GeroScience (2017) 39:241–244
DOI 10.1007/s11357-017-9969-7

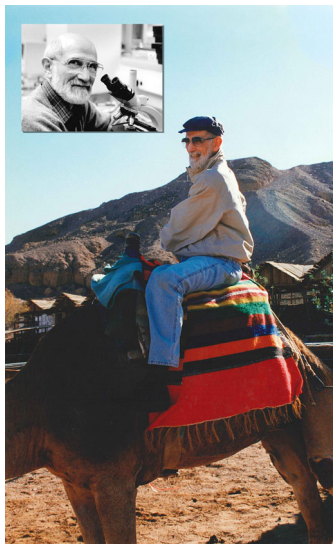
OBITUARY

Norman S. Wolf, D.V.M., Ph.D., 1927–2017: experimental pathologist and geroscientist

George M. Martin

Published online: 5 April 2017

Keywords Obituary · Norman S. Wolf · University of Washington · AAA Presidents · Hematopoiesis · Ocular cataracts · SIRT1 · Comparative gerontology



This marvelous photo of Norman Wolf riding a camel was provided by Susan Herring. It was taken during a break at a 1999 meeting Norm was attending in Eilat, Israel. It provides more evidence of Norm's love of large animals! The inserted photo was taken during the latter part of his career in the Department of Pathology of the University of Washington. Norm's love of large animals was also manifested during his service in the US Army near the end of WW2, when he volunteered to care for a herd of elephants while stationed in Hawaii!

G. M. Martin (✉)
Departments of Pathology and Genome Sciences, University of Washington, Seattle, WA 98195, USA
e-mail: gmmartin@uw.edu

Norm Wolf, the 2003–2004 President of our American Aging Association, passed away in Seattle, Washington on January 24, 2017, some 6 months shy of his 90th birthday. The cause was congestive heart failure, the result of a mitral prolapse of undetermined etiology suffered some 40 years ago but which did not dampen his enthusiasm for his research and teaching career, his cheerful demeanor, and his devotion to his beloved wife, Professor Susan Herring (https://dental.washington.edu/people/susan-herring), and to his devoted son Jeremy, both of whom were with him at the end of his life.

Norm was born in Kansas City, the son of a stockyard owner, from whom he got his love of large animals. This led to a D.V.M. from Kansas State University, where he was the valedictorian of his class. During a clerkship at a pig ranch in Iowa, however, he contracted Brucellosis, which led him to a career shift via a Ph.D. at Northwestern University, where he worked with Edwin T. Nishimura in the Department of Pathology, from whom he developed interests in cell biology. His mentor's pioneering work on catalase perhaps also set the stage for his much later interest in oxidative damage as a mechanism of aging. After a postdoc at the Pasteur Institute in Paris and a year of research at Oak Ridge, Norm joined the faculty of the Baylor College of Medicine until we recruited him to the Dept. of Pathology at the University of Washington in 1968, where he played key roles both as a teacher and as part of our research group associated with our Nathan Shock Center and our NIA Program Project grant. He also was a member of the faculty of our excellent Department of Comparative Medicine.

Norm loved to travel. His trips abroad included his NSF Fellowship at the Pasteur Institute, a sabbatical year with Peter MacCallum at the Cancer Research Institute in Melbourne, and numerous trips to the Stem Cell Group of the Radiobiological Institute in Rijswick, The Netherlands, as an invited scientist in residence.

Norm's research career can be divided into two major periods. His primary efforts were initially devoted to the study of hematopoiesis in the bone marrow. He was best known for his investigations of the role of the microenvironment on stem cell proliferation. A 1974 paper, the first of a series on "Dissecting the hematopoietic microenvironment," is still referenced in the 2014 edition of Wintrobe's famous textbook on Clinical Hematology. A nice summarization of his pioneering contributions to this field can be found in his single-authored 1999 review (Wolf 1999). How wonderful that he lived long enough to witness the relatively recent explosion of basic aging research in this field, notably the fascinating studies on heterochronic parabiosis conducted in the lab of Tom Rando and his colleagues (Conboy et al. 2005). His interest in hematopoiesis and its reconstitution in response to ionizing irradiation began during his year at the Pasteur Institute and resulted in a paper written in French (Wolf and Duplan 1961). His focus upon changes in the microenvironments of stem cells in old animals date back to at least 1968 (Wolf and Trentin 1968) and was coupled with a growing interest in the biology of aging, e.g., (Pietrzyk et al. 1989). One wonders what Norm would have thought of the current translational research attempting to "fix" stem cell microenvironments via infusions of "young plasma" (Kaiser 2016)! Norm's last publication in this field was carried out with colleagues here at the University of Washington (Papayannopoulou et al. 1995). This highly cited PNAS paper was an early contribution to the molecular dissection of the early stages of the homing of transplanted hematopoietic stem cells. It demonstrated the importance of cytoadhesion molecules for the recognition of transplanted hematopoietic cells by the sinusoidal endothelium of the bone marrow.

The second major focus of Norm's career began shortly after his recruitment to the University of Washington. The group of geroscientists in our Dept. of Pathology was beginning to expand, thanks particularly to the efforts of Peter S. Rabinovitch, who continued the development of my former Program Project grant and who was the PI of the nation's first round of Nathan Shock Centers for Excellence in the Basic Biology of Aging. We were delighted that Norm had chosen to develop a group of investigators with a focus on the pathogenesis of ocular cataracts, an essentially ubiquitous geriatric phenotype that Norm found to be easily studied in rodent models of aging. A particularly active early member of his team was William R. Pendergrass, a biochemist and geroscientist interested in replicative senescence. Before Norm's switch to the study of cataracts, they had worked together to show age-related declines in the replicative potentials of two cell types of the bone marrow microenvironments in mice (Jiang et al. 1992); declines in the replicative potentials of cells within six different tissues of mice overexpressing growth hormone (Pendergrass et al. 1993); and the conservation of replicative capacity with caloric restriction both in vitro (Pendergrass et al. 1995) and in vivo (Wolf et al. 1995).

Some highlights of the research on age-related cataracts include the demonstration, both in vitro and in vivo, that there is a significant decline in the replicative potential of lens epithelial cells with murine aging and that this decline can be delayed by caloric restriction (Li et al. 1997). Caloric restriction also protected lens epithelial cells from oxidative damage induced by H_2O_2 (Li et al. 1998). A very careful study of the controversial effects of fluorescent light exposure upon age-related murine cataracts failed to reveal any significant impacts, including experiments in which the animals were kept without any lighting for most of their lives (Wolf and Penn 2001). Norm and his colleagues demonstrated, in Brown-Norway rats, that telomere attrition was associated with aging and that this decline could be ameliorated by caloric restriction (Pendergrass et al. 2001). In another study, old rat lenses were shown to have lost more than 50% of their lens epithelial cells, organelle debris of which were found in the cortex in association of high levels of reactive oxygen species (Pendergrass et al. 2006). In a study that cries out for a follow-up with recent advances in genomics, a group of nonagenarians with good cognitive function was shown to exhibit a reduction in age-specific rate and lifetime cumulative incidence of age-related cataracts (Zubenko et al. 2007).

Norm's reputation as an expert on the evaluation of age-related cataracts in experimental animals, particularly in mice, quickly spread among geroscience colleagues around the country who realized the importance of his cataract research as a marker of healthspan. He was therefore recruited to systematically evaluate rates of development of cataracts in living mouse colonies around the country. Examples included the evaluation of

the effects of Resveratrol (Pearson et al. 2008) and Metformin (Martin-Montalvo et al. 2013). Both of those publications continue to be highly cited.

Apart from his work on mice, Norm was also interested in comparative geroscience and was an "early adopter" of the dog as a model for aging. Among other studies, he demonstrated that the replicative potential of young adult fibroblasts taken from dogs of different sizes is inversely correlated with body size (Li et al. 1996) and that the histopathology of age-related cataracts are significantly different in mice as compared to other species (Pendergrass et al. 2011). Norm's last trainee, Silvan Urfer, a DVM, was recruited for his research program on breed-specific variations in the rates of development of cataracts in dogs and their associations with body size and lifespan (Urfer et al. 2011). Norm would have been delighted to have known that Silvan is now part of a very exciting translational project on the effects of rapamycin upon multiple health parameters in dogs, a project conceived by my close UW colleagues, Matt Kaeberlein, and Daniel Promislow (https://www.technologyreview.com/s/542591/scientists-hope-to-lengthen-dog-years/).

Norm's personal review of his research interests in aging were expressed in one of a series of publications of interviews with distinguished geroscientists (Wolf 2003).

His many associates and trainees especially remember Norm's passion for teaching. Greg Priestley, his long-serving lab manager, also fondly recalls his wry sense of humor and his passion for social justice, including his interest in universal health care, a passion that Norm and I shared. But when I now think of my friend Norman Wolf, I reach for something he was especially proud of, a copy of a book he edited that he gave me as a gift. The title is "The Comparative Biology of Aging," published in 2010 by Springer and available via Amazon.com (https://www.amazon.com/Comparative-Biology-Aging-Norman Wolf/dp/940079083X/ref=sr_1_1?s=books&ie=UTF8&qid=1488417996&sr=1-1&keywords=the+comparative+biology+of+aging).

Acknowledgments The author is indebted to Susan Herring for graciously answering his many questions about Norm's life experiences. He also extends his thanks to William R. Pendergrass, Silvan Urfer, Greg Priestley, and Thalia Papayannopoulou for their helpful comments.

References

Conboy IM, Conboy MJ, Wagers AJ, Girma ER, Weissman IL, Rando TA (2005) Rejuvenation of aged progenitor cells by exposure to a young systemic environment. Nature 433:760–764

Jiang D, Fei RG, Pendergrass WR, Wolf NS (1992) An age-related reduction in the replicative capacity of two murine hematopoietic stroma cell types. Exp Hematol 20:1216–1222

Kaiser J (2016) Biomedicine antiaging trial using young blood stirs concerns. Science 353:527–528

Li Y, Deeb B, Pendergrass W, Wolf N (1996) Cellular proliferative capacity and life span in small and large dogs. J Gerontol A Biol Sci Med Sci 51:B403–B408

Li Y, Yan Q, Wolf NS (1997) Long-term caloric restriction delays age-related decline in proliferation capacity of murine lens epithelial cells in vitro and in vivo. Invest Ophthalmol Vis Sci 38:100–107

Li Y, Yan Q, Pendergrass WR, Wolf NS (1998) Response of lens epithelial cells to hydrogen peroxide stress and the protective effect of caloric restriction. Exp Cell Res 239:254–263

Martin-Montalvo A, Mercken EM, Mitchell SJ, Palacios HH, Mote PL, Scheibye-Knudsen M, Gomes AP, Ward TM, Minor RK, Blouin MJ et al (2013) Metformin improves healthspan and lifespan in mice. Nat Commun 4:2192

Papayannopoulou T, Craddock C, Nakamoto B, Priestley GV, Wolf NS (1995) The VLA4/VCAM-1 adhesion pathway defines contrasting mechanisms of lodgement of transplanted murine hemopoietic progenitors between bone marrow and spleen. Proc Natl Acad Sci U S A 92:9647–9651

Pearson KJ, Baur JA, Lewis KN, Peshkin L, Price NL, Labinskyy N, Swindell WR, Kamara D, Minor RK, Perez E et al (2008) Resveratrol delays age-related deterioration and mimics transcriptional aspects of dietary restriction without extending life span. Cell Metab 8:157–168

Pendergrass WR, Li Y, Jiang D, Wolf NS (1993) Decrease in cellular replicative potential in "giant" mice transfected with the bovine growth hormone gene correlates to shortened life span. J Cell Physiol 156:96–103

Pendergrass WR, Li Y, Jiang D, Fei RG, Wolf NS (1995) Caloric restriction: conservation of cellular replicative capacity in vitro accompanies life-span extension in mice. Exp Cell Res 217:309–316

Pendergrass WR, Penn PE, Li J, Wolf NS (2001) Age-related telomere shortening occurs in lens epithelium from old rats and is slowed by caloric restriction. Exp Eye Res 73:221–228

Pendergrass WR, Penn PE, Possin DE, Wolf NS (2006) Cellular debris and ROS in age-related cortical cataract are caused by inappropriate involution of the surface epithelial cells into the lens cortex. Mol Vis 12:712–724

Pendergrass W, Zitnik G, Urfer SR, Wolf N (2011) Age-related retention of fiber cell nuclei and nuclear fragments in the lens cortices of multiple species. Mol Vis 17:2672–2684

Pietrzyk ME, Wolf NS, Priestley GV (1989) Cycling patterns of hemopoietic stem cell subpopulations in young and old BDF1 mice. Mech Ageing Dev 49:79–86

Urfer SR, Greer K, Wolf NS (2011) Age-related cataract in dogs: a biomarker for life span and its relation to body size. Age (Dordr) 33:451–460

Wolf NS (1999) The hematopoietic microenvironment: stromal cell types: characterization and function in situ and in vitro. Hematology 4:241–254

Wolf NS (2003) An interview with Norman S. Wolf, D.V.M., Ph. D. by Vicki Glaser. J Anti Aging Med 6:5–9

Wolf NS, Duplan JF (1961) Production by the fetus and localization of cells gifted with restorative activity on irradiated mice. C R Seances Soc Biol Fil 155:1895–1897

Wolf NS, Penn PE (2001) The effect of high and very low fluorescent light exposure levels on age-related cataract in a pigmented mouse strain. Exp Eye Res 73:37–43

Wolf NS, Trentin JJ (1968) Hemopoietic colony studies. V. Effect of hemopoietic organ stroma on differentiation of pluripotent stem cells. J Exp Med 127:205–214

Wolf NS, Penn PE, Jiang D, Fei RG, Pendergrass WR (1995) Caloric restriction: conservation of in vivo cellular replicative capacity accompanies life-span extension in mice. Exp Cell Res 217:317–323

Zubenko GS, Zubenko WN, Maher BS, Wolf NS (2007) Reduced age-related cataracts among elderly persons who reach age 90 with preserved cognition: a biomarker of successful aging? J Gerontol A Biol Sci Med Sci 62:500–506