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Hydrogen: A Small Molecule with Great Clinical Significance

Tyler LeBaron

Founder & Executive Director of MHF

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2016 ILADS Annual Conference
Lyme Disease: An Evolving Paradigm from Chronic Illness
Sheraton Philadelphia Downtown Hotel
Philadelphia, PA, November 4 – 6, 2016

Disclosure Statement

I am a *consultant for the manufacturer of* *H_2 Absorb, Researched Nutritionals®*

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http://www.molecularhydrogenfoundation.org

Molecular Hydrogen Foundation is a science-based nonprofit, focused on advancing the research, education, and awareness of hydrogen as a therapeutic medical gas.

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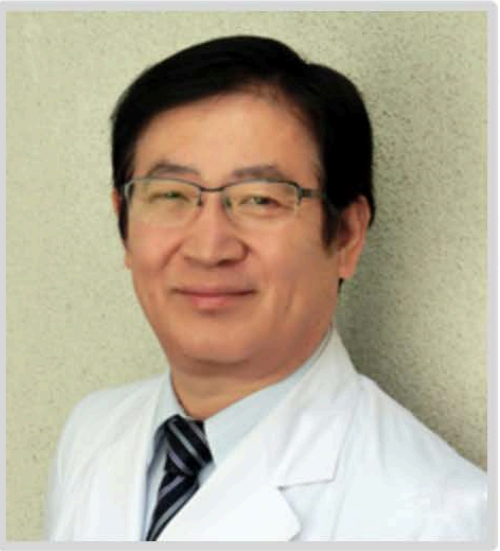
DR. SHIGEO OHTA, PHD., (NIPPON MEDICAL SCHOOL)

SENIOR ADVISOR



"When I was exploring an ideal anti-oxidant that lacks adverse effects, I came across hydrogen. By the first experiment on January 2005, I was amazed at the great protective effects of hydrogen against oxidative stress and decided to devote my life to hydrogen medicine. In 2007, we succeeded in the publication of the first paper in Nature Medicine. This first paper was accepted with a surprise and some doubts, but we overcame them by continuous publications. My mission is to develop not only hydrogen medical sciences, but also hydrogen industry as the pioneer of hydrogen medicine."

Dr. Shigeo Ohta, Nippon Medical School, Graduate School of Medicine.

Oxidation: aging and disease

- Damage DNA, RNA, cell membranes, proteins
- Cause cell death and aging
- Linked to every disease:
  - Inflammation
  - Cardiovascular
  - Cancer
  - neurological

Knight, J. A. Ann. Clin. Lab. Sci 28.6 (1998): 331.

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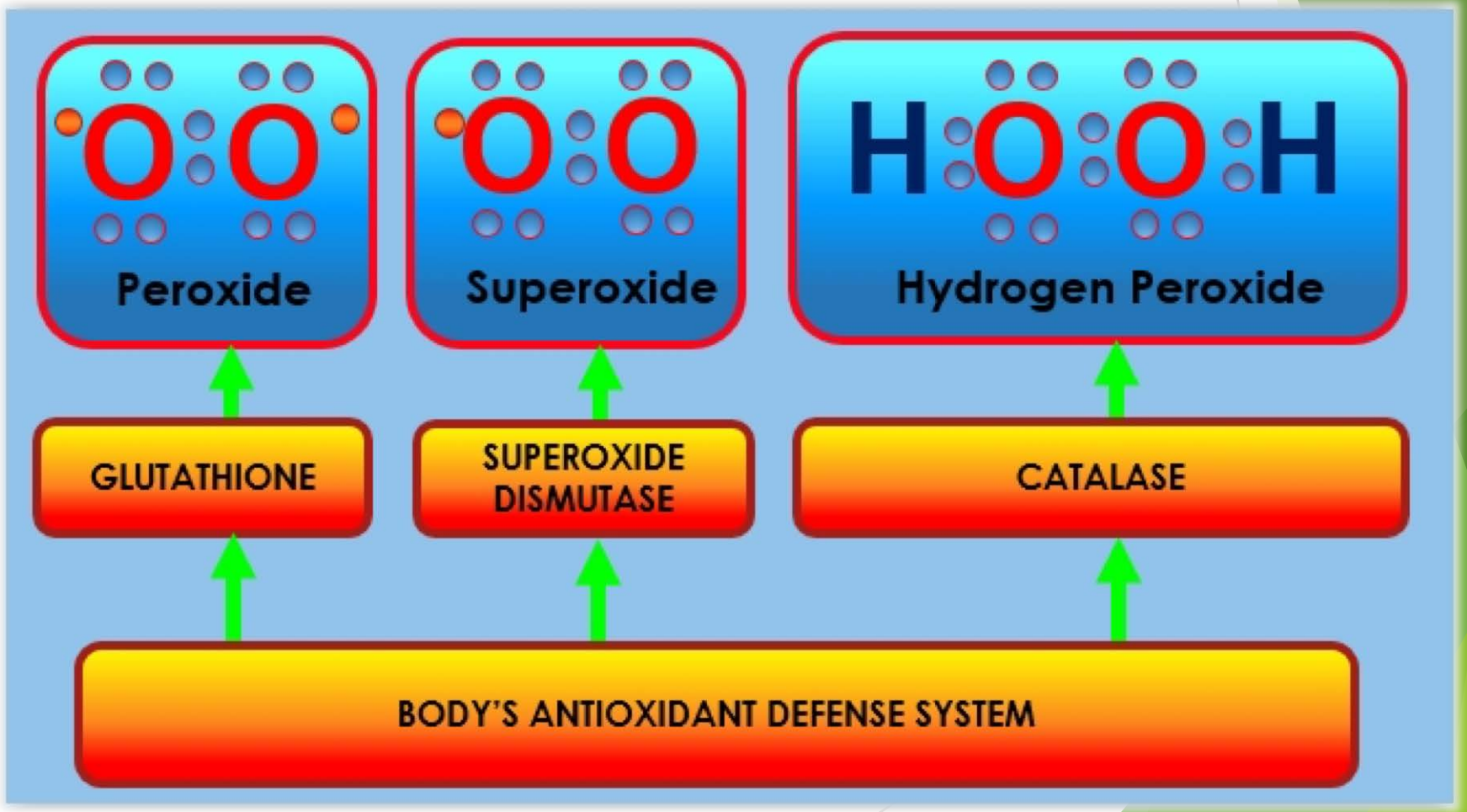
The body has its own endogenous antioxidant self-defense system (e.g. SOD, GSH, CAT) that regulates and controls redox homeostasis



Sen, Saikat, et al. Int J Pharm Sci Rev Res. 3.1 (2010): 91-100.

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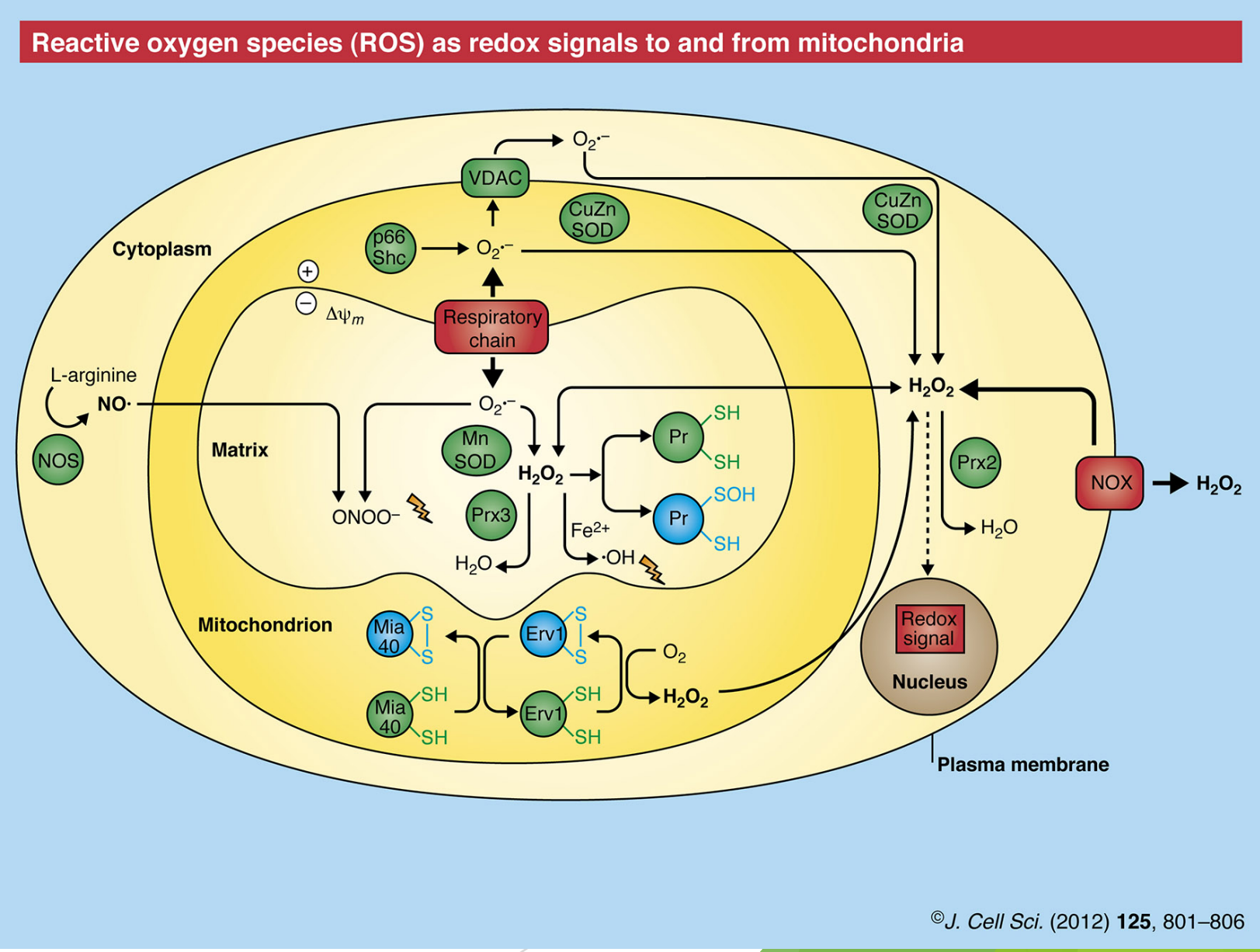
Benefits of ROS (Free Radicals)

- Signal transduction
- Immunity
- Vasodilation
- Activation of transcription factors



Y. Collins, et al. *J Cell Sci.* 125.4 (2012): 801-806

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Perhaps this is why clinical trials with supplemental antioxidants often have deleterious effects

Current Opinion in
Clinical Nutrition and Metabolic Care

Antioxidant supplements and mortality

Bjelakovic, Goran[a]; Nikolova, Dimitrinka[a]; Gluud, Christian[a,b]

SUMMARY: ANTIOXIDANT SUPPLEMENTS DO NOT POSSESS PREVENTIVE EFFECTS AND MAY BE HARMFUL, WITH UNWANTED CONSEQUENCES TO OUR HEALTH…

Summary: Antioxidant supplements do not possess preventive effects and may be harmful with unwanted consequences to our health, especially in well-nourished populations. The optimal source of antioxidants seems to come from our diet, not from antioxidant supplements in pills or tablets.

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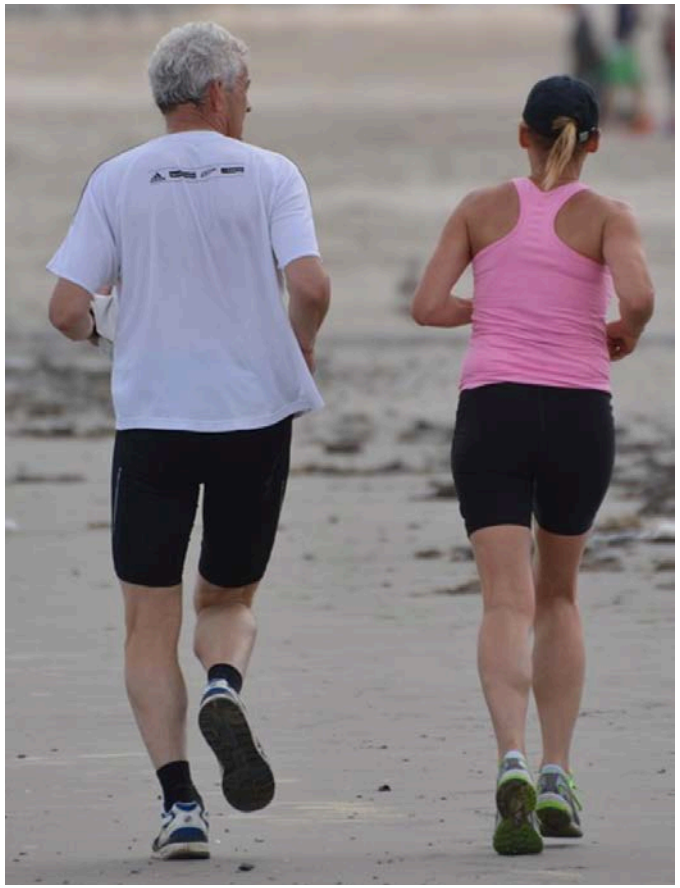
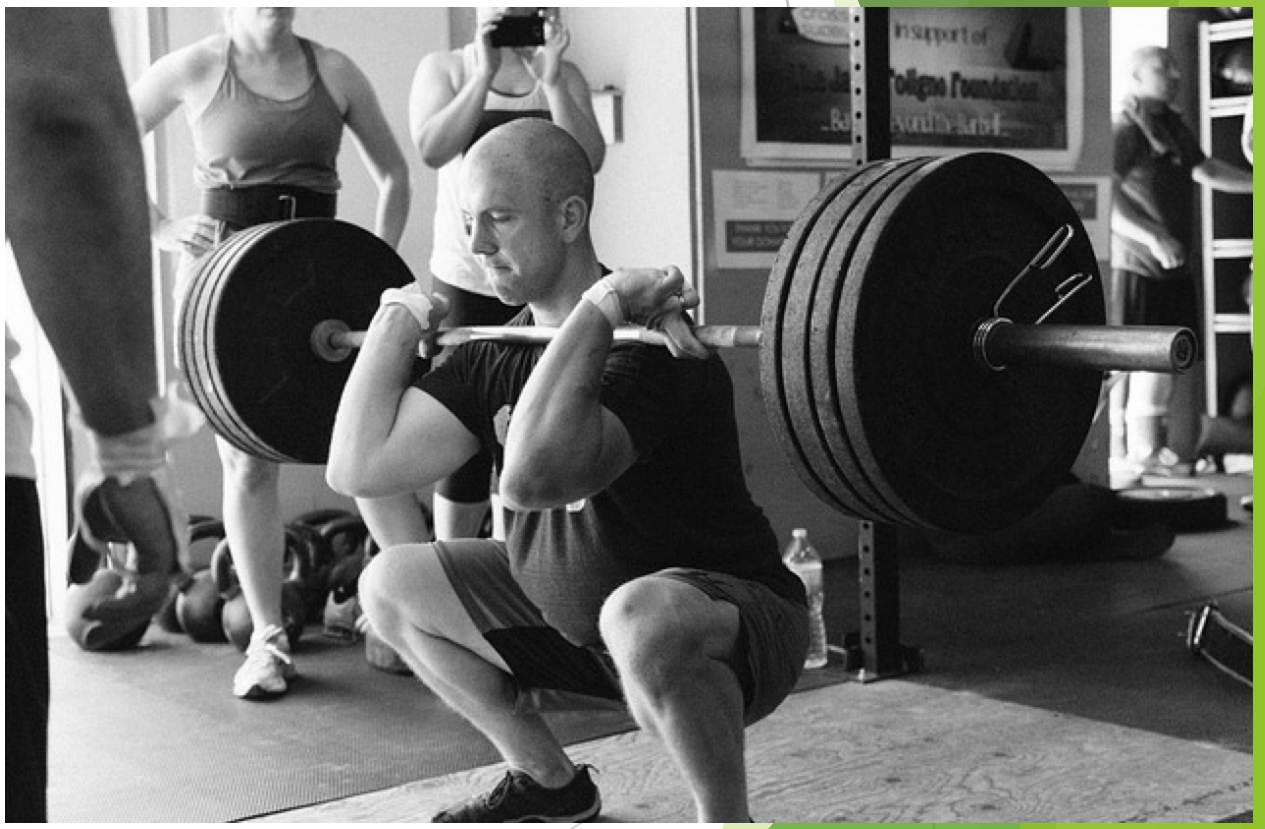
Exercise-induced ROS are important for training adaptations, vascularization, mitochondrial biogenesis, etc.





DA. Hood, *Appl Physiol Nutr Metab* 34.3 (2009): 465-472.

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Conventional antioxidants: potential pros & cons

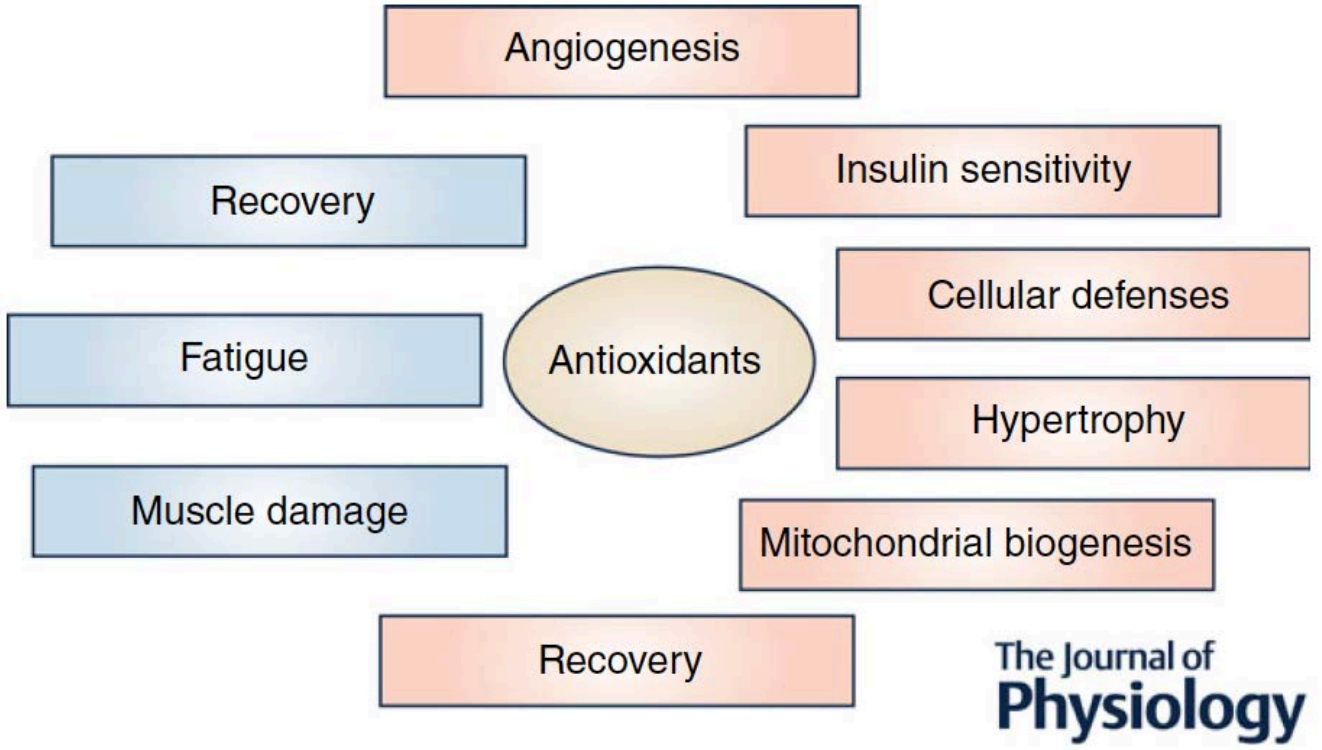

Figure 1. Effects of antioxidants on skeletal muscle during exercise training
Effectors of antioxidants that may be negatively affected are marked in red, effectors of antioxidants that may be beneficially affected are marked in blue.

Merry T. & Ristow M. J. Physiol 0.0 (2015) p. 1-13

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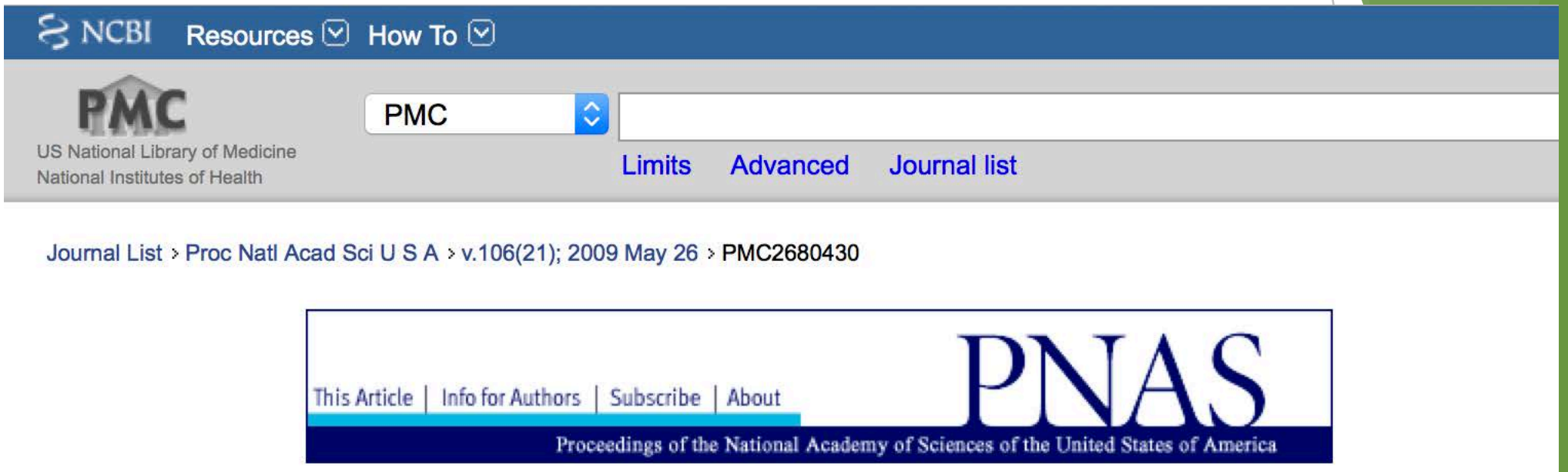
Conventional antioxidants may negate exercise benefits



Proc Natl Acad Sci U S A. 2009 May 26; 106(21): 8665–8670.
PMCID: PMC2680430
Published online 2009 May 11. doi: 10.1073/pnas.0903485106
Medical Sciences

Antioxidants prevent health-promoting effects of physical exercise in humans

Michael Ristow,[a,b,1,2] Kim Zarse,[a,2] Andreas Oberbach,[c,2] Nora Klöting,[c] Marc Birringer,[a] Michael Kiehntopf,[d] Michael Stumvoll,[c] C. Ronald Kahn,[e] and Matthias Blüher[c,2]

Author information ▶ Article notes ▶ Copyright and License information ▶

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Hydrogen does appear to reduce oxidative stress

Markers of oxidative stress		Markers of antioxidant status	
MDA	↓	Superoxide Dismutase (SOD)	↑
TBAR	↓	Glutathione (GSH)	↑
8-OHdG	↓	Catalase (Cat)	↑
HNE	↓	Glutathione peroxidase(GPx)	↑
Protein carbonyl	↓	Glutathione S-transferase (GST)	↑
dROM	↓	Glutathione reductase	↑
13-HODE	↓	Total Antioxidant Status (TAC)	↑

*Review of studies show these markers are altered by H_2 administration

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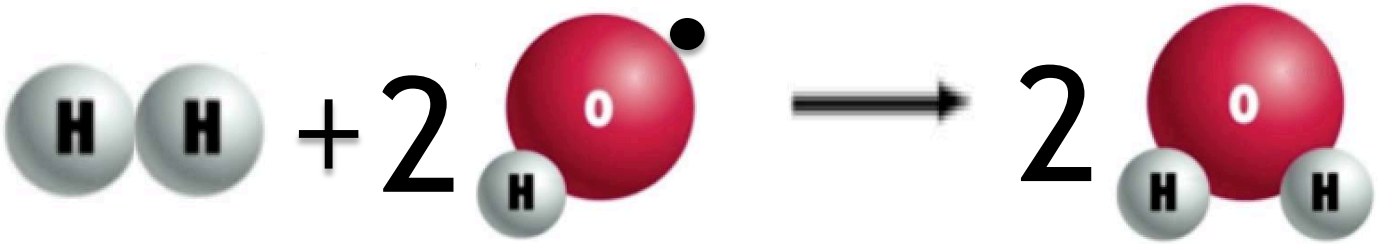
H_2 may scavenge hydroxyl radicals



nature medicine

Hydrogen acts as a therapeutic antioxidant by selectively reducing cytotoxic oxygen radicals

Ikuroh Ohsawa, Masahiro Ishikawa, Kumiko Takahashi, Megumi Watanabe, Kiyomi Nishimaki, Kumi Yamagata, Ken-ichiro Katsura, Yasuo Katayama, Sadamitsu Asoh & Shigeo Ohta

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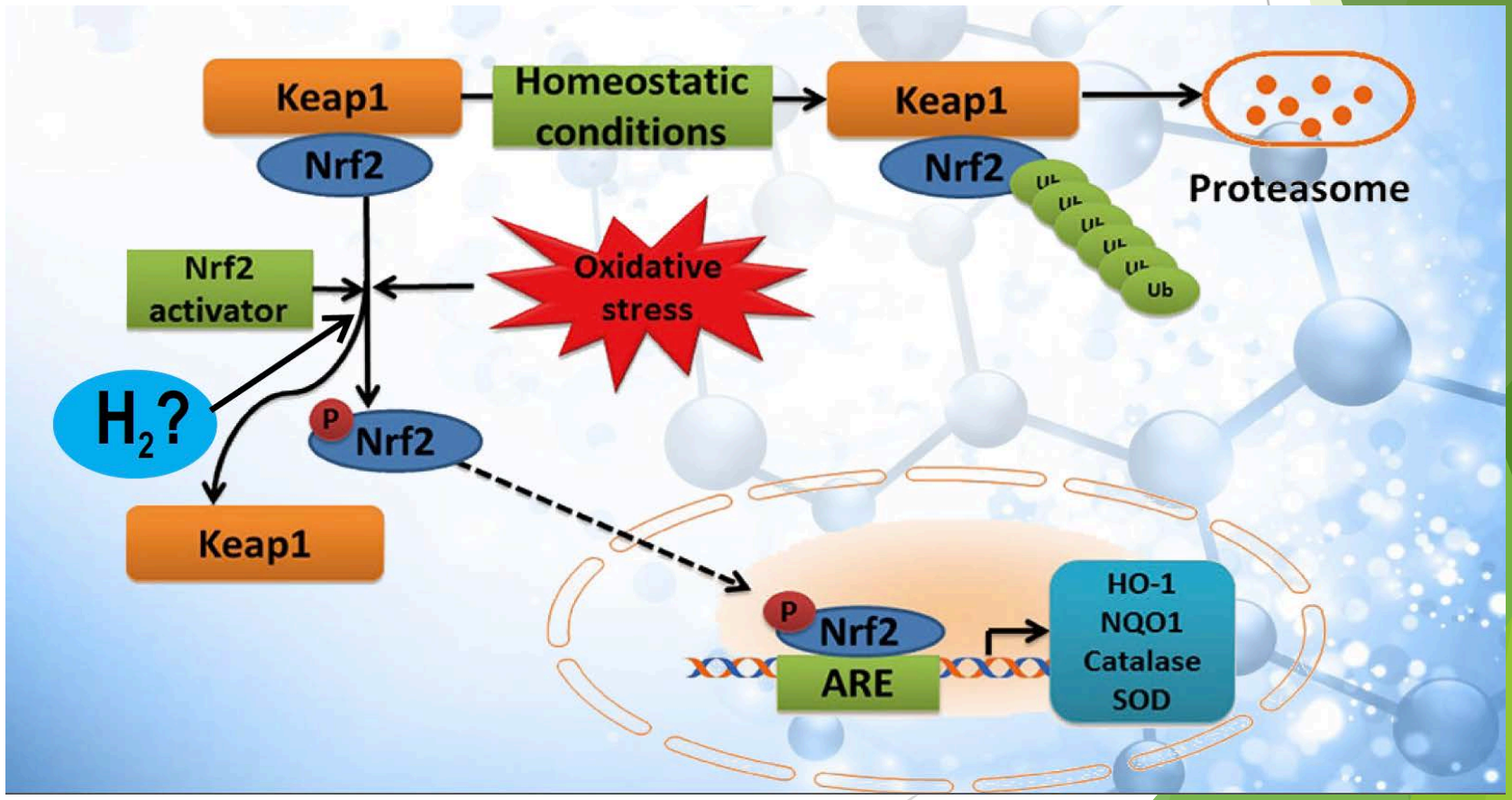
Hydrogen gas can activate the Nrf2 pathway, leading to increased production of SOD, GSH, CAT, etc.



- H. Chen, et al. *Int Immunopharmacol* 28.1 (2015): 643
- J. Yu, et al. *Toxicology letters* 238.3 (2015): 11

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Hydrogen prevents ROS formation by cell modulation

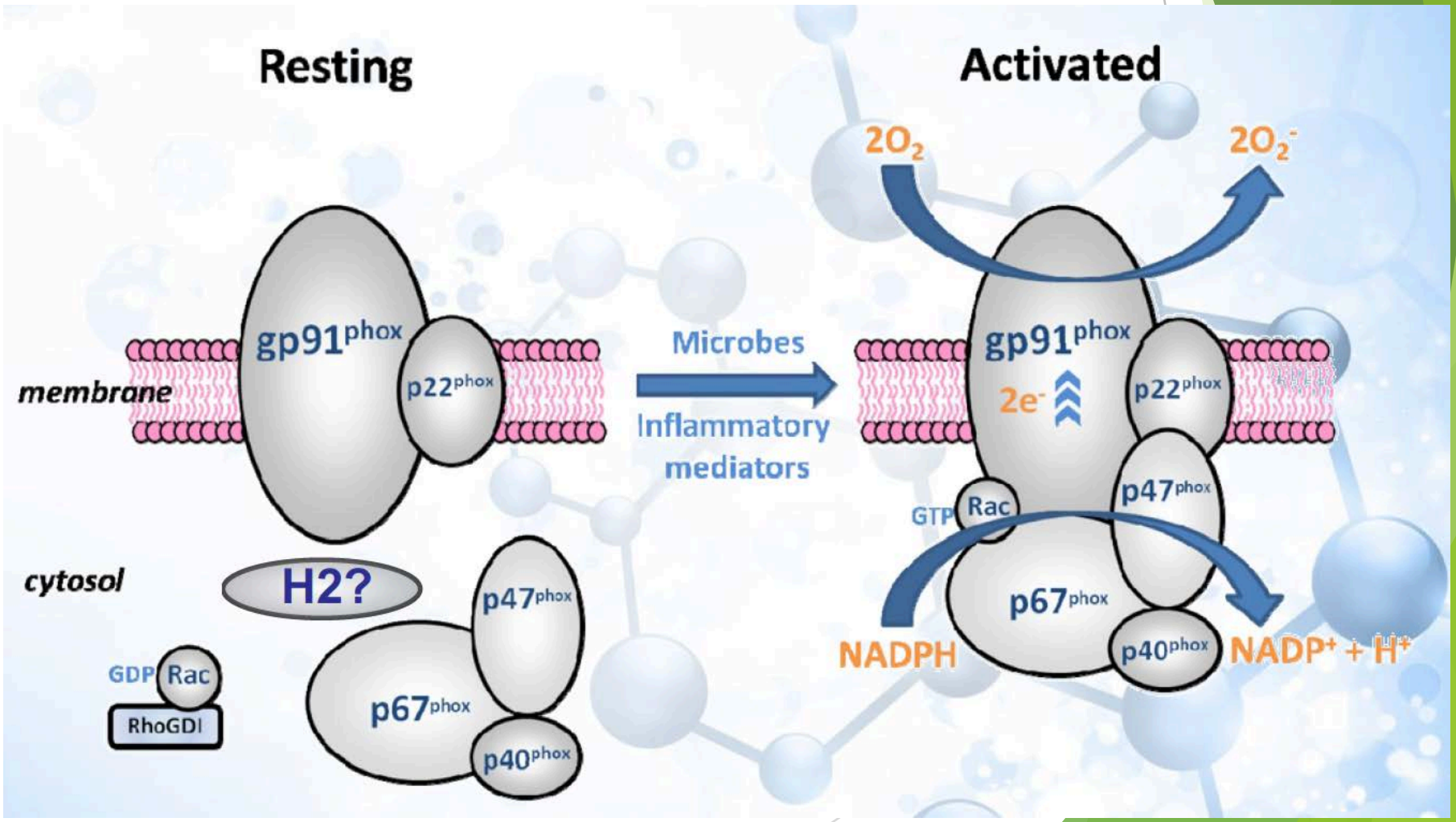

Fig. is example only.

I. Tomohiro, et al. Biochem. Biophys. Res. Commun. 411.1 (2011): 143-149.

S. Yasunori, et al. Biochem. Biophys. Res. Commun. 375.3 (2008): 346-350.

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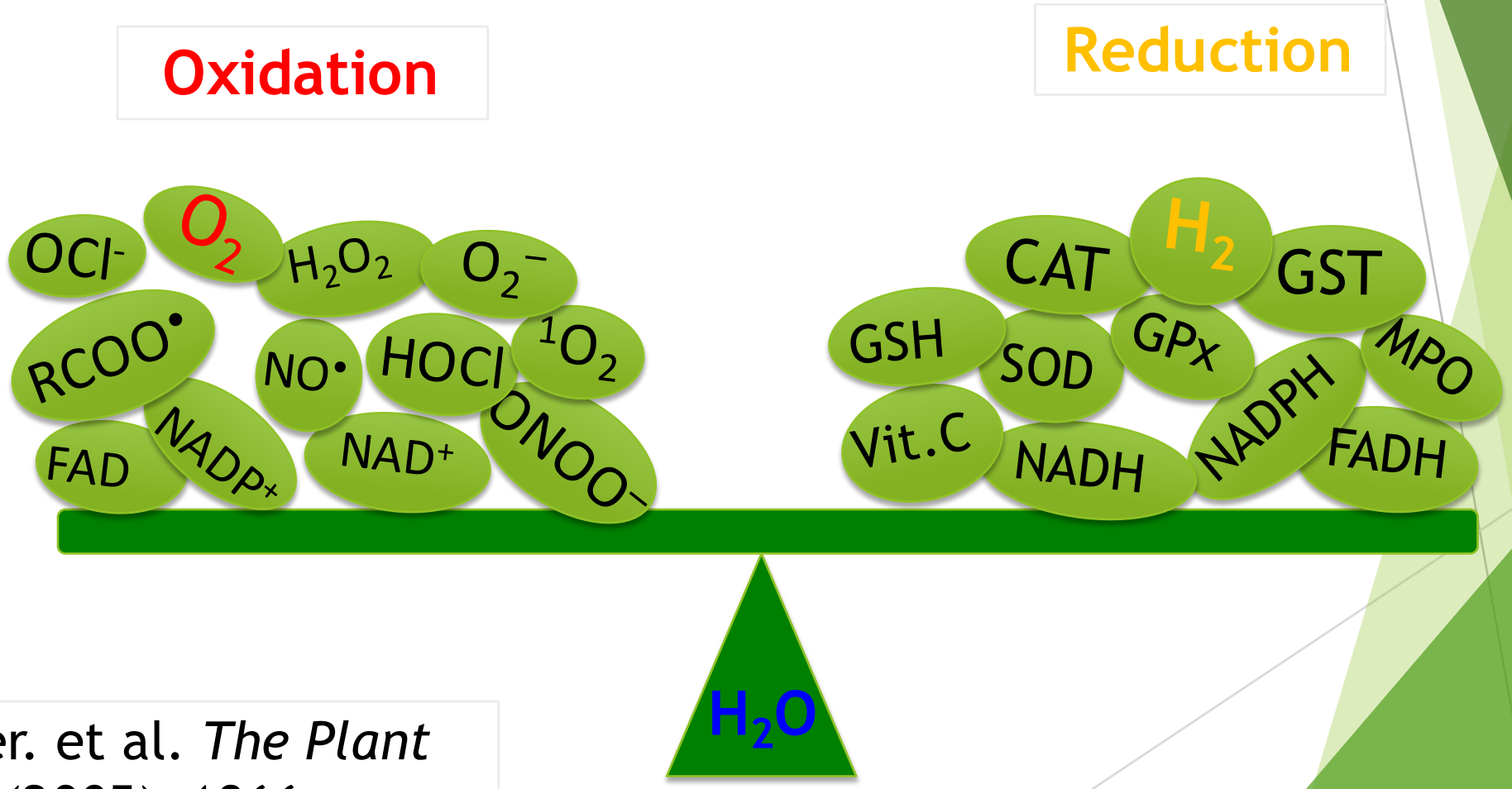
Life is balanced between Oxidation and Reduction



CH., Foyer. et al. *The Plant Cell* 17.7 (2005): 1866

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Oxidative stress

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Reductive stress

Zhang X, Min X, Li C, et al. Involvement of reductive stress in the cardiomyopathy in transgenic mice with cardiac-specific overexpression of heat shock protein 27. Hypertension. 2010;55: 1412-1417.

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Both oxidative and reductive stress can occur simultaneously in the same cell

Kirstein, J. The EMBO Journal (2015) 34: 2334–2349

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Redox dysregulation

Loscalzo J.
Free Radic Biol Med.
2014 Oct;75 Suppl
1:S2

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Superiority of Hydrogen compared to other antioxidants

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National Institutes of Health

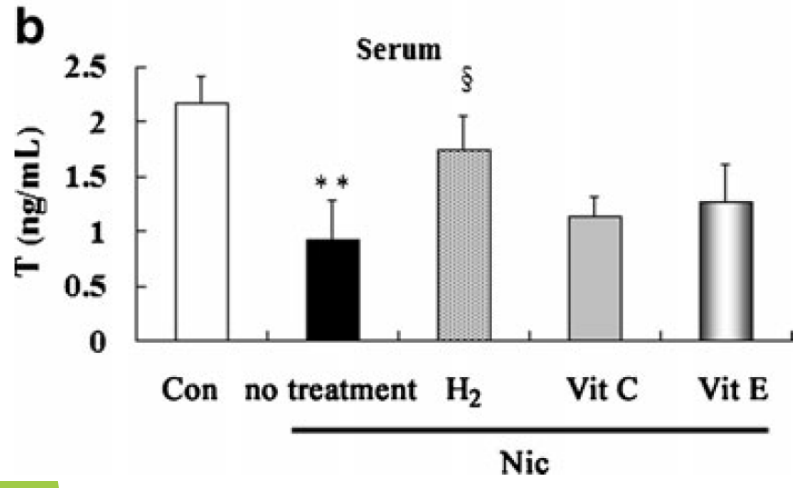
PubMed | Sea

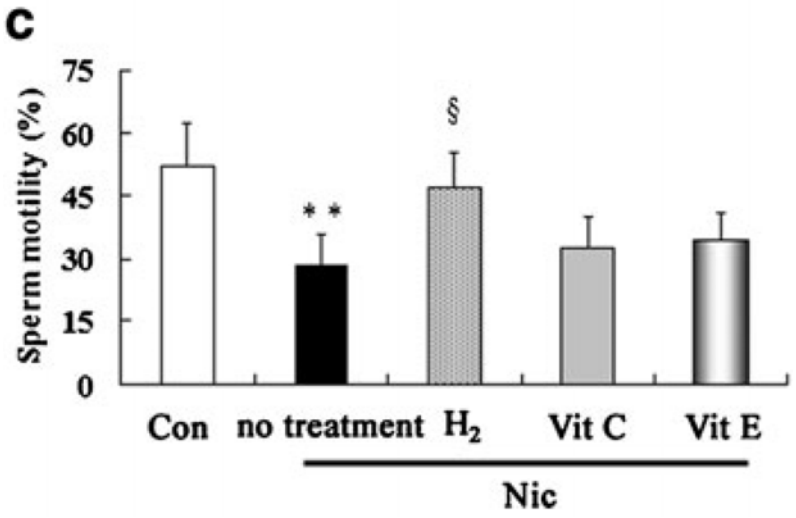
Advanced

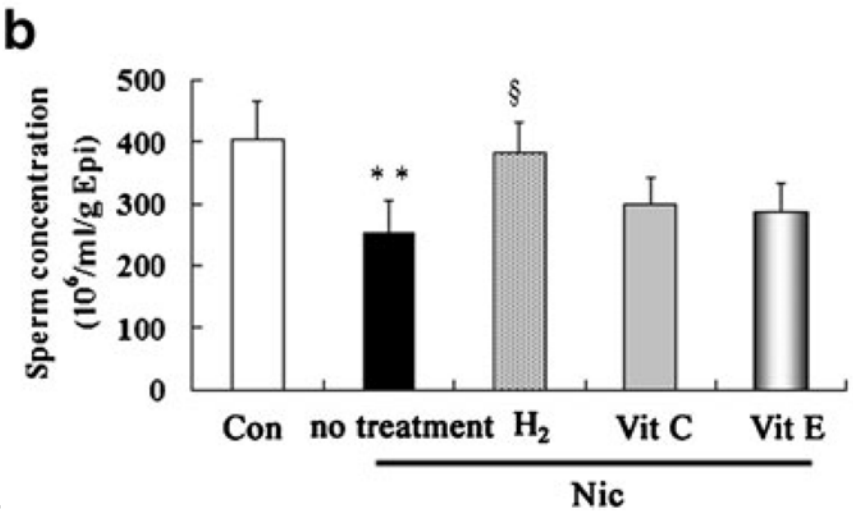
Abstract Send to:

J Assist Reprod Genet. 2014 Jan;31(1):109-14. doi: 10.1007/s10815-013-0102-2. Epub 2013 Nov 13.

Long-term treatment of hydrogen-rich saline abates testicular oxidative stress induced by nicotine in mice.







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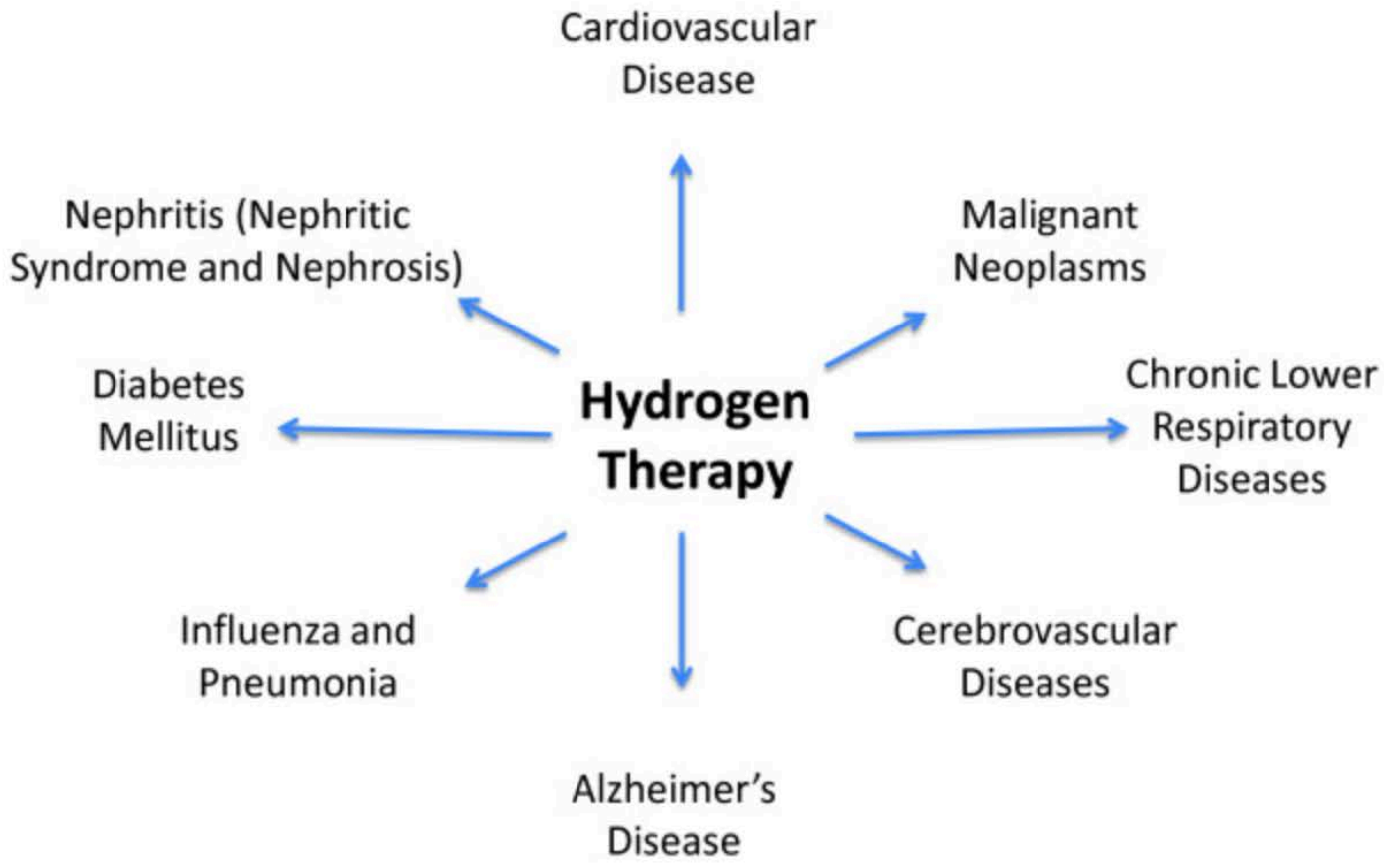
Hydrogen therapy has potential for the top 8 disease-causing fatalities as listed by CDC

Med Gas Res

Figure 4



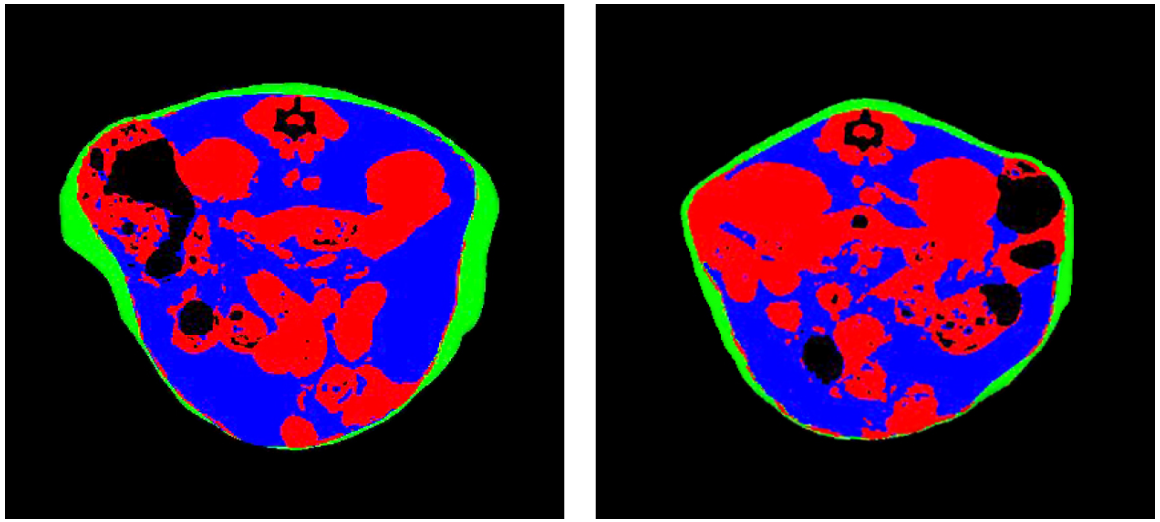
Hydrogen therapy potential for top causes of death in the US. The potential for molecular hydrogen in the top causes of death in the United States (excluding deaths caused by suicide and accidents) [23].

Med Gas Res

H_2 suppresses obesity

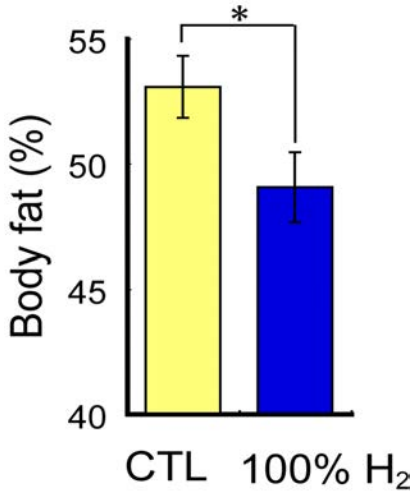
CT scan :18-week-old db/db mice

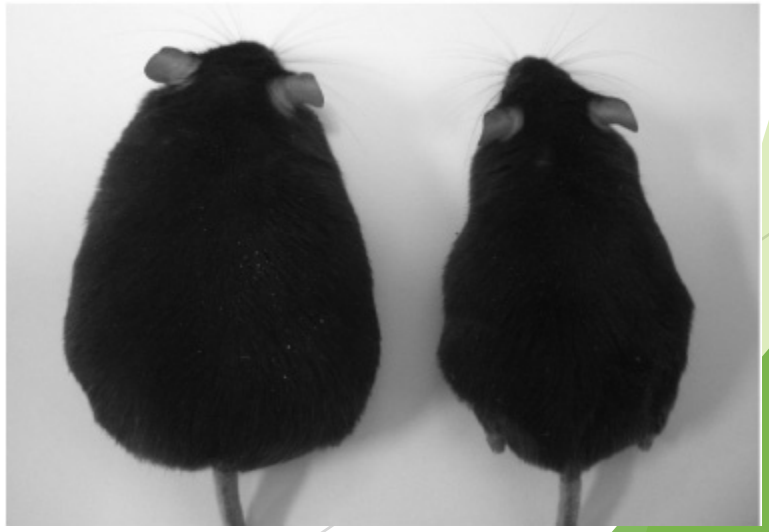
CTL H_2



Red: muscle
Blue: internal fat
Green: subcutaneous fat

Body fat





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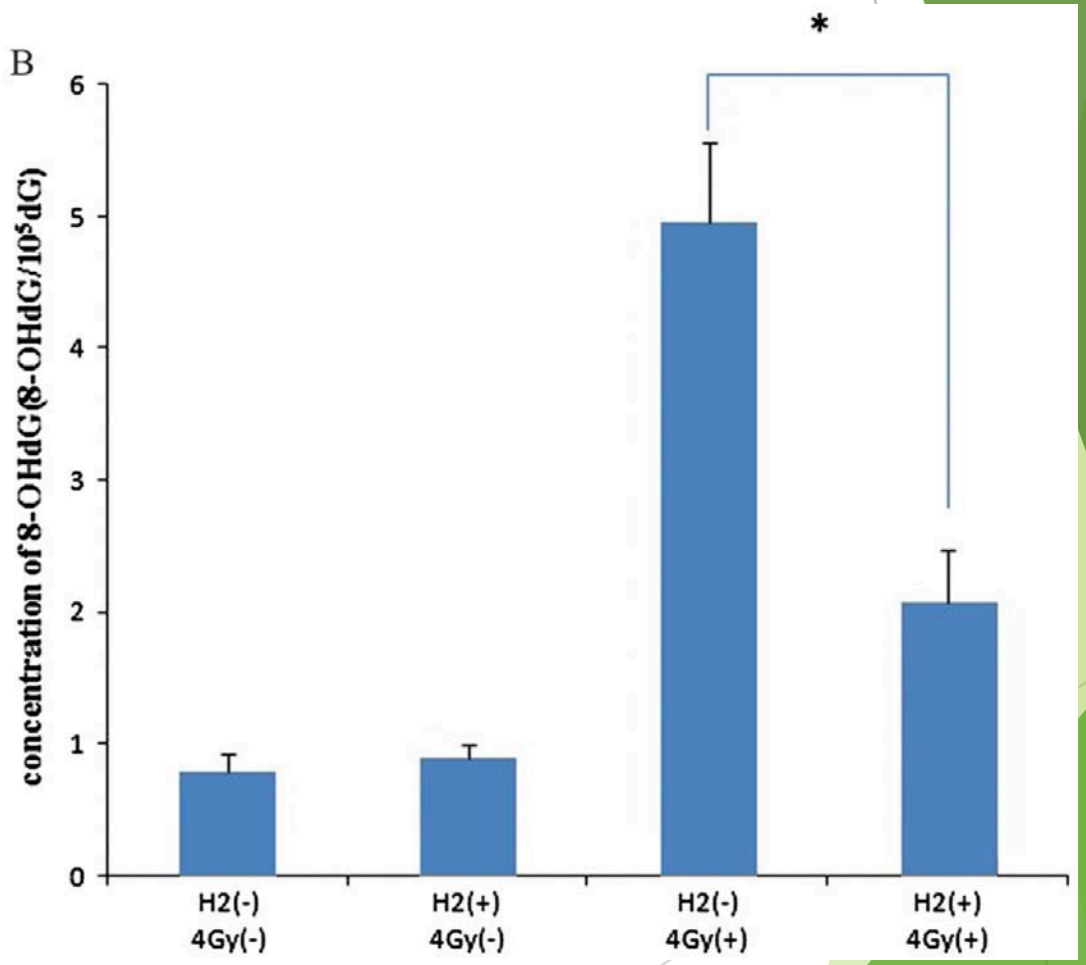
Helps maintain redox homeostasis



Qian, Liren, et al. "Radioprotective effect of hydrogen in cultured cells and mice." *Free radical research* 44.3 (2010): 275-282.

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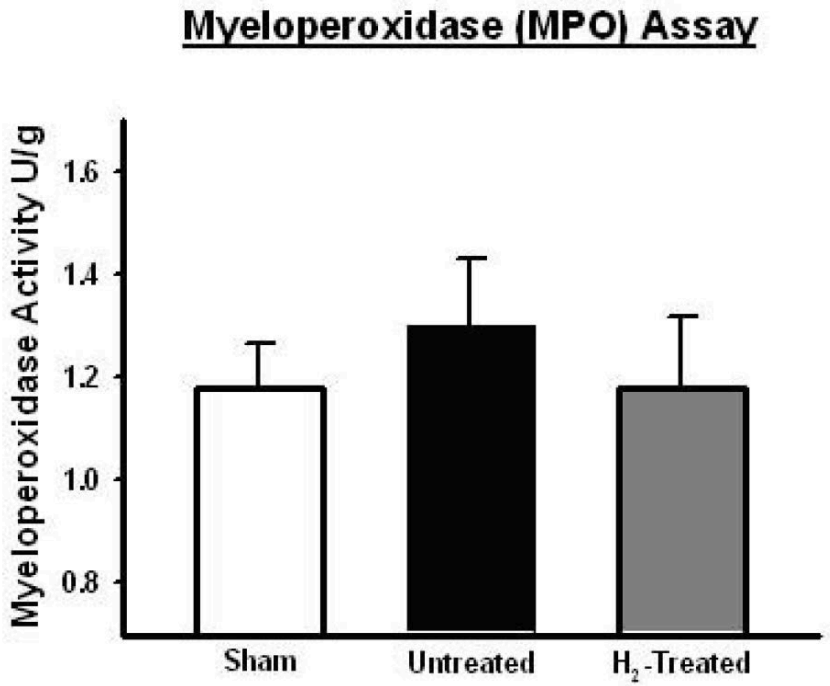
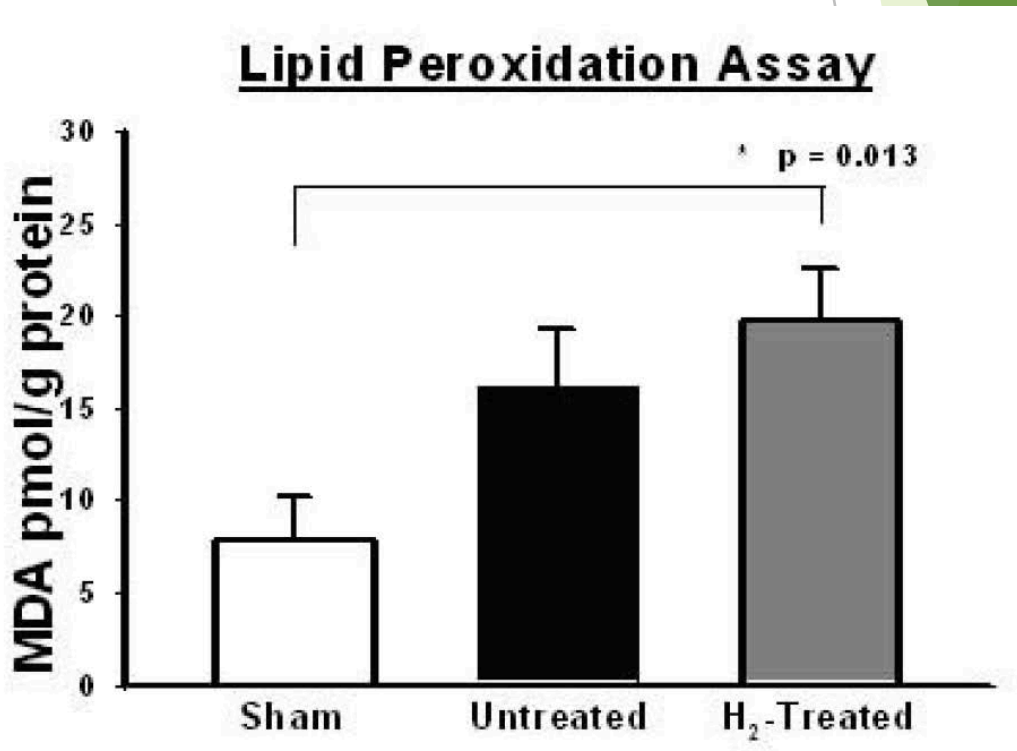
In rat model of surgically induced brain damage, hydrogen decreases inflammatory marker, but increases oxidation





Eckermann J. et al. Med Gas Res. 2011 May 18;1(1):7.

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Under certain conditions, the benefits or hydrogen are associated with increased ROS production

Yanjie X., et al. Plant Physiol. 2
Apr 14;165(2):759-773.

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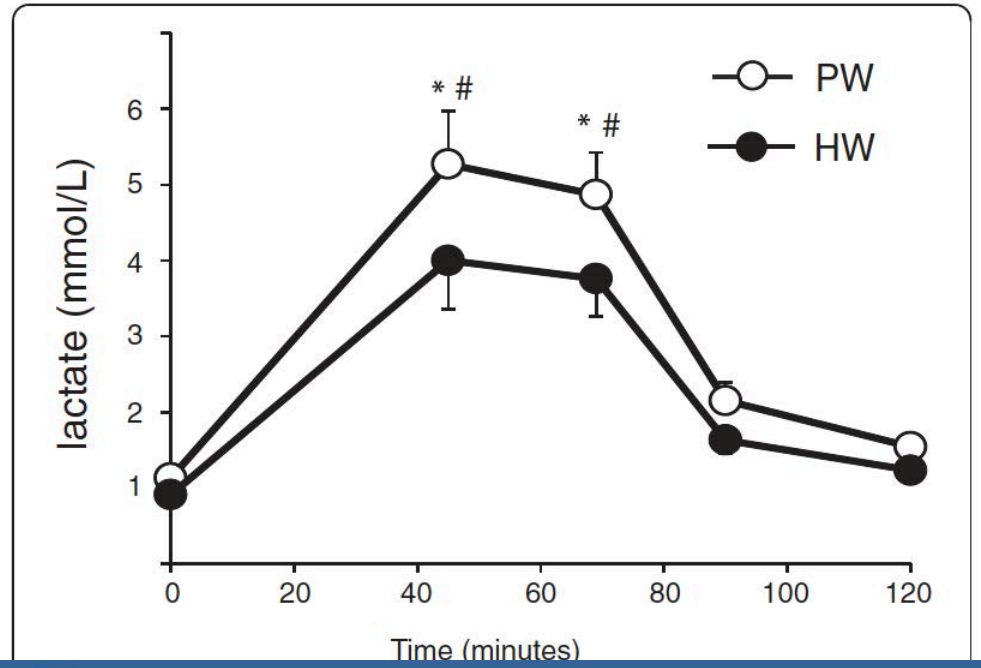

Reduced lactate, but did not reduce oxidant markers

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National Institutes of Health

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Med Gas Res. 2012 Jul 12;2:12. doi: 10.1186/2045-9912-2-12. eCollection 2012.

Pilot study: Effects of drinking hydrogen-rich water on muscle fatigue caused by acute exercise in elite athletes.

Aoki K[1], Nakao A[2], Adachi T[1], Matsui Y[1], Miyakawa S[1].

Author information

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Maybe more than just an antioxidant

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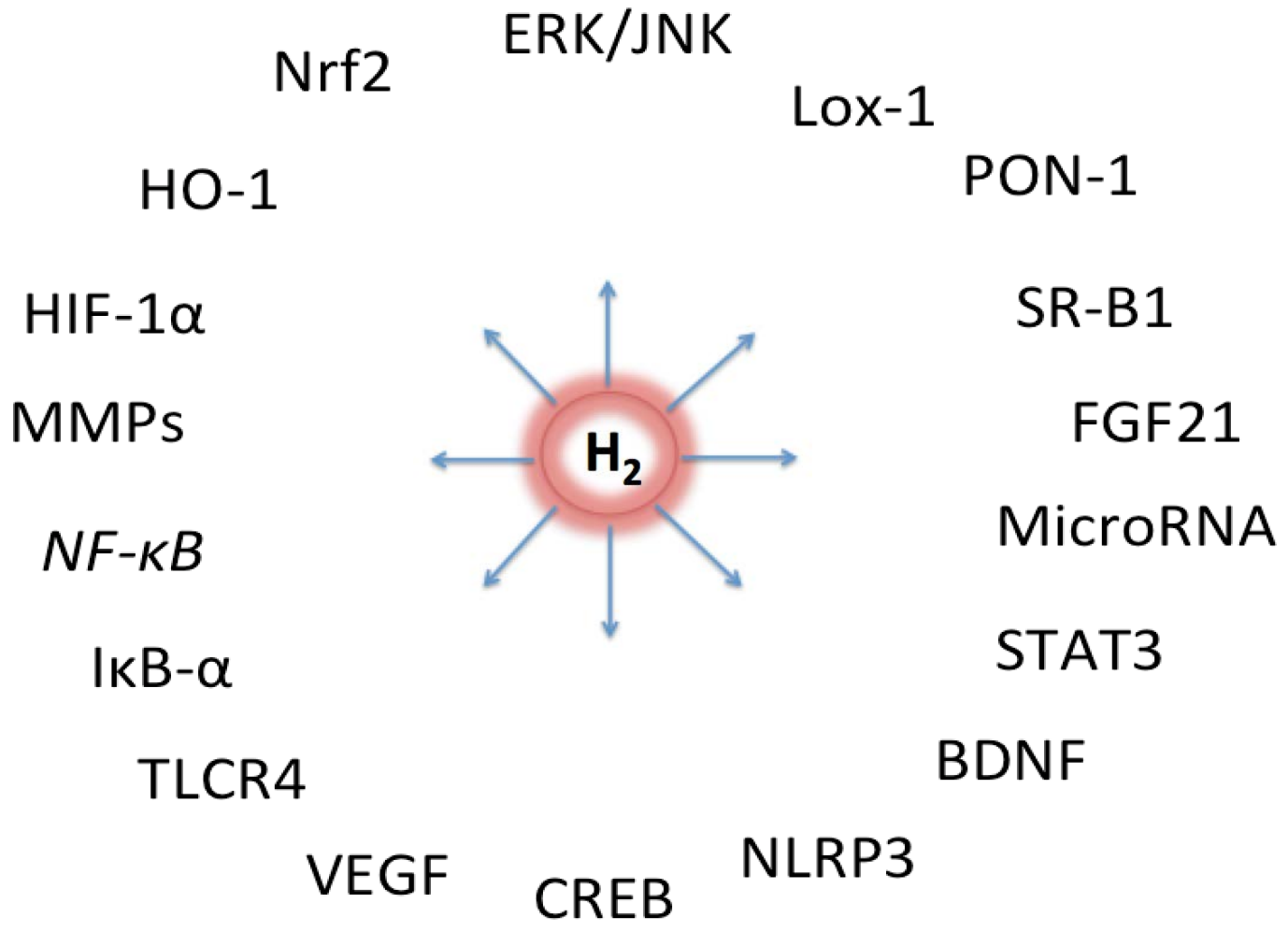
H_2 may act as a signaling molecule[1]

Under the right conditions, hydrogen can alter the levels/activities of over 200 biomolecules[2]



1. Itoh, T. et al (2009)., *389*(4), 651-656.

2. Personal review of 500+ papers

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JIANKANG LIU (XI'AN JIAOTO UNIVERSITY)

ADVISOR

The discovery of the antioxidant effect of hydr revolution in gas medicine and the following st an important area, i.e., Hydrogen Medicine.
My group's interest is targeting mitochondria t treat age-related degenerative diseases. Our r has unique effect on improving mitochondrial f mitochondrial dysfunction-related diseases, su cardiovascular disease. These exciting finding Hydrogen Medicine will have a brilliant future a important role in human health.

Professor and Dean， School of Life Science and Technology, Xi'an Jiaotong Univers

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DR. JIANGANG LONG, PHD. (XI'AN JIAOTONG UNIVERSITY)

ADVISOR

Mitochondrion is the key organelle for cellular ATP supply and apoptosis signaling. We are engaged in exploring mitochondrial metabolism under physiological and pathological conditions, and pursuing the mitochondrion-targeted molecules to improve mitochondrial function and maintain mitochondrial homeostasis damaged during neurodegeneration and nutritional imbalance.
Since the discovery of the antioxidant effect of H2 in 2007, we recently identified the beneficial effects of H2 on mitochondrial respiratory capacity and phase 2 enzymes activation. Therefore, we considered that H2 acts as a "mitochondrial nutrient", which will be very promising molecule in preventing and treating age-related disease and metabolic syndromes.

Professor and Vice Dean of School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, China

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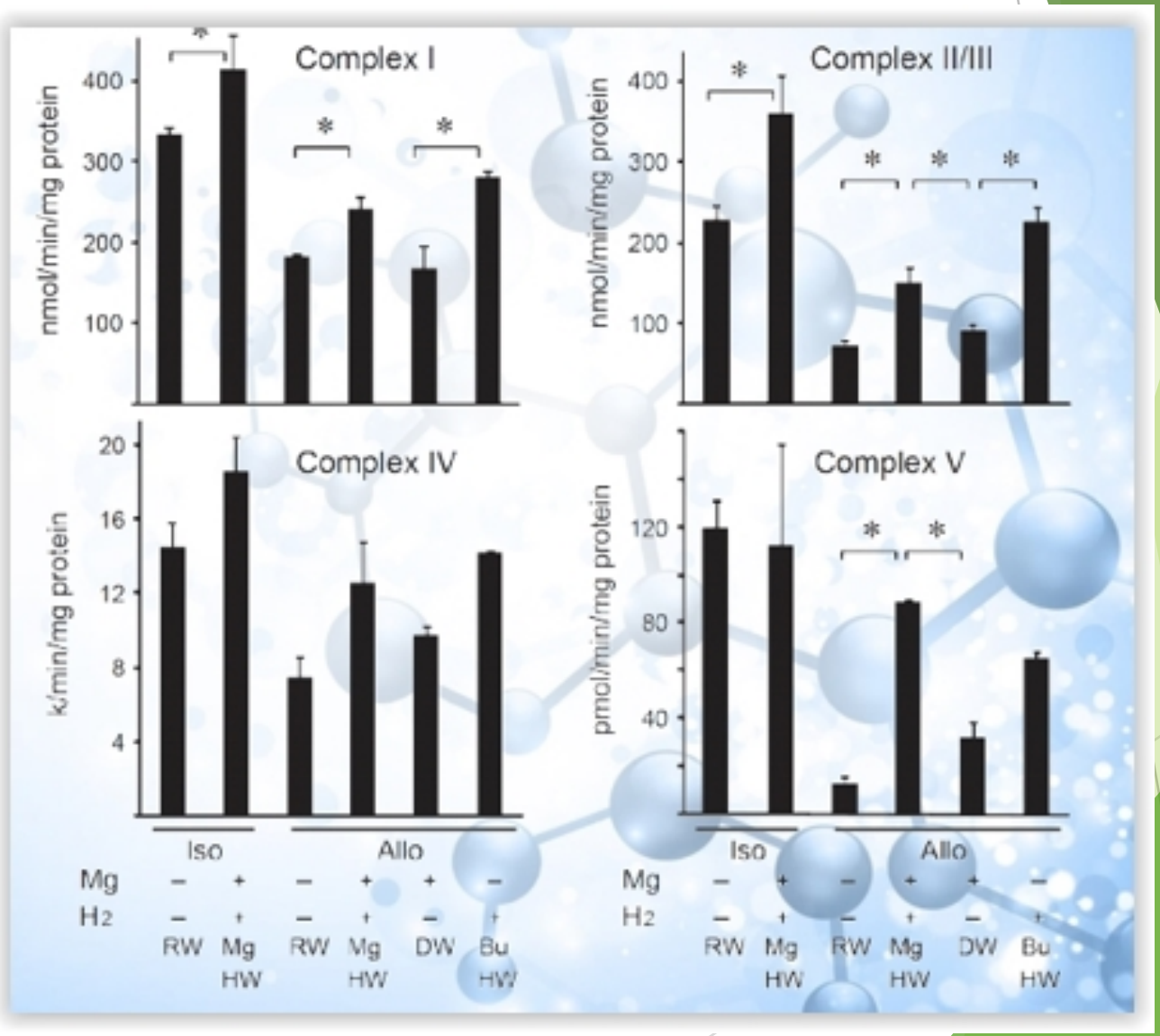
H_2 stimulates mitochondrial function



N. Kentaro, et al. (2012) "Hydrogen-supplemented drinking water protects cardiac allografts from inflammation-associated deterioration." Transpl Int. 25.12; 1213-1222

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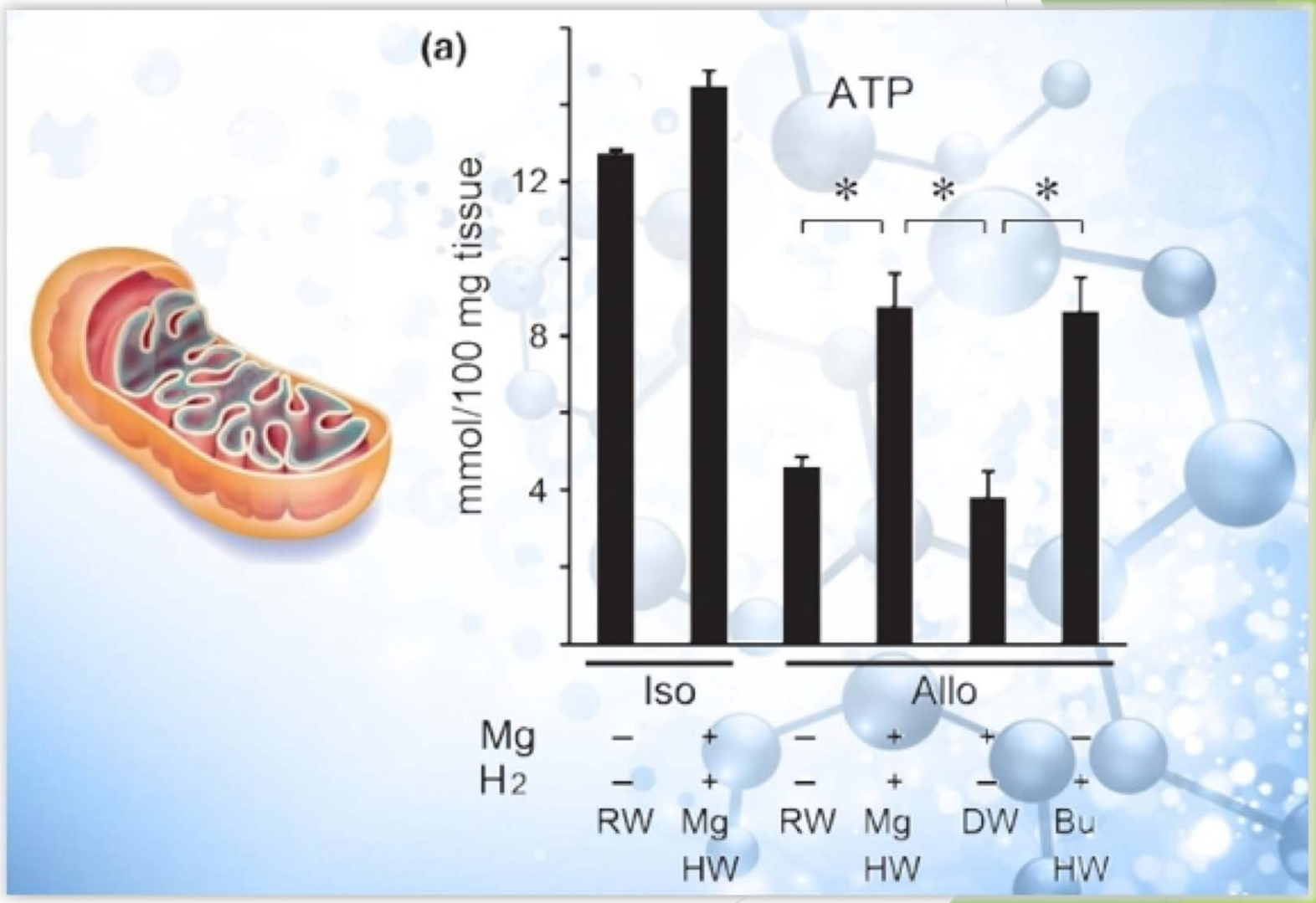
H_2 promotes production of ATP



N. Kentaro, et al. (2012) "Hydrogen-supplemented drinking water protects cardiac allografts from inflammation-associated deterioration." Transpl Int. 25.12; 1213-1222

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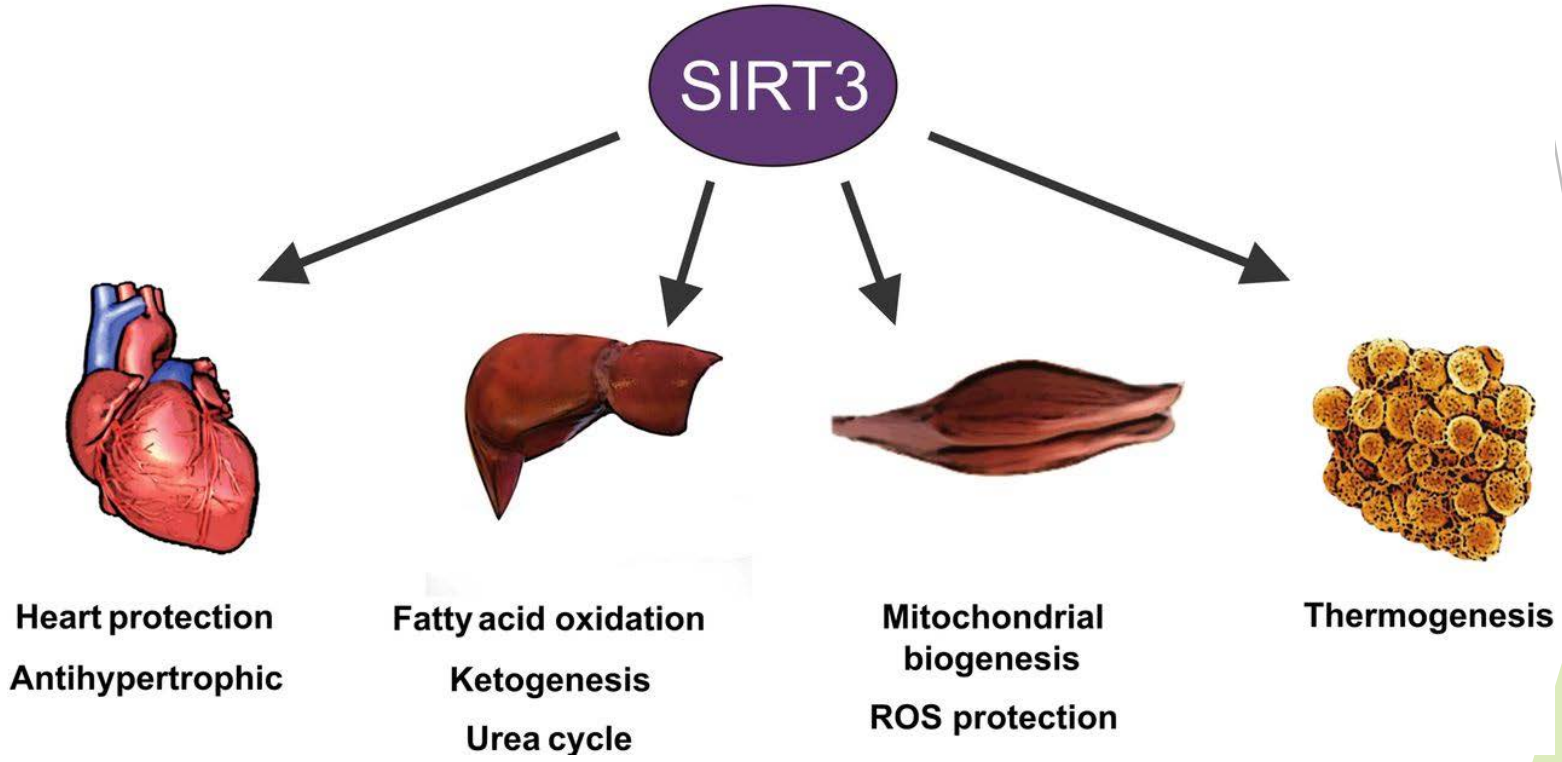
Increased Sirt3 expression



Wang L., et al. Chinese J.of Tissue Engineering Research July 9, 2015 Vol.19, No.29

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High Safety Profile

- Hundreds of studies
- Use in deep sea diving
- Intestinal bacteria

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PREDICTION

The market is generally 10 years behind the science

2007 marked the beginning of focused Hydrogen research

2017 will be the year of H_2 Awareness!

As the Molecular Hydrogen Foundation's role is to promote and disseminate scientific research, it does not endorse any specific product. The Molecular Hydrogen Foundation is not affiliated with Researched Nutritionals®.

H_2 Absorb™

PROMOTE HEALTHY OXIDATIVE STRESS LEVELS*

We are excited to introduce molecular hydrogen in an easy-to-use, effervescent tablet. Since 2007, over eighty published studies[1] have proven molecular hydrogen's role in supporting healthy mitochondrial function, exercise recovery, and metabolic processes.*

The effects of oxidative stress and the importance of antioxidants are well documented in the scientific community. Each **H_2 Absorb™** tablet allows your patients to turn regular water into a powerful health promoting beverage.* With hydrogen's low molecular weight, it is able to penetrate biomembranes and diffuse into the cytosol, mitochondria and nucleus.[2]

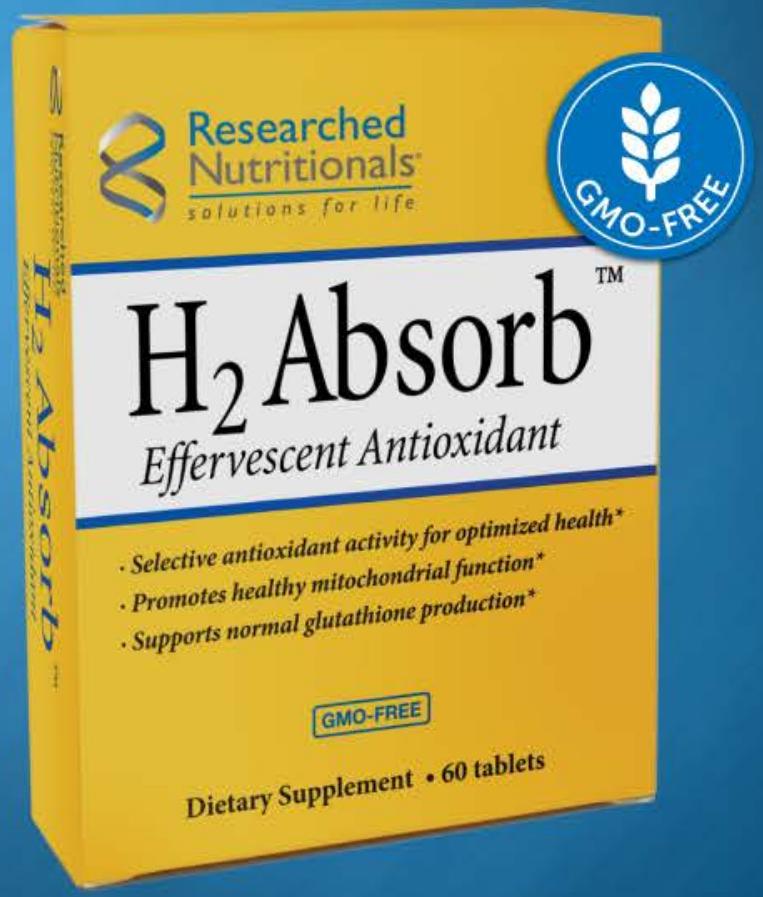
H_2 Absorb™ *- the optimized molecular hydrogen delivery system.*

1 Nicolson, Garth, et al. (2016) Clinical Effects of Hydrogen Administration: From Animal and Human Diseases to Exercise Medicine. International Journal of Clinical Medicine, 2016, 7, 32-76.

2 Ohsawa, I., Ishikawa, M., Takahashi, K., Watanabe, M., Nishimaki, K., Yamagata, K., Katsura, K., Katayama, Y., Asoh, S. and Ohta, S. (2007) Hydrogen Acts as a Therapeutic Antioxidant by Selectively Reducing Cytotoxic Oxygen Radicals. Nature Medicine, 13, 688-694.

Joseph Burrascano Jr., MD

"Due to the research basis of molecular hydrogen, I think this product would be an important part of a practitioner's arsenal."



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*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure or prevent any disease.

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