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"HYDROGEN: THE SECRET INGREDIENT TO LONGEVITY?

TYLER W. LEBARON

EXECUTIVE DIRECTOR OF

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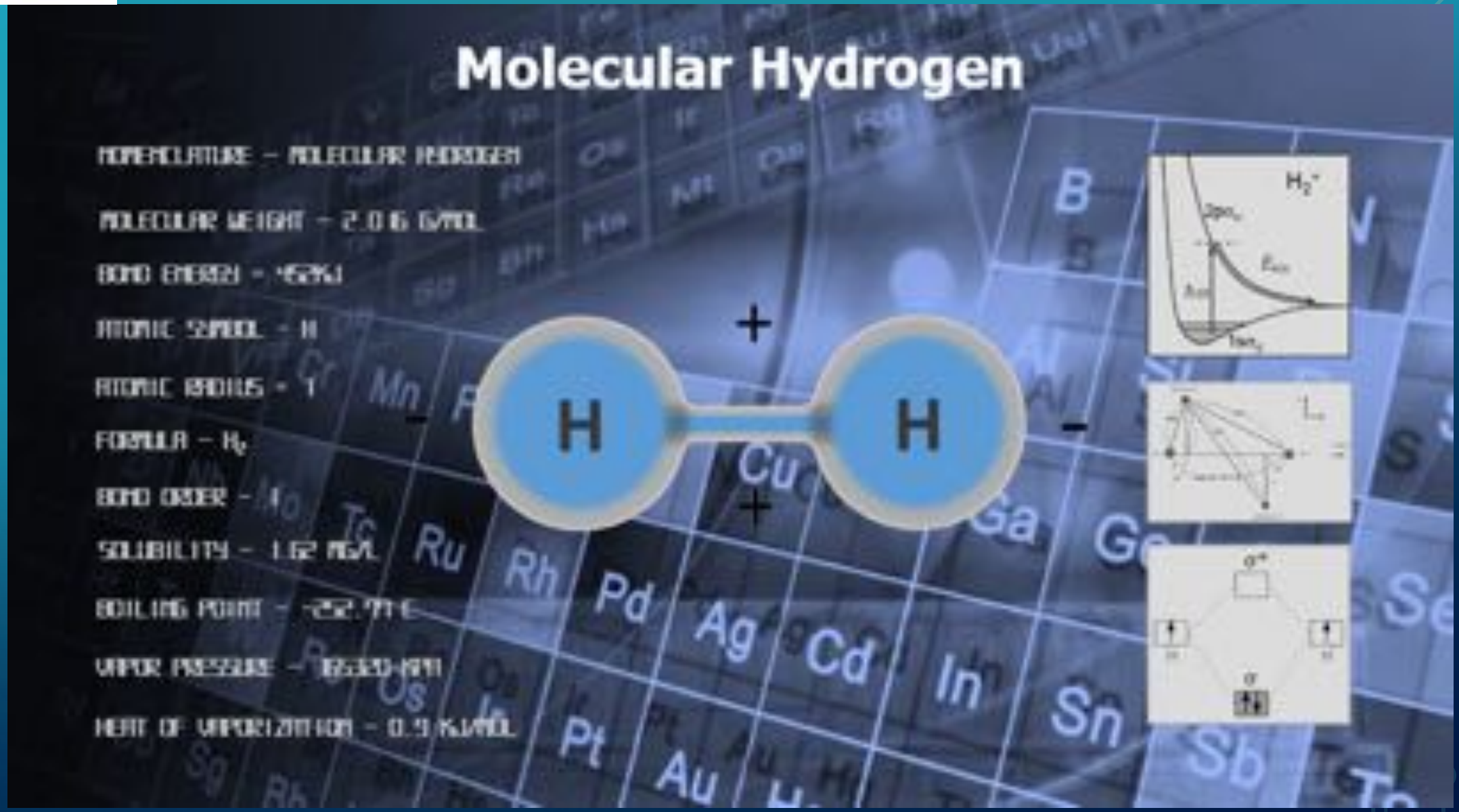
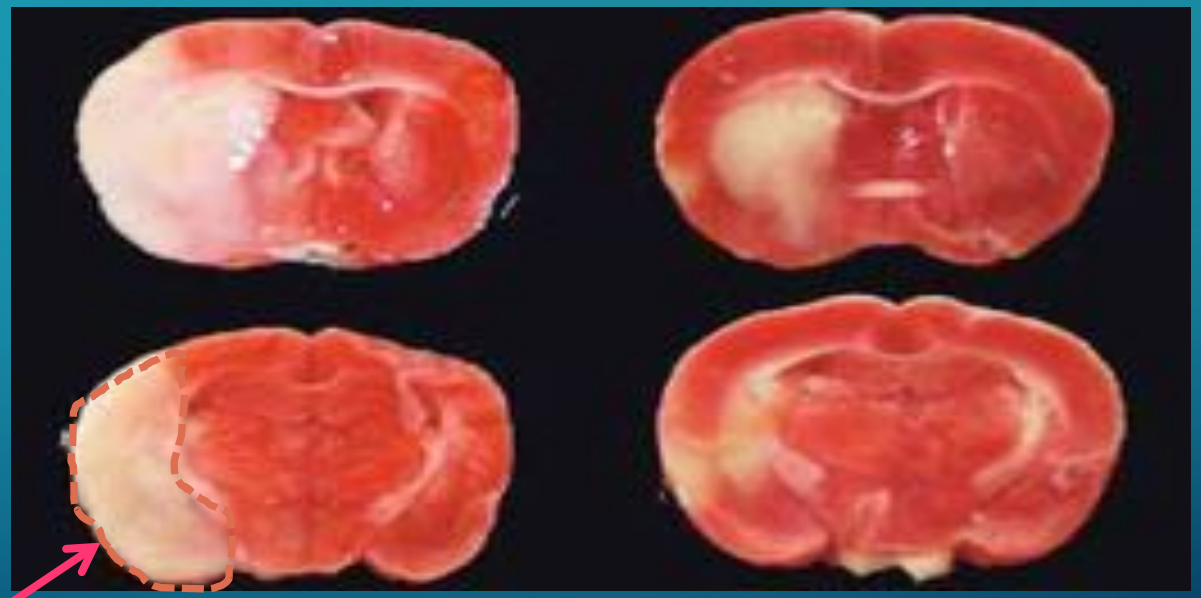
The Basics



H_2 gas suppressed cell death of the brain due to cerebral infarction

(there is no effect with helium gas)

0% H_2 gas 2 %



Dead area in rat brain

nature medicine

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

Hydrogen-rich water Parkinson's disease

Fu, Y., et al. "Molecular hydrogen is protective against 6-hydroxydopamine-induced nigrostriatal degeneration in a rat model of Parkinson's disease." *Neuroscience letters* 453.2 (2009): 81 & PLoS One. 2009 Sep 30;4(9):e7247

Control water

H_2 water

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Hydrogen gas from bacteria exerts therapeutic biological effects

- 1988: Hypothesized that hydrogen from bacteria could be therapeutic
- 2009: Confirmed by a report from the Forsyth Institute in Boston and the University of Florida

- Neale, R.J. Medical Hypotheses, 1988. 27(1): p. 85-87
- Kajiya, M., et al. Biochem. Biophys. Res. Commun. 2009. 386(2): p. 316-321.

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Molecular hydrogen has been shown to be therapeutic in over 170 different human and animal disease models and essentially every organ of the human body.

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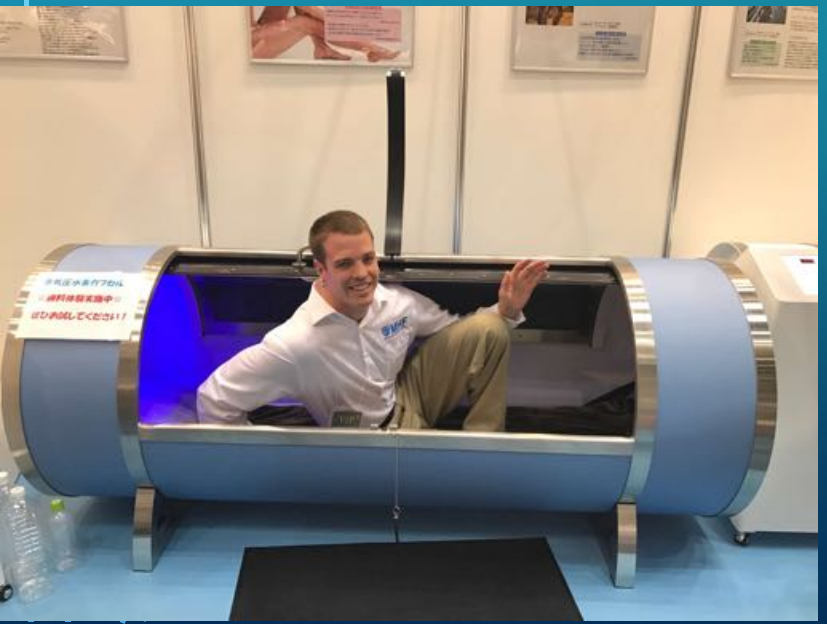
Methods of Administration

- Inhalation of hydrogen gas
- Hyperbaric hydrogen chamber
- Hydrogen-rich saline injection
- Taking a hydrogen water bath
- Ingestion of hydrogen-rich water



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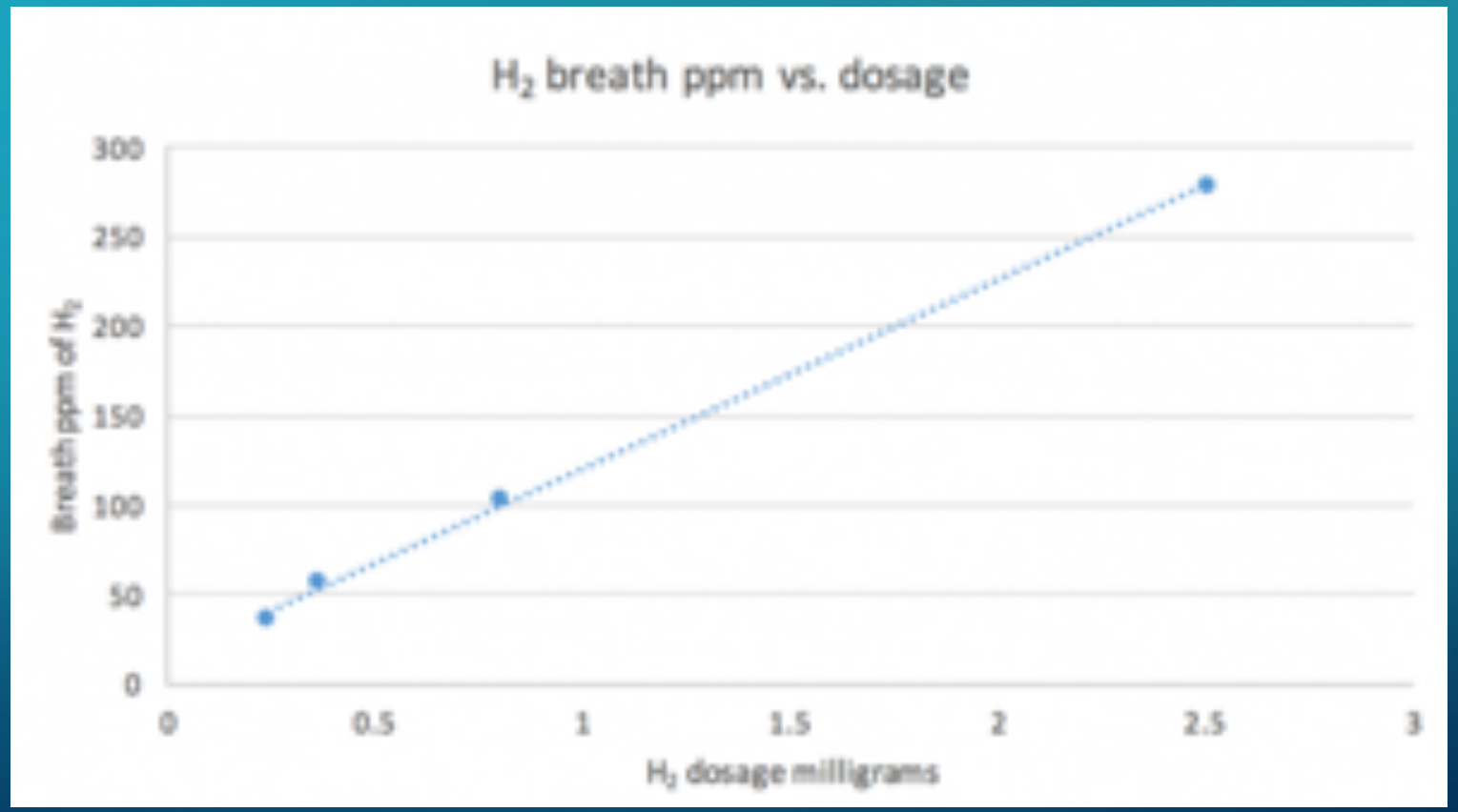
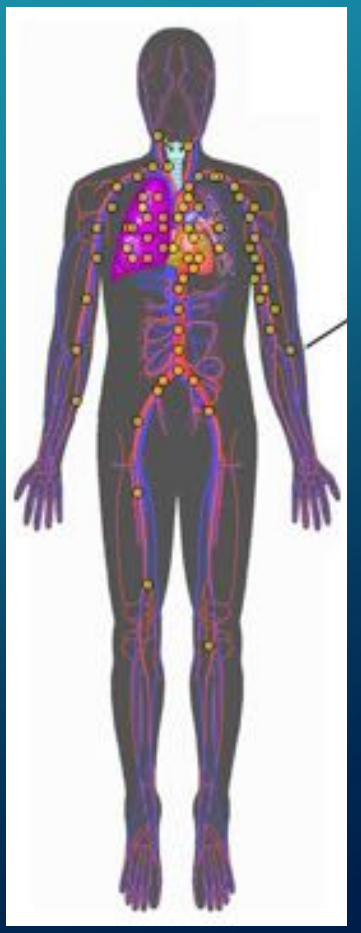
Pharmacokinetics





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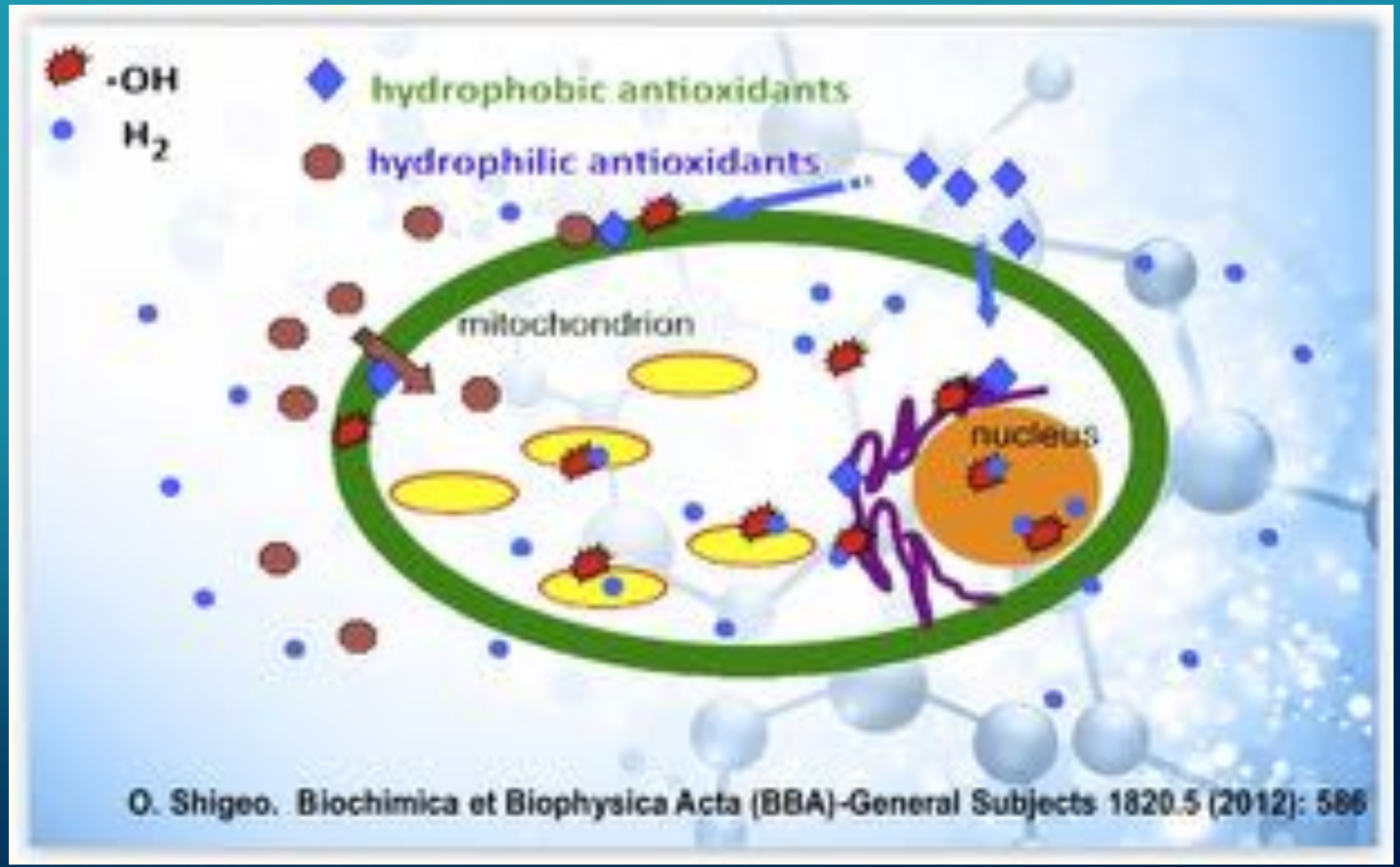
- Rapid diffusion
- Small molecule

- Hydrophobic
- No byproduct (water)



Ohta, S. (2012). *Biochimica et Biophysica Acta (BBA)-General Subjects*, *1820*(5), 586

Free radical/antioxidant marketing

Conventional antioxidants may negate exercise benefits

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PMC
US National Library of Medicine
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PMC Limits Advanced Journal list

Journal List › Proc Natl Acad Sci U S A › v.106(21); 2009 May 26 › PMC2680430

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PNAS
Proceedings of the National Academy of Sciences of the United States of America

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]

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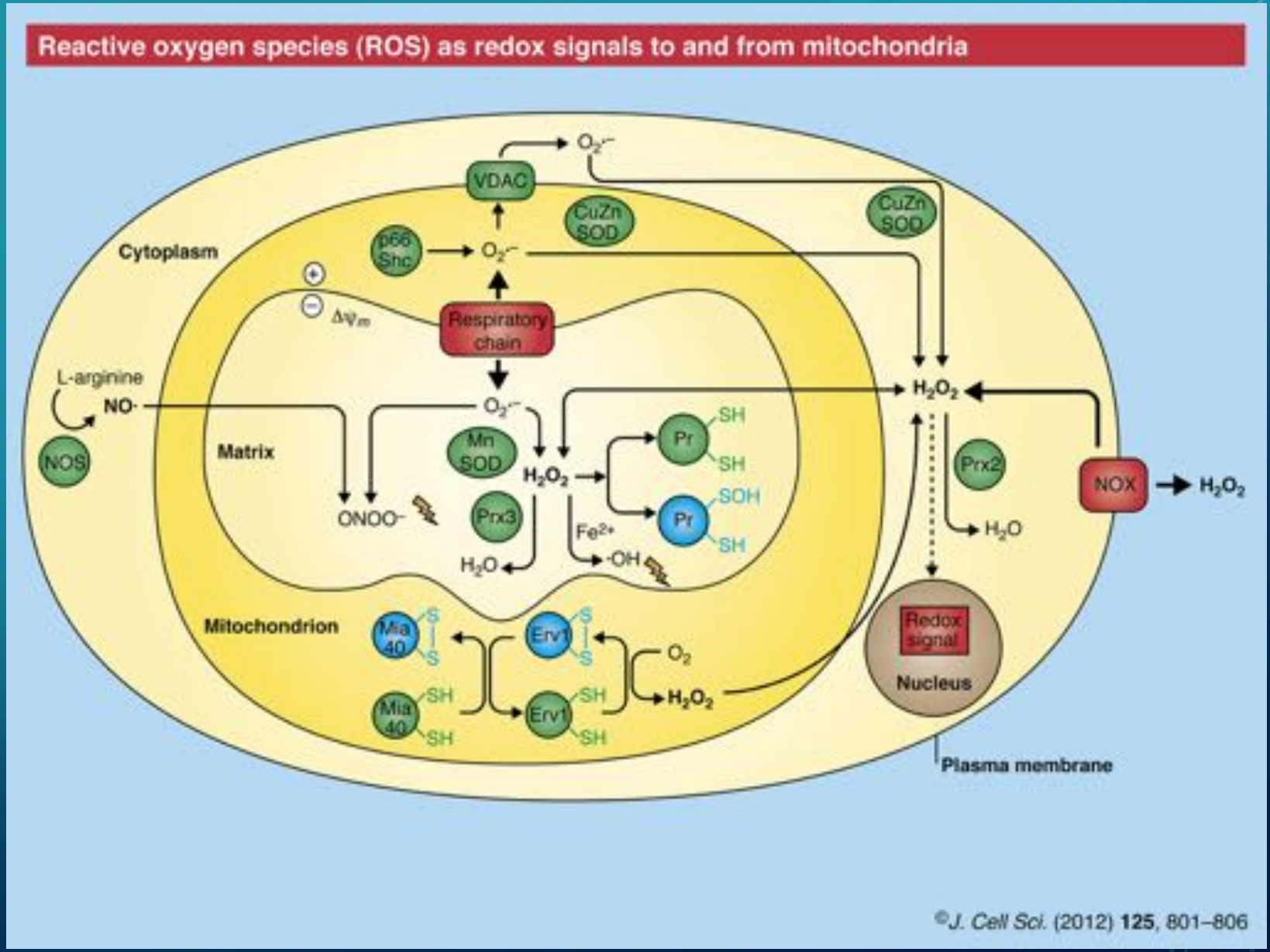
Proc Natl Aca

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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Hydrogen ameliorates oxidation

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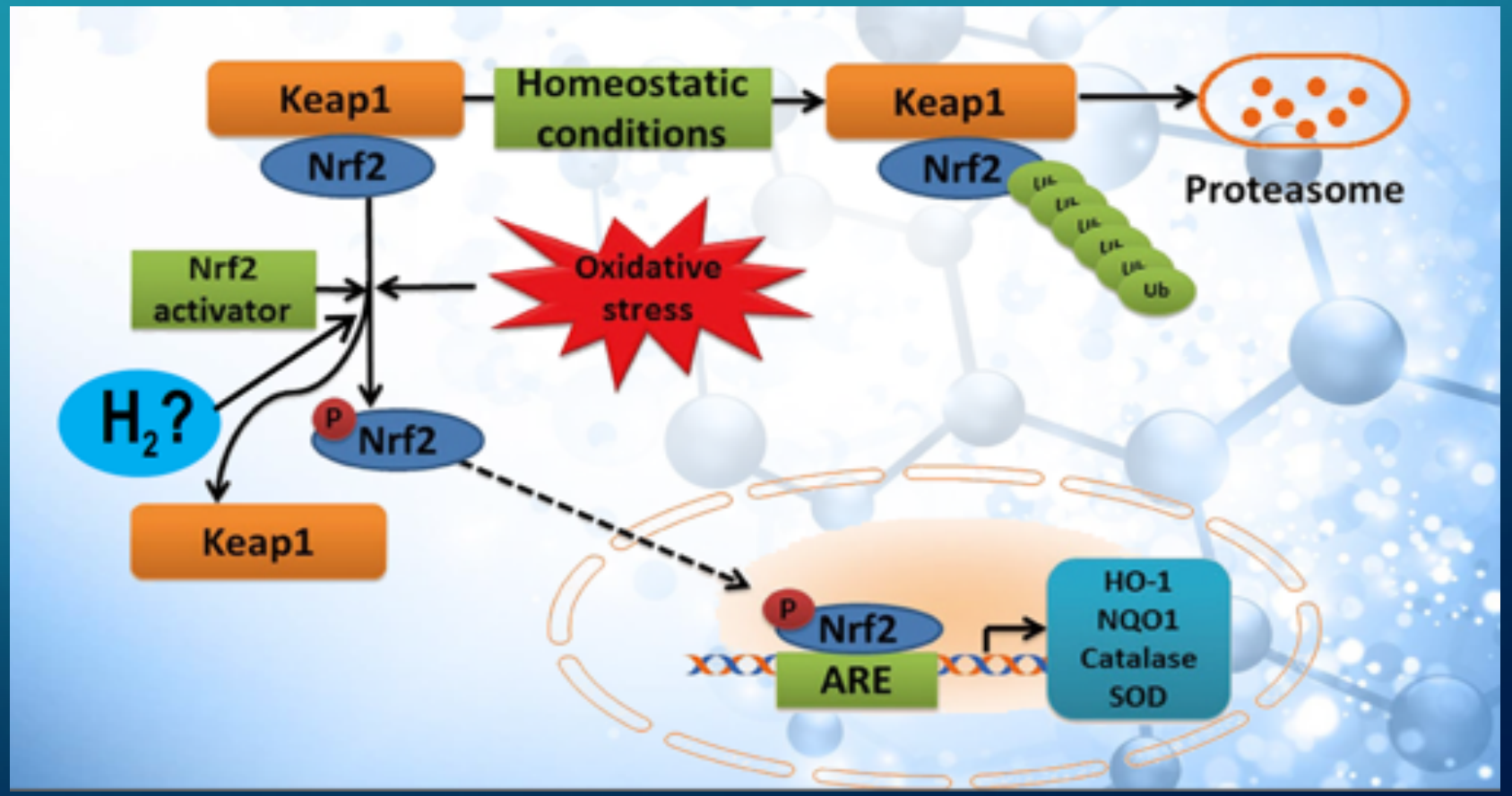
Hydrogen gas can activate the Nrf2 pathway, leading to increased production of SOD, GSH, CAT, etc.



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

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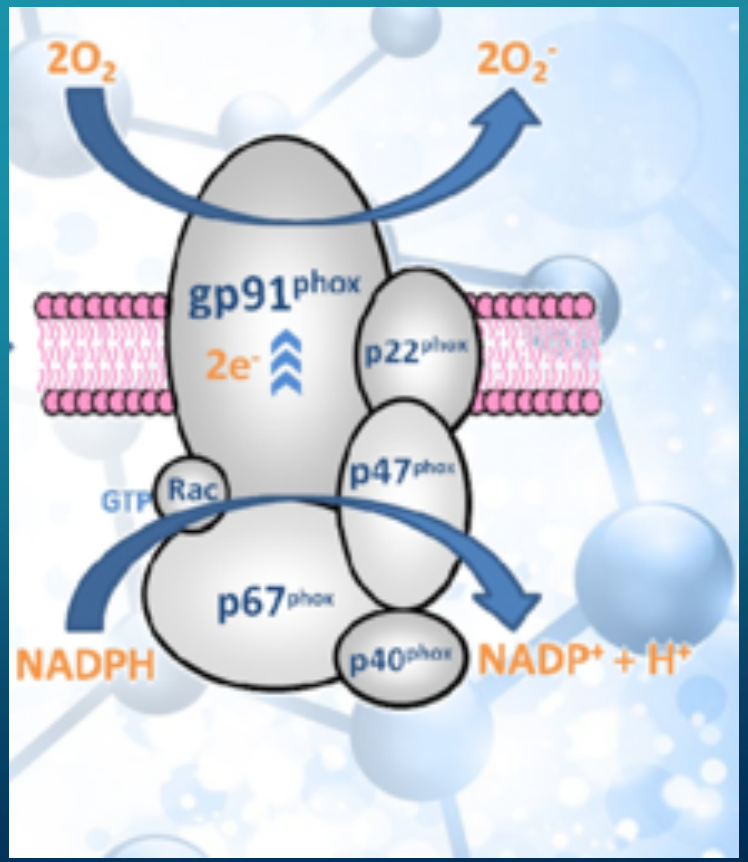
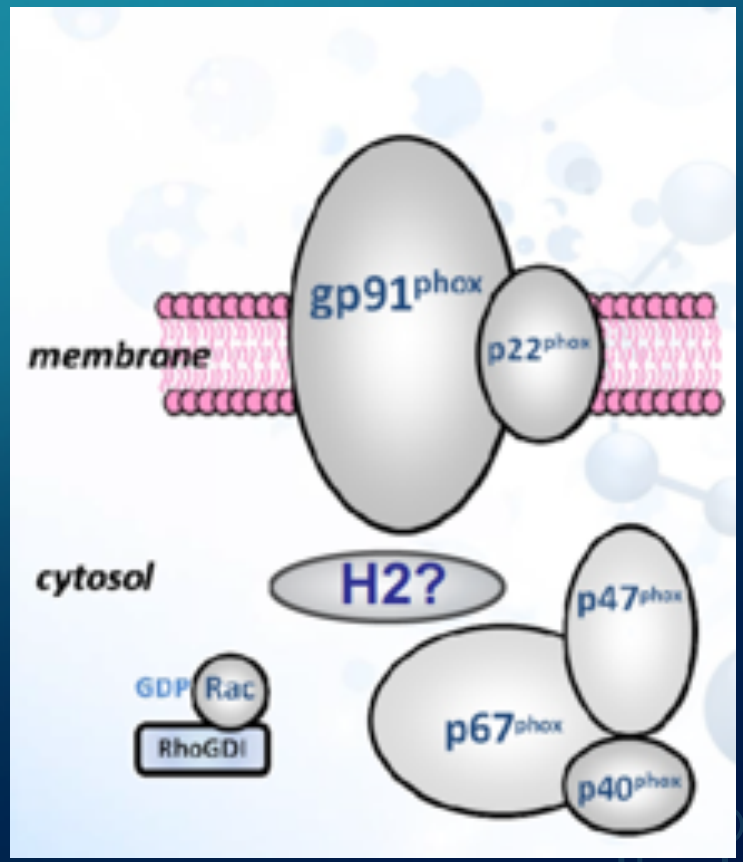
H_2 prevents ROS formation by cell modulation

Fig. is example only.

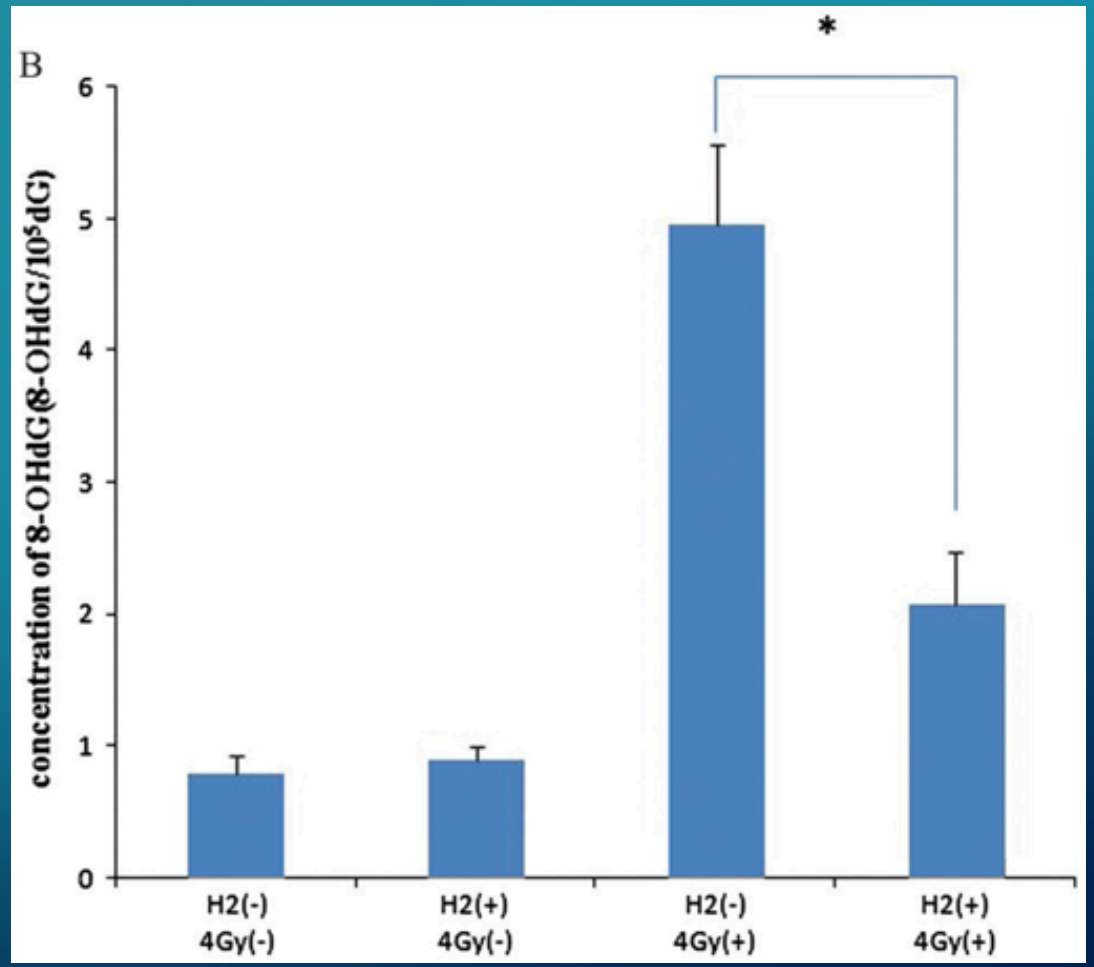
I. Tomohiro, et al. Biochem. Biophys. Res. Commun. 411.1 (2011): 143-149.

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





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.

Superiority of Hydrogen compared to other antioxidants

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US National Library of Medicine
National Institutes of Health

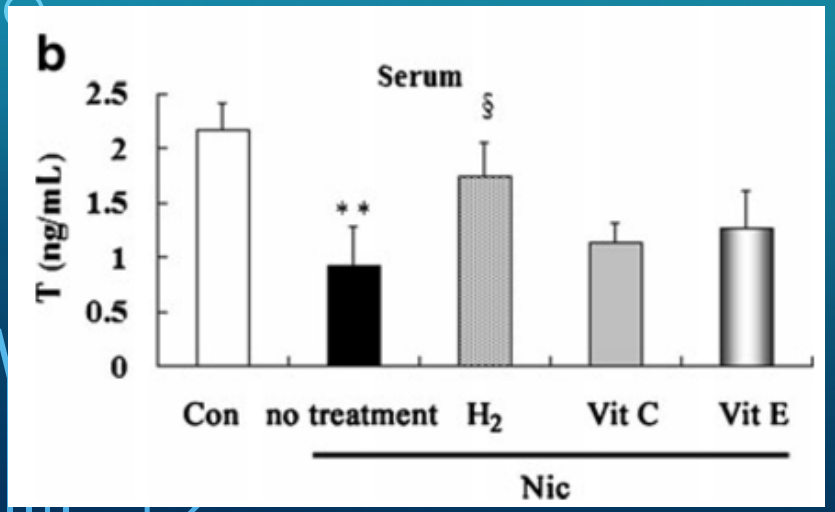
PubMed | Sea

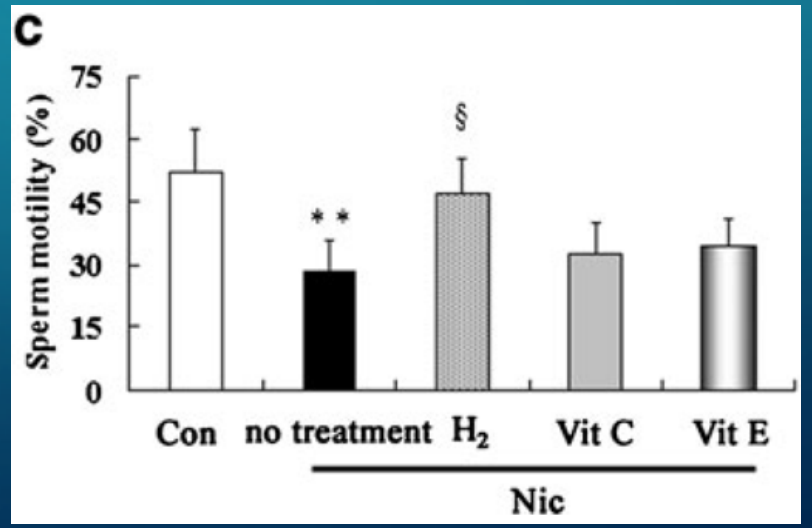
Advanced

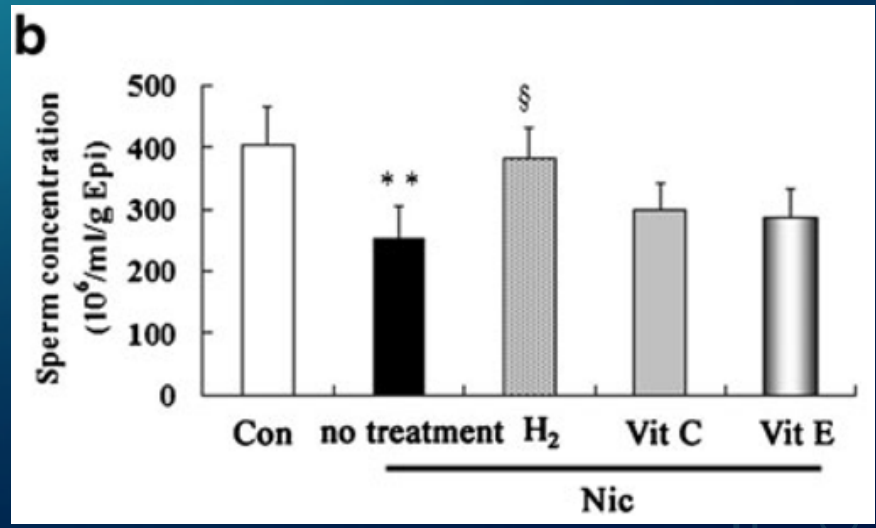
Abstract Send to:

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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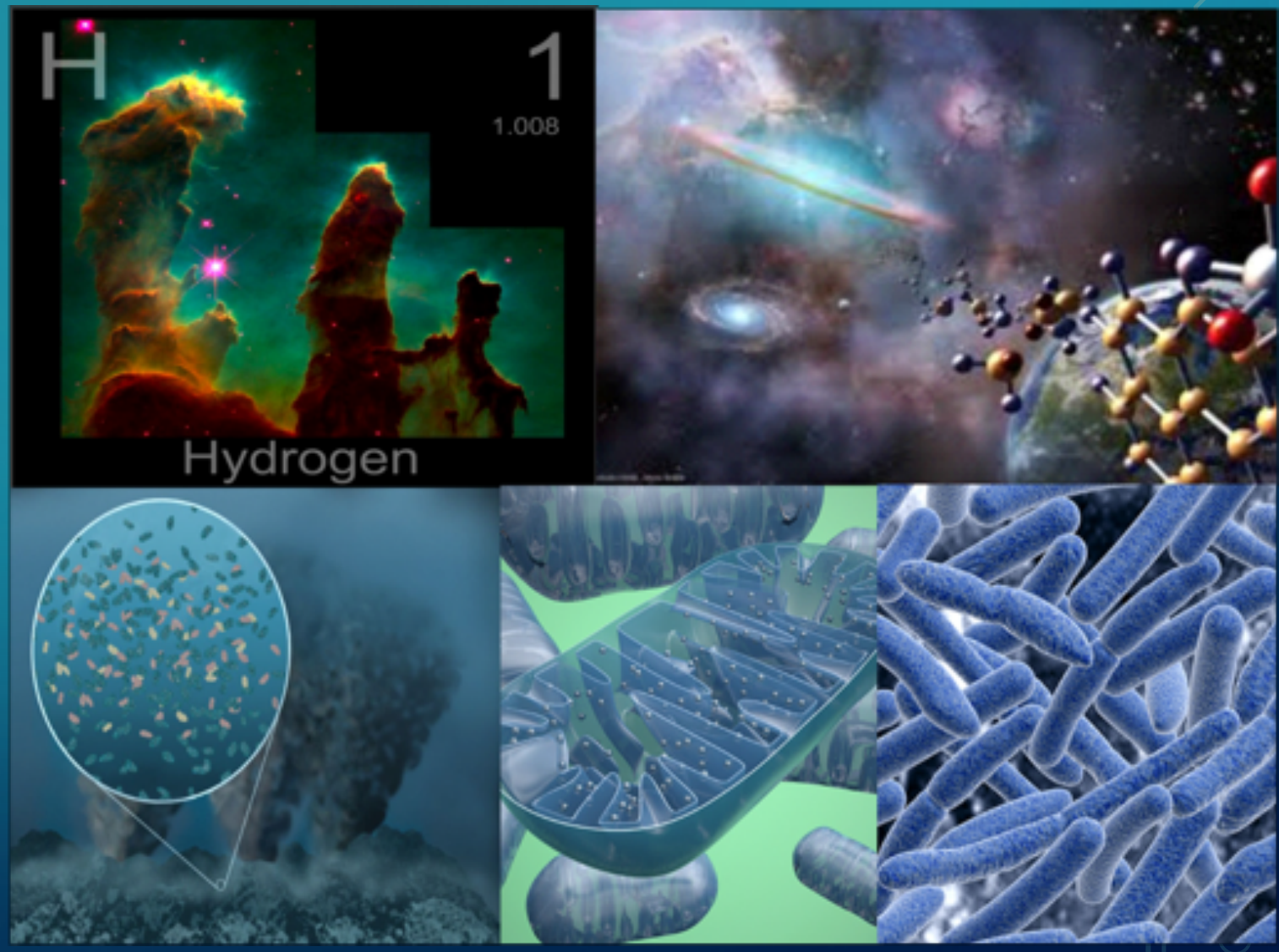
Perhaps the reason H_2 exerts a biological effect is because H_2 has been intimately involved in:

- *The origins of the Universe*
- *The genesis of life*
- *The evolution of eukaryotes (plant & animal cells)*



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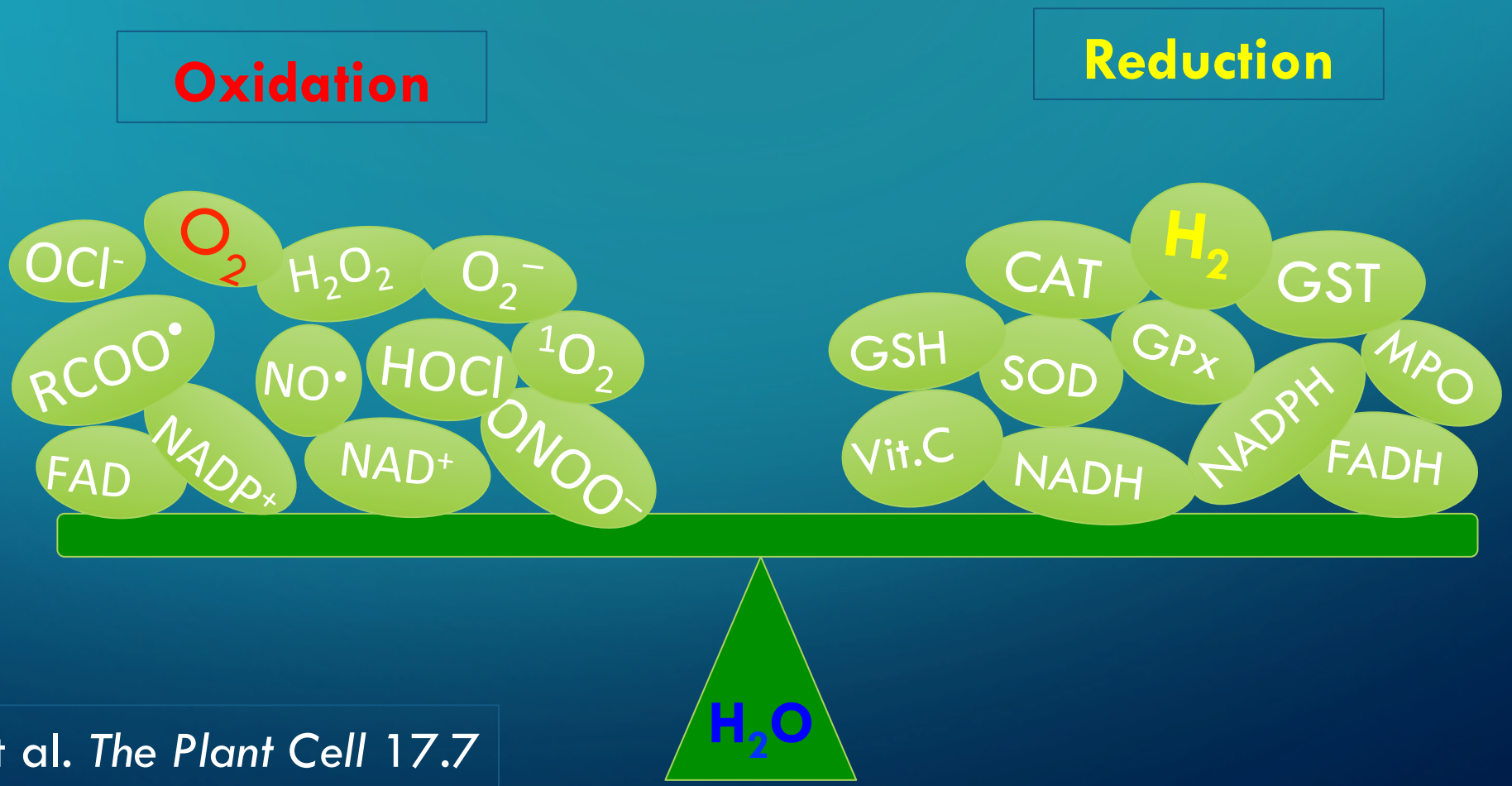
Life is balanced between Oxidation and Reduction



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

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Oxidative stress

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.

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

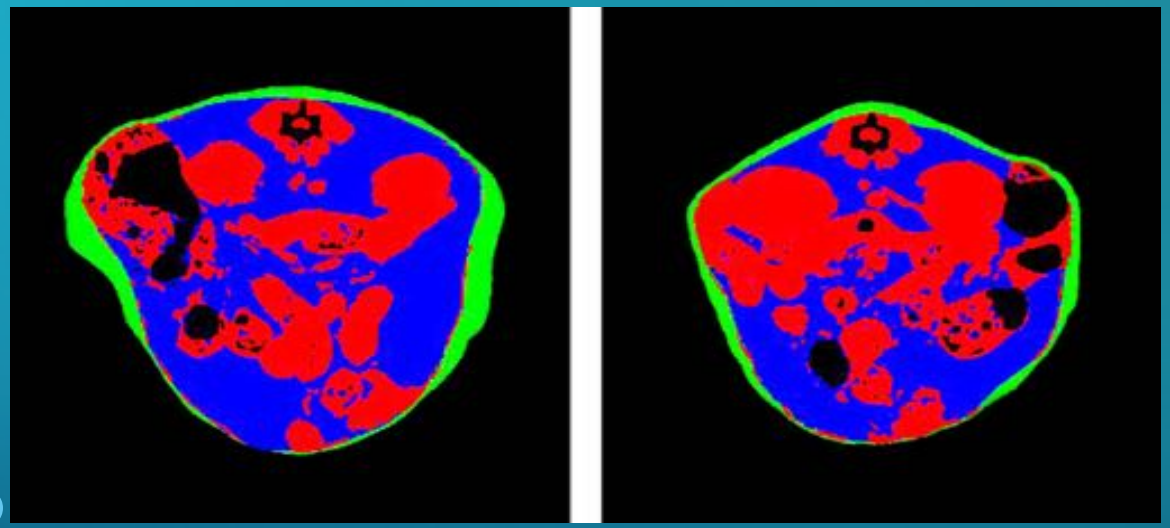
Kirstein, J. The EMBO Journal (2015) 34: 2334–2349

Redox dysregulation

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

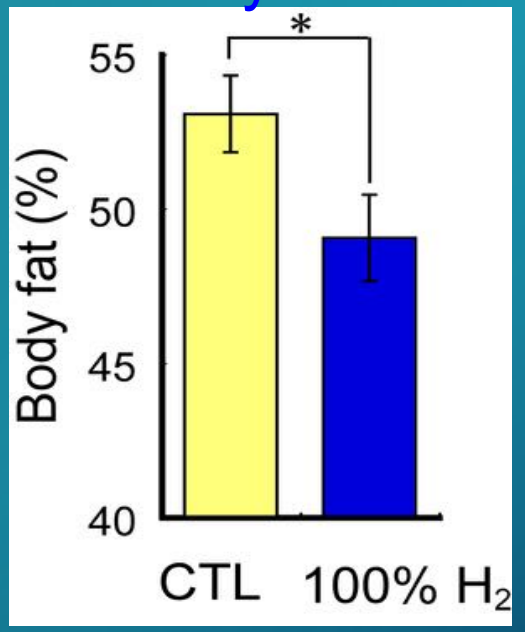
H_2 suppresses obesity

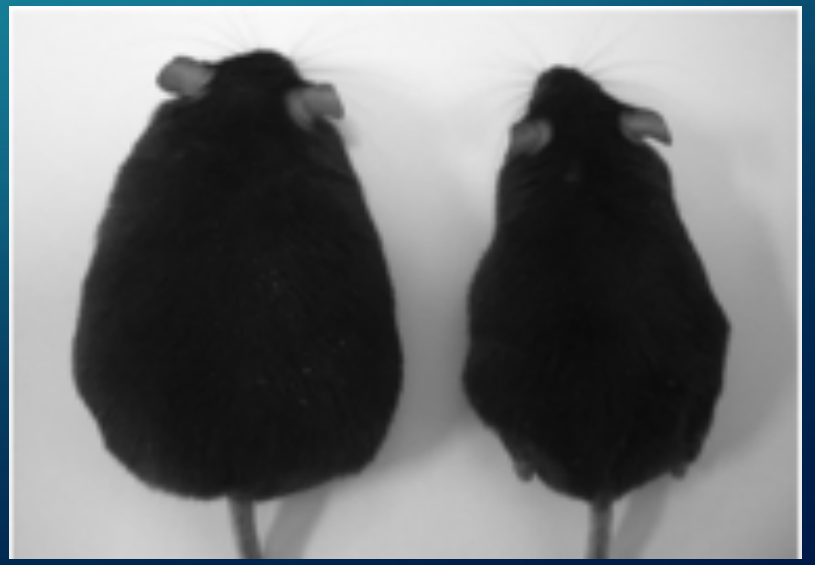
CTL H_2



Red: muscle
Blue: internal fat
Green: subcutaneous fat

Body fat





Kamimura, N., et al. *Obesity* 19.7 (2011): 1396-1403.

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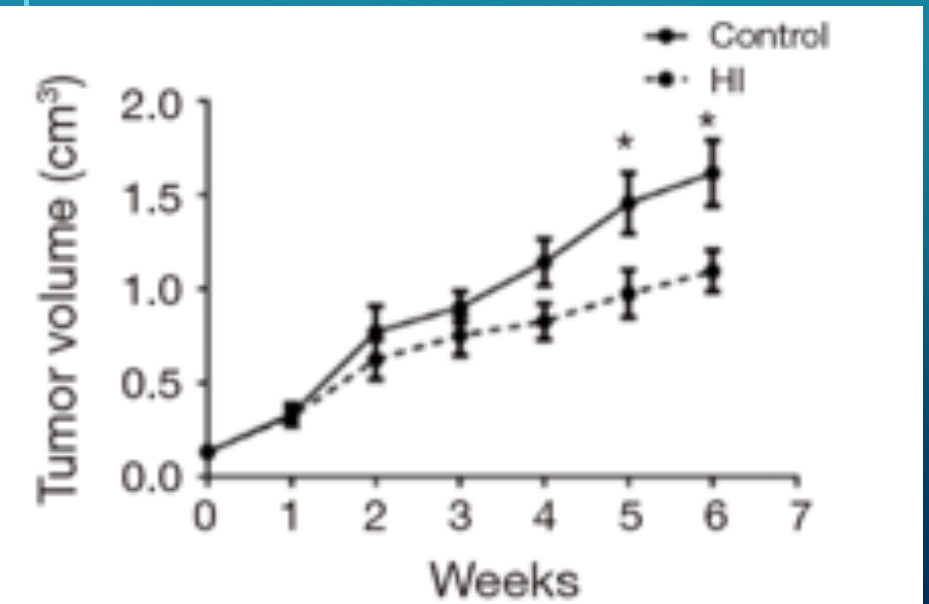
TCR TRANSLATIONAL CANCER RESEARCH
ADVANCES CLINICAL MEDICINE TOWARD THE GOAL OF IMPROVING PATIENTS' QUALITY OF LIFE

Original Article

Therapeutic potential of molecular hydrogen in ovarian cancer

Lei Shang[1,2#], Fei Xie[1,2#], Jiala Li[1,2], Yating Zhang[1,2], Mengyu Liu[1,2], Pengxiang Zhao[1,2], Xuemei Ma[1,2], Tyler W. Lebaron[3]



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www.nature.com/scientificreports

Likely mediated by inhibiting the hypothalamic-pituitary-adrenal axis and inflammatory responses to stress.

Hydrogen helps prevent autism

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US National Library of Medicine
National Institutes of Health

PMC Advanced Journal list

Journal List › Front Behav Neurosci › v.12; 2018 › PMC6087877

frontiers in Behavioral Neuroscience

Front Behav Neurosci. 2018; 12: 170.
Published online 2018 Aug 6. doi: [10.3389/fnbeh.2018.00170]
PMCID: PMC6087877
PMID: 30127728

Hydrogen-Rich Water Ameliorates Autistic-Like Behavioral Abnormalities in Valproic Acid-Treated Adolescent Mice Offspring

Qingjun Guo,[1,†] Xi Yin,[2,†] Meng Qiao,[3,†] Yujiao Jia,[3] Dandan Chen,[3] Juan Shao,[4] Tyler W. Lebaron,[5] Yuan Gao,[6,7] Haishui Shi,[6,7,8,9,*] and Bin Jia[7,10,*]

Front Behav

Sympathetic nerve activation and mood/anxiety (K6) were decreased by HRW

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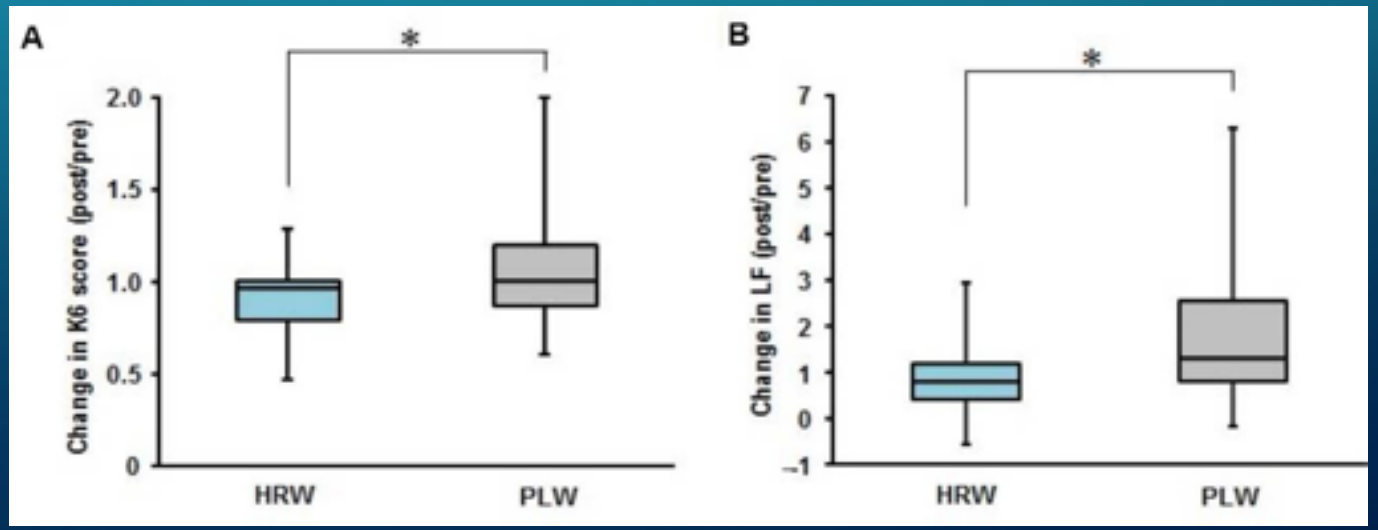
US National Library of Medicine
National Institutes of Health

PMC Advanced Journal list

Journal List › Med Gas Res › v.7(4); Oct-Dec 2017 › PMC5806445

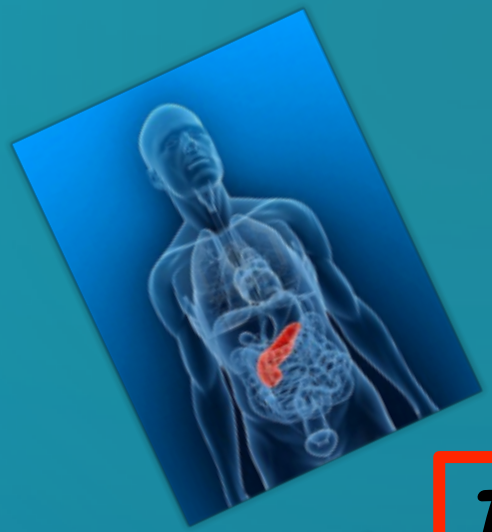
Med Gas Res. 2017 Oct-Dec; 7(4): 247–255.
Published online 2018 Jan 22. doi: [10.4103/2045-9912.222448]
PMCID: PMC5806445
PMID: 29497485

Hydrogen-rich water for improvements of mood, anxiety, and autonomic nerve function in daily life



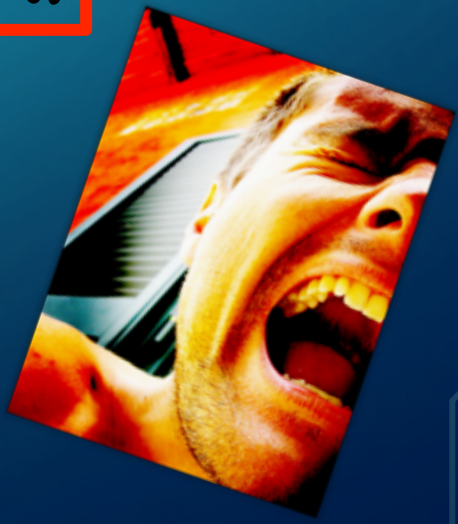
Hydrogen ameliorates inflammation

- Arthritis
- Pancreatitis
- Hepatitis
- Asthma
- Colitis
- Sepsis
- Pain



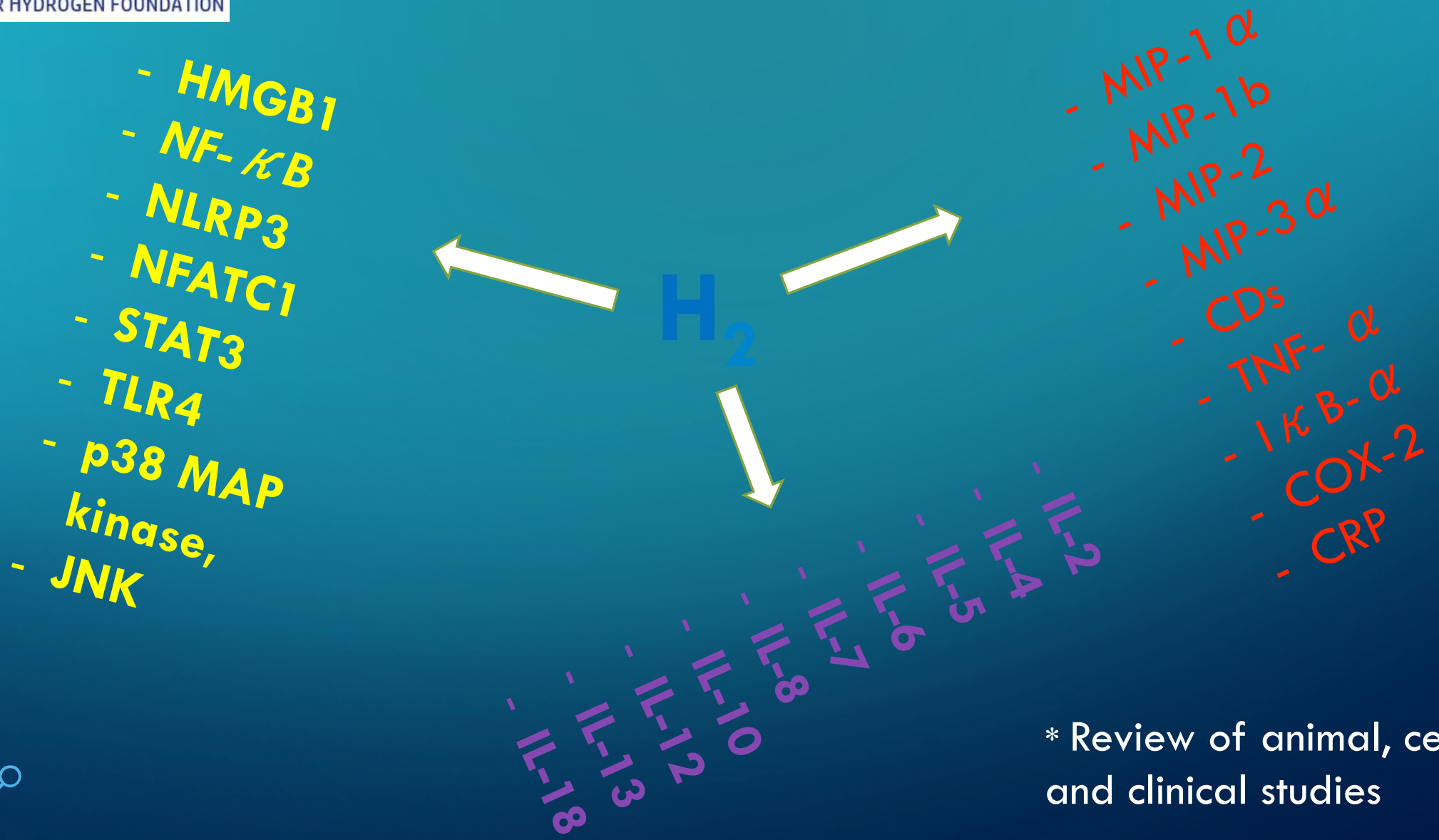
INFLAMMATION!





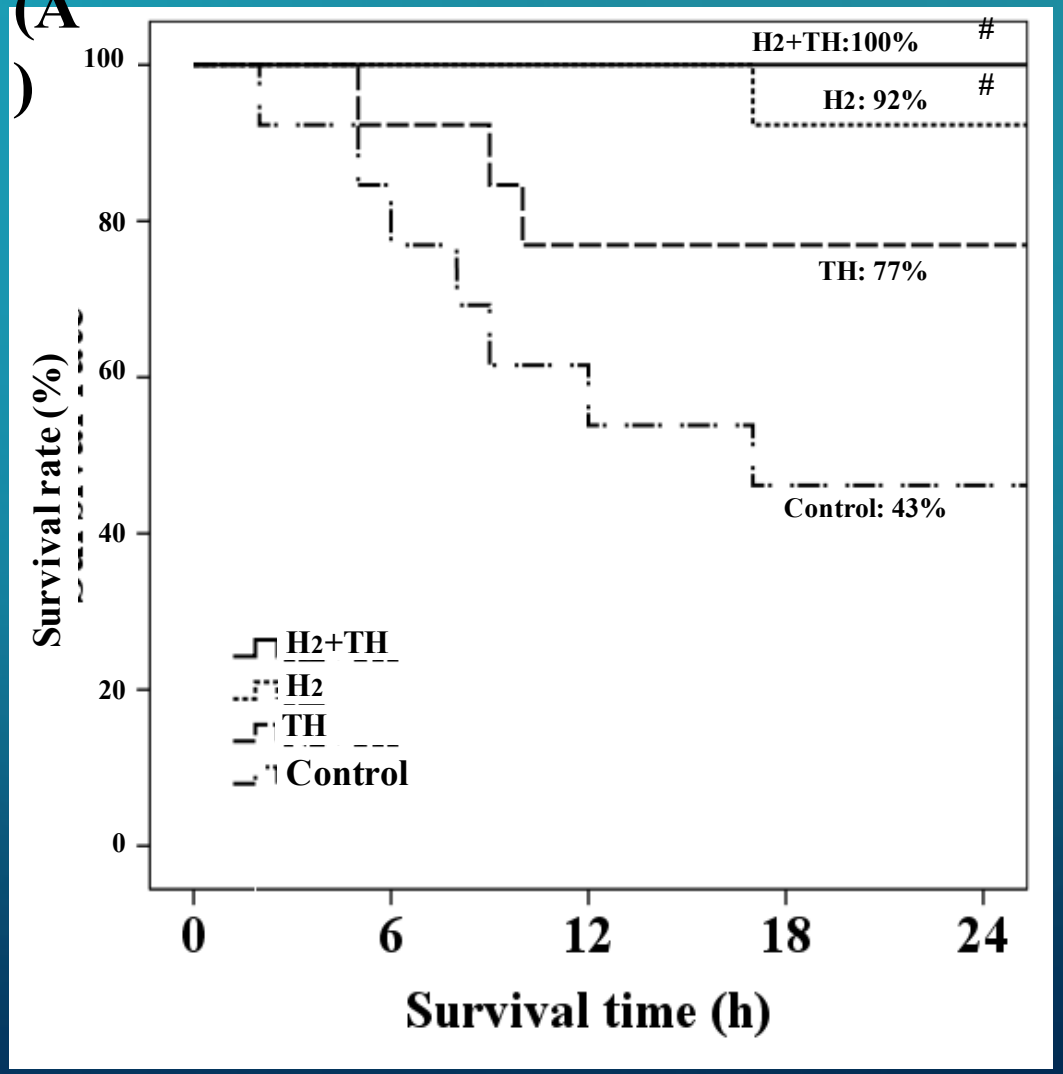
Xie, Keliang, et al. *Shock* 34.5 (2010): 495
Hong, Y.et al. : Exp Ther Med 11.6 (2016): 2590.

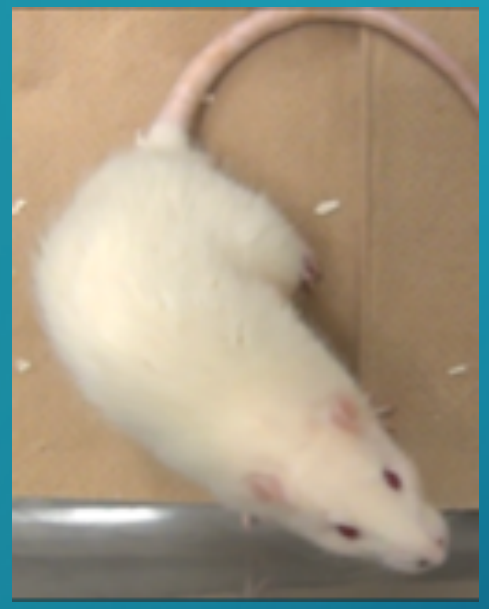
Hydrogen ameliorates inflammation



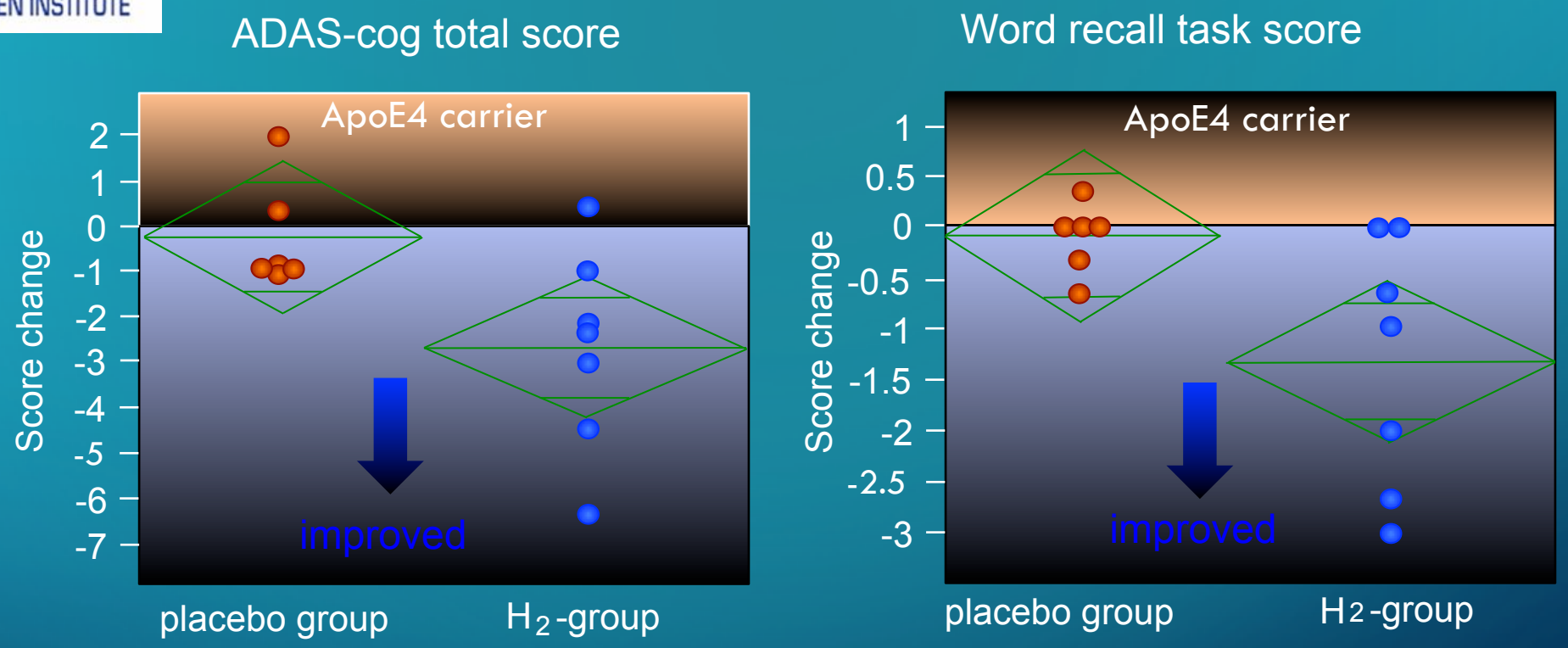
* Review of animal, cell, tissue and clinical studies

Post-Cardiac Arrest





H_2 water improved MCI with APOE4 genotype



Nishimaki, K., et al 2017. *Current Alzheimer research.*

Graphical abstract

Subjects with MCI carrying the APOE4 genotype were improved in ADAS-cog by drinking H_2-dissolved water for 1 year as assessed by a randomized double-blind placebo-controlled clinical study.

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J Stroke Cerebrovasc Dis. 2017 Nov;26(11):2587-2594. doi: 10.1016/j.jstrokecerebrovasdis.2017.06.012. Epub 2017 Jun 29.

Hydrogen Gas Inhalation Treatment in Acute Cerebral Infarction: A Randomized Controlled Clinical Study on Safety and Neuroprotection.

Ono H[1], Nishijima Y[2], Ohta S[3], Sakamoto M[2], Kinone K[2], Horikosi T[2], Tamaki M[4], Takeshita H[2], Futatuki T[2], Chishi W[2], Ishiguro T[2], Okamoto S[2], Ishii S[2], Takanami H[5].

Author Information

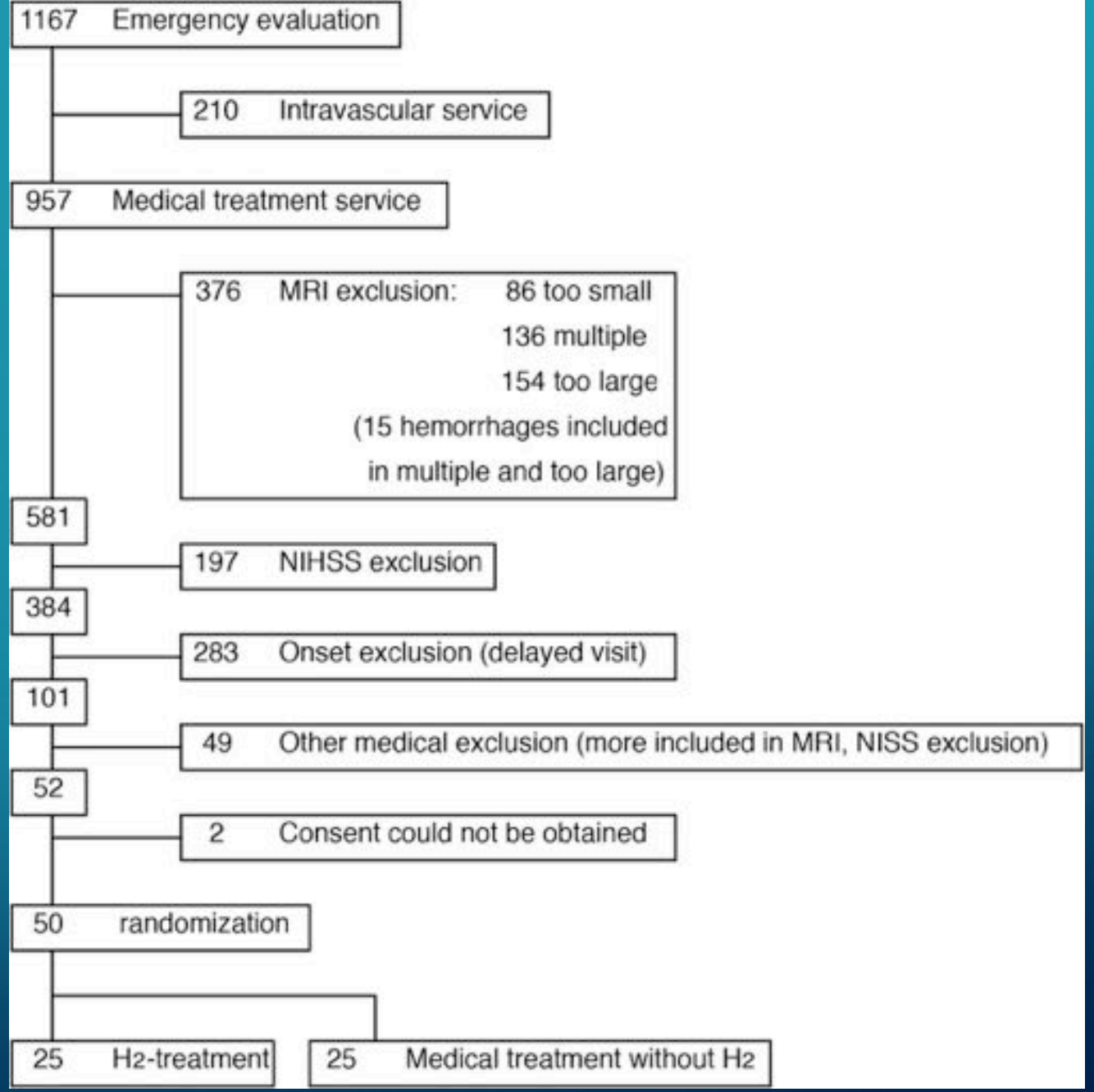
Abstract

BACKGROUND: Molecular hydrogen (H_2) acts as a therapeutic antioxidant. Inhalation of H_2 gas (1-4%) was effective for the improvement of cerebral infarction in multiple animal experiments. Thus, for actual applications, a randomized controlled clinical study is desired to evaluate the effects of inhalation of H_2 gas. Here, we evaluate the H_2 treatment on acute cerebral infarction.

METHODS: Through this randomized controlled clinical study, we assessed the safety and effectiveness of H_2 treatment in patients with cerebral infarction in an acute stage with mild- to moderate-severity National Institute of Health Stroke Scale (NIHSS) scores (NIHSS = 2-6). We enrolled 50 patients (25 each in the H_2 group and the control group) with a therapeutic time window of 6 to 24 hours. The H_2 group inhaled 3% H_2 gas (1 hour twice a day), and the control group received conventional intravenous medications for the initial 7 days. The evaluations included daily vital signs, NIHSS scores, physical therapy indices, weekly blood chemistry, and brain magnetic resonance imaging (MRI) scans over the 2-week study period.

RESULTS: The H_2 group showed no significant adverse effects with improvements in oxygen saturation. The following significant effects were found: the relative signal intensity of MRI, which indicated the severity of the infarction site, NIHSS scores for clinically quantifying stroke severity, and physical therapy evaluation, as judged by the Barthel Index.

CONCLUSIONS: H_2 treatment was safe and effective in patients with acute cerebral infarction. These results suggested a potential for widespread and general application of H_2 gas.



Journal of Stroke and Cerebrovascular Diseases 2017 26, 2587-2594DOI: (10.1016/j.jstrokecerebrovasdis.2017.06.012)

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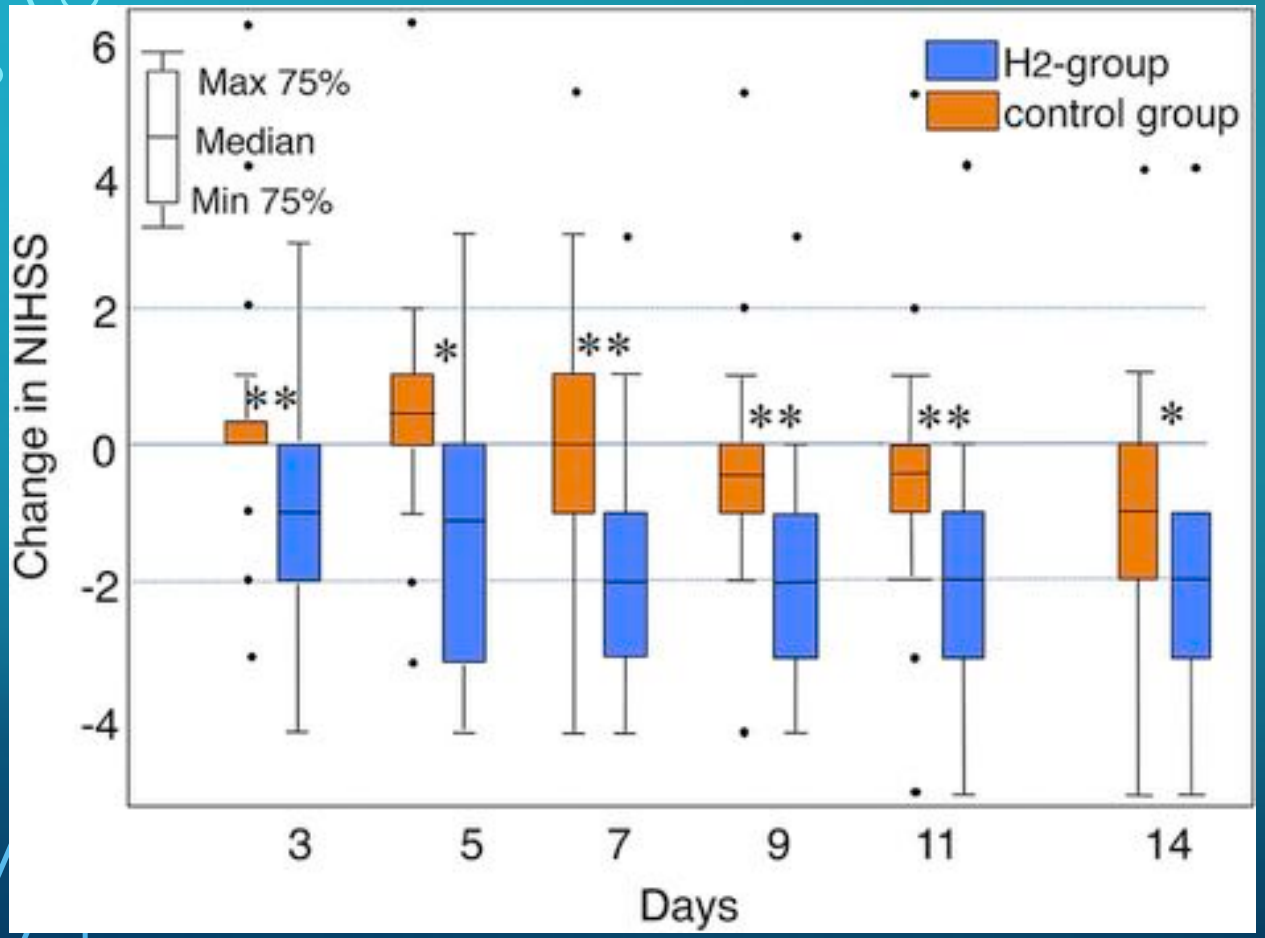

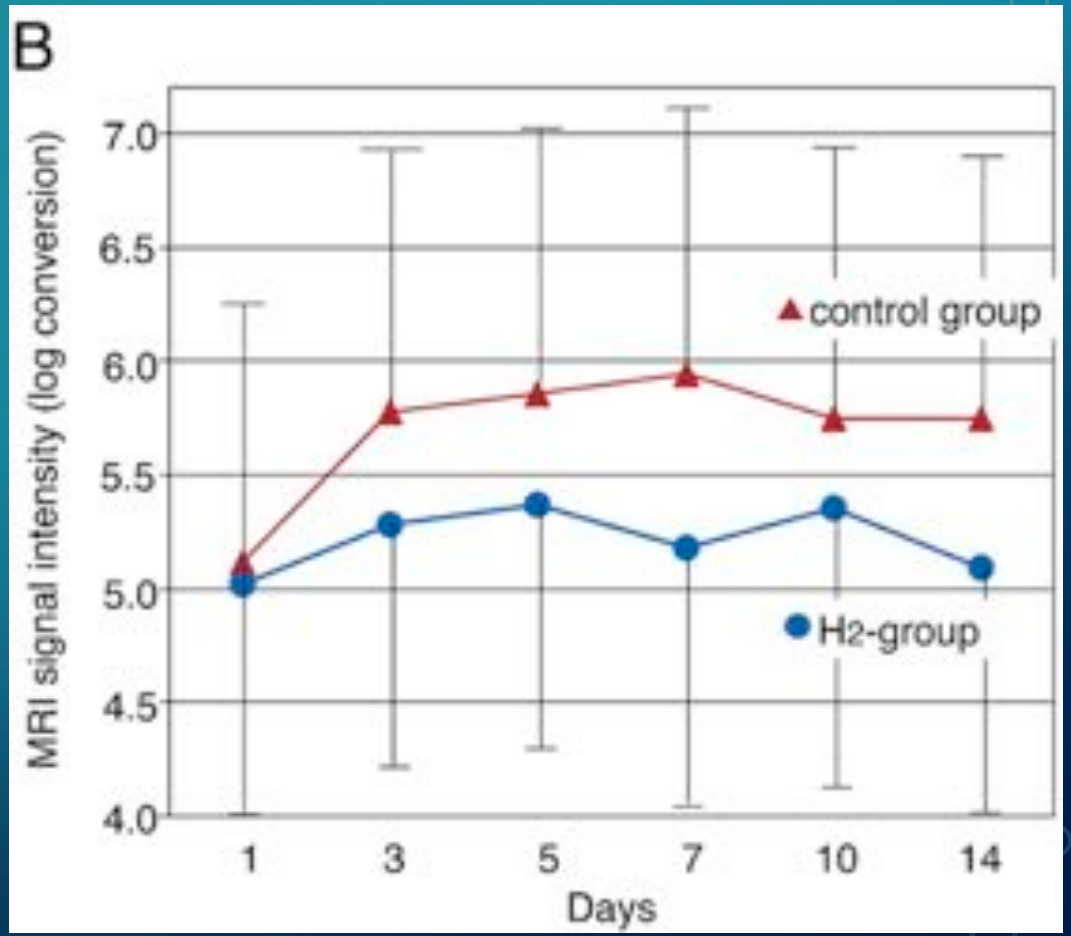

Journal of Stroke and Cerebrovascular Diseases 2017 26, 2587-2594DOI: (10.1016/j.jstrokecerebrovasdis.2017.06.012)

We need more studies

- Elucidate molecular mechanisms
- Which diseases most effective
- Dosing protocol/strategies
- Concentration
- Method of administration (comparisons)
  - Inhalation
  - Drinking
  - Intravenous
  - Bathing

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www.MolecularHydrogenInstitute.com

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Tyler W. LeBaron, Executive Director MHI