average lifespan and average life expectancy 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 understood and appreciated (Fig. 1b). Consequently, aging is one of the most broadly recognized societal challenges that we will face in the coming decades, with the goal of “healthy aging” already an urgent priority for the World Health Organization (WHO)<sup>3</sup>.

Active and healthy aging has been proposed as a keystone for a sustainable Europe. Danish policies and priorities reflect this approach to aging. Specifically, Danish welfare policies outline a range of intersectoral strategies focusing

on individual and structural factors affecting the ability to maintain health, and to live actively and independently into old age. This includes a law on preventive home visits targeting groups of elderly people at risk of functional decline; reablement, to help the elderly regain the ability to look after themselves; an 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 better innovative and holistic care for elderly people at the local community level.

From an individual perspective, a longer lifespan can be seen as progress, especially if it means more high-quality years of life. If we could guarantee such an increase of high-quality years, not only by smart welfare policies but also by an improved understanding and awareness of the aging process, as well as by improved mitigating strategies, the growing number of elderly people would not necessarily become the burden that many fear. Rather, a growing number of active elders would become a new resource, both in the general workforce as well as in civil society.

## 1.2 Challenges in aging research

Aging is a complex process that can only be fully understood by considering multiple perspectives (e.g., biological, social, psychological, and cultural). Consequently, the overarching challenges that should be addressed so that healthy aging is achieved traverse multiple areas. The major challenges in the field include the following:

1. **Improving the understanding of the basic biology of aging.** Despite the critical relevance of aging to the overall state of European society, understanding of the basic biological mechanisms that contribute to and influence aging, and how these mechanisms relate to disease development, is limited. This knowledge is crucial for improving healthy aging and counteracting chronic disease associated with increased age.
2. **Translating laboratory findings into clinical applications.** Interventions that target basic aging processes

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

2 Global status report on non-communicable diseases 2010, WHO: [https://www.who.int/nmh/publications/ncd\\_report\\_full\\_en.pdf](https://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



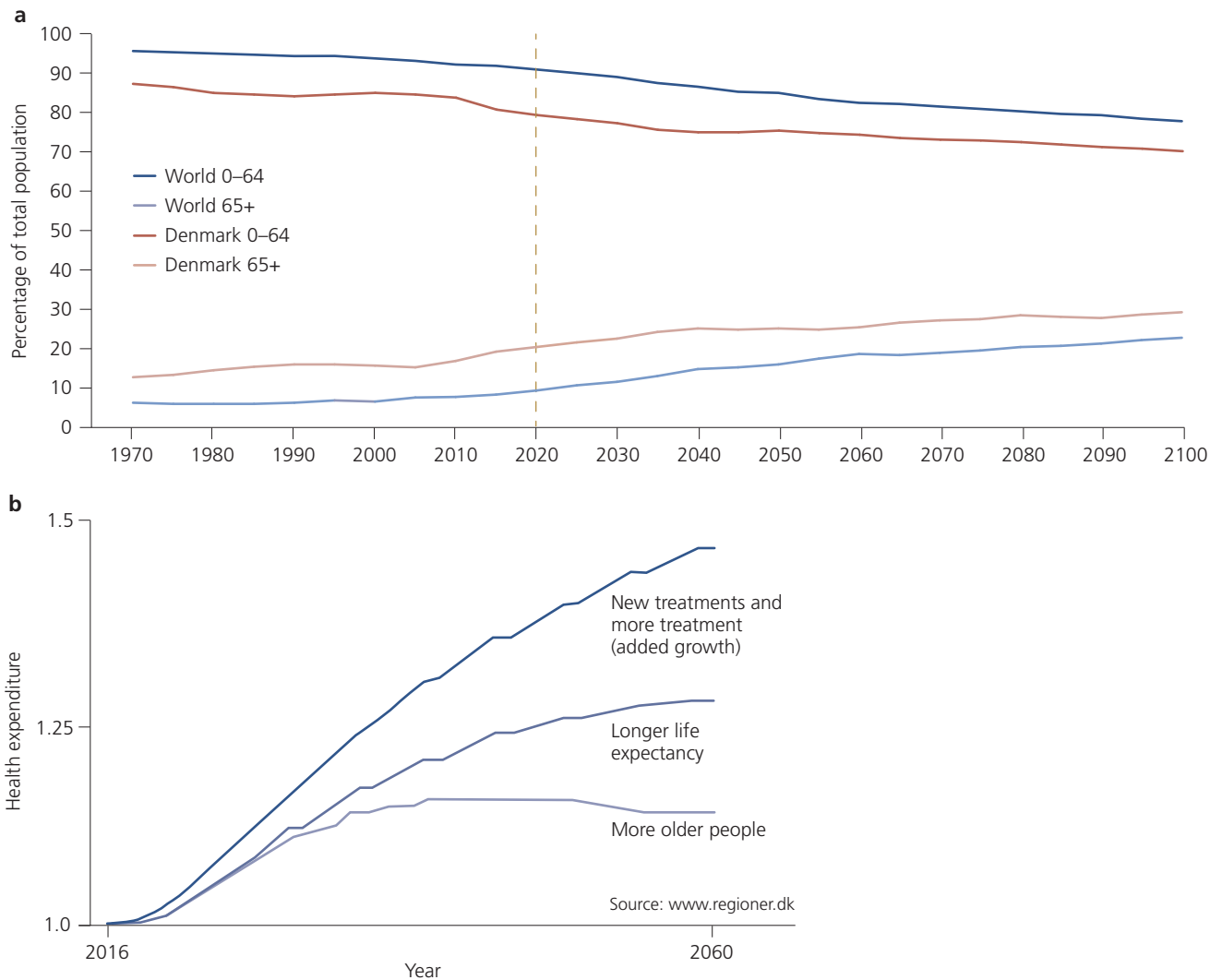


Figure 1: (a) Historical and forecasted demographic changes in Denmark and globally. (b) Projected increase in Danish health expenditure during the coming decades. It is estimated that expenditures will increase by 47% (58 billion DKK) from 2016 to 2060 if current development trends continue. The precise increase depends on a combination of demographic and technological changes: healthier aging will ameliorate future increases, but new technologies will boost them. Source: Statistics Denmark.

have been discovered that enhance the healthy lifespan and delay age-related disease in the laboratory setting. Furthermore, biomarkers for the 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.

3. **Improving the understanding of the link between aging and the environment.** Understanding how the environment contributes to aging in humans—and, more importantly, how the biological and environmental factors interact in aging—is incomplete. This knowledge is essential for defining strategies that extend the “health span” (i.e., the number of years lived without disability), during which people can stay active.
4. **Improving the understanding of the link between genes, lifestyle, and health.** The effect of genetic and lifestyle factors on health parameters has not yet been extensively analyzed. This knowledge is fundamental to addressing the unsustainable burden of the aging population on the healthcare system.
5. **Improving accounting for local community**

**heterogeneity during aging policy development.** The local community (neighborhood) plays a major role in an individual’s health. However, understanding of the role of the heterogeneity of local community in health and energy promotion among aging citizens is lacking. This knowledge is crucial for devising specific interventions for the local organization and implementation of care for the elderly.

Considering the complexity of the overarching challenges in the field, a multidisciplinary, holistic, cell-to-society research approach is needed to develop effective interventions and policies to promote the healthy aging of individuals and societies. With this in mind, we set up CEHA in 2009.

### 1.3 CEHA: Raison d’être, unique approach, and history

With the aging of society, societal institutions and socioeconomic environments are changing rapidly, rendering obsolete the traditional perceptions of aging, and catering to the needs of an aging population. It is therefore imperative that scientists work together with health professionals,



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

politicians, stakeholders, and citizens to gain a comprehensive understanding of the aging process; develop effective ways of preventing and treating age-related diseases; develop appropriate strategies to provide healthcare services, social networks, and pensions; and facilitate disruptive innovations to foster healthy aging.

Accordingly, we launched CEHA in 2009 as a multidisciplinary and mainly Danish center to address the individual and societal challenges associated with aging (Fig. 2). Specifically, we did several integrative biological studies to improve the understanding of the basic biology of aging. We investigated the link between aging and environment. We also addressed the need for improved insight into the link between genes, lifestyle, and health. Furthermore, we focused on building partnerships to translate laboratory findings into clinical applications. This approach to aging research was groundbreaking at the time. Since CEHA's foundation, we have honed and revised our approach, and we have evolved into a multidisciplinary international center at the forefront of aging research.

At CEHA, we emphasize multidisciplinary collaborations among scientists—locally, nationally, and internationally—because we understand that collaboration stimulates creativity

and growth, leading to synergy between participating groups. We thus strive to facilitate progress, and we allow each researcher to accomplish more than they could accomplish working independently. Our approach is unique in that as well as bridging multiple disciplines to foster a holistic understanding of aging and scientific excellence, we are invested in outreach and capacity building, and we constantly evolve and challenge stereotypes. This approach enables us to employ a common conceptual framework for understanding the complex interplay of biological, psychological, social, and cultural factors that influence health and well-being at the individual and societal levels.

### Multidisciplinary

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



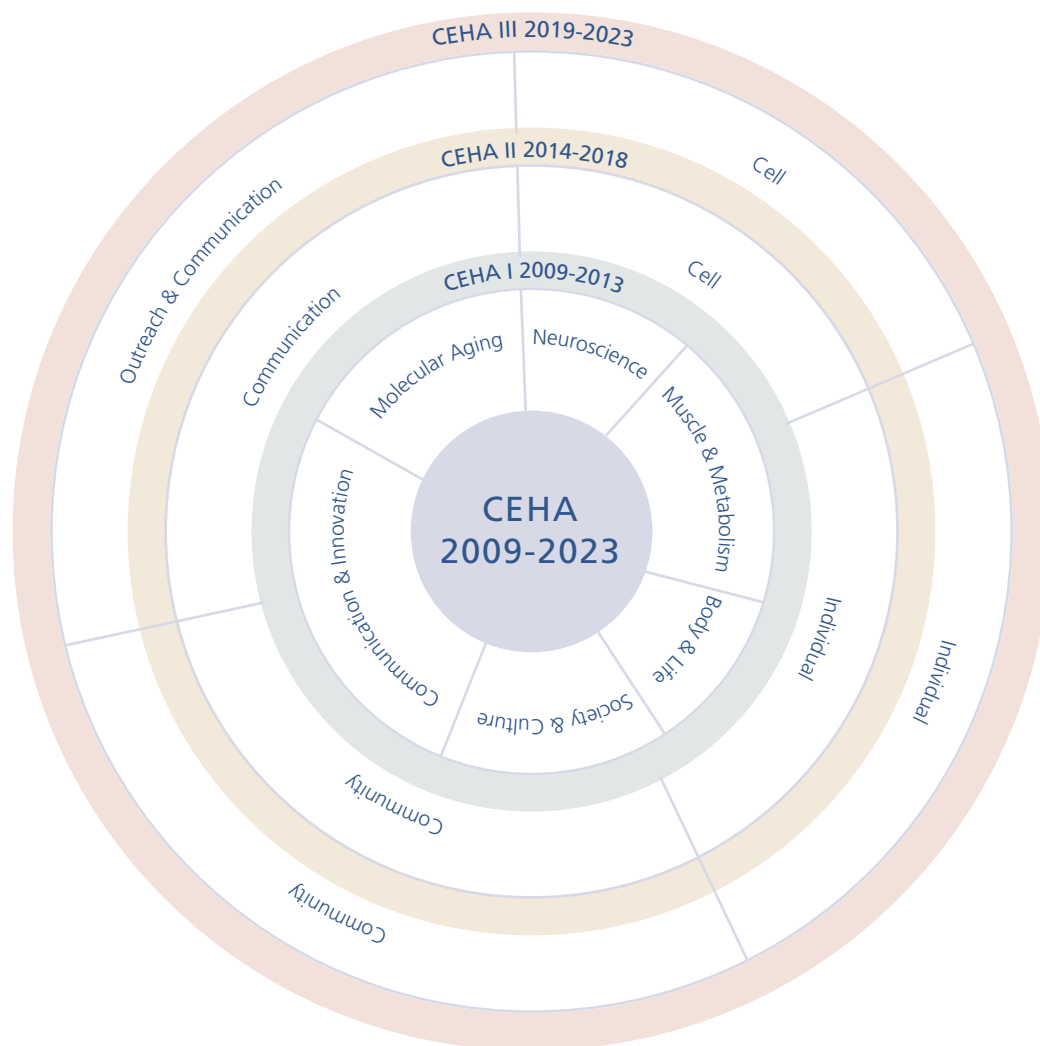


Figure 3: CEHA's evolution through the years.

### Holistic approach

We seek to understand all dimensions of aging—biological, social, psychological, and cultural—and on all scales, ranging from the cellular through to the individual and the societal. This holistic approach is rare, as only a few institutions in the world have the capacity to adopt it.

### Scientific excellence

We promote rigorous and innovative research into aging by bringing together top international scientists to address important biological, societal, and other questions from multiple perspectives. This common conceptual framework for all CEHA researchers, regardless of discipline, ensures that we stay focused on our main priorities and that we are successful in translating our findings into innovative health-promoting interventions to aid healthy aging.

### Outreach

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

### Constant evolution and challenging of stereotypes

We are a dynamic center that tunes our research and adapts

our engagement with various stakeholders to respond to changing scientific and social issues and needs. We are committed to contributing to the education of citizens by challenging ageism in our society and the habitual thinking about the life course that postulates that aging is inevitably associated with becoming dependent and disabled.

### Capacity building

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

### 1.4 CEHA: Coming of age

Since its founding in 2009, made possible by a generous donation from Nordea-fonden, CEHA has championed an interdisciplinary approach to aging based on our medical and scientific interest in age-associated disease and frailty. In the second grant period (2014–2018), CEHA's focus expanded to include prevention and health promotion, and we became involved in collaborative projects with Danish municipalities.

The Center, which began with 110 employees in 2009, now boasts 241 employees (as of August 2021). This has

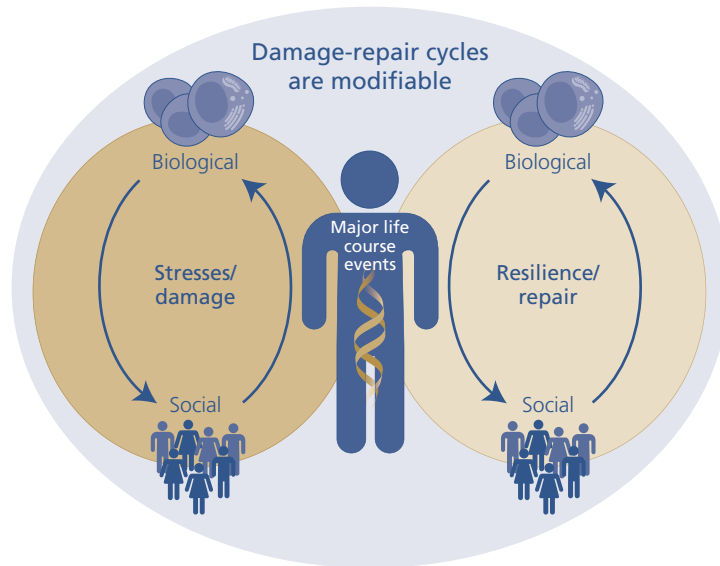


Figure 4: The complex interplay between internal (biological) and external (environmental, behavioral, and social) factors.

resulted in a steadily growing number of individual research collaborations, and participation in prestigious international collaborations and networks, such as the International Alliance of Research Universities (IARU), the Alliance for Biology of Ageing Research and Healthy Ageing Multidisciplinary Biobanking Approaches (ABRAHAM), and the European Institute of Innovation and Technology (EIT) Health.

Hence, over the years, CEHA has grown from a center bringing together high-level monodisciplinary researchers, primarily from UCPH, to one for high-level multidisciplinary researchers from UCPH and beyond (as described below), and a world-renowned center for aging research, driving societal change for healthy aging.

### 1.5 CEHA (2019–2023): Toward a holistic approach

Aging is a complex and multidimensional process that needs to be explored from multiple scientific perspectives—including biological, social, psychological, and cultural—and by taking a multilevel approach that includes the individual, community, and societal levels. Such research entails scientific, technological, organizational, and ethical challenges. Consequently, developing the interventions and policies to promote healthy aging of individuals and societies necessitates a multidisciplinary, holistic, cell-to-society approach, in full consultation with citizens, stakeholders, and policymakers, and we champion this philosophy at CEHA (Fig. 3).

#### Vision, mission, and strategic objectives

Since its launch in 2009, CEHA has advocated interdisciplinary research emphasizing the biomedical dimensions of healthy aging. In 2014, CEHA turned its attention to disease prevention and health promotion, simultaneously addressing the societal and cultural dimensions of aging via interactive projects involving Danish municipalities. We have continued this trajectory by further refining the existing interdisciplinary research approaches and developing new approaches across complementary disciplines within a common conceptual framework. Interdisciplinary projects became the core of CEHA, while the widely recognized merits of pursuing “bench-

to-bedside” translational models were balanced by a novel emphasis on “bedside-to-bench” exploratory research, with the involvement of diseased elderly, to understand age-related changes in the human body.

Ultimately, we at CEHA came to understand that the accumulation of aging damage is malleable to a far greater extent than previously imagined because of the complex interplay between internal (biological) and external (environmental, behavioral, and social) factors (Fig. 4). CEHA took its cue from these findings in pursuing a holistic perspective by exploring the complex interplay between the cellular, organismal, and societal factors that influence how people age. This is reflected in our current mission, vision, and strategic objectives.

Our **vision** is to become a world-leading interdisciplinary research center that empowers people to live longer, healthier, and more meaningful lives.

Our **mission** is to employ a common conceptual framework to understand the complex interplay of biological, psychological, social, and cultural factors that influence health and well-being at the individual and societal levels.

Accordingly, we work toward the following strategic objectives:

- To employ a systems approach to understanding aging, i.e., one that encompasses the individual and societal levels, as well as biological, cultural, ethical, and psychological perspectives
- To achieve a multifaceted understanding of the aging process by performing cutting-edge multidisciplinary research
- To foster healthy aging and boost awareness by undertaking meaningful stakeholder engagement
- To challenge the negative public discourse on aging, frailty, and dependency by focusing the public’s attention on

damage/repair, energy, resilience, intrinsic capacity, and psychosocial (functional) abilities of healthy older people and those with chronic disease.

- To contribute to new knowledge on human aging by intensifying jointly planned and executed research programs.

### Approach

The ambition of CEHA is to use a holistic approach to address the grand challenges of aging research. The approach is built on fostering interdisciplinarity, scientific excellence, stakeholder engagement, and capacity building.

Over the years, we have significantly strengthened the interdisciplinary nature of our research in CEHA while ensuring scientific excellence.

We take pride in fostering scientific excellence, which is enabled by CEHA's vibrant infrastructure, particularly its integration in UCPH, one of the top-ranked universities in continental Europe. This embedment is complemented by strong ties with three university hospitals in the Copenhagen area (Rigshospitalet, Hvidovre, and Bispebjerg hospitals) that substantially invest in CEHA, for instance through the clinical academic groups (see section 7). At CEHA, we are well positioned to take full advantage of the aging-research resources unique to Denmark. These include the well-established nationwide health registries covering several generations of Danes, a strong scientific infrastructure, and the relatively small size and high homogeneity of the Danish population.

Furthermore, in CEHA (2019–2023), we emphasize collaborative approaches that involve citizens and other major societal stakeholders in research and outreach projects.

### Milestones and achievements

Below, we present a selection of CEHA milestones and major achievements for the years 2019–2023 that support our mission and vision. See appendices for details: the full list of our scientific accomplishments is provided in Appendix A1; all publications for that period are provided in Appendix A2;

our capacity building and educational activities are itemized in Appendix A3; and an overview of all our research projects is provided in Appendix A4.

### Center-level milestones

#### 1. **Scientific publications and knowledge dissemination.**

We generate over 150 peer-reviewed publications per year, of which 90 percent are published in open-access journals and 20 percent are in high-impact international (interdisciplinary) scientific journals. Furthermore, to communicate our findings to various stakeholders in Denmark and abroad, we have engaged in communication partnerships with a broad range of stakeholders, participated in public events, and achieved an annual 5 percent increase of mentions in stakeholder media.

#### 2. **Educational and research training activities.** Academic development. As part of our dedication to capacity building, we teach undergraduate courses at UCPH and develop initiatives to ensure that aging Research Themes are included in the teaching curricula whenever appropriate. In this context, we also organize a series of symposia, internal multidisciplinary seminars, and workshops. We organize annual summer schools for MSc students. We also engage with our Network of Young Scholars (NYS) members in the organization of such activities.

#### 3. **Key awards.** In 2019, we were awarded Center of Excellence status from the Danish National Research Council and Novo Nordisk Foundation. In 2020, Professor Michael Kjær received the Grand Hagedorn Prize in recognition of his excellent research in internal medicine in Denmark.

#### 4. **Funding success.** We aim to attract additional funding for CEHA III activities to equal that received from Nordea-fonden. Collectively, we have obtained 255 million DKK (34 million EUR) in additional funding between January 2018 and August 2021.

# 2 Research

Below, we present an overview of the rationale, developments, and key achievements of research during the different Center for Healthy Aging (CEHA) grant periods: 2009–2013 (section 2.1), 2014–2018 (section 2.2), and 2019–2023 (sections 2.3–2.6). Detailed information on the most recent CEHA research activities and accomplishments is provided in appendices A1–A4.

## 2.1 CEHA retrospective: 2009–2013

From 2009 to 2013, CEHA aimed to conduct 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. We also worked to identify mechanisms to develop and implement diagnostic and/or preventive interventions that minimize health burdens associated with normal and accelerated aging and with aging-related chronic disease. The common thread running through this research period was ‘frailty,’ and the research was centered on five Research Programs. These Programs are briefly described below, followed by a description of the major cross-disciplinary projects conducted during this funding phase and the key outcomes.

### Programs

#### 1a. Molecular aging:

This Program focused on oxidative stress, lactate signaling, calcium homeostasis, mitochondrial dysfunction, and neurodegenerative diseases, and their contribution to aging and age-related diseases.

Program leader: **Ian Hickson**

#### 1b. Neuroscience:

This Program focused on oxidative stress, genomic instability, calcium homeostasis, neuroenergetics, mitochondrial dysfunction, and neurodegenerative diseases in the context of aging and age-related diseases.

Program leader: **Martin Lauritzen**

#### 2. Muscle and matrix:

This Program focused on understanding the metabolic, genetic, and lifestyle factors that influence skeletal muscle function throughout the life course, with the aim of preventing and/or postponing functional decline in old age.

Program leaders: **Michael Kjær and Flemming Dela**

#### 3. Body and Life:

This Program focused on the life-course perspective on aging; specifically, the aim was to contribute new knowledge on the life-course determinants of health and early aging in mid- and late life, designed with a particular emphasis on the earlier stages of the aging process.

Program leaders: **Kirsten Avlund and Erik Lykke Mortensen**

#### 4. Society, Culture, and Healthcare Policy:

This Program focused on preventive medication, health services, and the health of an aging population, with a view to understanding decisions by different actors (e.g., managers, health professionals, and patients) related to prescribing and using preventive drugs, and identifying factors influencing these decisions (e.g., the evidence behind the decisions) and tools for improved coordination of interventions. Furthermore, the research analyzed possible inequalities in the patterns of utilization of the health services related to social and ethnic background; the aim of this research was to identify barriers to the optimal use of preventive medication and ways of achieving greater equity in its distribution, and consequently to improve healthy aging for all population groups.

Program leader: **Allan Krasnik**

#### 5. Health in Everyday Life:

This Program looked at how individuals deal with aging in their everyday life and how they maintain or increase their quality of life, by exploring new strategies for addressing the everyday health concerns of our aging population.

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

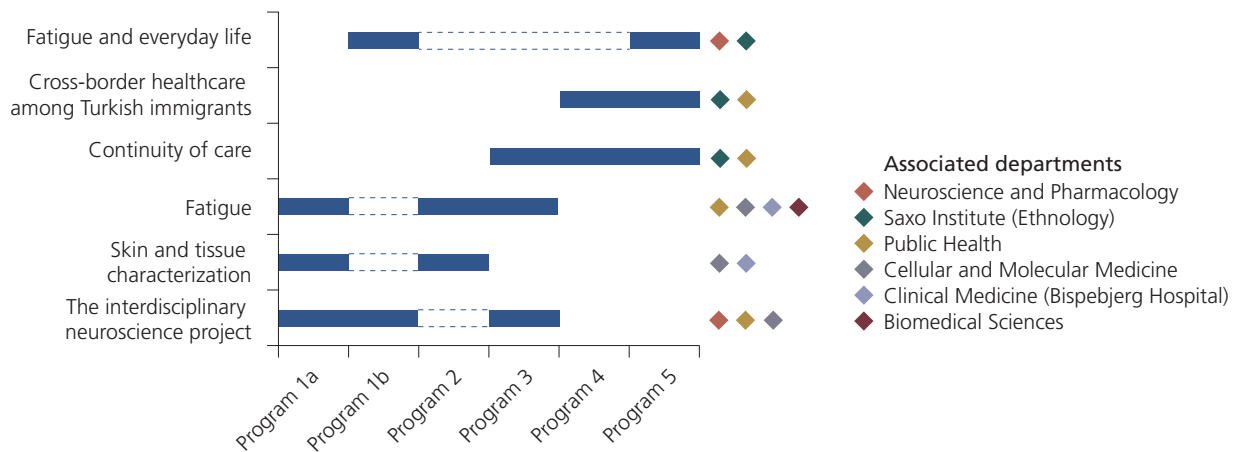


Figure 5: Overview of multidisciplinary projects in CEHA 2009–2013.

### Key multidisciplinary projects

In addition to the main focus of each Program described above, several multidisciplinary projects were conducted across the programs (Fig. 5), as follows.

#### Fatigue and everyday life:

This project focused on the experiences of fatigue among healthy people and people suffering from apoplexy (Programs 1b and 5).

Coordinator: **Lene Otto (Astrid Jespersen)**

#### Cross-border healthcare:

This project involved Turkish immigrants in Denmark, with a particular focus on the elderly (Programs 4 and 5).

Coordinator: **Lene Otto (Astrid Jespersen)**

#### Continuity of care:

This was devised as an international comparative analysis of tools and settings for the coordination of preventive drug medication (Programs 3, 4, and 5).

Coordinator: **Allan Krasnik**

#### Fatigue (low subjective vitality) in middle-aged men:

This project aimed to explore the links between fatigue and specific biological and physiological markers in individuals from the Copenhagen Aging and Midlife Biobank (CAMB) cohort (born in 1948–1961) (Programs 1a, 2, and 3). We tested the correlation between fatigue and levels of reactive oxygen species, deoxynucleoside triphosphates (dNTPs), DNA damage, body mass index, and physical performance. The project allowed us to identify important associations between biological and social factors and aging.

Coordinators: **Kirsten Avlund and Vilhelm Bohr**

#### Skin and tissue characterization of a patient with apparent dimorphic rates of skin aging:

This project explored the biological mechanisms underlying an individual showing a premature aging phenotype (Programs 1a and 2).

Coordinator: **Michael Kjær**

#### Interdisciplinary neuroscience project:

This project focused on the cumulative effect of morbidity on brain function at different life stages in a Danish birth cohort

composed of Danish men born in 1953. The primary aim of the project was to identify factors that influence or predict cognitive function, especially as relevant to cognitive decline in mid- or late life.

Coordinator: **Martin Lauritzen**

#### KEY ACHIEVEMENTS CEHA (2009–2013)

Science: 791 publications

Capacity building: 81 individual PhD students enrolled, and 54 individual post-docs employed during the first 5 years of CEHA

External funding: more than 223 million DKK (approximately 30 million EUR) in addition to the Nordea-fonden grant

Awareness: 672 media mentions (of which 47 on the radio, 41 on television)

### 2.2 CEHA retrospective: 2014–2018

During this 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 was ‘energy’ and the retention of vitality in its broadest sense, for healthy aging and for society. In this second phase of CEHA, our research specifically focused on the significance of ‘energy’ in the aging processes, not only as it relates to individual bodies and processes at the cellular level, but also in relation to psychological and social dimensions, including interest in one’s surroundings and engagement with other people. This reorganization was a natural development from the initially monodisciplinary approaches in the first phase of CEHA (2009–2013) toward a more-encompassing interdisciplinarity.

Building on the knowledge gained from CEHA’s first phase, and the large number of successful interdisciplinary collaborations facilitated by the establishment of the Center, we reorganized the Center around three Research Themes, established to enhance multidisciplinary collaborations at CEHA (see Fig. 6). We also established a Communication and Outreach Platform to put knowledge about healthy aging on the agenda and ensure that aging research is prioritized by politicians and health decisions and recommendations are carried out that target specific challenges and citizens.

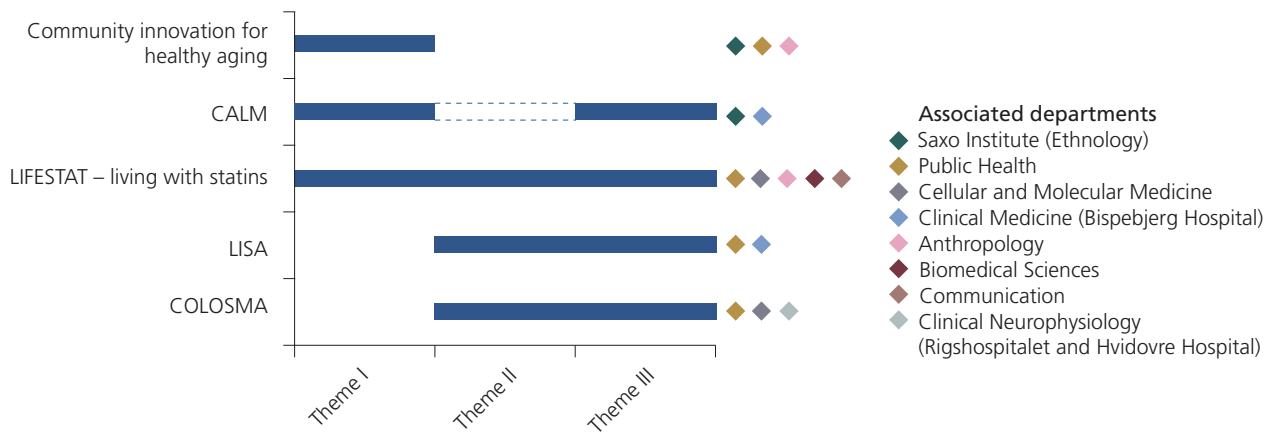


Figure 6: Overview of multidisciplinary projects during CEHA (2014–2018).

## Research Themes

### I. Community Innovation for Healthy Aging:

This Theme focused on the significance of the local community, and on opportunities for promoting the health and energy of the elderly in the last stage of life. Much of this work was done in collaboration with four Danish municipalities, by also studying how historical and social changes have influenced relations between people and between generations.

Research Theme leader: **Astrid Jespersen**

### II. Life Course Aging Processes: Lifespan Exposures and Healthy Aging:

This Theme focused on exploring the different factors that influence the aging processes throughout life; how citizens could be motivated to follow an active lifestyle; and what happens to cells, muscles, and the brain as we get older. It also involved an intervention project focusing on the protective effect of physical activity against age-related changes in the musculature and the brain.

Research Theme leader: **Martin Lauridsen**

### III. Energy Balance in Humans:

This Theme focused on the cellular and physiological mechanisms that cause energy levels to dwindle with age by taking a highly integrated approach examining biomedical, physiological, and psychological aspects of aging in humans. This theme exploited CEHA's unique access to and relationships with local Danish municipalities and this theme participated in outreach activities designed to engage the general public in CEHA's aging research initiatives.

Research Theme leader: **Ian Hickson**

## Key multidisciplinary projects (Fig. 7)

### CALM: Counteracting Age-Related Loss of Skeletal Muscle Mass (Themes I and III):

This project was an interdisciplinary research collaboration focusing on age-related loss of skeletal muscle mass and the contribution of dietary protein and physical activity to elderly people achieving a healthier and more active lifestyle. Furthermore, a systems approach (both qualitative and quantitative) was used to address the roles of biological, sensory, clinical, physiological, and cultural factors in the

context of the project. CALM aimed to generate scientific evidence, recommendations, and innovative solutions to counteract the age-related loss of skeletal muscle mass in elderly Danes.

### LIFESTAT: Living with Statins (Themes I–III):

This was an interdisciplinary project that leveraged approaches and knowledge from medicine, the humanities, and social sciences to analyze the impact of statin use on the health, lifestyle, and well-being of 40- to 60-year-old Danes. The project showed that mitochondrial function was affected in statin users. CALM and LIFESTAT were both launched in 2013 with grants from the University of Copenhagen (UCPH) Excellence Programme for Interdisciplinary Research (<https://www.research.ku.dk/strengths/excellence-programmes>).

### LISA: Live Active–Successful Aging (Themes II–III):

This project is ongoing (since 2014) and investigates the impact of different training types on muscle function over a prolonged time period. The project involves healthy individuals and those with chronic disease. In the project, after 1 year of interventions, the participants are followed for 10 years to assess their long-term ability to adhere to exercise training and to potentially change their behavior and attitude toward exercise. Results suggest that heavy-resistance training improves muscle mass and strength, that this effect is not as pronounced with medium-intensity training, and that strength training stimulates the release of anti-inflammatory cytokines. The observations will be compared to the results of similar studies in animal model systems (also see section 3.2).

### COLOSMA (Copenhagen Longitudinal Study of Male Cognitive Aging, Themes II–III):

This is an ongoing clinical project (started in 2009). It focuses on the associations between cognitive function and biological and brain parameters. The data obtained to date indicate that cognitive decline can be predicted with high sensitivity by recording changes in cerebral rhythmic activities evoked by complex visual stimuli (also see section 3.4).

## 2.3 The next stage: CEHA (2019–2023) overview

For this phase of CEHA, we have built on our experience in the preceding funding periods to evolve toward our main strengths that are research excellence, involvement of other stakeholders,



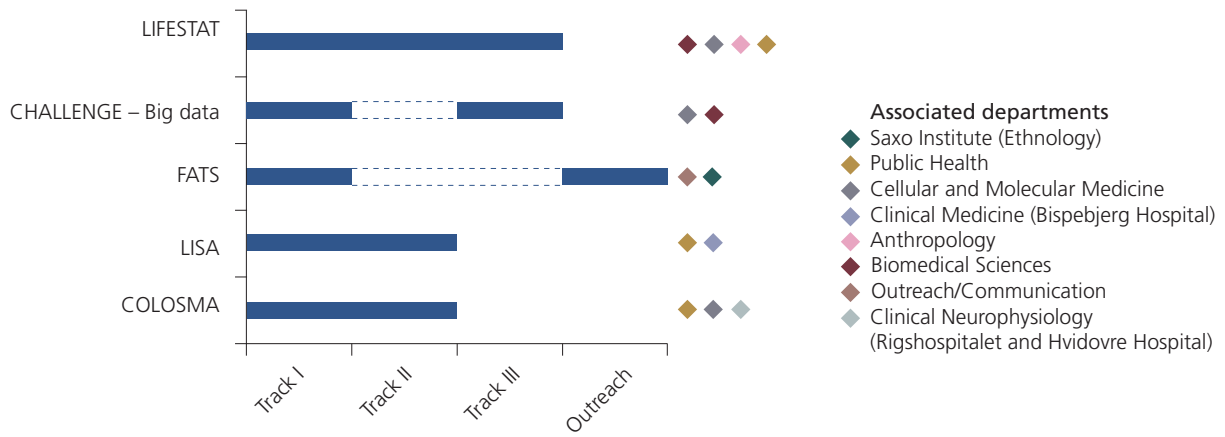


Figure 7: Overview of multidisciplinary projects during CEHA (2019–2023).

and a better use of big data. The research activities fall into three broad Research Tracks (Fig. 8). Track I, “Modifiable pathways of damage and repair in aging,” focuses on the basic biology of aging, especially in skeletal muscle and brain. Track II, “Retirement and transitions,” examines how behavior and social contexts interact in shaping successful responses to critical transitions in later life. Track III, “Individualized health,” pursues the issues associated with individual aspects of health and aging. Together, these Research Tracks support CEHA’s mission and vision by employing a common conceptual framework for understanding the complex interplay of biological, psychological, social, and cultural factors that influence health and well-being at the individual and societal levels. These Tracks allow us to foster interdisciplinarity by engaging actively with a variety of stakeholders to develop interventions and policies that promote healthy living and social participation in old age. They further strengthen our scientific excellence and empower us to contribute to people to living longer, healthier, and more meaningful lives. We describe these Research Tracks in detail below, with major organizational developments and key achievements.

### 2.4 Track I: Modifiable pathways of damage and repair in aging

The achievements of Track I researchers are detailed in Appendix A1.1; the publication list is provided in Appendix

#### TRACK I IN NUMBERS

Number of publications: **196**

2019: **66**

2020: **87**

January–August 2021: **43**

PhD Students: **36**

2019: **7**

2020: **13**

January–August 2021: **16**

External funding (excluding the Nordea-fonden grant)

Total: **104,377,373 DKK (14 million EUR)**

2019: **27,231,082 DKK (3,7 million EUR)**

2020: **54,953,430 DKK (7,4 million EUR)**

January–August 2021: **22,192,861 DKK (3 million EUR)**

A2.1; capacity-building activities (education) are listed in Appendix A3.1; and research projects are presented in Appendix A4.1.

#### Group leaders

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

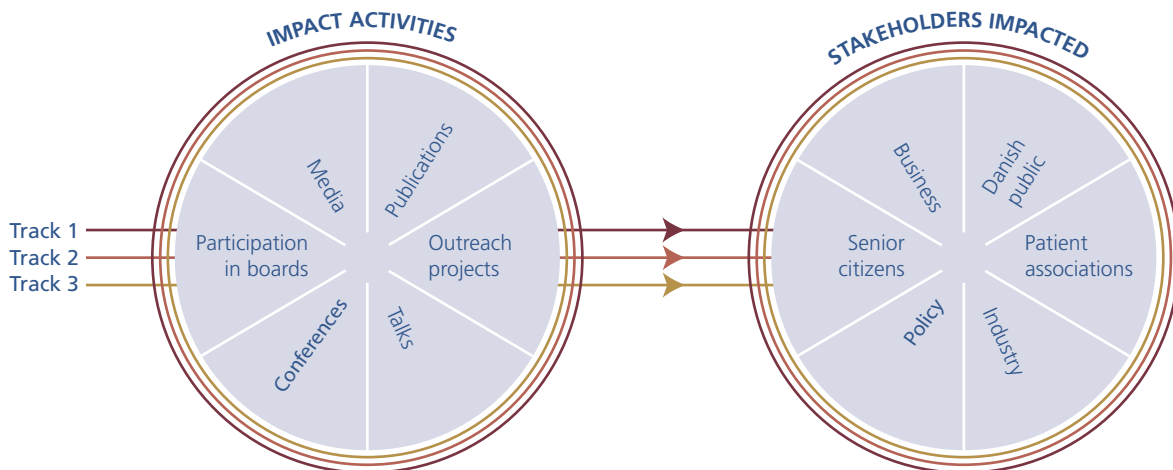


Figure 8: Organization of CEHA (2019–2023) research into Research Tracks. These Tracks allow us to create impact by actively engaging with a variety of stakeholders to develop interventions and policies that promote healthy living and social participation in old age.

*Expertise:* Skeletal muscle and tendon tissue, aging, physical activity, and injury

**Simon Holst Bekker-Jensen**, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences  
*Expertise:* Cell stress responses, signal transduction, MAP kinases, DNA damage response, and aging

**Ian Hickson**, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences  
*Expertise:* Aging, chromosome stability, DNA repair, and age-associated disease

**Martin Lauritzen**, Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences, and Department of Clinical Neurophysiology, Rigshospitalet, Glostrup, Denmark  
*Expertise:* Aging, human brain function, and neurodegenerative disorders

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

**Morten Scheibye-Knudsen**, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences  
*Expertise:* Aging, accelerated aging, and aging interventions

**Linda Hildegard Bergersen**, Department of Neuroscience, Faculty of Health and Medical Sciences  
*Expertise:* Aging, physical activity, and human brain function

### Rationale, focus, and aims

Every day, the human body experiences cycles of tissue breakdown, damage, or trauma followed by subsequent regeneration, recovery, or repair to re-establish homeostasis. The ability of the body to heal itself is important for overall homeostasis and health. However, although the major potential signaling pathways and factors that regulate bodily homeostasis in general are known, many questions regarding their role and importance remain unanswered. For instance, we do not know how DNA stability, damage, and repair is regulated during human aging, or how ribotoxic stress influences metabolic health and tissue pathology. Crucially, the knowledge of how these processes are affected by aging is incomplete. Furthermore, the regulation of brain blood flow, brain energy supply, and musculoskeletal adaptation, and how all these factors are associated with cognitive decline with aging, is unknown. This is a major knowledge gap because impairments in the regulation of these processes will result in detrimental health conditions for the elderly in brain function and other organ functions. Accordingly, Track I focuses on the effect of aging on these processes in both the skeletal muscle and the brain. By addressing the effect of aging on these processes at the cellular level, we will create a basis for counteracting the functional and cognitive decline that occurs with advanced age. This Track firmly supports the mission and vision of CEHA and feeds into Tracks II and III by providing

biological mechanistic insights into aging processes.

### The Track's principal aims are:

- To understand the cellular responses leading to DNA instability, damage, and repair in relation to aging
- To understand how DNA damage and ribotoxic stress impact metabolic health, tissue pathology, and disease related to aging
- To understand the importance of blood flow and energy supply to the brain during aging as well as cognitive decline with advanced age
- To understand the impact of physical activity (or lack thereof) on skeletal musculature and connective tissue, and its potential long-term coupling to cognitive function

### Organizational developments

Since its inception, Track I has focused on biological processes with human aging and we have increased the collaborative effort to develop integrated knowledge on cell and organ adaptation to aging. There has been a constant development of molecular, imaging, and intervention techniques that has allowed us to gain advanced insight into the biological mechanisms behind the aging process. Over the past 3 years, five researchers in the Track have been promoted to Associate Professor and three to Assistant Professor. Of these, two have become Principal Investigators in the Track, and several post-docs have obtained positions in other labs.

### Key achievements

The Track boasts many seminal publications and major scientific discoveries in the field. Since the last self-evaluation, we have published 537 papers in high-impact journals.

In terms of scientific discovery, we have made important inroads into addressing the Track's principal aims. The most important points are listed below.

**Aim 1.** We discovered mitochondrial defects in some DNA repair-defective diseases with severe neurodegeneration. Furthermore, we identified a novel component of the human mismatch repair pathway and its activity. We showed that DNA repair is defective in various types of cancer. We also identified new genes that affect the rate and/or extent of single-strand DNA break repair, and showed that they play a role in the suppression of neurodegeneration. Furthermore, we revealed the role of folate deficiency in genomic instability of the entire human genome. In addition, we characterized the mechanism by which cells respond to DNA replication stress and identified mechanisms by which telomeres maintain stability during periods of DNA damage/replication stress.

**Aim 2.** We identified key aspects of the activation of the ribotoxic stress response, and we have made critical discoveries about the physiological and pathological ramifications of this signaling pathway. We also discovered the mechanism underlying p38 and JNK activation in a contracting skeletal muscle, which can impact its plasticity in response to exercise and could play a role in aging muscle. We showed

that metabolic changes in several monogenic premature aging diseases are caused by the hyperactivation of a DNA damage-responsive enzyme, poly-ADP-ribose polymerase 1 (PARP1). This and related studies facilitated the realization that we can intervene in the aging process by inhibiting PARP1, and perhaps by augmenting NAD<sup>+</sup> levels and increasing acetyl-CoA.

**Aim 3.** We identified brain precapillary sphincters that affect the rate of cerebral blood flow and brain energy supply. We also revealed that stroke in aged mice causes a widespread increase in brain astrocyte activity. Furthermore, we characterized the mechanisms by which vascular mural cells in brain arterioles and capillaries respond to brain aging and identified decreases in the reactivity of brain precapillary sphincters as a key mechanism for brain vascular aging. Finally, we identified the electroencephalogram (EEG) characteristics of cognitive decline in brain aging and demonstrated that specific changes in the EEG signal differ between individuals with preserved and reduced cognitive function.

**Aim 4.** We demonstrated that age-related loss of skeletal muscle can be counteracted with moderate strength training at an advanced age, and the muscle hypertrophy ability and regenerative potential are maintained in individuals who are up to 70 years old. Furthermore, hospitalized geriatric patients with muscle loss can undertake physical training, which impairs the proteolytic activity associated with inactivity, although high levels of inflammation are associated with a poorer effect. Finally, in healthy and chronically diseased elderly people, long-term resistance training can be implemented with good compliance, inducing consistent positive changes in muscle mass, strength, mental health, and a decline in abdominal fat levels.

We have been actively involved in disseminating our findings to various stakeholders, and our Principal Investigators have received prestigious awards in recognition of their scientific excellence. For example, Professor Simon Bekker-Jensen was awarded Lundbeck Foundation's Research Prize for Young Scientists in 2019, and Professor Michael Kjær received the KFJ prize in 2019 and the Hagedorn Prize in 2020. Finally, we have had some external funding success and received more than 104 million DKK (14 million EUR) on top of the main grant from Nordea-fonden.

## 2.5 Track II: Retirement and transitions

The achievements of Track II researchers are detailed in Appendix A1.2; the publication list is provided in Appendix A2.2; capacity-building activities (education) are listed in Appendix A3.2; and research projects are presented in Appendix A4.2.

### Group leaders

**Karsten Vrangbæk**, Department of Public Health, Faculty of Health and Medical Sciences

*Expertise:* Health policy and health economics

**Marco Piovesan**, Department of Economics, Faculty of Social Sciences

### TRACK II IN NUMBERS

Number of publications: **88**

2019: **36**

2020: **32**

January–August 2021: **20**

PhD Students: **4**

2019: **1**

2020: **2**

January–August 2021: **1**

External funding (excluding the Nordea-fonden grant)

Total: **8,360,999 DKK (1,1 million EUR)**

2019: **922,999 DKK (124,000 EUR)**

2020: **6,649,000 DKK (894,000 EUR)**

January–August 2021: **789,000 DKK (106,000 EUR)**

*Expertise:* Social preferences, self-control problems, unethical behavior, peer effects, and behavioral contract theory

**Rikke Lund**, Section of Social Medicine, Department of Public Health, Faculty of Health and Medical Sciences

*Expertise:* Social epidemiology, public health, intervention studies, and life course

**Stine Møllegaard**, Department of Sociology, Faculty of Social Sciences

*Expertise:* Social stratification in socioeconomic and health outcomes, intergenerational transmission of inequality, sociogenomics, and quantitative methods

**Paul Maurice Conway**, Department of Psychology, Faculty of Social Sciences

*Expertise:* Work and organizational psychology, occupational health psychology, social media data analysis, and intervention studies

**Line Hillersdal**, Department of Anthropology, Faculty of Social Sciences

*Expertise:* Obesity, cancer, aging, food and eating, welfare technology, personalized medicine, interdisciplinarity, cultures of science, the body in biomedical contexts, prevention, and complex intervention research

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

*Expertise:* Anthropology of life and health, aging, technologies, and community studies

**Maria Kristiansen**, Department of Public Health, Faculty of Health and Medical Sciences

*Expertise:* Health services research, mixed methods, public health, intervention studies, and person-centered healthcare

### Rationale, focus, and aims

Aging should be viewed as a process of physical, mental, and social transitions. While such transitions can have a profound impact on an individual's capabilities and quality of life, the perceptions and responses to such transitions vary

significantly. For some people, they accelerate a decline in quality of life and capabilities, whereas other people find ways to mobilize resources and bounce back or even extend their previous capabilities based on the experience gained in the process. Currently, it is not known why some people are better able to mobilize resources than others, or which interventions we should use to target different types of capabilities. Likewise, resilience is a key concept that captures the diversity of response patterns facilitated by social- and individual-level resources, but too little is known about factors that support resilience and the effectiveness of potential interventions to strengthen such factors. Retirement is an example of a critical transition event that can have profound consequences for an individual's health and well-being. It also is a crucial societal and political issue, because the sustainability of the welfare state relies on retaining more seniors in the workforce.

While retirement is a key focus area, we extend the analysis to include other aging-associated transitions, such as onset of disease, bereavement, functional decline, and change of living conditions. This enables us to gain a broader understanding of the antecedents, dynamics, and consequences of such transitions. Accordingly, Track II focuses on retirement and transitions, and it was specifically devised to provide insights into critical transition events in later life and to enable us to understand how we might strengthen the capacity to prepare, absorb, react, and recover when experiencing adversity in old age. It brings together researchers from different academic disciplines, including public health science, economics, psychology, anthropology, and sociology. This Track supports the mission and vision of CEHA by exploring the interaction between healthy aging and critical life transitions in old age from a multidisciplinary perspective, and it complements Tracks I and III by providing a better understanding of the macro- and meso-level societal context for interventions based on discoveries in Tracks I, II, and III.

#### The Track's principal aims are:

- To understand how behavior and social contexts interact in shaping successful responses to critical transitions in later life
- To collaboratively develop interventions and outreach projects to support coping with transitions in later life
- To contribute knowledge and tools for strengthening resilience and the capacity to handle critical life transitions in later life
- To inspire policy solutions at all levels that will strengthen the interaction between individuals and their social environment and support an active and meaningful aging experience

#### Organizational developments

The Track has been devised with a main focus on critical life transitions, how these affect individuals in later life, and how their detrimental effects on the various aspects of later life could be mitigated. This has been developed in subprojects focusing on retirement, welfare and digital technology, ageism and age-friendly work environments, and behavioral

intervention options in later life.

The main strength of Track II is the diversity of academic disciplines represented, and research methods implemented, by the members. Since its inception, Track II has expanded to recruit a number of researchers from psychology, anthropology, health policy, and economics. These additions have allowed us to expand our capabilities for advanced quantitative and qualitative research, specifically in state-of-the-art behavioral economics, workplace psychology, welfare and digital technologies, and the combination of registry and survey data to form life-course perspectives. We take advantage of access to national and international data sources, and new cohort survey data designed and collected in collaboration with the CAMB database. Furthermore, we have evolved close collaborations with societal partners, which have allowed us to conduct specific intervention studies and activities, such as participation in think tanks and working closely with patient organizations, healthcare professionals, and municipalities to analyze developments and apply new interventions to support the aims of the Track.

#### Key achievements

Track II in CEHA is built on an interdisciplinary approach, where researchers from different departments interact with external partners to generate results in the context of complex real-life problems specifically related to critical life-course transitions such as retirement. Despite the fact that Track II and most of the social science groups are recent extensions to the CEHA community, our work has resulted in 88 scientific publications and programs that have provided important novel contributions in several fields, bridging the many facets of age research.

Examples of recent Track II publications include a paper by Kristiansen et al. (2021) titled "Targeting preventive home visits to older adults in disadvantaged communities" and a paper by Mikkelsen and Kristiansen (2021) titled "Implementation and potential of a social intervention at nursing homes in Denmark." Both of these papers exemplify the close interaction between Track II research and critical issues in the organization of care for older citizens. A publication by Lassen and Vrangbæk (2021) provides a scoping review of retirement transitions in the 21st century in Europe as a background for registry and survey-based analysis of developments in Denmark. All of these papers exemplify how Track II takes on contemporary issues related to the complex societal challenge of dealing with critical life-course events in old age.

We participate in various academic and stakeholder networks to develop research infrastructure and knowledge that could be applied in designing and testing interventions to support resilience in the context of critical transitions in old age. We have produced new survey-based data in collaboration with the CAMB database project that, in combination with cohort and registry data, provide a rich resource for understanding transition patterns in later life, allowing us to probe retirement patterns and the relationship between retirement, individual motivation, and health. We have also engaged with societal partners in investigating the use of new technological solutions to support healthy aging. For example, we have looked at the use of digital communication in dementia care and for rehabilitation. We have also worked closely with

patient organizations and clinical partners to evaluate new intervention modes; examples include multiple sclerosis and heart failure. Furthermore, researchers in psychology have explored perceptions of seniors in the workforce to develop recommendations and interventions for particular workplaces.

We participate in *Altinget's "Ældre Politiske Netværk"* and Tryg's "Tænketanken for Fremtidens Velfærd," which are networks for developing policy ideas and recommendations, and we regularly contribute to popular journals such as *Altinget*, *Kommunal Sundhed*, and *Berlingske Tidende*, which provide further avenues for engagement with the broader society. We also engage with other universities and research projects, and collaborate with stakeholders outside academia. For instance, we have established research collaborations with Aalborg University, the management of the Technical University of Denmark (DTU), the Center for Team Sport and Health at UCPH, the Danish Alzheimer Association, and several municipalities (e.g., Vordingborg, Århus, Ishøj, and Copenhagen) and Local Government Denmark (the association of Danish municipalities). Through these collaborations, we are able to disseminate knowledge about our research and to establish new interdisciplinary projects, influencing the work done in workspaces and non-government organizations. Worthy examples of the latter are the Danish Heart Association and DaneAge.

Our researchers are instigators of important research projects and recipients of major awards and funding. For example, Rikke Lund is engaged in the Nordic interdisciplinary research project "Social Inequalities in Aging", funded by NordForsk, which investigates life-course influences, trends, and trajectories in health and functioning within a context of welfare state changes and how inequality impacts on recent social reforms. This provides important input to the Track II aim of understanding how behavior and social contexts interact in shaping successful responses to critical transitions in later life.

Furthermore, Maria Kristiansen, one of the key Track II researchers, completed the UCPH Forward: Talent Programme for Excellence in Research at UCPH in 2019. She was also awarded a Research Collaborator Agreement at the Mayo Clinic (Rochester, MN, USA) in 2020. In addition, Karsten Vrangbæk and Nete Schwennesen were awarded a network collaboration grant to develop research into technology-assisted healthy aging with Osaka University in Japan. Unfortunately, this project and other Track II projects have been delayed due to travel restrictions and other barriers related to COVID-19.

## 2.6 Track III: Individualized health

The achievements of Track III researchers are detailed in Appendix A1.3; the publication list is provided in Appendix A2.3; capacity-building activities (education) are listed in Appendix A3.3; and research projects are presented in Appendix A4.3.

### Group leaders

**Flemming Dela**, Professor, Xlab, Department of Biomedical Sciences, Faculty of Health and Medical Sciences, and Affiliate Professor, Department of Geriatrics, Bispebjerg-Frederiksberg University Hospital

*Expertise:* Aging, geriatric medicine, sarcopenia, type 2

### TRACK III IN NUMBERS

Number of publications: **151**

2019: **52**

2020: **59**

January–August 2021: **40**

PhD Students: **5**

2019: **2**

2020: **-**

January–August 2021: **3**

External funding (excluding the Nordea-fonden grant)

Total: **30,860,169 DKK (4,1 million EUR)**

2019: **2,738,579 DKK (368,000 EUR)**

2020: **12,330,590 DKK (1,7 million EUR)**

January–August 2021: **15,791,000 DKK (2,1 million EUR)**

diabetes, exercise training and inactivity, and energy metabolism

**Vilhelm Bohr**, Affiliate Professor, Department of Cellular and Molecular Medicine, Faculty of Health and Medical Sciences, and Senior Investigator at the National Institute of Aging, National Institutes of Health, Laboratory of Molecular Gerontology, USA

*Expertise:* Aging, DNA repair, neuroscience, metabolism, and neurodegeneration

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

*Expertise:* Geriatrics, gerontology, and epidemiology

**Amy Clotworthy**, Assistant Professor, Department of Public Health, Faculty of Health and Medical Sciences

*Expertise:* Gerontology, anthropology, and healthcare services provision

**Jørn Wulff Helge**, Professor, Xlab, Department of Biomedical Sciences, Faculty of Health and Medical Sciences

*Expertise:* Aging, training, substrate utilization, metabolism, and inactivity

**Steen Larsen**, Associate Professor, Xlab, Department of Biomedical Sciences, Faculty of Health and Medical Sciences

*Expertise:* Mitochondrial physiology and bioenergetics

**Clara Pratts**, Associate Professor, Xlab, Department of Biomedical Sciences, Faculty of Health and Medical Sciences, and Core Facility for Integrated Microscopy

*Expertise:* Compartmentalization of energy stores in cells, aging, training, skeletal muscle substrate utilization, and metabolism

### Rationale, focus, and aims

Aging is associated with a general decline in energy levels or 'vitality.' At the cellular and tissue levels, the reduction in vitality correlates with a diminished ability to properly replace or repair damaged tissue and cellular components. We still do not fully know how these processes drive the aging process, or whether they can be modified to achieve healthy aging.



Importantly, these processes are shaped by factors unique to the individual. Thus, both a general and an individual-based perspective are needed for effective interventions to promote healthy aging. Aging is the biggest risk factor for chronic diseases. Inflammation is a common condition many age-related diseases. Therefore, a better understanding of the underlying mechanisms of age-related inflammation is the key to promoting healthy aging. Accordingly, Track III focuses on various aspects of health and aging to influence the underlying molecular processes and to prevent the occurrence of degenerative diseases. Specifically, we are broadening the understanding of the phenotypic characteristics that render each individual unique. We also explore how the classical ways of determining age may differ from an individual's understanding and experience of age, with the goal of enabling people to live healthier lives for longer. To achieve this, we integrate biomedical research with human physiology and psychology, and we utilize CEHA's unique links with local municipalities to engage the public with aging research and empower them to make informed lifestyle decisions to control and restrain age-related diseases. Track III thus constitutes one of the research pillars of CEHA and supports Tracks I and II.

#### The Track's principal aims are:

- To decipher the molecular mechanisms responsible for age-related pathologies and loss of vitality
- To investigate the underlying causes of age-related inflammation
- To identify novel and reliable biomarkers of age-related pathologies
- To explore novel strategies to promote healthy aging
- To identify the mechanisms translating physical training into physiological changes in muscle tissue, to improve vitality
- To collect the life histories of people with fast and slow aging rates

#### Organizational developments

The individual aspects of health and aging are the focus of Track III. We have expanded the scope of the principal aims to include specific projects (see below). The Track III researchers are based at the Department of Public Health (Rudi Westendorp and Amy Clotworthy), the Department of Cellular and Molecular Medicine (Vilhelm Bohr), and Department of Biomedicine (Flemming Dela, Steen Larsen, Jørn Wulff Helge, and Clara Prats). We have also developed important collaborations. For instance since 2019, we have been collaborating with Professor Charlotte Suetta (Bispebjerg-Frederiksberg University Hospital), and this collaboration has resulted in various research projects and the establishment of CopenAge, Copenhagen's Center for Clinical Age Research (<https://copenage.ku.dk/english/>). CopenAge brings together all the clinical aging researchers in East Denmark to develop basic and clinical aging research.

#### Key achievements

Since the last self-evaluation, we have published more

than 200 papers in high-impact journals, such as *Nature Neuroscience* (impact factor 20). This has cemented the position of our researchers as leaders in the field of individualized health and aging. Also, Professor Vilhelm Bohr received the Olav Thons International Prize for Science and Medicine (5 million DKK) (672 thousand EUR).

**Mitochondria and DNA damage.** Mitochondrial dysfunction can lead to altered bioenergetics and several secondary cellular changes that contribute to age-related pathologies. These include increased DNA damage and altered nucleotide metabolism, which we have shown to be associated with cognitive decline and reduced subjective vitality.

**Inflammation.** Elevated systemic inflammation and innate immune responses are hallmarks of the aging process as well as of age-associated diseases. Aging is the consequence of a lifelong accumulation of stochastic damage to tissues and cellular components. We have identified compounds that modify a key inflammatory response system that is activated by damaged cellular components.

**Method development.** We have expanded our research portfolio to include the study of mouse and *Caenorhabditis elegans* models of human pathologies and premature aging disorders. These models have provided unique insights into the physiological mechanisms of aging, and they facilitate experimental investigations to improve the health span.

**COVID-19 and inactivity.** In studies involving human volunteers, we have demonstrated that muscle mass and functional deterioration (e.g., during periods of inactivity) can be counteracted by functional electrical stimulation. This has also been tested in geriatric patients and in patients in intensive care units during the COVID-19 pandemic. The findings will help to counteract permanent muscle loss in all patients in general, as well as in acutely ill patients on bed rest who experience inactivity for a short time.

**Sarcopenia.** Physical training as a means to counteract sarcopenia has emerged as a research area in Track III, with contributions from clinical geriatric departments in CopenAge, as well as from Xlab, Department of Biomedicine. In the aging population, polypharmacy represents a real problem. We have tested controlled discontinuation of statins in healthy volunteers over 65 years old who had been prescribed statins as primary prevention of cardiovascular diseases. Preliminary results indicate that muscle function improves with statin discontinuation and returns to sub-optimal levels upon restarting statin therapy, which raises questions about the consequences of the widespread use of statins in the aging population.

**Type 2 diabetes.** The worldwide incidence and prevalence of type 2 diabetes is rapidly increasing, in part because of physical inactivity, positive energy balance, and advanced age. We investigated the interaction between the pharmacological treatment of type 2 diabetes and physical training. We demonstrated that the insulin secretory capacity improves with training and shows additive effects with the concomitant use of GLP-1 analogues. Furthermore, we are currently delineating



the molecular basis of training-induced improvements in skeletal muscle insulin sensitivity, using single-nuclei transcriptomics. This is being done in collaboration with industrial partners (Novo Nordisk A/S).

**Extreme exercise in old athletes.** Exercise has beneficial pleiotropic effects on metabolism and physiology in humans. These include positive effects on body composition, cardiorespiratory fitness, metabolic flexibility, and increased muscle oxidative capacity. However, it is not known whether an upper limit exists to the health benefits of extreme physical activity and, if so, whether it is influenced by age. We addressed this by studying young and old (~60 years) individuals cycling 7–10 h per day (approximately 3000 km in 15 d) and found that, indeed, the older individuals were close to or had met their central cardiovascular tolerance and adaptability level. This means that while moderate-intensity exercise is beneficial for health in both young and old individuals, this endeavor probably represents an upper limit of what is beneficial for health.

**Attenuated effect of training on fat oxidation with age.**

Whole-body maximal fat oxidation rate (MFO) increases with training, and it is most often associated with good metabolic fitness and flexibility. In men, MFO declines with age; this is especially apparent in older trained men (60+ years of age), which suggests that the effect of training attenuates with age. However, the data are sparse for women. To address that, we have just completed a major study involving matched young and middle-aged menopausal women classified into three groups—“lean trained,” “lean untrained,” and “obese untrained”—with an additional group of older women (aged 70–80 years) in the “lean trained” category. Compared with younger women, the latter groups displayed reduced MFO (also per lean mass), indicating a qualitative change in muscle.

**Biological age.** Biological age is a measure that incorporates functional status and vulnerability to disease, which does not necessarily correspond to chronological age. In other words, biological age assessment provides a measure that is meaningful for the general population. Accordingly, we have explored the estimation of biological age as a tool to help and support health promotion of the general population. We are currently developing and validating a novel methodology for estimating biological age.

**Obesity starts in childhood.** With globalization, the western lifestyle is becoming popular worldwide, and with it there is an increasing incidence of obesity and associated metabolic diseases. According to the World Health Organization (WHO), the number of overweight infants and children in Europe has increased steadily since 1990 and over 60 percent of children who are overweight before puberty will be overweight in early adulthood. Childhood obesity is a strong risk factor for cardiovascular disease, type 2 diabetes, mental disorders, underachievement in school, and reduced self-esteem. Under the Cross KIC EIT project “Eat Healthy to Keep Healthy,” we have created educational material for primary school children to teach them about the link between diet and health, how

their body uses food components, and why a balanced diet is important for healthy aging. In 2019, we created educational material in collaboration with education experts at Københavns Professionshøjskole [University College Copenhagen], as well as with food experts at Universidad Autónoma de Madrid [Autonomous University of Madrid], Università degli Studi di Torino [University of Turin], and Queen’s University Belfast. To date, the material has reached more than 3500 children in six European countries.

**Sudden death in the Faroe Islands.** For several decades, many cases of sudden death in young Faroese individuals with untreated carnitine transporter deficiency (CTD) were reported. The extent of undiagnosed CTD remained unknown until 2009, when a nationwide voluntary screening program was initiated. The screening revealed that the incidence of CTD in the Faroe Islands is 50–100 times higher than that reported elsewhere. CTD is an autosomal recessive disorder of fatty acid  $\beta$ -oxidation associated with a lack of the functional organic cation transporter 2 (OCTN2). Because hyperinsulinemia is associated with elevated muscle carnitine content in otherwise healthy people and a 2.3-fold increase in OCTN2 mRNA levels, the question arose as to whether co-administration of carnitine and insulin could benefit patients with CTD. In February 2019, we moved our laboratory to the National Hospital of the Faroe Islands to investigate the mechanisms behind insulin-induced upregulation of carnitine transport in CTD patients and matched controls.

**Beetroot supplementation for improvement of blood circulation.** Aging and type 2 diabetes are associated with impairments in muscle blood flow, submaximal exercise capacity, and mitochondrial function. This reduces oxygen delivery to the exercising muscle and is strongly associated with limitations in physical performance in the affected individuals. Beetroot supplementation may restore the blood flow to the exercising muscle. Currently, we are investigating whether the underpinning mechanism involves mitochondrial efficiency in the skeletal muscle.

**Harnessing the power of big data to address the societal challenge of aging.** Rudi Westendorp was awarded a Novo Nordisk Foundation Awards Challenge Programme Grant (<https://novonordiskfonden.dk/en/news/novo-nordisk-foundation-awards-challenge-programme-grants-of-dkk-360-million-for-six-research-projects/>) of 60 million DKK (~8 million EUR) to explore the prevention and delay of infirmity in old age to shape personalized therapy for a healthier and longer life. The project builds on the strength of Danish data repositories and scientific research into aging and is embedded within an appropriate socio-ethical-legal framework.

**COVID-19 and mental health.** Amy Clotworthy is coordinating the research project “Standing together – at a distance: How Danes are living with the corona crisis” (<https://coronaminds.ku.dk/english/>). This interdisciplinary project is documenting mental health in Denmark during the COVID-19 pandemic through a series of timed online surveys and qualitative interviews with specific population groups.

# 3 Intervention studies, outreach, and interdisciplinary projects

Working across research disciplines and co-creating solutions with clinical and societal practitioners are the cornerstones of the Center for Healthy Aging (CEHA). The Center brings together researchers from various fields that all contribute to understanding what happens when we grow old, what we can do to improve life for individual seniors, and how we can protect and develop our welfare system at a time of substantial population aging. Researchers from the Center's three Research Tracks, experts from our extensive network, and brothers-in-arms across society are brought together in collaborations and interventions that conjoin research and the people it can benefit. The following projects are examples of this approach.

## 3.1 FATS: From work life to retirement (2020–2023)

**Project manager:** Outreach Consultant Barbara Kjølbye Zinckernagel; **CEHA Tracks:** special outreach project grant from Nordea-fonden; **Collaborators:** Aarhus, Vejle, and Vordingborg municipalities plus trade unions and companies with many employees in the target group

**Rationale and aims.** Every year, approximately 40,000 Danish citizens retire from the active workforce. While some enjoy the freedom and quickly fill their days with various activities, many find the transition difficult. A weakened sense of identity and direction, often combined with a decreased physical and social activity, causes their health and well-being to suffer. To address this, CEHA researchers within the fields of the humanities and health sciences, together with Aarhus, Vejle, and Vordingborg municipalities, are engaged in a comprehensive outreach and intervention project to develop scalable formats that support seniors in preparing for and maintaining a healthy, meaningful pensioner life. The outcome will be a series of evidence-based recommendations and concepts, which, it is hoped, could be replicated in other Danish municipalities and impact the national retirement agenda.

**Activities.** The target group is seniors with little or no education. In the project's lifespan, approximately 4000 citizens will be enrolled (e.g., as senior ambassadors, test

persons, volunteers, or participants in activities). Through co-creation and involvement, the project will define and test formats for peer mentoring and local activities involving exercise, social events, volunteer work, and activities at the seniors' (former) workplaces.

**Key achievements.** The municipalities, CEHA, and the first groups of seniors are engaged in promising activities. For example, a group of eight men in the target group in Vordingborg are currently testing social and physical activities based on advice from researchers, and 100 men in the target group will participate in a summit on 7 October 2021 about preparing and timing retirement well (the latter in cooperation with the trade union 3F). About 10 seniors in Aarhus are currently taking part in developing a senior guidance concept along with researchers and municipal project managers, and recruitment of target group seniors at local companies is well underway. Moreover, CEHA and Aarhus Municipality are planning a large knowledge festival for seniors and relevant stakeholders to take place in Aarhus on 28–29 January 2022. A joint retreat with CEHA-anchored education activities for senior ambassadors will take place in March 2022.



Image: Bus driver. Credit: Simon Skipper.

### 3.2 LISA: Live Active – Successful Aging (2015–2025)

**Project manager:** Professor Michael Kjær; **CEHA Tracks:** I; **Collaborators:** Bispebjerg Hospital

**Rationale and aims.** Previous CEHA research has shown that reduced stem cell function, increased inflammation, and altered cell interplay causes muscle loss with aging. However, physical activity seems to counteract this process significantly. Accordingly, the LISA project was initiated in 2015 by CEHA and Bispebjerg Hospital to investigate how different types of training affect the muscle function of people aged 62–70 years and provide guidelines regarding training of the aging human body in health and disease. The findings will inform an improvement of rehabilitation and prevention practices, as well as general health recommendations and knowledge on what motivates good exercise habits.

**Activities.** During the first year of the project, we performed interventions involving healthy individuals and individuals with chronic disease. A blinded assessor allocated each of the 451 participants aged 62–70 years to one of three groups: supervised heavy-resistance training, moderate-intensity resistance training, or non-exercise cultural activity. The participants are being surveyed over the course of 10 years to assess the effect of the specific intervention on their physical ability, evaluated by detailed physical and cognitive assessments and annual MRI scans of the brain and thighs.

**Key achievements.** Preliminary results suggest that heavy-resistance training improves muscle mass and strength. The effect of medium-intensity training on muscle mass and strength is not as pronounced as that of heavy-resistance training. Furthermore, strength training seems to reduce abdominal fat mass and stimulate the release of anti-inflammatory cytokines, such as interleukin 6. As at 2021, 380 of the participants are still involved in the study.

### 3.3 STRIT: Health, well-being, and social relations at Taastrupgaard (2018–2020)

**Project manager:** Professor Rikke Lund; **CEHA Tracks:** II; **Collaborators:** Inhabitants at Taastrupgaard, Taastrup Municipality and Illustrator Mette Jeppesen

**Rationale and aims.** Taastrupgaard is one of Denmark's most ethnically diverse and deprived social housing areas, and it has a large share of senior residents—some dealing with cultural differences, low trust in authorities, and language barriers, on top of physical aging. The area also has designated senior housing. STRIT is a CEHA observational and interventional study that seeks to improve health, well-being, and social relations among the middle-aged and older residents while the area's built environment is undergoing structural changes. Interventions designed for and by residents at Taastrupgaard can eventually benefit similar housing areas and seniors from ethnic backgrounds other than Danish.

**Activities.** The project involves three types of interventions: (1) facilitating cultural and communal activities for residents across ethnicities; (2) helping the residents voice and visualize



Image: Associate Professor Maria Kristiansen at a CEHA-facilitated resident meeting at Taastrupgaard.

their concerns and wishes for the area's redevelopment process; and (3) developing effective health information formats with residents from ethnic minority backgrounds during the COVID-19 pandemic.

**Key achievements.** Preliminary outcomes include a series of social outings chosen by residents (e.g., the zoo; Egeskov Castle; and Lübeck, Germany), building social relations in the community across ethnicities (e.g., by communal debate meetings and visualization workshops), and a participatory process involving the residents and a graphic facilitator to produce narratives about life during the COVID-19 pandemic as a means to explore ways of engaging hard-to-reach groups in research. During the process, residents took part in producing COVID-19 guideline communication materials targeting social housing residents, health professionals, and older adults from ethnic minority backgrounds, as well as the free book *I count the stars while I wait—Corona stories from public housing* (2021). These materials and the book are examples of health communication that takes residents' needs and cultural prerequisites into account and gives them the confidence to voice their perspective.

### 3.4 COLOSMA: Copenhagen longitudinal study of male cognitive aging (2009–2023)

**Project manager:** Professor Martin Lauritzen; **CEHA Tracks:** I and II; **Collaborators:** Rigshospitalet and Glostrup Hospital

**Rationale and aims.** The clinical project COLOSMA is one of the oldest and most successful multidisciplinary CEHA projects. It investigates how aging influences cognitive functioning and the biological and brain parameters of a large cohort of 383 Danish men born in 1953. COLOSMA is one of the first studies in the world to use draft board IQ results as a basis for evaluating midlife cognitive performance. The participants' IQ scores were similar when cognitive function was assessed at draft board examination (baseline) when they were 18 years old, but they performed differently when data were collected when the participants were 58, 61–63, and 66–67 years old. By following up these men, we have identified several predictive markers for aging-associated cognitive decline. We have also replicated these findings in rodents, which has provided important information on brain aging. We are currently further investigating the predictive markers in a

follow-up study. Ultimately, this research will lead to novel strategies for diagnosing and preventing brain aging, thus promoting healthier late-life years.

**Activities.** The current project activities are performing MRI studies and relating structural findings to known genetic risk factors for cognitive decline. By implementing a new method combining electroencephalogram (EEG) and MRI, we are looking at neurovascular coupling and how it can reflect cognitive differences.

**Key achievements.** The study indicates that cognitive decline can be predicted with high sensitivity by recording changes in cerebral rhythmic activities evoked by complex visual stimuli. Differences in sleep quality, telomere length, and structural and functional MRI have been demonstrated between participants with preserved and with decreased cognitive performance. Recent results have shown that decreased activity of the mitochondrial complex 1 and increased mitochondrial size heterogeneity point to declining mitochondrial quality control as an initial event in brain aging.

### 3.5 CHALLENGE platform: Harnessing the power of big data to address the societal challenge of aging (2019–2024)

**Project manager:** Professor Rudi Westendorp; **CEHA Tracks:** III; **Collaborators:** Statistics Denmark, Zealand University Hospital, and Newcastle University

**Rationale and aims.** Today, life expectancy is continuously on the increase—we all want to age healthily and for longer. Therefore, it is crucial to understand how our bodies

accumulate damage over time, becoming increasingly dysfunctional and in need of repair. The CHALLENGE Platform aims to harness the power of big data to gain a more comprehensive understanding of the aging process at the population, organismal, and molecular levels, and to contribute to personalized medicine. CEHA researchers collaborate with Statistics Denmark, Region Sjælland, and Newcastle University.

**Activities.** This interdisciplinary initiative combines the strength of basic research, the potential of Danish data registries, and the unexplored biorepository in the Danish National Pathological Data Archive. In the project, researchers systematically trace individuals over time to identify key events in people's lives that result in different histories of disease and disability. This is combined with using machine-learning to dissect the complex relationship between the morphology of cells and their biological behavior, as well as an in-depth investigation of the dynamic interaction between nuclei and mitochondria in response to experimental perturbation.

**Key achievements.** Denmark's comprehensive set of electronic population registers provides longitudinal data that cover individual and household socio-demographics and medical history. Using these data, CHALLENGE Platform researchers have developed and applied recurrent neural networks to predict the risk of a need for care services in the future and thus identify individuals who would benefit the most from the municipalities' prevention strategies. Register data have also been used to identify Danish hotspots for long lives, which are now being investigated further. For example, you are 37 percent more likely to turn 100 if you live in Sydfoyn, Ærø, Tåsinge, Langeland, or Vestlolland compared to other areas in Denmark.



# 4 Communications and engagement

Center for Healthy Aging (CEHA) aims to help people live longer, healthier, and more meaningful lives, by informing practices in healthcare, social services, and individual behavior. Therefore, the Center gives high priority to research communication, stakeholder relations, and public engagement. We liaise with the health and care sectors, municipalities, patient and interest organizations, and policy makers, through collaborations, public debate, and research dissemination in the form of press releases and events, as well as networks, councils, think tanks, and strategic meetings. Importantly, all Center staff are actively encouraged to participate in these activities. The engagement work is coordinated by an Outreach Consultant, in close collaboration with CEHA management, as described below. Discussed elsewhere in this report are the Center's efforts to bring research into social and clinical practice through outreach (section 3 and elsewhere in section 4), collaboration (section 7), and training activities (section 5), as well as intervention studies (section 3).

## 4.1 CEHA communication and engagement activities: The foundation we build on

Since its founding in 2009, CEHA has strived to be an internationally recognized aging center known for excellent research and an outgoing approach.

**During CEHA 2009–2013**, we laid the foundations for our strategy of reaching a broad audience with research insights. We did that by building a strong media and online presence, and by participating in and organizing aging-research awareness events.

We created two CEHA websites: a Danish version (<https://sundaldring.ku.dk>) and an English version (<https://healthyaging.ku.dk>). The sites were (and are) parallel in some aspects, but the Danish version is primarily targeted at employees in elderly-focused organizations, health professionals, and politicians, while the primary target groups of the English site are researchers, foundations, students, and international partners. Later, we launched a CEHA Facebook

page in Danish (<https://facebook.com/sundaldring>) as a forum for advice, awareness, and debate about healthy aging and for CEHA branding, targeting the general public. It attained over 10,000 followers within a year. The page is still active and now has 19,000 followers.

The year 2012 was the EU Year for Active Aging, which put healthy aging on the public agenda both in Denmark and abroad. This provided an excellent outreach platform for CEHA. We participated in a lot of aging-dedicated conferences, public meetings, lectures, exhibitions, and a science theater during that year, which was the kick-start of CEHA's continued engagement in a wide range of outreach activities.

Furthermore, CEHA research was featured several times on Danish national television. For example, channel DR2 aired the documentary series "Fauli, Fat and Finished?", in which CEHA researchers designed and supervised physiological and clinical experiments to help the main character, Søren Fauli, live a healthier life. The series had approximately 825,000 viewers. Furthermore, some CEHA researchers undertook projects with a built-in communication component during that CEHA installment. Examples include Adrian Bertoli's work on social media-based disease management, Morten Bülow's work on the history of the 'successful aging' concept, and Lucy Lyons' postdoctoral project "Drawing Aging".

**During CEHA 2014–2018**, more resources were invested into outreach and communication, and a handful of people were employed to work strategically to put knowledge about healthy aging on the public agenda and reach decision-makers and citizens with research-based recommendations; this was called the Outreach and Communication Platform.

The Outreach and Communication Platform instigated many important outreach activities. For instance, at Medical Museion, the Platform, together with a diverse group of researchers, created engaging exhibitions with surprising, dialogue-stimulating perspectives on aging, including the *Kintsugi—Golden Body Repair* exhibition. This later became the basis of an awareness project integrated in the education of future healthcare professionals. Another Medical Museion

activity was the *Life on the Line* game, which was based on CEHA research outcomes. Its home was at Medical Museion, but it was also played at the People's Political Meeting on Bornholm, the school science fair "Science Forum 2018," PKA Pensions "Pensions Day," and the University of Konstanz (Germany), among others.

During that time, we also explored ways to stimulate meaningful, lasting engagement through meetings and events. Accordingly, CEHA hosted more than 100 research dissemination events at the University of Copenhagen (UCPH), at the People's Political Meeting on Bornholm, at the Danish Science Festival, and at various stakeholder venues. Creative dissemination formats—such as cross-disciplinary science slams in which three researchers from different fields presented their most important points in 3 minutes each—were a hit both among general guests and among researchers. Furthermore, we promoted public events on social media, for example as videos, which were seen by thousands of people (one such video, starring the comedienne and author Hella Joof, has been viewed 168,000 times on Facebook alone). A major outreach activity was the project "Keep Your Brain Healthy," developed in close collaboration with DGI (Danish Gymnastics and Sports Associations) and the Agency for Culture and Palaces, aimed at seniors aged 55–75 years. This involved physical and cultural activities and had more than 1000 participants. "Keep Your Brain Healthy" activities still take place all over Denmark, with the participants reporting that they had experienced a lasting improvement in their health and/or well-being following participation.

Finally, the Outreach and Communication Platform worked strategically with stakeholders to influence the public agenda through research results and dialogue. The primary target groups were organizations for the elderly, municipal decision-makers, pension companies, government agencies, healthcare professionals, and selected patient organizations. As a result of these activities, CEHA developed a close relationship with the most influential organization for the elderly in Denmark, DaneAge (750,000 members), and arranged joint events during the People's Political Festival in the years 2015–2018 and a series titled "The Good Life" in the Danish newspaper *Politiken*. The Center also hosted a CEHA retreat, attended by the Minister of Senior Citizens, among others.

**In CEHA 2019–2023**, we draw on the solid scientific background of our researchers, the strong networks we have built, and communication and collaboration experience from previous years. While these experiences continuously inform our communication and engagement strategies, the Communication and Outreach Platform has now been replaced by one Outreach Consultant, and the Center's communication strategy emphasizes collaborative projects, stakeholder communications, and dialogue with policymakers rather than the broader public. CEHA continues to strive to be a visible and communicative research institution, and to help as many people as possible live healthier and happier lives. The current CEHA communications activities are described in detail below.

#### 4.2 Agenda setting in CEHA 2019–2023: Changing our nation's approach to aging

For more than a decade now, CEHA has been key in changing the tone in the aging debate in Denmark, from talking about a 'burden' and a 'ticking time bomb' in western economies

to a more positive discourse. As a result of our efforts and the efforts of others, today's aging debate typically avoids the 'burden' rhetoric and focuses on improving the well-being of seniors, promoting a healthy lifestyle, and making the labor market more flexible. The Center engages in the aging debate in the mass media and social media, as well as in direct dialogue with major stakeholders such as politicians, healthcare providers, patients, and interest organizations.

While still invested in communicating our findings to the public, currently CEHA emphasizes collaborative projects, stakeholder communications, and dialogue with policymakers rather than the broader public. Accordingly, we are advocating the creation of a politically backed national aging initiative that would bring together foundations, relevant organizations, public and private health and welfare providers, and aging researchers from Danish universities. The Center has voiced this ambition in the mass media, such as *Altinget*, *Dagens Medicin*, and *Berlingske*, and it participates in an ongoing dialogue with several stakeholders regarding the initiative. These stakeholders include the National Association of Municipalities; the Deans of health and medical Sciences at the University of Southern Denmark, Aalborg University, and Aarhus University; PFA Pension; the DaneAge Association; the Minister for Social Affairs and Senior Citizens; and several foundations and patient organizations. CEHA is planning a seminar in the coming year involving all the potential partners, which we hope will reveal the shape and purpose of the national aging initiative.

In addition, CEHA researchers frequently participate in political hearings on topics related to the elderly. Two to three times a year, our researchers are invited to help qualify legislation concerning, for example, social services, quality of homecare standards, preventive homecare, dignity standards in eldercare, and the use of digital communication tools with the elderly. CEHA has also recently earned a coveted place in Tænketanken for Fremtidens Velfærd [Thinktank for Future Welfare]. This enables us to continuously and readily share our knowledge and results with very important stakeholders.

#### 4.3 Media spotlight on research breakthroughs

In close collaboration with the Communications Department at the Faculty of Health and Medical Sciences, University of Copenhagen, the Center has continued to strengthen the relationships between CEHA researchers and journalists, and to disseminate research results to the public using the mainstream media. Our major strategies in this regard include direct media notification in advance of major announcements, liaising via specific channels, and approaching science and health editors. Consequently, Danish and international journalists often seek out CEHA researchers for knowledge on aging-related issues, and the Center's research and activities often receive coverage in Danish newspapers, radio programs, television, as well as media targeting health professionals. Examples of coverage in Danish media include an invitation from *Dagens Medicin – Kommunal Sundhed* to be featured with regular expert columns, and an interview about aging and the welfare economy in the Danish newspaper *Berlingske*. The project "From Work Life to Retirement" (FATS) is also regularly portrayed in local newspapers. CEHA researchers have been invited to participate in the radio program "20 Spørgsmål til Professorens" [20



Questions for the Professor] and the UCPH podcast “Tankelyn,” among others. In addition, Associate Professor Morten Scheibye-Knudsen has been asked by the Danish national television channel TV 2 to participate in a program about ways to counteract aging (which has not yet aired), and the Copenhagen area local channel Lorry are interested in doing a series on the FATS agenda with local seniors.

Several significant research results from the Center have enjoyed widespread recognition in the Danish and international media, sometimes leading to changed practice. This was the case for CEHA studies on how social relations affect health and on what happens to your muscles when you are inactive for 14 days.

To make sure CEHA results keep reaching the media and the public even with fewer resources for press work in the CEHA organization, the Outreach Consultant will coordinate media training and strengthen researchers’ own awareness of communication tools.

We also continue our engagement via social media and our website, initiated during earlier installments of CEHA. Specifically, we have an active presence on Facebook and LinkedIn. The CEHA websites continue to attract traffic and will receive a thorough update in the fall of 2021.

#### 4.4 Events and stakeholder engagement

In CEHA 2019–2023, we use event concepts and skills developed during our previous public and stakeholder events. These range from lectures to specialized seminar series, workshops, and science festivals. Some major examples are listed below.

CEHA researchers give lectures to various audiences, locally and all over Denmark. Examples include dedicated teaching at Folkeuniversitetet. These courses will run during the spring of 2022 and are aimed at mature adults with an interest in aging; they are very well attended. Our researchers are also actively involved in showcasing CEHA research and aging-related concepts at such recognized events as the Copenhagen Culture Night. This event takes place annually and brings together thousands of Copenhagen citizens.

During Copenhagen Culture Night, CEHA researchers measure people’s biological age in the minilab, give the talk “Living to be 1000 years old—medicine or miracle?”, and showcase public health research that involves co-creation with citizens. Finally, CEHA researchers present talks all over the country; examples include clubs and organizations at education institutions, libraries, organization headquarters, and the Danish Science Festival.

We have also been trying out new formats and paths for engagement. For example, in January 2019, Associate Professor Maria Kristiansen (Group Leader and CEHA Vice-Director) initiated a seminar for 200 health sector representatives interested in person-centered care. The seminar took place at the Center for Health and Society, University of Copenhagen, and it was open to decision-makers, researchers, and practitioners in healthcare. At the event, Victor M Montori, Professor at the Mayo Clinic and author of the renowned book *Why We Revolt: A Patient Revolution for Careful and Kind Care*, gave the keynote address and—together with Maria Kristiansen and other speakers—sparked a fruitful conversation about how the health sector could be improved.

In terms of notable workshops, CEHA and the then newly established CopenAge hosted a workshop with representatives from 19 municipalities about the physical rehabilitation of seniors. The workshop was held on 28 November 2019 at the University of Copenhagen. The speakers included Professor Flemming Dela and Clinical Professor Charlotte Suetta. Through a series of presentations and discussions, the workshop shed light on how to support rehabilitation centers with research-based knowledge.

Most opportunities for generating awareness and engagement through in-person events and meetings have been cancelled or postponed during the COVID-19 pandemic. We expect to take up dissemination and engagement activities again in the fall of 2021. For instance, together with our partners in the outreach project “From Work Life to Retirement” (see section 3), we are planning to host a festival for hundreds of seniors and relevant professionals in January 2022.

# 5 Capacity building

Educating the next generation of aging researchers as means of capacity building is one of the top priorities of the Center for Healthy Aging (CEHA). To this end, we are making a concerted effort to provide high-quality educational resources to CEHA students and trainees via lectures, online courses, and mentorship; to organize research training via summer schools, networks, and the PhD Academy; and to recruit junior and senior scientists with appropriate research interests and/or expertise to the Center by identifying and nurturing young talent and securing further employment. A full list of our activities in this area is provided in Appendix A3.

## 5.1 Education

With more than 200 unique PhD (60%) and postdoc (40%) positions, CEHA has done more than any other program to advance aging research, in a broad sense, within Denmark, and possibly in the entire Scandinavian region and Europe. Building up the academic capacity has been one of the great successes of CEHA.

We support aging researchers at various levels of training: pre-graduate, BA, MA, and post-graduate students, as well as post-docs. In the past few years, the numbers of students in these groups have been relatively stable, with the exception of growth of the pre-graduate, BA, and MA student populations (Table 1).

Since the founding of CEHA in 2009, the portfolio of educational activities offered has increased every year, beginning with PhD courses and now including summer schools, BA/MA/PhD courses, and a massive online open

course (MOOC) focusing on aspects of healthy aging, interdisciplinarity, and innovation.

Specifically, our educational programs include undergraduate- and graduate-level courses on aging. These courses are conducted by all faculties and embedded in their affiliated departments' course offerings.

We also offer opportunities for postdoctoral mentorship of the Faculty of Health and Medical Sciences, in which CEHA is based.

## 5.2 Research training

CEHA is at the forefront of advancing aging research and will continue to promote and invest in the development of new talent to facilitate breakthroughs in aging research.

Growing the academic capacity of the Network for Young Scholars (NYS) has been one of the great successes of CEHA. We will continue nurturing talent. Building on the successful activities of the NYS network, CEHA will continue the development of a career flow program to ensure that the considerable investment in aging research capacity is put to the best possible use, both inside and outside the University of Copenhagen (UCPH).

Concomitantly, CEHA has exposed early-career researchers to a variety of outreach tasks, trained them to build their capacity to engage in public dialogue and dissemination, and worked in collaboration with external stakeholders and other enterprise.

In addition to actively supporting local early-career researchers, CEHA, under the auspices of UCPH, develops specific research-application support services for early-career researchers from abroad. These early-career researchers have been encouraged to apply for independent research grants or fellowships, and to become affiliated with CEHA. Such funding may be obtained from many Danish funders (e.g., Lundbeck and the Novo Nordisk Foundation) and international funding programs (e.g., the European Research Council's Marie Skłodowska-Curie Actions). Collectively, by engaging in these activities, CEHA promotes the brightest young minds in aging research to establish long-term commitment to the defined research goals and to realize the CEHA vision.

**Table 1 Number of individuals from various categories that were trained by CEHA since its launch**

	2018	2019	2020	2021
Pregraduate/BA/MA	30	53	59	59
Research assistants	14	14	14	10
PhD Students	55	49	55	52
Postdoc	31	31	31	30

## International Alliance of Research Universities (IARU) Summer School: Interdisciplinary aspects of healthy aging

The IARU Summer School course Interdisciplinary Aspects of Healthy Aging is part of the IARU Courses initiative (previously known as the IARU Global Summer Program). It was devised as an intensive series of lectures and seminars conducted by CEHA staff and international recognized scientists, covering all aspects of aging research. The Summer School takes place at UCPH. It lasts 3 weeks and is directed at students from around the world. It provides the students with opportunities to explore diverse research methods across different disciplines, from the cellular to the societal level; to get to know the CEHA faculty; and to interact with students from all over the world. Summer School courses emphasize interdisciplinary knowledge and approaches, and they provide an opportunity for research experience in the field of aging. At the end of the Summer School, students write a grant application under the supervision of the course faculty. This requires the use and/or consideration of interdisciplinary research methods and provides hands-on experience with the process of developing a research program or agenda that addresses critical questions or problems in the study and understanding of aging.

## Network for Young Scholars (NYS)

The CEHA NYS is a network for all young researchers affiliated with the Center (<https://healthyaging.ku.dk/education/network-for-young-scholars>). It was initiated in 2010, with the goal of building a platform for research assistants, PhD students, and post-docs to promote educational and research activities in the field of aging, and to provide opportunities for social networking for these young scientists. In 2020, the NYS arranged a PI Lunch series, wherein young researchers met with the Center's affiliated Principal Investigators to discuss career development in an informal setting. Typically, such events have relatively high numbers of participants, and they are attended by young researchers from across the three Research Tracks.

In 2021, the NYS Steering Group had seven members:

- PhD Student Anna Constance Vind, Institute for Cellular and Molecular Medicine (Track I)
- PhD Student Michael Ben Ezra, Institute for Cellular and Molecular Medicine (Track I)

- PhD Student Zhiqian Li, Institute for Cellular and Molecular Medicine (Track I)
- Research Assistant Sarah Zaccagni, Department of Economics (Track II)
- Postdoc Linn Gillberg, Department of Biomedical Science (Track III)
- PhD Student Arthur Ingersen, Department of Biomedical Science (Track III)
- PhD Student Casper Søndénbroe, Department of Biomedical Science (Track III)

## PhD Academy for Interdisciplinary Aging Research (PAIAR)

CEHA's PAIAR aims to develop and organize high-level, internationally recognized interdisciplinary PhD courses in the field of aging research (<https://healthyaging.ku.dk/education/phd-academy-paiar>). The intent is to strengthen the research focus on aging, now and in the future. The courses primarily target the Center's PhD students, but they are open to all students at UCPH, as well as students from other universities in Denmark and other countries.

In 2021, the PAIAR Steering Group consisted of:

- Associate Professor Claus Desler
- Senior Researcher Jakob Agergaard
- Assistant Professor Sasmita Kusumastuti

## 5.3 Recruitment and career development

In terms of recruitment, we continue the development of a career flow program to ensure that the considerable investment in the capacity of aging research is put to the best possible use, both within and outside UCPH. Furthermore, Principal Investigators identify PhD students and post-docs who demonstrate excellence in aging research, mentor them, and (if necessary) intervene to help secure extended or permanent employment in their home departments. Such interventions include holding meetings with department heads and/or providing teaching opportunities, pedagogical training, and mentorship programs for early-career scientists.

# 6 Organization and governance

## 6.1 Organization

The research of the Center for Healthy Aging (CEHA) is organized as a network of research units. By the end of 2021, it spanned seven different departments within three University of Copenhagen (UCPH) Faculties (Humanities, Social Sciences, and Health and Medical Sciences) and at three hospitals in the Greater Copenhagen Area (Hvidovre, Rigshospitalet, and Bispebjerg). The research units are organized into three multidisciplinary Research Tracks (I–III) (section 2).

Since August 2017, the many CEHA researchers and the Secretariat have been brought together on the 2<sup>nd</sup> and 3<sup>rd</sup> 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 basic biology, physiology, neuroscience, behavior, anthropology, economics, and psychology.

## 6.2 Management and advisory boards

The administrative duties of the Center are carried out by the Executive Director, three Deputy Directors, a Steering Committee, an International Scientific Advisory Board (SAB), and administrative staff. The Executive Director, Lene Juel Rasmussen, reports to the Dean of the Faculty of Health and Medical Sciences, Professor Ulla Wewer, who is ultimately responsible for all CEHA activities.

Operational tasks at CEHA—including strategic planning and development, and coordination between Tracks—are agreed upon by the Dean of the Faculty of Health and Medical Sciences, the Executive Director, and the three Deputy Directors. The administrative staff are organized in a Secretariat; they manage administrative tasks and support the Center's research and educational activities. The Secretariat is centrally located in the Faculty of Health and Medical Sciences.

The Executive Director, Deputy Directors, Steering Committee, and administrative staff deliver management



Image: Mærsk Tower

and leadership to CEHA and provide oversight for research activities, financial issues, recruitment, strategic planning, and outreach. The Steering Committee acts as the oversight committee for CEHA. It includes leaders of the three CEHA Themes (Figs. 9 and 10), with the Executive Director acting as the Chair of the Steering Group (see Appendix A5 for the list of members).

CEHA is supported by an International SAB, which reports to the Dean. The SAB includes nine distinguished scientists who represent broad scientific expertise relevant to CEHA research and whose selection was based on the areas of scientific expertise in CEHA. The role of the SAB is to provide advice on the strategic planning, recruitment, feasibility, progress, and development of the Research Tracks. The Board proposes the 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 the CEHA leadership ensure that the CEHA Research Programs meet the highest international standards and achieve optimal scientific impact.

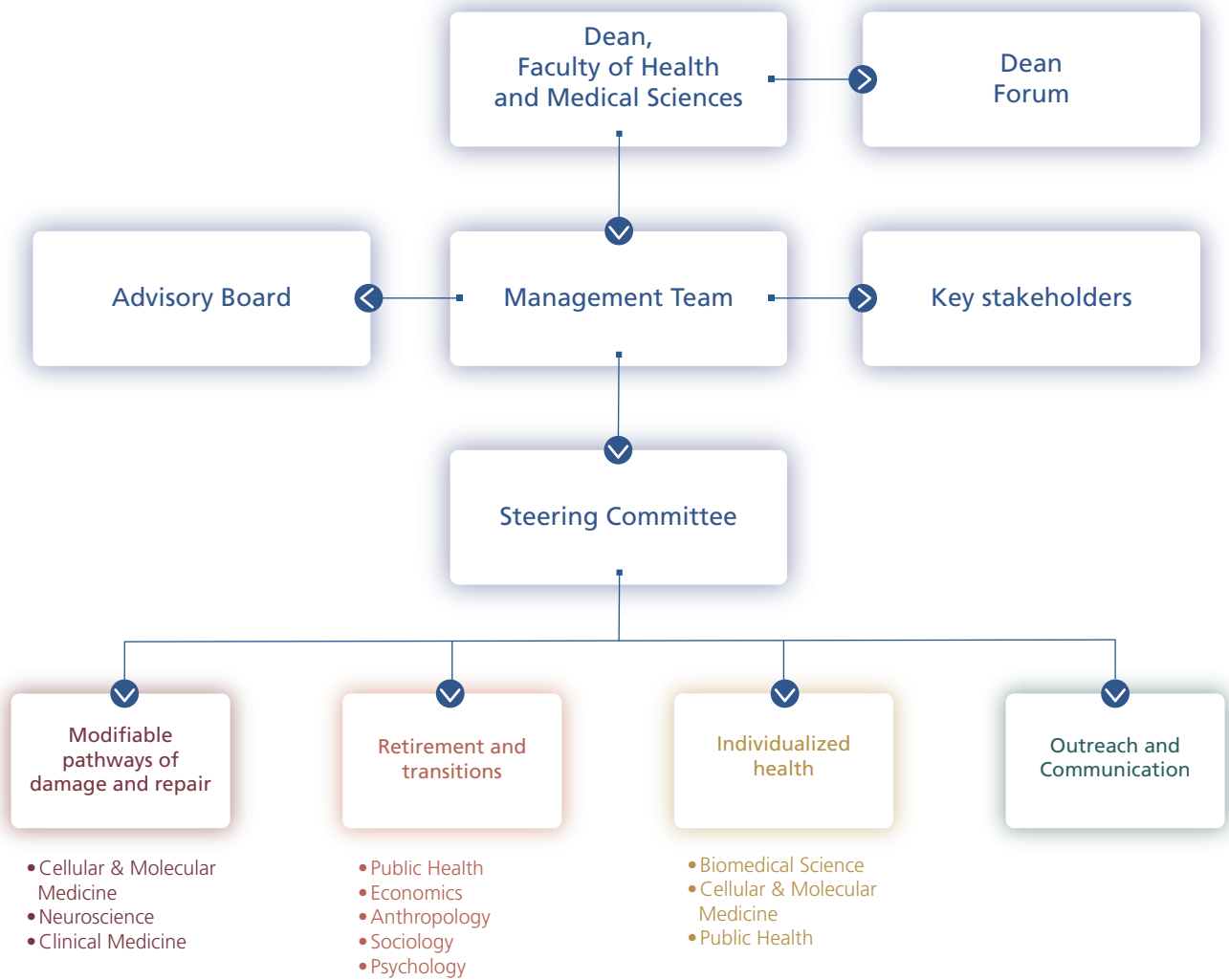


Figure 9: Organization of CEHA. Departments associated with a Track are listed below the respective Track.



Figure 10: Organization of CEHA Steering Group.



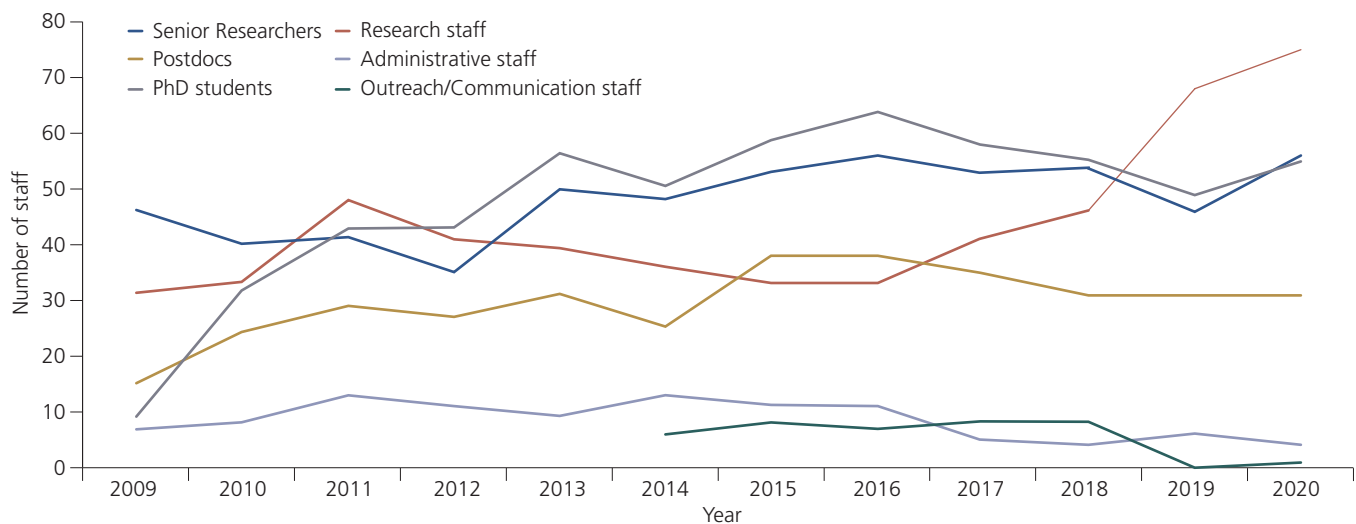


Figure 11: Staff composition over time.

### 6.3 Staff

As at 1 September 2021, CEHA had 47 full-time and part-time employees (funded by the Nordea-fonden grant), plus 194 employees paid by UCPH and various external funders. These numbers include employees from Tracks I-III, the Outreach Consultant, the Secretariat, and the Management (see Fig. 11).

#### CEHA 2018–2021 complete staff list

- Full and part-time employees (funded by the Nordea-fonden grant)
- Employees paid from external funding (non-Nordea-fonden funding), including staff paid by UCPH

#### CEHA (2018–2021) staff funding (Table 2)

2018 Total: **240 persons**

Paid or partly paid by CEHA: **78 persons**

Paid from sources other than CEHA: **162 persons**

2019 Total: **246 persons**

Paid or partly paid by CEHA: **52 persons**

Paid from sources other than CEHA: **194 persons**

2020 Total: **265 persons**

Paid or partly paid by CEHA: **53 persons**

Paid from sources other than CEHA: **212 persons**

2021: Total: **241 persons**

Paid or partly paid by CEHA: **47 persons**

Paid from sources other than CEHA: **194 persons**

Table 2 CEHA III Staff funding

	2018			2019			2020			2021 <sup>†</sup>		
	*	**	***	*	**	***	*	**	***	*	**	***
Senior researchers	9	10	37	10	4	42	4	7	45	4	8	41
Postdocs	5	3	23	0	5	26	2	6	23	3	3	25
Guest researchers	0	0	10	0	0	8	0	0	8	0	0	2
Guest students	-	-	-	0	0	2	0	0	8	0	0	10
PhD students	14	7	34	2	9	38	2	11	42	2	9	40
Research assistants	3	0	7	0	3	11	0	5	11	1	3	7
Bachelor/master/pregraduate research students	5	0	25	0	3	50	0	3	56	0	2	61
Student assistants	-	-	-	0	4	6	0	3	7	1	1	3
Lab assistants	1	4	8	0	2	7	0	2	8		2	1
Secretaries	0	1	4	1	0	1	0	1	2	0	1	2
Other key persons	1	0	3	0	3	3	1	2	2	1	2	2
Center Administration	4	0	0	3	3	0	4	0	0	3	0	0
Communication and Outreach	5	1	2	-	-	-	-	-	-	1	0	0
<b>Total</b>	<b>47</b>	<b>26</b>	<b>153</b>	<b>16</b>	<b>36</b>	<b>194</b>	<b>13</b>	<b>40</b>	<b>212</b>	<b>16</b>	<b>31</b>	<b>194</b>

<sup>†</sup> 2021 Jan-Aug; \*paid by CEHA (funded by Nordea-fonden grant); \*\*partly paid by CEHA (plus external funding); \*\*\*paid from sources other than CEHA (external funding).

# 7 Research collaborations and networks

Center for Healthy Aging (CEHA) actively collaborates with several institutions and networks—locally, within Denmark, and around the world. In addition to having scientific and outreach advantages, these collaborations stimulate the mobility of researchers and students, and play a key role in CEHA's recruitment at all levels. We describe some of our major collaborations below.

## 7.1 International collaborations

### International Alliance of Research Universities (IARU; ongoing)

University of Copenhagen and CEHA is closely linked with the prestigious IARU (<http://www.iaruni.org>). IARU is an alliance of universities (Fig. 12). It is a forum for enhancing collaboration and promoting future research activities of member universities. The association of CEHA with IARU is a cornerstone of our efforts to internationalize the Center, which provides valuable networking opportunities for CEHA members.

The specific CEHA–IARU collaboration is the joint research initiative *IARU Aging, Longevity & Health (ALH)*, which was started in 2014. The aims of ALH are to increase engagement across IARU campuses and to promote joint activities and funding opportunities for IARU ALH participants within the international aging-research community. The ALH initiative is led by a Steering Committee composed of internationally recognized aging researchers. Until fall 2019, the Committee has been chaired by Professor Sarah Harper from Oxford University. Professor Nicolas Cherbuin, from the Australian National University, was recently appointed the Chair for the period 2019–2021. As of 2021, the Committee members are:

- Professor Lene Juel Rasmussen, University of Copenhagen
- Professor Nicolas Cherbuin, Australian National University
- Professor Angelique Chan, National University of Singapore
- Professor Katsuya Lijima, The University of Tokyo
- Dr Louise Lafortune, University of Cambridge (Chair)
- Professor Sarah Harper, University of Oxford

- Professor David Lindeman, University of California, Berkeley
- Professor Xiaoying Zheng, Peking University
- Dr Sebastiana Kalula, University of Cape Town

As part of the IARU collaboration, CEHA also hosts an annual *Summer Course on Interdisciplinary Aspects of Healthy Aging*. Another example of IARU-instigated collaboration is the *IARU Online Course on Sustainable Aging*, initiated in 2020 by CEHA together with the University of Tokyo. In the fall of 2020, CEHA received financial support from UCPH and IARU to offer it as a graduate course during week 15, 2021. The course focuses on the following four questions: What is sustainable aging? What shapes sustainable aging? How do we move toward realizing the goal of healthy lives and well-being during old age for all? And what can we learn by taking a global, comparative approach to this challenge? The course was aimed at students from IARU universities, although students from universities that are not IARU members were also eligible.

### European Institute of Innovation and Technology (EIT) Health (ongoing)

EIT Health is a consortium of EU partners founded 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. It was founded in response to the 2014 EIT call for Knowledge and Innovation Communities (KICs), as part of a larger EU initiative, Horizon 2020. The KICs aim to encourage stakeholders in education, technology, research, business, and entrepreneurship to establish excellence-driven partnerships and provide innovative solutions to tackle the grand challenges (health, climate, bio-economy, etc.) facing the EU. Today, EIT Health consists of more than 50 core partners and their 90 associate organizations. These include leading businesses, public partners, research centers, and universities (including UCPH) from nine EU countries.

EIT Health revolves around three programs: (1) Accelerator for Business Development; (2) Campus for Educational

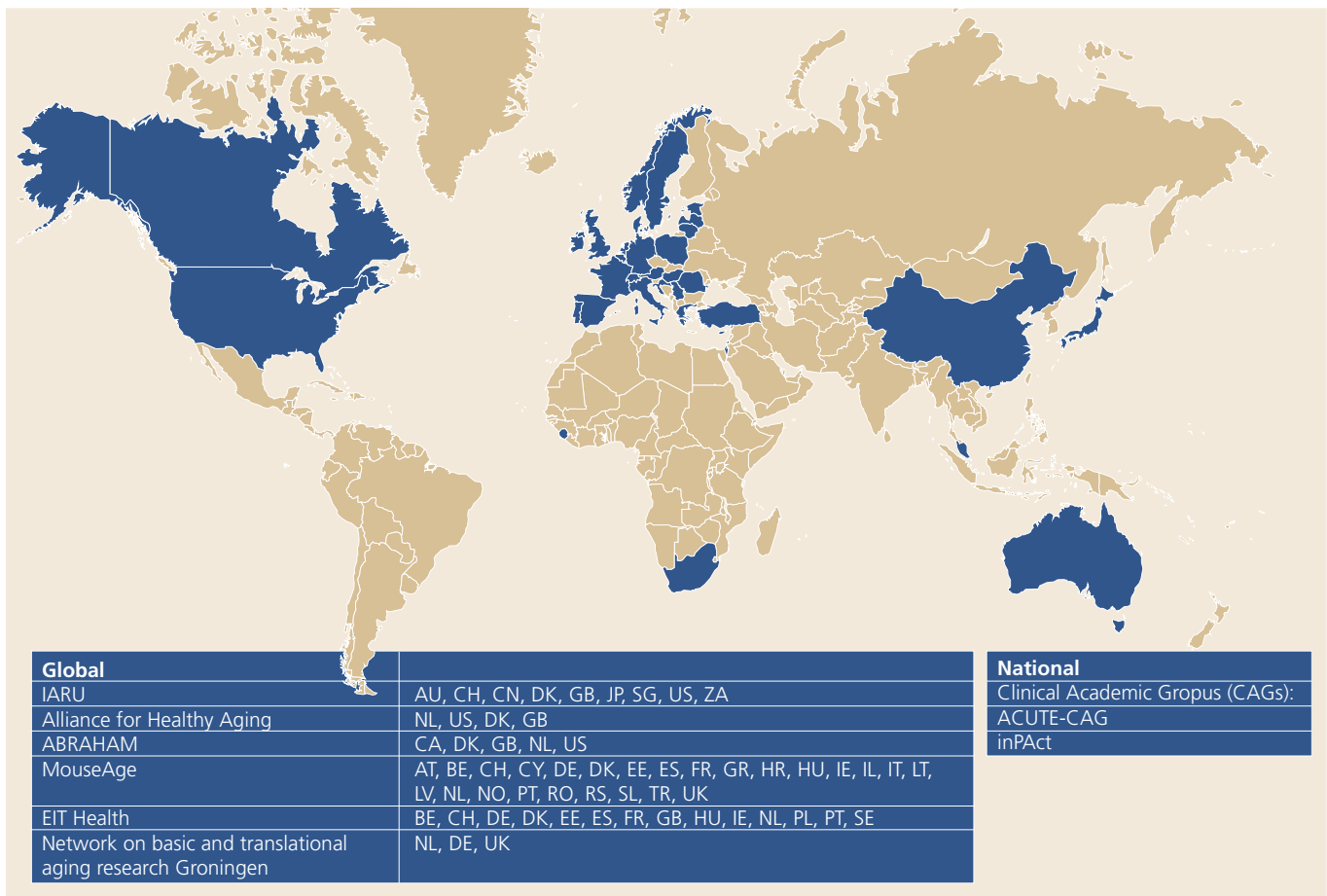


Figure 12: International collaborations: International Alliance of Research Universities (IARU; ongoing).

Activities; and (3) Innovation Projects. EIT Health provides opportunities for new and strengthened collaborations between CEHA, UCPH, IARU universities, and beyond. Since the launch of EIT Health, CEHA has been involved in several activities in the Campus program. One such activity is the “Innovating Solutions for Aging Populations” summer course, developed in collaboration with the Copenhagen Business School, Novo Nordisk A/S, and the innovation and entrepreneurship hub SUND Vækst (2016). Another example is BRIDGE—a network involving UCPH, Copenhagen Business School, Uppsala University, and Erasmus University Rotterdam—set up to share and implement pedagogic and digital didactic practices in connection with a summer school at each campus (2017). We are also involved in “Healthy Aging in 6 Steps”, a massive open online course (MOOC) on healthy environments and citizen involvement, in collaboration with the Leyden Academy on Vitality and Ageing and Delft University of Technology (2017).

Furthermore, within EIT Health, CEHA participates in *EpiDEMPrev*, a pan-European PhD program on the epidemiology of aging and dementia prevention, in partnership with the University of Coimbra and Imperial College London (2018) (<https://eithealth.eu/project/eit-health-ageing-phd-school>). The program brings together an EIT Health consortium consisting of academic and non-academic partners. *EpiDEMPrev* trains a new generation of PhD-level specialists in gerontology, neuroscience, and epidemiology, with the goal of establishing competencies in innovation and entrepreneurship. As part of

the doctoral program, on 25–27 May 2020, the Center offered an online PhD course on the methodology of aging research, “Why Do We Age—Molecular Models of Ageing.” The course included in-depth lectures from international renowned experts on molecular and cellular processes of aging and was led by Associate Professor Claus Desler.

**Alliance for Biology of Ageing Research and Healthy Ageing Multidisciplinary biobanking approaches (ABRAHAM) network (not active)**

CEHA was active in the ABRAHAM network, which was created in 2010 and includes researchers, companies, governmental institutions, and patients/citizens. ABRAHAM aimed to create a transatlantic network with partners from the EU, US, and Canada to enhance integration in the field of biobanking and basic aging research, to contribute to the goal set by the European Commission to give its citizens two additional healthy years of life by 2020. This collaborative effort harmonizes, standardizes, and facilitates exchanges of data and materials from biobank and cohort studies; facilitates the shared use of infrastructures, facilities, and expertise; and enables exchange visits of personnel to participating institutes to explore options for new projects and/or pilot studies. The founding partners of the ABRAHAM network are the University Medical Center Groningen (Netherlands), UCPH (Denmark), Newcastle University (UK), Mayo Clinic (MN, USA), and McGill University (QC, Canada). All of them have extensive collaborations with industries in the food,

pharmaceutical, and medical technology sectors, as well as experience in human clinical trials.

The network builds on several existing projects of the founding members, some of which involve transatlantic partnerships that focus on aging-related issues, such as genome stability and metabolism, and systems biology. Since 2013, CEHA and the ABRAHAM network have participated in the Annual Alliance for Healthy Aging conference series, the EU Marie Curie Integrated network of Researchers (ITN) MARRIAGE, and EU research and infrastructure applications.

### MouseAge (not active)

MouseAge was launched in 2014 as a European COST Action network for the preclinical testing of interventions in mouse models of age and age-related diseases. It links major research centers in Europe, including CEHA. The network was established in response to the low availability of mouse models for preclinical research studies, and a need for standardized methodologies to test and evaluate interventions. Specifically, MouseAge was set up as a highly interactive and flexible European network to create a critical mass of cross-disciplinary scientists, clinicians, and industrial partners to reach a consensus on ways to test preclinical interventions in aging mice. It consolidates current best practices across leading European institutions and researchers, maximizes resource efficiency, and provides a platform to help train the next generation of scientists. It thus improves the quality of European aging research, standardizing methodologies and guidelines for animal welfare, and defining endpoints, as well as providing a centralized model for storing and disseminating information about these models and technologies.

### Alliance for Healthy Aging (ongoing)

The Alliance for Healthy Aging was founded by the Robert and Arlene Kogod Center on Aging at Mayo Clinic (MN, USA) and some institutes from the Netherlands, namely, the University Medical Center Groningen, the University of Groningen, the Noaber Foundation (Lunteren), and Vita Valley (Ede). It was founded to bring together scientists, clinicians, and engineers, providing a forum for the exchange of ideas. CEHA joined in 2019. Accordingly, the Alliance holds a series of annual meetings dedicated to translational research on aging. The first meeting was held in June 2010. Entitled “The Next Step in Aging Research: From Bench to Bedside: A Forum for Collaboration between Clinicians and Researchers,” it focused on the basic biology of aging and its relationship to clinical practice. The meeting was a resounding success. Since then, meetings have been held regularly on such topics as “Healthy Aging and Independent Living: Countering Frailty and Maintaining Independence” (Groningen, 2011), “Senescence and Healthspan” (Rochester, 2012), “Molecular Mechanisms of Age-Related Multi-Morbidity” (Groningen, 2013), and “Frailty and Healthspan: Bench to Bedside to Home” (Rochester, 2014). In 2015, Newcastle University’s Institute for Ageing teamed up with the University of Coimbra to support the creation of the new Multidisciplinary Institute of Ageing, in Coimbra, Portugal. The Alliance welcomed the collaboration with Newcastle/Coimbra; together, these institutions hosted the 6<sup>th</sup> Annual Alliance for Healthy Aging Conference: “Interventions to Slow Down Aging” UK in November 2015.

In 2016, the conference was unexpectedly cancelled because of Hurricane Matthew. In 2017, the University Medical Center Groningen hosted the 8<sup>th</sup> Annual Conference, “Metabolism and Ageing,” which was followed by the conferences “Molecular Mechanisms of Organ System Crosstalk and Failure with Aging” (Rochester, 2018) and “Intervention: From Mice to Humans” (UK, 2019).

### National Institute on Aging at National Institutes of Health (NIA/NIH)

CEHA has an active collaboration with the NIH/NIA, who are world-leaders in aging research. CEHA collaborates via Professor Wilhelm Bohr, who is a Group Leader in Track III and has been instrumental in the establishment of CEHA. This has enhanced the Center’s ability to recruit accomplished scientists to the Center over many years, such as Professors Ian Hickson and Linda Bergersen, and Associate Professor Morten Scheibye-Knudsen.

## 7.2 National collaborations

### Stakeholder strategy

The primary target groups for CEHA stakeholder engagement are organizations for the elderly, municipal decision-makers, healthcare professionals, and selected patient organizations. We aim to engage with these groups to highlight and discuss healthy aging through events, workshops, seminars, and lectures organized by CEHA, and during joint projects and events. A successful example is CEHA’s participation at the People’s Political Festival in 2016–2019. More importantly, our strong communication efforts and work with stakeholders have paved the way for new types of collaborations that integrate research, communication, and implementation. This stakeholder strategy has provided a framework for engagement and external collaborations of CEHA in the past 5 years.

### Collaborating with municipalities

Much of CEHA’s research is done in a dialogue with citizens as well as with 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.

## 7.3 Connecting national researchers to solve complex issues

Greater Copenhagen Health Science Partners is a partnership between the University of Copenhagen (UCPH), the Technical University of Copenhagen, Region Zealand, and the Capital Region of Denmark. It hosts clinical academic groups (CAGs), which act as forums for close collaboration between university and hospital researchers, allowing the participants to learn from each other and develop new ideas, for rapid scientific progress and improved treatment of patients. To bring aging-related university research, clinical research, and clinical practice closer together, Center for Healthy Aging (CEHA) researchers chair and participate in two CAGs: ACUTE CAG, and the CAG on Physical Activity and Sports in Clinical Medicine. These CAGs focus, respectively, on improving acute treatments of people suffering from multimorbidity, and on using physical activity in the prevention and treatment of

chronic diseases and prolonged injuries. Examples of CEHA CAG activities are provided below.

#### **ACUTE CAG: Predicting acute recovery capacity based on biological age**

**Chairs:** Professor Ove Andersen (Amager-Hvidovre Hospital) and Professor Lene Juel Rasmussen (Track I)

The clinical academic group ACUTE CAG was formed in 2019 by 30 researchers from CEHA and Amager-Hvidovre Hospital, with different specialties, to enable personalized treatments of acute illness in patients with multimorbidity (two or more chronic health issues).

Approximately 1.2 million Danes suffer from multimorbidity, and age is the greatest risk factor. In fact, half the population over 65 years old lives with more than two medical conditions. This complicates the treatment of acute illnesses among these individuals because the acute issue disturbs the chronic conditions and because of possible inexpedient interactions between drugs. Accordingly, ACUTE CAG uses biological data, medical history, and lifestyle information to estimate each person's biological age and to predict how a person will react to treatment. The ultimate aim is to develop an index to measure a person's biological age based on the 50 most relevant biomarkers for someone's individual recovery

capacity. This contributes to better treatment and recovery of individuals with multimorbidity.

#### **ImPAct: Exploring the role of physical activity in recovery and rehabilitation**

**Chairs:** Professor Flemming Dela (Track III) and Professor Michael Kjær (Track I)

The CAG on Physical Activity and Sports in Clinical Medicine was formed in 2018. It couples laboratory and clinical research groups to explore the recovery and rehabilitation potential of physical activity and generally increase the synergy between research, clinical activity, and education within the area.

Physical inactivity and sedentary behavior represent the new public health challenge. They are considered responsible for 40 million deaths worldwide each year and for four major disease types: cardiovascular diseases, cancers, respiratory diseases, and diabetes. Regular physical activity is beneficial for the prevention and treatment of chronic diseases that affect many elderly people. Furthermore, physical activity can improve the treatment and rehabilitation of patients after trauma and injury, and prevent future musculoskeletal disorders. However, the use of physical activity in daily clinical medical practice is limited, and the interplay between physical activity and pharmacological treatment is poorly understood.



# 8 Center performance and impact

## 8.1 Center for Healthy Aging (CEHA) impact strategy: Impact definition and measures

The interdisciplinary research, education, and outreach of CEHA deals with society's needs at a time of vast population aging. We exist to help solve the major challenges associated with a diminishing workforce and an increasing pressure on the health and care sector. We have a very extroverted and open approach to our research and knowledge production, and we seek to connect with stakeholders beyond academia to maximize the short- and long-term impact of our activities. We define 'impact' as:

1. Producing research results that increase the understanding of the aging process at the cellular, organ, individual, and societal levels
2. Educating future experts in aging, who can contribute to solving society's aging-related challenges
3. Conducting intervention and outreach projects with relevant stakeholders e.g., municipalities and organizations for the elderly
4. Developing research-based guidelines and policy documents to increase citizens' quality of life
5. Participating in ongoing dialogue with stakeholders such as politicians, interest organizations, and people in the health and care sector, as well as the wider public, to qualify debates and projects with the newest research-based knowledge

## 8.2 Reflection on the Center's performance to date, in light of the defined impact

Using the above definitions as a guide, we assess the Center's performance from 2018 to 2021 as well as in the previous 10 years as very strong in all our five impact areas. Specifically, for increasing the understanding of the aging process (1, above) we have shown how exercise can improve muscle function even late in life and that strength training is the most effective type of exercise (projects CALM and LISA), and we have found out that the coenzyme NAD<sup>+</sup> can improve cell repair and halt the aging process.

For educating future experts (2), we have educated more

than 200 PhD students who are now implementing their knowledge in the health and care sector or in research at Danish and foreign universities, and we have held summer schools and massive open online courses (MOOCs) each year and inspired, for example, future doctors to take an interest in aging issues.

Concerning outreach projects (3) and research-based guidelines, etc. (4), we have shown how our knowledge and approaches can be used to improve the health of vulnerable (e.g., minority) groups of seniors (see Track II and section 3, "STRIT"), and CEHA researchers often help formulate guidelines and reports that qualify efforts in Denmark and internationally—such as through the council Science Advice for Policy by European Academies or reports for the Danish Health Authorities.

When it comes to dialogue with stakeholders and the general public (5), CEHA has from the beginning been a very actively communicating research center in the media and in direct dialogue such as public events and stakeholder meetings. These efforts have led to several research results reaching the point of common knowledge and changing practices, such as our results on how and why social relations impact our health and what exactly happens if you are physically inactive for an extended period of time.

### Strategic focus

CEHA's impact strategy builds on achievements, results, and networks throughout the Center's first 10 years of existence and is deeply integrated in our research approach (i.e., research projects in direct collaboration with stakeholders) and in our communication and outreach efforts, which are described in sections 3 and 4. CEHA's long-term goal is to build a national multi-stakeholder aging initiative based on the Center's extensive aging research, research from Aarhus and Aalborg Universities and the University of Southern Denmark, and the demands of society as defined through dialogue with Local Government Denmark (KL) and Health Sector leaders, among others. By formally assembling the accumulated Danish aging research efforts in a strategic, practice-oriented



Figure 13. Strengths–Weaknesses–Opportunities–Threats (SWOT) analysis.

collaboration, Denmark can become an international frontrunner in handling aging-related societal challenges. The national aging initiative’s shape and form as well as several concrete research products are to be defined in a co-creation process with key stakeholders who are working closely with the citizens and have hands-on experience with the aging-related challenges western welfare societies need to address.

CEHA is currently nurturing this agenda by showing the value of aging research by participating in various collaboration projects and having ongoing dialogue with relevant stakeholders (as always), through public affairs efforts in the (social) media, and at meetings and conferences (see appendix A3 under “Other activities” and section 3 of this self-evaluation). CEHA has already shaken hands with the three other universities and is now planning to bring together other potential partners to investigate the potential further. Our key stakeholders are:

- Organizations for the elderly—specifically DaneAge
- Decision-makers, specifically in municipalities and regions as well as the Ministry of Social Affairs and Senior Citizens
- Patient associations, specifically the Danish Heart Association and the Danish Cancer Society
- Health professional organizations, e.g., the Danish Medical Association
- Foundations, Danish and international
- Pensions funds, specifically PFA Pension
- Trade Unions (because of their impact on the Danish labor market)

### Impact measures

We apply both qualitative and quantitative methods to measure CEHA’s impact. We will measure impact at the Center by continuously estimating how we are achieving impact according to the five definitions above. We will do this by evaluating projects ourselves, by collecting relevant data, and by performing surveys of our collaborators and the users benefiting from our research. This will be supplemented by impact cases that give illustrative examples of CEHA research and outreach projects with a high relevance to our surrounding society, including how we succeeded in making a difference.

Notwithstanding the above definition, impact is dynamic and changes over time. We recognize that new potential impact develops throughout the CEHA lifespan. We therefore strive to bring openness and flexibility to our impact measures to be able to include unforeseen developments. Impact will be reported on an annual basis, when we will also evaluate and revise our strategic impact goals and measurements in accordance with the Milestones Report. At the final reporting, we will summarize and report on impact for the full project period.

### 8.3 Strengths–Weaknesses–Opportunities–Threats (SWOT) analysis

The CEHA management has conducted a SWOT analysis (Fig. 13) based on input from a bottom-up self-evaluation exercise of Group Leaders. This analysis is a simple way of guiding new efforts by capitalizing on strengths and minimizing weaknesses. It also helps us to identify possible strengths, weaknesses, opportunities, and threats. We employed this analysis as a basis for discussion with the leadership of the University of Copenhagen (UCPH) to decide how to continue CEHA after 2023.

# 9 Perspective

The Center for Healthy Aging (CEHA) has for 13 years made giant strides to become a unique hub of knowledge about aging across disparate research disciplines. It was launched as a response to the increasing realization that major demographic changes across the globe require know-how, interventions, and policies that catalyze cutting-edge research across the natural and social sciences and the humanities, while engaging with key stakeholders across major societal sectors.

We have risen to the task and gone from strength to strength since CEHA's inception in 2009. At the outset, CEHA was the first multidisciplinary center in Denmark to address the individual and societal challenges associated with aging by understanding the biology of aging, its link to the environment, and the role and interplay of genes, lifestyle, and health. In its second installment (2014–2018) we then built on these initial successes to hone a unique approach to not only bridge multiple disciplines to foster a holistic understanding of aging, but also to invest in outreach and capacity building, and constantly evolving and challenging stereotypes associated with aging.

In the second installment of CEHA we also introduced the common thread of “energy” in the aging processes, not only as it relates to individual bodies and processes at the cellular level, but also in relation to psychological and social dimensions, including interest in one's surroundings and engagement with other people. This reorganization was a natural development from the initial *multidisciplinary* approach of CEHA to an increased *interdisciplinarity*.

We have continued this trajectory toward increasing interdisciplinarity in CEHA's third installment (2019 onwards) where we have developed new approaches across complementary disciplines within a common conceptual framework.

CEHA is now recognized internationally for its high-quality research. We educate the next generation of basic scientists, clinicians, and health sector professionals at the forefront of interdisciplinary aging-related research. However, our work is far from done.

Drawing from our most recent SWOT analyses, we have identified great opportunities to build closer collaborations between UCPH and hospitals and to foster the career development and recruitment of young Group Leaders in interdisciplinary aging research. In addition, we believe that Denmark needs a politically backed national aging initiative that can bring together foundations, relevant organizations, public and private health and welfare providers, and aging researchers from Danish universities to create a comprehensive aging strategy.

Therefore, during the coming years we will: (1) increase collaborations by taking advantage of our existing national and international collaborations and establishing new ones; (2) contribute to increasing the critical mass within aging research at UCPH by establishing a research network; (3) apply for external funding for aging research from public and private national and international foundations; (4) collaborate with other universities in Denmark to establish a national aging initiative, which could include a joint PhD program; and (5) continue to build on our outreach and partnership activities, including university–hospital collaborations.

This strategy will further cement the position of CEHA as a key player in the international aging-research community while building crucial know-how, awareness, capacity, and synergies to make Denmark the best country in the world to grow old in.



UNIVERSITY OF COPENHAGEN

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