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ORIGINAL ARTICLE

University of Washington Nathan Shock Center: innovation to advance aging research

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Abstract The University of Washington Nathan Shock Center of Excellence in the Basic Biology of Aging provides leadership and resources to support the geroscience community locally, nationally, and internationally. Services are provided through our Resource Cores and funds are available annually to support pilot projects by external investigators. Aging-related studies involving proteomics, metabolomics, invertebrate model organisms, and bioinformatics/artificial intelligence are supported by our Cores. The UW Nathan Shock Center also serves as the administrative home for a Geropathology Research Resource. In addition, the Center works in conjunction with the University of Washington Healthy Aging and Longevity Research Institute to organize and support an annual Seminar Series in the Biology of Aging, an annual 1-day Geroscience Symposium, didactic training for the Biological

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Mechanisms of Healthy Aging Training Program, and other strategic initiatives. Our Center also supports the American Aging Association Annual Meeting, and we have recently partnered with the American Aging Association and the JAX Aging Center to create a set of video lectures on select topics in geroscience as part of the AGE Presents Video Lecture Series.

Keywords Aging · Systems biology · Yeast · Worms · Machine learning · Mass spectrometry · National Institute on Aging

Introduction

The University of Washington Nathan Shock Center of Excellence in the Basic Biology of Aging (UW-NSC) has served the local, national, and international aging research community for more than two decades. Since its inception in 1995, the Center has focused on expanding access to new technologies and research areas, with a primary emphasis on supporting junior investigators or established investigators new to aging research. Early efforts focused on creating world-class programs for production of transgenic rodents and for analysis of genome-wide mRNA expression levels dedicated for aging-related studies. As these technologies became more widely available, the Center shifted its efforts toward developing new technologies and providing services for proteomic and metabolomic studies of aging along with building the bioinformatic expertise needed to rigorously analyze high-dimensional data sets.

The UW-NSC currently consists of six cores. The Program Enrichment and Administrative Core provides overall leadership, identifies and acts on strategic opportunities to positively impact the field, and coordinates all center activities. The Research and Development Core oversees the solicitation, review, and administration of Pilot Project Awards. The four Resource Cores work interactively to support the geroscience community and enhance aging research in the areas of metabolomics, proteomics, invertebrate model organisms, and artificial intelligence and bioinformatics. In addition to providing access to cutting-edge methodologies in aging research that are not widely available elsewhere, each of our Resource Cores has active technology development programs, often overlapping between two or more Cores. Creating and exporting these new tools to the scientific community allows the UW-NSC to have an outsized impact that benefits the research of investigators around the world.

Research cores

Program enrichment and administrative core

Core leaders: Matt Kaeberlein (kaeber@uw.edu) and Peter Rabinovitch (petersr@uw.edu).

The UW-NSC Program Enrichment and Administrative Core provides effective leadership for all aspects of Center function. The Core Directors consult regularly with the Center Executive Committee to ensure that Center goals are being achieved. In addition to providing overall Center leadership and strategic planning, the Core has supported strategic initiatives to advance the field of aging research.

One such initiative is the Geropathology Research Resource (GRR), which is led by Dr. Warren Ladiges. Geropathology is the study of aging and age-related diseases in the form of whole necropsies/autopsies, surgical biopsies, histology, and molecular biomarkers and has become recognized as a critical component of studies examining health during aging [1]. The GRR has held a series of Center-sponsored virtual workshops and will be participating in the 2021 American Aging Association annual meeting with a session devoted to geropathology.

The Core has also supported outreach and education by co-organizing a virtual 1-day Geroscience Symposium held on October 23, 2020, which was made freely available to the public and attended by more than 300 participants from 13 countries. The Center worked in conjunction with the Healthy Aging and Longevity Research Institute on this objective. The symposium was divided into three sessions: (I) organ aging and growth signaling, (II) neurodegeneration and metabolism, and (III) innovative approaches in geroscience and aging research. Nine speakers affiliated with the University of Washington and three invited guest speakers, predominantly trainees and junior faculty, presented their research. Proceedings

from this symposium were collected into a series of articles published in *GeroScience* [2].

The Core has also supported the production of a series of didactic video lectures on foundational topics in aging research. The UW-NSC collaborated with the JAX Aging Center and the American Aging Association to commission a total of 10 lectures that were recorded by Zoom between Jan 1 and March 31, 2021. These lectures will be lightly edited and provided on the AGE YouTube channel under the AGE Presents brand.

Research and development

Core leaders: Peter Rabinovitch (petersr@uw.edu) and Jessica Young (jeyoung@uw.edu).

The Research and Development Core facilitates the use of UW-NSC Cores by investigators worldwide in order to obtain data that will aid in new aging-relevant projects and career development. This is accomplished by granting competitive awards for pilot projects in the basic biology of aging. Support involves access to key resources provided by our Resource Cores. All pilot project recipients are required to consult with the UW-NSC Biostatistician, Dr. Lu Wang (Artificial Intelligence and Biostatistics Core), prior to initiation of Core services in order to ensure rigorous and efficient experimental design. The great majority of awards are made to investigators from institutions outside of the UW, with a strong preference for junior investigators or investigators who are new to aging research.

Protein phenotypes of aging

Core leaders: Mike MacCoss (maccoss@uw.edu) and Judit Villén (jvillen@uw.edu).

The Protein Phenotypes of Aging Core is designed to provide support to the aging research community by providing access to state-of-the-art proteomics technologies. The UW-NSC has been at the forefront of developing technologies to perform large-scale targeted proteomics assays that generate near complete data matrices, accurate quantitation, and high reproducibility—even across multiple laboratories. A new emphasis for this Core is the application of quantitative proteomic technologies aimed at identifying protein post-translational modifications regulated during aging, particularly changes to the phosphoproteome [3]. The primary goal of the Core is to apply these methods to studies of aging, to obtain accurate quantitative measurements of peptides from samples provided by its users, and to aid geroscience researchers in linking these high-dimensional data to biologically meaningful outcomes. In addition, the Core will continue to develop and apply new proteomic assays especially suited to aging. The Core works closely with, and shares some facilities with, the Metabolite Phenotypes of Aging Core, to apply common technological and software solutions to both proteomic and metabolomic studies. The Core also collaborates with the Artificial Intelligence and Bioinformatics Core in applying multi-omic data analysis approaches to aging for Center users whose projects include multiple types of big data.

Metabolite phenotypes of aging

Core leader: Daniel Promislow (promislo@uw.edu).

The Metabolite Phenotypes of Aging Core develops and implements state-of-the-art experimental and statistical methods to provide targeted and global metabolite phenotyping to the geroscience community. The Core performs metabolomic "discovery" assays to identify novel pathways and discover potential biomarkers of aging and has developed a low-cost profile for researchers interested in very large-scale studies with hundreds to thousands of samples. The Core has also developed a small targeted pathway focused on NAD-related metabolites and a steroid panel to facilitate studies of sex differences in aging.

The Metabolite Phenotypes of Aging Core works closely with the Protein Phenotypes of Aging Core on method development in three realms, including novel Data Independent Acquisition (DIA) metabolomics, enhancing the Skyline/Chorus suite of tools [4] for metabolomics data, and developing a standalone statistical package to facilitate integrated proteomic-metabolomic multi-omic network analysis. The DIA method will enable the Core to incorporate new analytes into previous data sets without having to run all the previous samples. The Skyline/Chorus tools will provide powerful resources for data sharing and collaboration.

The Metabolite Phenotypes of Aging Core also works closely with the Artificial Intelligence and Bioinformatics Core to provide comprehensive statistical support, from experimental design to data analysis to manuscript preparation. The reports generated are rigorous, elegant, and easy to read and interpret, and have formed an integral part of manuscripts and grants developed using UW-NSC metabolomic data. The Core continues to develop novel statistical tools, including network models and metabolomic clock models that will be made available to Core users.

Invertebrate longevity and healthspan core

Core leaders: Matt Kaeberlein (kaeber@uw.edu), Maitreya Dunham (maitreya@uw.edu), and Alex Mendenhall (alexworm@uw.edu).

The Invertebrate Longevity and Healthspan Core assists investigators in quantifying a variety of longevity and healthspan measures in two of the major invertebrate model organisms: the budding yeast *Saccharomyces cerevisiae* and the nematode *Caenorhabditis elegans*. This is accomplished through direct collaboration, training and outreach, and the development and dissemination of new tools and technologies. Services provided include consultation on experimental design and appropriate genetic backgrounds for aging/healthspan studies, construction of new transgenic strains or reporters, lifespan analysis in both yeast and nematodes, and a panel of health metrics in both organisms. The data generated by this Core can often be correlated with high dimensional protein and metabolite phenotypes studied in the other UW-NSC Cores.

A major focus of this Core has been, and continues to be, the development of new technologies of broad utility for the aging research community. We have previously developed and disseminated powerful microfluidic systems for analysis of lifespan and detailed cell-biological changes with age in yeast [5, 6], a toolbox of fluorescent reporters for use in nematodes [7], and a robotic system for high-throughput nematode lifespan analysis (the WormBot) [8]. Current technologies in development include an improved chemostat-based system for purification of large populations of aged yeast mother cells and, in collaboration with the Artificial Intelligence and Bioinformatics Core, a neural network algorithm for detecting individual nematodes and quantifying their lifespan and health metrics in conjunction with the WormBot system.

Artificial intelligence and bioinformatics core

Core leader: Su-In Lee (suinlee@cs.washington.edu).

The Artificial Intelligence and Bioinformatics Core offers integrated statistical and bioinformatics consulting for all Center-supported projects from experimental design through to publication. This ensures that our Center resources have the greatest opportunity to support high-impact studies in aging research and also meets an important goal of enhancing rigor and reproducibility in biomedical research. The Core also brings state-of-the-art computational approaches, particularly in the area of AI, to support Center users and maximize the impact of the other Resource Cores.

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