Review article

The American Aging Association honors Huber R. Warner, PhD., Retiring Associate Director, National Institute on Aging

George M. Martin

Alzheimer's Disease Research Center, University of Washington, Seattle, WA 98195, USA

Author for correspondence (e-mail: gmmartin@u.washington.edu)

Received 1 July 2005; accepted in revised form 1 August 2005

Key words: aging, antioxidant, apoptosis, NIA, Hutchinson–Gilford syndrome, mitochondrial dysfunction, phospholipids, replicative senescence

Abstract

On behalf of American Aging Association and his many biogerontological colleagues, the author thanks Huber R. Warner for his 21 years of exemplary service at the National Institute on Aging (NIA). In so honoring Dr. Warner, we also honor his many associates at that “user friendly” branch of the National Institutes of Health. Some highlights of Dr. Warner’s scientific training, academic career and special contributions while serving in a leadership position at the NIA are reviewed. We wish him well as he returns to the University of Minnesota, this time as Associate Dean of Research in the College of Arts and Sciences.

Andy Bartke, President of the American Aging Association, phoned me to ask if I could introduce Huber Warner at the 2005 annual meeting of the society, in Oakland, California. Huber was about to retire from government service and had accepted a position as Associate Dean of Research in the College of Arts and Sciences at the University of Minnesota. He was to be honored at the meeting for his 20+ years of service at the National Institute on Aging. My immediate response was, “I would go to China to introduce Huber!” (Alas, had I been born a comedian, I would have said “I would even go to Auckland, New Zealand!”)

I have known and admired Huber during all of his 20+ years at the NIA. When he signed on, the news of the recruitment of a nucleic acid biochemist was greeted with considerable enthusiasm by my biogerontological colleagues. We got much more than a well trained biochemist, however: we got a colleague with marvelous human qualities. He was and still is a gentle, modest, thoughtful and dedicated administrator. A good listener, he was always open to various points of view and cautious and constructive with any

criticisms. Friends who have had considerable experience with different branches of the National Institutes of Health have often commented that the NIA staff has been by far the best in terms of their dedication to their field and their hard work on behalf of applicants, whether they have been successful or unsuccessful with their proposals. In honoring Huber, we therefore honor his entire staff and the NIA as a whole.

Huber did his undergraduate work at Ohio Wesleyan (BA) and MIT (BS in Chemical Engineering). His PhD (U. Michigan) was in the difficult field of lipid biochemistry. He became an expert on plasmalogens, a class of phospholipids. How interesting that recent work has suggested that an antioxidant scavenging function may be among the properties of these compounds (Brites et al. 2004)! Returning to MIT as a postdoctoral fellow, he pursued training in molecular virology and nucleic acid biochemistry. He stuck with these themes during his long academic career at Minnesota. Among his particularly influential papers was a PNAS publication he first-authored on the role of apurinic endonuclease in the repair of

pyrimidine dimers and other DNA lesions (Warner et al. 1980), something quite relevant to his subsequent career in biogerontology. To 'escape' the cold climate of Minnesota, he took two sabbaticals in the even colder climate of Sweden, in the labs of A. Holmgren and P. Reichard at the famed Karolinska Institute. He also worked with Stuart Linn at UC-Berkeley.

With his move to the NIA [date], Huber became a catalyst in the promotion of several major new initiatives, all of which are of great relevance today: replicative senescence, apoptosis, oxidative stress, mitochondrial dysfunction, longevity assurance genes, an intervention testing program employing four-way crosses of inbred mice, as well as studies of various models of putative accelerated or premature segmental aging. The latter is the most recent, so I will say a few words about that program.

Although the study of gene actions that appear to accelerate features of aging and shorten life span have been controversial, Huber and his colleague, Filipe Sierra, have been quite articulate in pointing out the advantages – as well as the disadvantages – of these approaches (Warner and Sierra 2003). To his credit, Huber was the only administrator at the NIH who provided encouragement to Leslie Gordon in her pioneering effort to gather together groups of scientists with the requisite skills to identify the genetic defect in one of the most striking of these progeroid disorders, Hutchinson–Gilford syndrome (also known as 'Progeria of Childhood'). He was motivated not only by the challenge of the basic science, but also by his compassion for the fate of the unfortunate children with this fatal disorder. I was at that first workshop, along with Francis Collins, whose group soon was able to demonstrate that the disease was caused by a dominant negative mutation at a locus coding for lamin A/C, which lines the inner nuclear membranes of our cells (Eriksson et al. 2003).

This area of research is now beginning to be integrated with several of Huber's other initiatives, notably his long-standing interest in apoptosis (Warner 1997; Warner and Sierra 2003) and very recent work on mitochondrial dysfunction and apoptosis (Kujoth et al. 2005). As Huber suggests in his review in this issue of AGE, recent findings now seem to point to the importance of research on stem cell biology for elucidating fundamental processes of aging. There are likely to be a number of pathways

leading to the death of cells during aging, including oxidative stress. In mammals, the eventual decline in the ability of stem cells and their progeny to maintain cellular and functional homeostasis may be key components of aging, perhaps including, paradoxically, the many dysfunctional hyperplasias that could be steps towards such major disorders as cancer, atherosclerosis and osteoarthritis (Martin 1979). A failure of appropriate rates of apoptosis could also contribute to the loss of proliferative homeostasis. This would be consistent with the very attractive ideas and experiments from the Campisi lab, as briefly discussed in Huber's review (Campisi 2005).

Huber will have many responsibilities in his new role as a Dean. Among these, I am sure, will be efforts to enhance the contributions of his Minnesota colleagues to our understanding of the biology and pathobiology of aging. Coincidentally, his new institution is the home of one of the world's leading centers for research on stem cell biology (Lakshmipathy and Verfaillie 2005).

References

- Brites P, Waterham HR and Wanders RJ (2004) Functions and biosynthesis of plasmalogens in health and disease. *Biochim Biophys Acta* 1636: 219–231
- Campisi J (2005) Senescent cells, tumor suppression, and organismal aging: good citizens, bad neighbors. *Cell* 120: 513–522
- Eriksson M, Brown WT, Gordon LB, Glynn MW, Singer J and Scott L et al. (2003) Recurrent de novo point mutations in lamin A cause Hutchinson–Gilford progeria syndrome. *Nature* 423: 293–298
- Kujoth GC, Hiona A, Pugh TD, Someya S, Panzer K and Wohlgemuth SE et al. (2005) Mitochondrial DNA mutations, oxidative stress, and apoptosis in mammalian aging. *Science* 309: 481–484
- Lakshmipathy U and Verfaillie C (2005) Stem cell plasticity. *Blood Rev* 19: 29–38
- Martin GM (1979) Proliferative homeostasis and its age-related aberrations. *Mech Ageing Dev* 9: 385–391
- Warner HR (1997) Aging and regulation of apoptosis. *Curr Top Cell Regul* 35: 107–121
- Warner HR and Sierra F (2003) Models of accelerated ageing can be informative about the molecular mechanisms of ageing and/or age-related pathology. *Mech Ageing Dev* 124: 581–587
- Warner HR, Demple BF, Deutsch WA, Kane CM and Linn S (1980) Apurinic/apyrimidinic endonucleases in repair of pyrimidine dimers and other lesions in DNA. *Proc Natl Acad Sci USA* 77: 4602–4606