



# PROGRESS REPORT 2016 - 2019



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## KNOEBEL INSTITUTE FOR HEALTHY AGING

QUALITY IN LIFE, WELLNESS & COMMUNITY



## EXECUTIVE SUMMARY

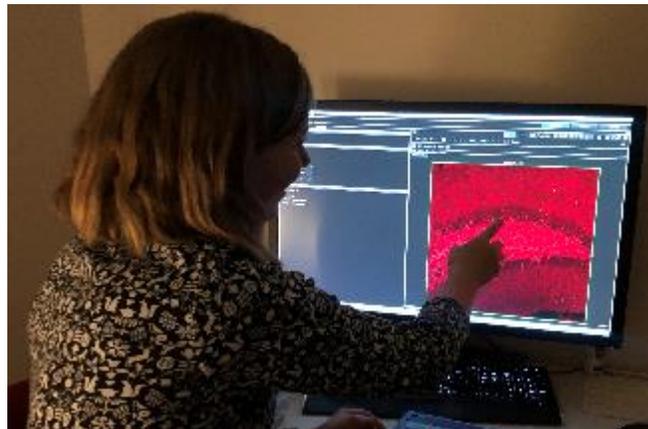
**KIHA** moved into its new space in the Engineering building in early fall of 2016. We have submitted more than 100 grant applications to federal grant agencies. This has resulted in more than \$4.7 million in funded grants to date. We have raised \$1.03 million fundraising dollars the last three years. The Eleanor Roosevelt Institute (ERI), which joined KIHA in January of 2018, has raised an additional \$193,000 in gifts and foundations since the merge. We have recruited 10 research groups. Together, KIHA and KIHA-affiliated researchers have published close to 50 peer-reviewed publications during the last 3 years and formed interdisciplinary research groups focused on healthy aging, dementia, movement disorders, intergenerational programs, financial security, and gerontechnology. We have also partnered with clinics in Colorado to initiate translational studies.

We have active collaborations with 25 faculty from other Departments at DU, in nine different colleges and with other Universities in 13 US states and 10 countries. We have implemented two collaborative networks: **CoCARE** (Colorado Coalition for Aging Research and Education), which consists of seven Colorado-based Universities, and the **DSBC** (Down Syndrome Biobank Consortium), which consists of eight Universities in the US and three in Europe. We have held close to 200 events.



In comparison with other Aging Institutes in the US and abroad, the growth of KIHA infrastructure and research groups as well as community engagement is beyond the expected growth, attributed to strong leadership, the highly accomplished scientists involved, and the strong belief in team science and interdisciplinary work in the DU leadership. In addition, strong support from the community organizations outside of DU has allowed a rapid increase in community outreach and education.

*“Working at KIHA has given me the opportunity to be continually inspired by the diverse community focused on groundbreaking research”.*  
*Kaitlin Smith, sophomore Mathematics and Computer science double major.*



# HISTORY

**DU** established the Knoebel Center for the Study of Aging in 2010 with a generous gift from Betty Knoebel, widow of Denver food services pioneer Ferdinand “Fritz” Knoebel. **Dr. Lynn Taussig, MD, Special Advisor to the Provost at DU**, headed the effort (see below). In 2012, a pilot grant program was established that sought proposals with a focus on aging and awarded pilot grants, with recipients of grants in almost all DU colleges and schools. Several of these early grants have led to federal funding. The name was changed in 2015 to the Knoebel Institute for Healthy Aging. This change reflects the vibrant role the Institute has as an umbrella for cooperation and partnerships between natural sciences, engineering, social sciences, the arts, lifelong learning and the University’s professional research and education programs in law, business, social work and psychology. In April of 2015, Dr. Lotta Granholm-Bentley was named the Founding Executive Director for KIHA. KIHA’s state-of-the-art research lab and office space are on the 5th floor of the \$60 million complex that houses the Daniel Felix Ritchie School of Engineering and Computer Science. We are eternally thankful to the Knoebel family for their continued support and interest in KIHA.

## Lynn Taussig, MD, Special Advisor to the Provost

“After retiring as President/CEO at National Jewish Health, I was asked by DU to assess the academic profiles of the various academic units and determine if DU should be considering establishing certain new programs. I suggested that, building on some already existing small age-related studies, DU should consider establishing a multidisciplinary program on “Aging.”. After extensive study by faculty and staff, a Center on Aging (the name later changed to the Knoebel Institute for Healthy Aging recognizing a \$10 million-dollar gift from the Knoebel family) was created and an Executive Director (Dr. Lotta Granholm-Bentley) recruited. From its inception, the Institute was charged with developing outstanding programs/activities/initiatives in clinical and basic science research, educational programs for students, scientists and community service. This brochure highlights the outstanding achievements KIHA has accomplished in all these areas in a relatively short time and how it is now positioned for a continuing exciting and productive future”.



## Dr. Lotta Granholm-Bentley, Executive Director

Dr. Granholm (PhD/DDS) was born in Göteborg, Sweden and received her PhD in Neuroscience from the Department of Histology at the Karolinska Institutet in Stockholm in 1984. She has published more than 160 peer-reviewed journal articles and been funded by the NIH, Bright Focus Foundation, and the Alzheimer’s Association since the early 90s. Dr. Granholm is a Guest Professor in the Alzheimer program at Karolinska Institutet in Stockholm since 2015. The Karolinska Institutet is highly prestigious and gives out the Nobel Prize in Physiology or Medicine. Her research is focused on Alzheimer’s disease and Down syndrome, working on animal models, basic mechanisms, and biomarkers of disease. Before Dr. Granholm came to DU as the inaugural Executive Director for the Knoebel Institute for Healthy Aging (KIHA), she was Director for the Center on Aging at the Medical University of South Carolina (MUSC) for 16 years and Director for the South Carolina Brain Bank. She is married to Stephen Bentley and has one son, Lars Bentley, who is a recent graduate of DU. Dr. Granholm-Bentley was one of the highest NIH-funded researchers at DU in 2019.





# STRATEGIC OBJECTIVES

These transformative directions and specific objectives were developed in 2015-2016 by an interdisciplinary **Strategic Work Group**, consisting of faculty from many different colleges at DU.

## KIHA Transformative Directions:

### 1. Develop Interdisciplinary Research Programs

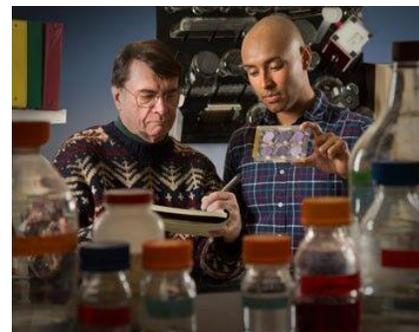
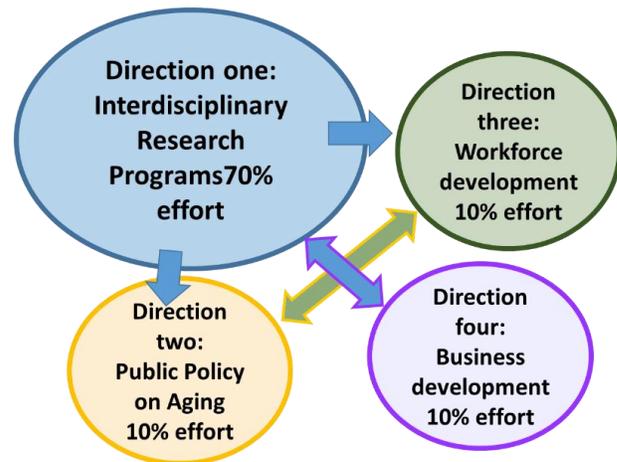
- Build interdisciplinary research teams
- Provide pilot funding, grant writing and mentoring
- Develop a Biobank and data repository for aging research
- Form partnerships in programmatic grant funding
- Provide seminars and conferences on aging

**Progress summary:** 4.7 million dollars in research funding, development of multiple interdisciplinary research groups, development and funding of the Down Syndrome Biobank Consortium, consisting of 11 different sites in the US and Europe, and recruitment of 6 additional research groups to KIHA. Monthly scientific “chalk talks” and 5 annual Grand Rounds.

### 2. Transform Public Policy and Attitudes on Aging

- Develop a multi-disciplinary and intergenerational community think tank on aging
- Provide and enhance student immersion projects in the community
- Work with other organizations regarding aging policies and laws in Colorado
- Support intergenerational programming

**Progress summary:** We have engaged more than 50 organizations and businesses in the area. We have placed many students in internships around the Denver area, and we serve on both government committees and non-profit boards. The CoCARE consortium was implemented with a one-day conference in 2018. Dr. Granholm serves on the Alzheimer Association Board. We have received 5-year funding to implement an Intergenerational Program, in collaboration with GSSW.



*“The work space of KIHA is relaxed and intellectually focused. The experience gained from working on a team consisting of a diverse group of engineering and scientific specialties has been of great value for my engineering education and research career. For me it has been a place where I can not only have thoughtful conversations but then do work that results in something tangible.” Andriy Novakov, Engineering Student*

### 3. Increase Competency of the Current and Future Workforce for Aging

- Support interdisciplinary educational opportunities on aging
- Expand learning opportunities on aging-related issues
- Integrate health and wellness disparities of aging
- Develop teaching materials on aging
- Provide educational opportunities for the community

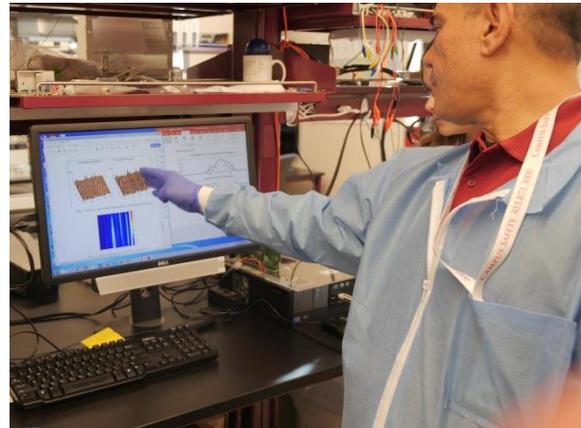
**Progress summary:** Educational opportunities for the community in collaboration with other organizations at least four times per year and are planning to provide more student training via training grants and internships. An interdisciplinary course was taught to Law and GSSW students in 2018 by Drs Granholm and Chess. Another course is planned with Engineering on Artificial Intelligence.



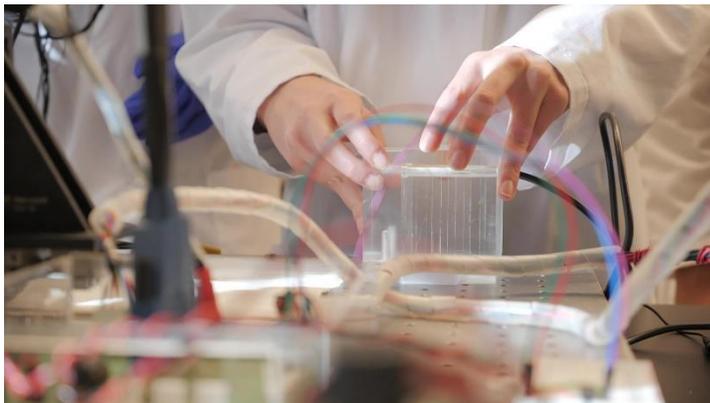
### 4. Support Business Development and Innovation Related to Aging

- Develop an aging-related incubator
- Provide SBIR funding support
- Partner with businesses and organizations
- Partner with the annual Aging 2.0
- Organize a job fair for DU students on age-related businesses
- Work with Project X-ite to develop Gerontechnology projects at DU

**Progress summary:** We have collaborated on a funded SBIR grant (PI Mahoor, Engineering) and submitted two others. We currently have three contracts with local businesses including clinical experience and support for 4 graduate students (Alumia and Resilience Code). We have participated in the Aging 2.0 conference two consecutive years.



*Dr. Paredes examines metabolomic pattern recognition data from patients with Parkinson's disease.*



*"Dr. Lotta Granholm-Bentley and her great team at KIHA are a great resource for the entire Denver area. I have worked with Dr. Granholm-Bentley over the past few years and find her to be knowledgeable, influential and a great collaborator on aging issues, particularly on the topic of Alzheimer's disease and dementia".*  
*JJ Jordan, Community Chair, Dementia Friendly Denver*

# RESEARCH IMPACT AREAS

The research and outreach areas summarized below are ongoing interdisciplinary research projects and span many colleges and departments at DU as well as collaborative partners nationally and internationally. **The added value of KIHA** is to provide startup funds and a scientific home for interdisciplinary research teams as well as grant writing support and student training and mentorship.

## Research Impact areas at KIHA:

1. Memory loss and aging
2. Movement Disorders and aging
3. Intergenerational Programs
4. Financial Security and aging
5. Gerontechnology

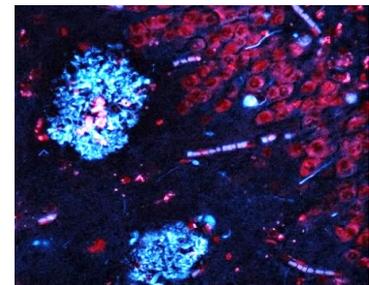


### 1. Memory Loss and Aging

#### ***Lifestyle factors, healthy aging and dementia***

***Principal Investigators:*** Lotta Granholm and Aurélie Ledreux. ***Collaborators:*** Kirk Daffner (Harvard), Abdul Mohammed (Karolinska Institutet). This research is focused on

understanding the biological mechanisms underlying detrimental effects of high-fat diets as well as protective effects afforded by exercise or cognitive training on the aging brain. The Western diet as well as a sedentary life style increases risk for dementia with aging, but mechanisms are not understood. Studies are conducted in animal models and also in healthy older adult humans, developing novel biomarkers and intervention paradigms. **This work has been funded by the National Institutes on Aging (NIA), Kamprad Foundation and Alzheimer Association.**



*Amyloid plaques in a brain with Alzheimer's disease.*

#### ***Down Syndrome and Alzheimer's***

***Principal Investigators:*** Lotta Granholm (KIHA), Aurelie Ledreux (KIHA), Guido Vacano (KIHA), David Patterson (KIHA), Dan Linseman (NSM/KIHA), Scott Horowitz (NSM/KIHA), Martin Margittai (NSM), Daniel Paredes (KIHA), Yan Qin (NSM), Sunil Kumar (NSM/KIHA). ***Collaborators:*** Liz Head (UC Irvine), Juan Fortea (Barcelona), Elliott Mufson (Barrow Neurological Institute), Brian Skotko (Harvard), Ed Goetzl (NIH), Stanley Prusiner (UCSF), Agneta Nordberg (Karolinska), Pablo Caviedes (Universidad de Chile). This research team has discovered novel potential treatment avenues and early biomarkers as well as a novel method for determining whether those with Down syndrome will convert to Alzheimer's disease before symptoms arise using innovative exosome biomarker technology. In collaboration with Yan Qin (Biology), altered mitochondrial movement in a human Down syndrome fibroblast cell line has been discovered and work in the Horowitz, Kumar, and Margittai laboratories focuses on understanding protein misfolding and aggregation and developing new tools to treat Alzheimer's disease. **Funded by Bright Focus Foundation and the National Institutes on Aging.**

#### ***Concussion Study in Athletes***

***Principal Investigators:*** Bradley Davidson (Engineering), Kevin Shelburne (Engineering), Kim Gorgens (Graduate School of Professional Psychology), Martin Margittai (NSM), Dan Linseman (NSM/KIHA), Julie Campbell (Athletic Performance), Aurélie Ledreux (KIHA), and Lotta Granholm (KIHA). ***Collaborators:*** Adam Wolff (Chief Neurology, Porter Hospital), Chad Prusmack (Neurosurgeon, CEO Resilience Code), Ed Goetzl (NIH).



*DU athletes waiting for a blood*

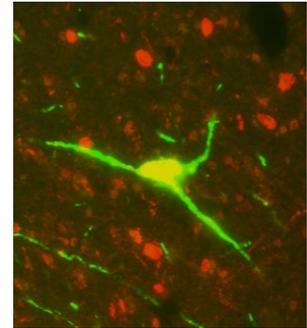
Research studies suggest that repeated concussions may lead to increased risk for Alzheimer's disease. This research team is utilizing a newly developed blood test called "exosome technology" coupled with novel dynamic balance measurements and has already enrolled a cohort of >350 of the DU Division 1 athletes to participate in the study. We use this novel technology to study brain health and disease biomarkers in athletes. The new technology will also be used to study whether repeated concussions lead to an increased risk for dementia with age. The Linseman laboratory has identified several natural compounds that can prevent post-concussion symptoms and promote long-term brain health.

## 2. Movement Disorders and Aging

### *Parkinson's Disease*

*Principal Investigator:* Daniel Paredes (KIHA), Daniel Linseman (NSM/KIHA), Adam Hebb (KIHA, Neurosurgery St Joe's/Kaiser), Sunil Kumar (KIHA/NSM), Mohammad Mahoor (Engineering).

*Collaborator:* Rajeev Kumar (Medical Director of the Rocky Mountain Movement Disorders Center). One goal of this translational project is to detect Parkinson's disease before clinical symptoms appear to prevent the disease. Investigators are using Artificial Intelligence (AI) to identify a "footprint" of beginning neurodegeneration in blood samples from patients long before symptoms appear. Drs. Hebb, Paredes and Mahoor received a DU PROF grant to develop new circuitry for Deep Brain Stimulation (DBS) to create a system capable of triggering the electrical stimulation selectively, only when it is needed. A collaboration between Dr. Kumar (NSM/KIHA), Dr. Ledreux (KIHA) and Dr. Paredes (KIHA) is to identify aggregating forms of alpha-synuclein (protein altered in Parkinson's disease). In addition, Dr. Granholm and Dr. Ledreux are collaborating with investigators at University of Kentucky to explore benefits of a neural transplant in patients with Parkinson's disease (see picture).



*Dopamine cell in the brain (green) surrounded by transplanted cells (red) providing protection.*

### *Amyotrophic Lateral Sclerosis*

*Principal Investigator:* Daniel Linseman (KIHA/NSM). Dr. Linseman's research is focused on elucidating molecular mechanisms of neuronal cell death in degenerative disorders with a emphasis on amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease). Biochemical, immunofluorescence, and molecular biological techniques are used to examine the roles of mitochondrial oxidative stress and cell death in neurodegeneration. Mouse models of



*Alec Smith and Lilia Koza plan an experiment*

neurodegenerative disorders are also used to study disease processes *in vivo*. Specific projects include investigating the role of Rho family GTPases in the motor neuron cell death that underlies ALS, the role of mitochondrial glutathione transport in protecting neurons from oxidative stress, involvement of Bcl-2 family proteins in the regulation of mitochondrial susceptibility to oxidative stress, and the antioxidant and neuroprotective properties of a variety of natural products. **This project has been funded by a grant from the KIHA pilot grant program and by the Ralph L. Smith Foundation via the Eleanor Roosevelt Institute and has led to numerous publications.**

## 3. Intergenerational Programs

*Principal Investigators:* Leslie Hasche (GSSW), Lotta Granholm (KIHA), and Carson De Fries (KIHA). *Collaborator:* Roddy MacInnes (Arts, Humanities & Social Sciences, DU). With five years of Strear Family Foundation funding, a formal partnership between DU and the community collaborative called LinkAGES is housed in KIHA to support evaluation of community-based

intergenerational programs. LinkAGES Colorado's mission is to prevent and reduce social isolation across the lifespan while fostering a culture of respect between the generations. Community members lead the LinkAGES collaboration and the offering of intergenerational programs, while DU leads evaluation across all intergenerational programs. Examples of LinkAGES intergenerational programs that are evaluated by DU include mentorship, music and art therapy, food and holiday traditions, and photography. LinkAGES collaborators include the following community partners: Kavod Senior Life, Shalom Park, Jewish Family Service, Denver Jewish Day School, Wish of a Lifetime, the Denver Public Library, the Staenberg-Loup Jewish Community Center, and Generations United. **The project has been partially funded by a grant from the Strear Family Foundation and by funding from KIHA.**



*A DU photography student shares an intergenerational moment with a senior resident during Dr. Roddy MacInnes's photography class.*

#### 4. Financial Security and Aging

*Director: Eric Chess MD/JD (KIHA, Daniels College of Business, Sturm College of Law). Program Manager: Ashley Taeckens-Seabaugh. Collaborators: Jennifer Greenfield PhD (Graduate School of Social Work), Kim Gorgens PhD (Graduate School of Professional Psychology), Matt Rutherford PhD (Engineering & Computer Science).*



*FSCH Team: Eric Chess MD/JD, Jessica King, Jennifer Greenfield PhD and Ashley Taeckens*

As our population ages, concerns regarding financial security and cognitive health loom large. KIHA's **Financial Security and Cognitive Health Initiative** is working on the development of practical and accessible testing methods for early identification of impaired financial decision-making, which is one of the first clinical signs of cognitive impairment and dementia. The *Initiative's* multi-disciplinary team is also developing evidence-based educational programs to show positive change in behavior regarding financial and cognitive health. We have also launched an innovative multi-disciplinary course in the University's Sturm College of Law, designed for graduate students in law, business, social work and psychology. The

team is working with financial industry partners and regulators to develop industry-wide guidelines and best practices with respect to impaired financial decision-making and cognitive impairment. Finally, the *Initiative* has been working with the Attorney General's office in Colorado to advance impactful policy initiatives and statewide educational programs. This *Initiative* stands to play a critical role in protecting financial security and preventing or delaying or lessening symptoms of cognitive impairment and dementia, affecting millions of lives and billions of dollars. **This research group is funded by a grant from Impact 2025 and the Next 50 Initiative.**

#### 5. Gerontechnology

**Engineering faculty are collaborating with KIHA faculty on several projects.** Among these can be mentioned the Social Bot Ryan, for which Dr. Mohammad Mahoor has received a Small Business Innovation Research grant (SBIR) with a subcontract to KIHA to develop Ryan for people with mild cognitive impairment. Another project involves dynamic balance measurements in athletes with multiple concussions (see above) and development of novel applications for assessment of cognitive impairment and financial planning.



*The "brain jig" can help dissect tiny areas of the brain*

**KIHA Biobank:** The Knoebel Institute for Healthy Aging hosts a national/international biobank focused on Down syndrome-related Alzheimer's disease, the *Down syndrome biobank consortium, DSBC*. Currently DSBC contains 11 sites, both in the US and Europe. The biobank has led to valuable collaborations both within DU and with other entities, in 10 different countries and in 13 different states within the US. **Dr. Granholm was recently funded by the Bright Focus Foundation to lead the effort in DSBC and collect blood and brain samples from individuals with DS.** A recent collaboration between KIHA (Granholm) and Engineering has led to the production of a novel "brain jig" used for brain dissections and using 3D printing.

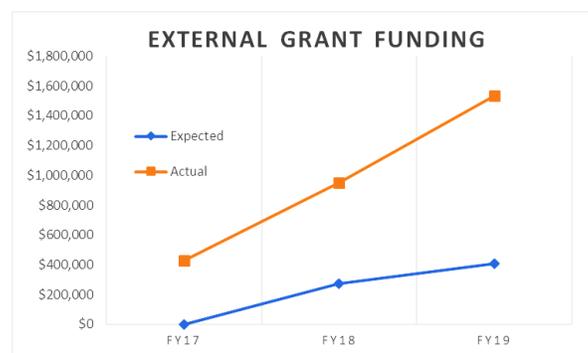
*"As a faculty member, the opportunity to work alongside the thought leaders in neuroscience and bioengineering is extraordinary. Our interdisciplinary concussion biomarker team is the perfect exercise in collaboration for the public good. This team is jointly addressing a public health crisis (dementing disease) and empowering young people to manage their brain health—the effects of this work cannot be overstated".*

*Dr. Kim Gorgens, Clinical Professor in the Graduate School of Professional Psychology*

## RESULTS

### Grant funding

KIHA researchers have been awarded more than **\$4.7 million dollars** since the inception and have **exceeded the expected grant levels all 3 years**. Funded projects include the Financial Security project, the Intergenerational project, Dementia, Healthy Aging, and the Down syndrome Biobank. Dr. Granholm recently received a multi-PI R01 grant from the National Institutes of Aging (NIA) with total awarded \$3,4 million dollars. We have also received a \$250,000 5-year grant from the Strear Foundation for the **Intergenerational Program**, a multi-year grant from the Next 50 Initiative Foundation for the **Financial Security Program**, and a 5-year Biobank grant from the Bright Focus Foundation. Despite our grant success, KIHA is still in its initial startup phase, since it is only 3 years since we moved into our labs and offices.



**Fundraising Progress** A successful Institute should receive equal parts of infrastructure funds, grant support and philanthropic funding. While we are still in our infancy, we have surpassed expectations for fundraising the last two years. Donated dollars are used for infrastructure, specific projects, bridge funding and startup funds for new projects and recruitment of new faculty. **We are thankful to our supporters! Continuous support is needed to propel our impact and enhance all areas of research at KIHA.**

*"The environment at KIHA offers researchers a truly unique environment unparalleled in the U.S. Many projects underway in the labs will be paradigm shifters in the senior care industry. These research scientists are collaborating to make a dent in a variety of neurological disorders. Additionally, the schools of engineering, law, business, computer science and social work are developing treatments and techniques to help our fast-aging population age-in-place as long as possible".*

*David Geras, CEO GoldLeaf HomeHealth*

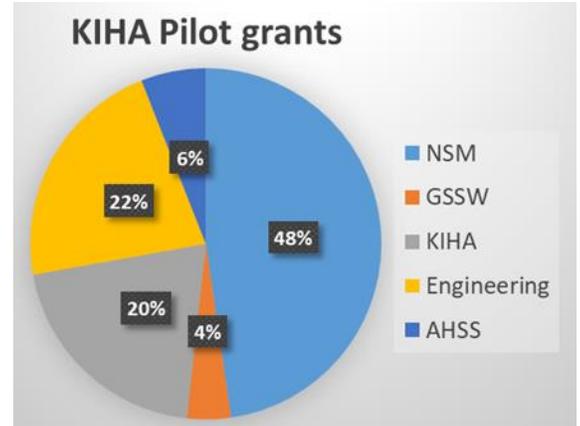
# RESULTS

## KIHA Pilot Grants

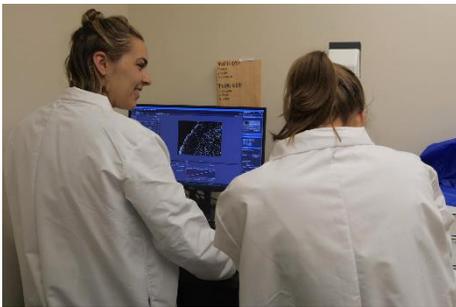
As part of the DU investment into KIHA, we are distributing 4-5 pilot grants to DU investigators in different departments and colleges each year. While this program is still in its infancy, return on investment will be more obvious in the next 2-3 years. Total KIHA pilot grant money awarded: \$707,255

Total Gain in External grants resulting from KIHA pilot grants to DU faculty: \$1,550,902

Return on investment: 219%



*KIHA pilot grants awarded by college*



*Graduate students Alex Sanberg and Lilia Koza work in Dr. Linseman's lab.*

**Students:**

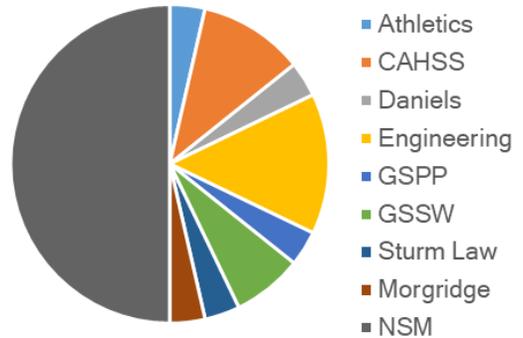
- 3 postdocs
- 24 graduate students
- >30 undergraduate students
- 12 graduate students supported by KIHA

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## DU Faculty and Departments Engaged in KIHA Projects

KIHA faculty have collaborated with 28 other DU faculty, located in 13 different departments and 9 different colleges. These interdisciplinary collaborations have resulted in close to **50 publications** by KIHA faculty, KIHA members and collaborators since the inception in 2016. One of the major objectives of KIHA was to unite colleges and research programs at DU. **We currently have active collaborations with nine colleges at DU.**

## Collaboration with DU colleges

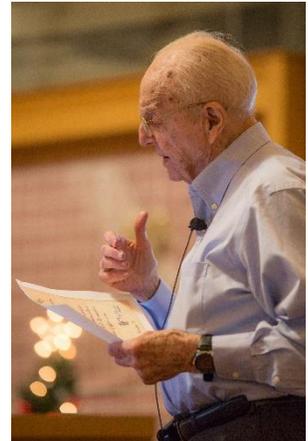


*"The future is too complex to be a doctor of everything. To make progress on a challenge as complex as aging, you need the support of every facet of STEM and the social sciences. Working in KIHA has shown me the importance of collaborating across fields and the power those partnerships have to make a real impact".*  
**Jordan A. Smith, B.S. in Electrical Engineering with a Concentration in Mechatronic Systems**

# COMMUNITY ENGAGEMENT

KIHA staff and faculty have held more than 200 events since moving into the new building. These include research seminars and workshops, community education sessions and fundraising events. **More than 55 different outside organizations** have engaged directly with KIHA faculty, staff and students during the last 3 years.

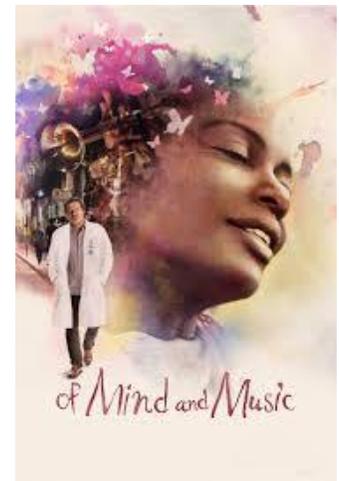
**Dr. William Koch**, 98-year old retired physicist, talked about his work with the Manhattan project in the 1940s. His presentation was so powerful and appreciated that he had to give his seminar twice.



**A record Croquet game** included one 2-year old and one 103-year old in the summer of 2018. KIHA co-organized this event with James Creasy of the Jiminy Wicket company.

KIHA and Mr. Creasy have submitted a SBIR application to measure beneficial effects of social engagement on memory in older adults.

**Dr. Nicolas Bazan**, LSU, showed his movie "Of Mind and Music" and discussed the effects of music on memory with Dr. Leah Weinberg, Lamont School of Music. Dr. Bazan (MD/PhD), is a true renaissance man - research scientist, teacher, mentor, community leader, author, screenplay co-writer/executive movie producer, patron of the arts, and entrepreneur. He is the Director of the Neuroscience Center of Excellence at the School of Medicine, Louisiana State University Health New Orleans and has an ongoing collaboration with Dr. Granholm.



Along with monthly scientific chalk talks and seminars, KIHA hosts a weekly Tai Chi class for the community, a mindfulness class and many education seminars. Via these community events, we have been able to connect with so many organizations. **We are thankful to the Yale Family Foundation**, through which we are able to host remarkable scientists from across the world.

## CoCARE

The Colorado Coalition for Aging Research and Education (CoCARE) was implemented in the fall of 2017. CoCARE consists of 7 Universities in Colorado (5 state Universities and 2 private). **CoCARE members:** University of Denver, Regis University, CU Anschutz, CU Boulder, UCCS, CSU, Metro State University. An immediate benefit will be increased collaboration between



# HOW CAN YOU HELP?

KIHA investigators are very successful in terms of grant funding and foundation grants. However, every organization needs help to raise funding for new projects and to support students, recruitment of new faculty, and acquiring novel technology that can propel success in a new area of research. There is also naming opportunities for endowed positions and for individual programs.

KIHA needs your help in the following areas:

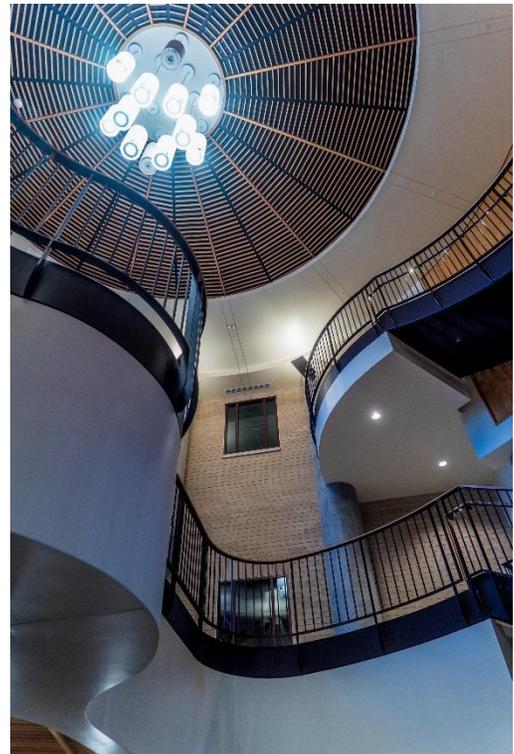
- ❖ Graduate student stipends
- ❖ Recruitment and retainment of faculty
- ❖ Equipment investments
- ❖ Support of educational programs

For more information, please contact:

Valerie Appelbaum

[valerie.appelbaum@du.edu](mailto:valerie.appelbaum@du.edu)

303-871-4056



KNOEBEL INSTITUTE  
FOR HEALTHY AGING

“The Knoebel Institute for Healthy Aging is of great importance for the Osher Lifelong Learning Organization (OLLI) in Denver. The information on aging research and the ability to connect to leading edge information allows OLLI members to plan for their own healthy aging”  
Barbe Ratcliffe Director, OLLI Denver

