



## Editorial

Int Neurorol J 2022;26(1):1-2

<https://doi.org/10.5213/inj.2222edi01>

pISSN 2093-4777 · eISSN 2093-6931



# Biomarkers of Aging: The proxy of Time

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Aging is a phenomenon that has gained wide traction in science for as long as the history of academia itself. As a social phenomenon its academic interest waxes and wanes according to the surplus of wealth in society. As physico-chemical phenomenon in that it is a process of endless battle between catabolism and anabolism that inevitably leads toward increased entropy. But despite these grandiose claims, it is essentially a biological phenomenon, in which most organisms experience time and ultimately succumb to deteriorating function, loss of upkeep and finally ceasing maintenance altogether [1,2].

Despite the torpid history of alchemists, the scientific approach to the study of aging has only recently crystallized into a few focused lines of investigation. The study of deteriorating telomeres, its upkeep and senescence, the study of accumulating epigenetic changes, blunting of hormonal signals, to say nothing of the probabilistic accumulation of comorbidities that eventually fell even the heartiest of mortals. Among such lines of study, one of the earliest avenues of research had been that of the reactive oxygen species and the reactive electrophile species (RES) [3].

As residents of a toxic planet where organisms are constantly bombarded by ultraviolet radiation and subjected to one of the most caustic of elements, oxygen, organisms have evolved to deal with such environments. Even simple organism such as bacteria have evolved to employ hydrogen peroxide as a defense against oxidative stress [4]. Superoxide dismutases, peroxidases and catalases form the basic background that is preserved even to higher organisms. More complex organisms have developed accordingly, as the necessity to prevent against damage to more sensitive genetic data increases, the organism develops defenses

against alternative sources of oxidative stress, such as deterioration of fatty acids.

Among many lipid oxidation reactions a major RES is formed; malondialdehyde (MDA) is a major small aldehyde that is produced in lipid oxidation reactions [5,6].

While at first glance, biomarkers, such as MDA, may seem like an accumulation of some waste product, the measurement of refuse filling up in a landfill. This comes from a distinct underestimation of the importance of energy efficiency in the biological entity, for frugality of biology dictates that waste product is a messenger in itself. MDA has been shown to regulate glucose metabolism, and affect mental states, as well as its marked position as an indicator of oxidative and/or post ischemic stress [6-8]. However, although MDA may be overproduced during stress, careful measurements have shown that MDA may decrease in some pathologic conditions. Furthermore, much study regarding MDA is based on nonspecific assays, and even when specific assays are used sometimes there is no obvious correlation between MDA and stress [9,10]. As such, reports specifying high-quality MDA specific assays with accordingly designed controls should only be considered when regarding the correlation between stress and MDA, to say nothing of extrapolating towards a vague concept such as aging.

In the current issue of the *International Neurourology Journal*, Khosla et al. present a systemic review of aging. While this encompasses not only MDA, but goes on to list more basic anti-oxidative mechanisms, it shows the budding interest and wide scope that requires to be attended to. Alternatively, while MDA may be the more popular choice as a biomarker for lipid oxidation stress, 4-hydroxy-2-nonenal (HNE) may be seen as a sup-



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plementary or alternative biomarker [11-13]. Future systematic reviews may wish to focus on a single aspect of the oxidative process than to cast such a wide and vague net such as “aging.”

When investigating aging, one must be reminded that age is the biological representative of time. We are, in effect, looking for a proxy variable that represents the effect in time, and that may range from any wide variety of biochemical or bioinformatic processes. Hence, approaching the subject it is best to be what we do best and remain scientific, specific, and focused.

• **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

## REFERENCES

1. Khosla L, Gong S, Weiss JP, Birder LA. Oxidative stress biomarkers in age-related lower urinary tract disorders: a systematic review. *Int Neurourol J* 2022;26:3-19.
2. Cho ST, Na HR. Urology and geriatrics in Korea: present status and future directions. *Int Neurourol J* 2022;26:20-5.
3. Farmer EE, Davoine C. Reactive electrophile species. *Curr Opin Plant Biol* 2007;10:380-6.
4. Storz G, Tartaglia LA, Farr SB, Ames BN. Bacterial defenses against oxidative stress. *Trends Genet* 1990;6:363-8.
5. Mas-Bargues C, Escrivá C, Dromant M, Borrás C, Viña J. Lipid peroxidation as measured by chromatographic determination of malondialdehyde. Human plasma reference values in health and disease. *Arch Biochem Biophys* 2021;709:108941.
6. Yonny ME, García EM, Lopez A, Arroquy JI, Nazareno MA. Measurement of malondialdehyde as oxidative stress biomarker in goat plasma by HPLC-DAD. *Microchem J* 2016;129:281-5.
7. Liu Z, Cai Y, Zhang X, Zhu Z, He J. High serum levels of malondialdehyde and antioxidant enzymes are associated with post-stroke anxiety. *Neurol Sci* 2018;39:999-1007.
8. Wang X, Lei XG, Wang J. Malondialdehyde regulates glucose-stimulated insulin secretion in murine islets via TCF7L2-dependent Wnt signaling pathway. *Mol Cell Endocrinol* 2014;382:8-16.
9. Muckenschnabel I, Goodman B, Williamson B, Lyon G, Deighton N. Infection of leaves of *Arabidopsis thaliana* by *Botrytis cinerea*: changes in ascorbic acid, free radicals and lipid peroxidation products. *J Exp Bot* 2002;53:207-14.
10. Weber H, Chételat A, Reymond P, Farmer EE. Selective and powerful stress gene expression in *Arabidopsis* in response to malondialdehyde. *Plant J* 2004;37:877-88.
11. de Jongh R, Haenen GR, van Koeveeringe GA, Dambros M, van Kerrebroeck PE. Lipid peroxidation product 4-hydroxynonenal contributes to bladder smooth muscle damage. *Urology* 2008;71:974-8.
12. Whongsiri P, Pimratana C, Wijitsettakul U, Jindatip D, Sanpavat A, Schulz WA, et al. LINE-1 ORF1 protein is up-regulated by reactive oxygen species and associated with bladder urothelial carcinoma progression. *Cancer Genomics Proteomics* 2018;15:143-51.
13. Orioli M, Aldini G, Benfatto MC, Maffei Facino R, Carini M. HNE-michael adducts to histidine and histidine-containing peptides as biomarkers of lipid-derived carbonyl stress in urines: LC-MS/MS profiling in Zucker obese rats. *Anal Chem* 2007;79:9174-84.