Published in final edited form as:

Ann N Y Acad Sci. 2009 July ; 1170: 680–681. doi:10.1111/j.1749-6632.2009.04491.x.

Symposium on the Chemical Senses and Longevity: Introduction and Overview

Claire Murphy, Ph.D. [Professor]

San Diego State University/University of California, San Diego Joint Doctoral Program, 6363
Alvarado Ct., Suite 101, San Diego, CA 92120-4913, cmurphy@sciences.sdsu.edu

Abstract

Dietary restriction is one manipulation that delays aging in every species in which it has been applied, including man. The mechanisms are not yet known. This symposium was designed to bring to ISOT 2008 leading scientists in the field of molecular mechanisms of aging/longevity to stimulate interest in novel research that may bridge the burgeoning interface between chemical senses and longevity. Speakers presented provocative research into the mechanisms underlying longevity that suggest that life span is regulated by both gene modification and environmental cues and that chemosensory perception of food-related environmental cues can modulate lifespan.

Keywords

chemosensory aging; longevity; olfactory impairment; gustatory; taste; smell; olfactory; odor; aging; *C. elegans*

Cynthia Kenyon discovered more than 10 years ago that a single change in the DAF2 (delay accelerating factor) gene, which codes a receptor similar to the human receptors for the hormones insulin and IGF-1, doubled the lifespan in *C. elegans*.¹ Dr. Kenyon discussed her findings that the regulation of lifespan in *C. elegans* is regulated by gustatory and olfactory input,² and then presented recent findings on modulation of longevity by thermosensory neurons. She and her colleagues have demonstrated that certain gustatory neurons inhibit longevity, whereas others promote longevity, most likely by influencing insulin/IGF-1 signaling. Dr. Kenyon has reported that in *C. elegans*, olfactory neurons also influence life span, and they act in a distinct pathway that involves the reproductive system. In addition, she finds that a putative chemosensory G protein-coupled receptor that is expressed in some of these sensory neurons inhibits longevity. Together her findings imply that the life span of *C. elegans* is regulated by environmental cues and that these cues are perceived and integrated in a complex and sophisticated fashion by specific chemosensory neurons.

Gert Jansen and his colleagues have identified multiple G proteins that extend lifespan, as well as a mutant that reduces life span, in *C. elegans*. His analyses have demonstrated that a number of G proteins, including *odr-3*, *gpa-1*, *gpa-11*, *gpc-1* and *pcrg-1* play a role in gustatory plasticity, which involves desensitization of gustatory neurons and sensitization of

Chair: Linda Buck

Organizers: Wen G. Chen and Claire Murphy

nociceptive neurons. In his manuscript, he discusses his proposal that the regulation of lifespan depends not only on chemosensory detection but also on the sensitivity of the sensory neurons.³ Anne Brunet and her colleagues have focused on FoxO transcription factors in studying changes in gene expression that extend lifespan. She has demonstrated that in addition to regulation by the protein kinase Akt in response to insulin/growth factor signaling, FoxO transcription factors are also regulated in response to nutrition deprivation by the AMP-dependent protein kinase (AMPK) pathway. Decreased energy or glucose levels and decreased leptin levels, as well as exercise, activate the energy sensing AMPK. Based on her findings, she proposes a model for the mechanism whereby dietary restriction activates target genes that facilitate resistance to cumulative damage by oxidative stress and thus, life extension.⁴ Scott Pletcher has demonstrated the expression of genes involved in resistance to stress and changes in dietary restriction in *Drosophila*, which suggest modulation of the effects of dietary restriction on longevity by olfaction.⁵ He presented research that established the very interesting finding that anosmia can increase the lifespan of *Drosophila* and simply smelling food can somewhat reverse lifespan extension by dietary restriction. His results suggest that small subsets of sensory neurons can have dramatic effects on lifespan.

An important aim of aging research is drug discovery that would not only prolong life but extend vitality. Linda Buck discussed her highly significant recent work using a high throughput screen for chemicals that delay aging.⁶ She and her colleagues have identified a drug, used as an antidepressant in humans, that increases lifespan in *C. elegans*, likely through a food perception pathway responsive to dietary restriction.

Thus, this symposium addressed the following aims: 1) To bring together scientists at the forefront of research on longevity and the chemical senses, 2) To stimulate investigation into the mechanisms that underlie longevity and the dramatic changes attributable to olfactory and gustatory input, 3) To facilitate the application of state of the art innovative technology, particularly genetic, molecular and cellular biological techniques, to research on longevity and the chemical senses, and 4) To identify directions for future research in chemosensory science. To these ends, the speakers introduced novel approaches and hypotheses that have the potential to stimulate research into the mechanisms of longevity and stimulate further chemosensory research that has the potential to identify treatments that delay aging and age-related diseases. The significance of this research is potentially profound.

Acknowledgments

Supported by Conference Grant #1U13AG032223 from the National Institute on Aging to Claire Murphy with NIA Program Support.

References

1. Kenyon C, et al. A *C. elegans* mutant that lives twice as long as wild type. *Nature*. 1993; 355:461–464. [PubMed: 8247153]
2. Alcedo J, Kenyon C. Regulation of *C. elegans* longevity by specific gustatory and olfactory neurons. *Neuron*. 2004; 41(1):45–55. [PubMed: 14715134]
3. Hannes L, Dekkers M, Hukema R, Bialas N, Leroux M, Jansen G. Signaling proteins that regulate NaCl chemotaxis responses modulate longevity in *C. elegans*, NYAS. in press (this volume).

4. Greer E, Banko M, Brunet A. AMP-activated protein kinase and FoxO transcription factors in dietary restriction induced longevity, NYAS. in press (this volume).
5. Pletcher S. The modulation of lifespan by perceptual systems, NYAS. in press (this volume).
6. Petrascheck M, Ye X, Buck L. A high throughput screen for chemicals that increase the lifespan of *Caenorhabditis elegans*, NYAS. in press (this volume).