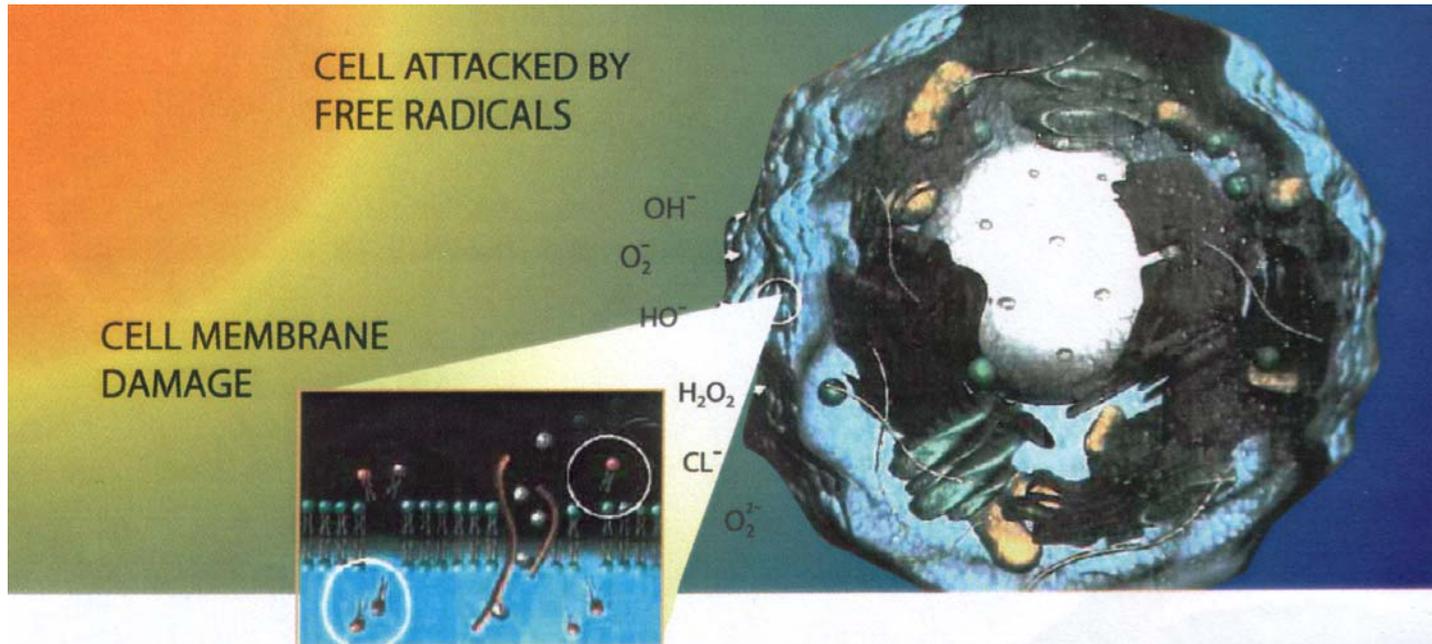


# Anti-Aging Medicine World Conference

April 10, 11, 12 – 2008 - Paris



**Speaker: Serge Jurasunas**

**Theme: Oncology how to live longer despite cancer**

**Topic: Oxidative stress and cancer – antioxidant therapy**

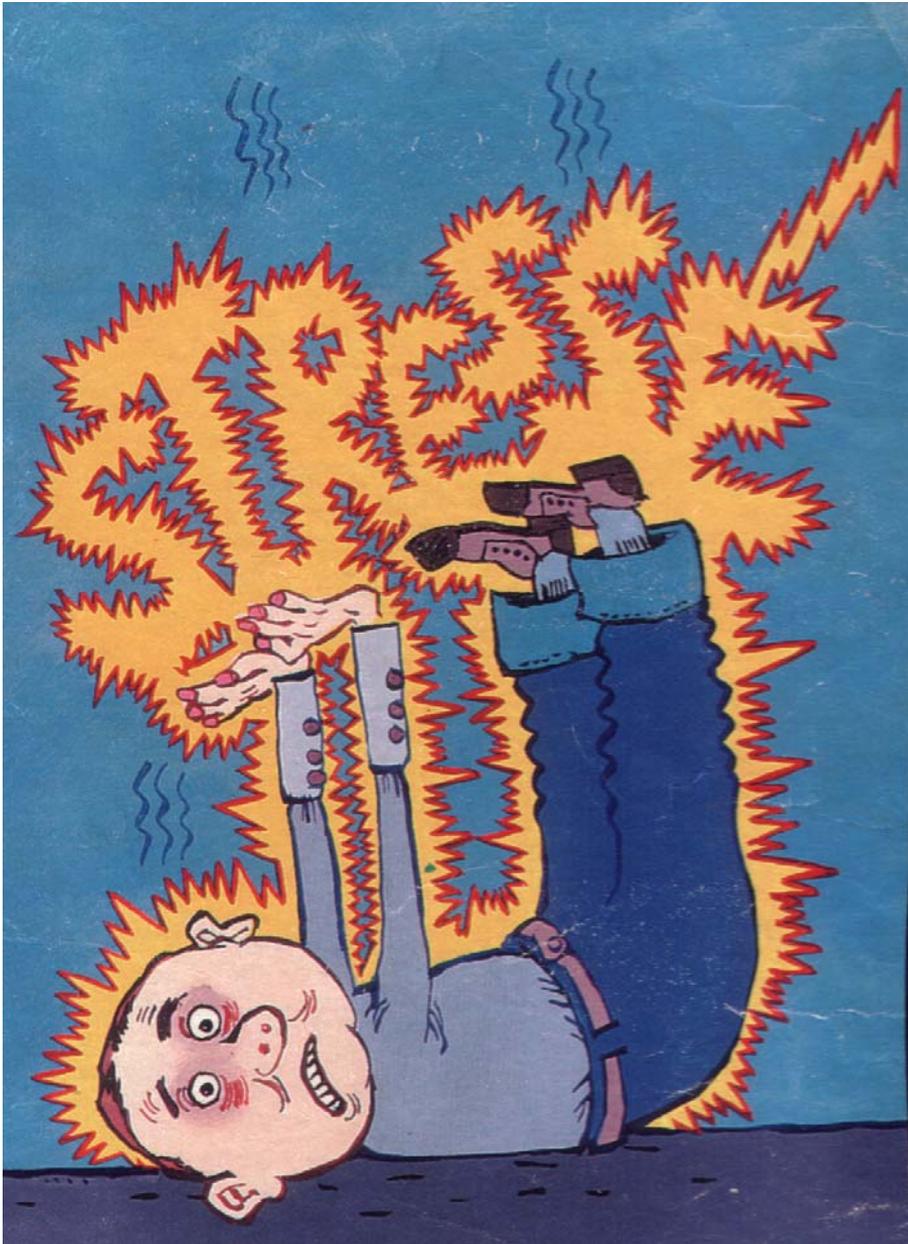
**Date/time: Saturday 12th April 2008 – 16.30-16.55 P.M.**

## INTRODUCTION

- Considerable evidence support the contention that excessive oxidative stress interfere with the cytotoxicity of antineoplastic agents.

- New evidence suggest that dietary antioxidants supplementation can influence the response of chemotherapy by modulating excessive ROS activity increase the effectiveness, reduce adverse effects,

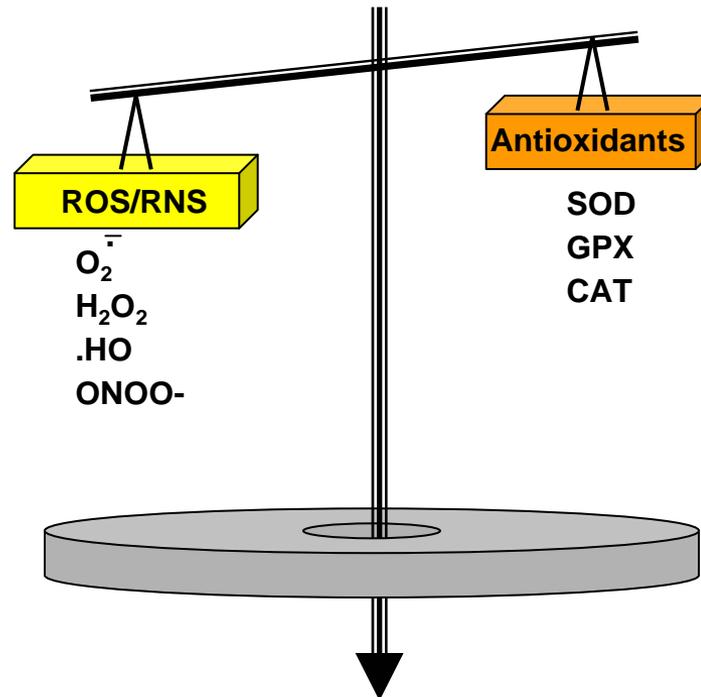
**increasing Quality of Life.**



**He was diagnosed with  
a cancer.**

**He looks like been  
under oxidative stress**

# Oxidative Stress



Imbalance between oxidants and antioxidants in favor to oxidants

Lost of proliferation  
Apoptosis resistance.

Metastasis and  
angiogenesis.

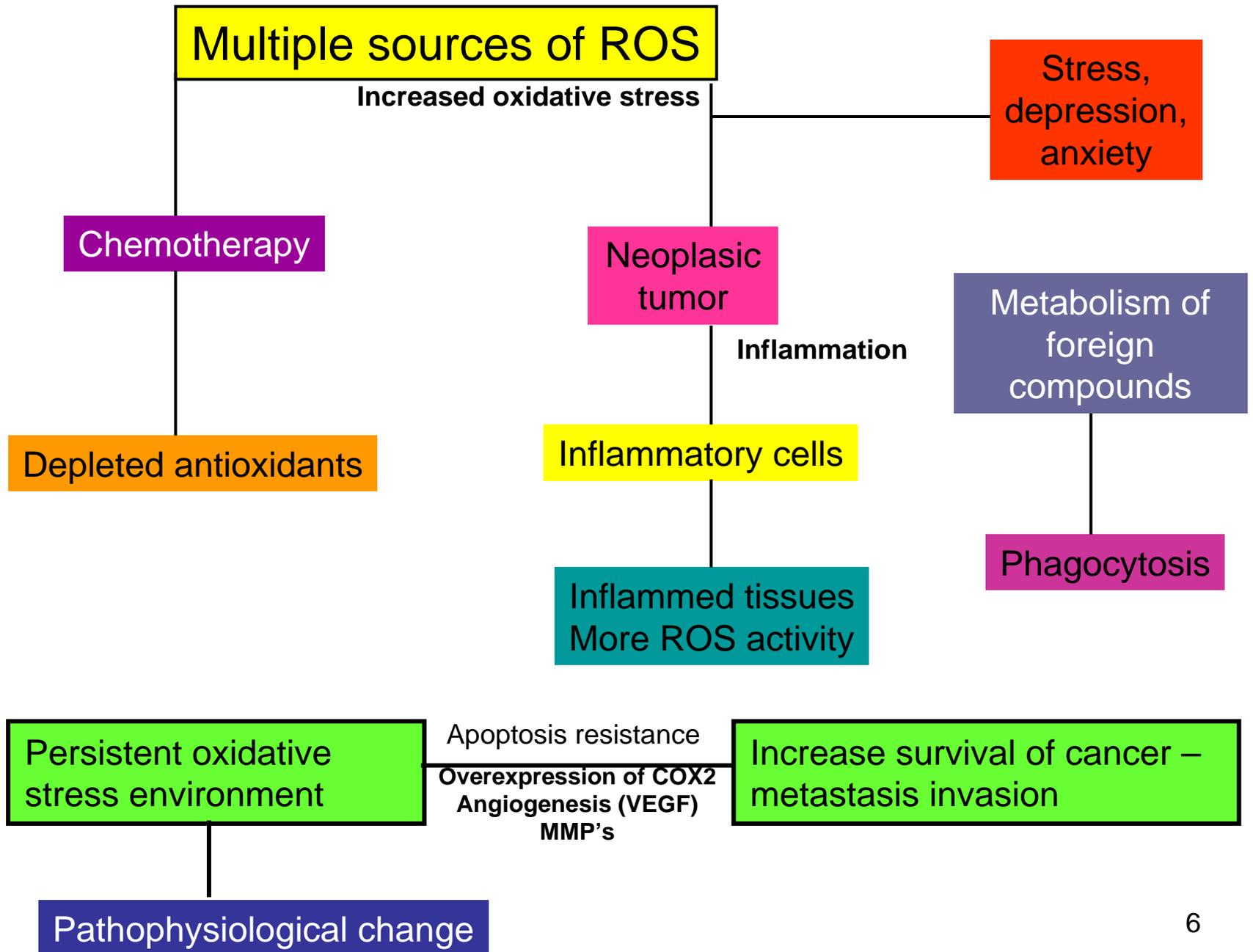
**Oxidative stress is caused by cellular excess of ROS/RNS activity and decreasing endogenous antioxidants defence.**

**Damage to DNA, protein, lipids and macromolecules.  
Interfere with many signal transduction pathway.**

## **Two main problems of chemo/radiation:**

- Toxicity to normal cells
- Failure to kill cancer cells

- Promote highly toxic free radicals to increase oxidative stress.
- Strong adverse effects in 80% of patients.
- Reduce antioxidants concentration levels in blood plasma.
- Vitamins – antioxidants are critical to active immune cells such as NK cells usually lower in cancer patients.
- Depleted antioxidants = Multiple source of ROS contribute to persistent stress environment that results in resistant cells to chemotherapy metastasis invasion, angiogenesis.

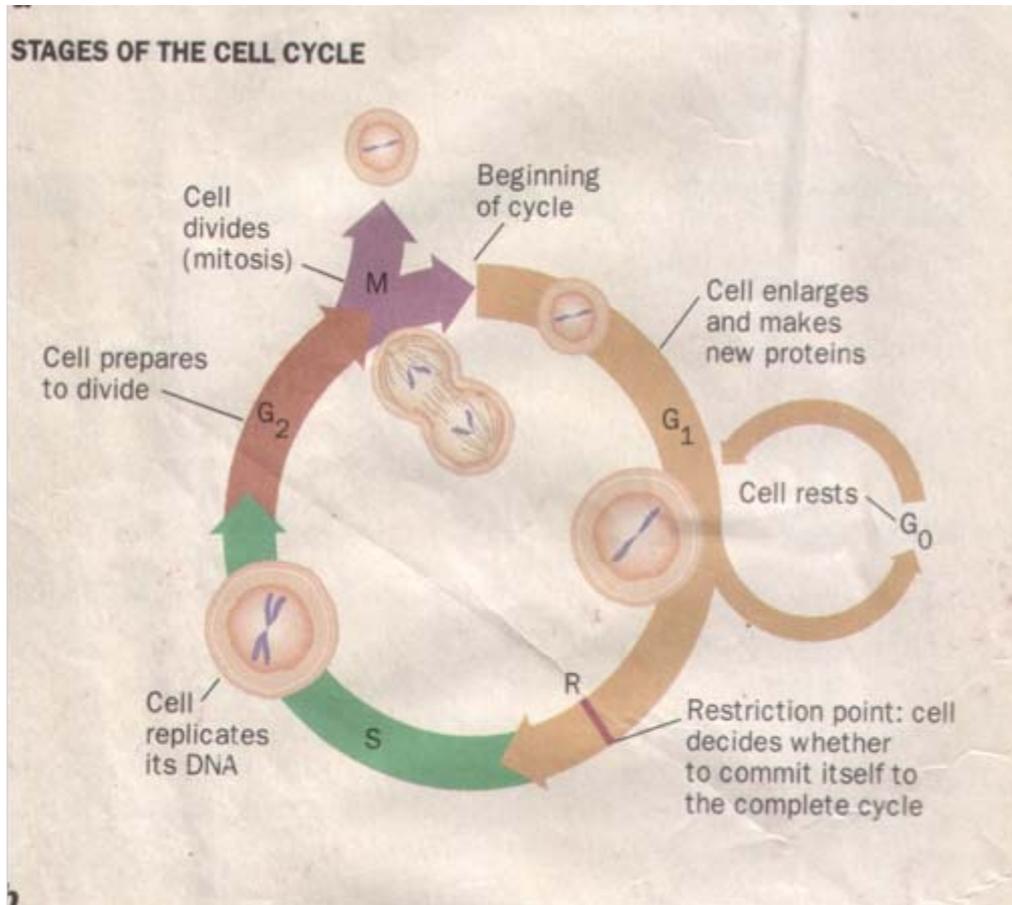


# **Oxidative stress interferes with the length of the cell's progression through the cell cycle.**

- 1- Anticancer drugs are cytotoxic only when tumor cells divide quickly.**
- 2- Rate of DNA synthesis and the rate of cell proliferation are related to the degree of lipid peroxidation.**
- 3- Oxidative stress from chemotherapy results in lipid peroxidation of cancer cells acting as negative growth regulator to slow down or arrest cell growth.**

# Interferes with the chemotherapy effectiveness

## Consequence:



-Oxidative stress prolong the G<sub>1</sub> phase and increase cancer cell resistance.

- Cancer cells may enter the nonproliferation dormant G<sub>0</sub> Phase for prolonged periods of time.

-Reenter the division after chemotherapy is completed unresponsive to chemotherapy. (active their DNA repair damage)

- Oxidative stress impair apoptosis by inhibition of caspases due to oxidation of their thiol groups by oxidants.

- Reduced environment.

# Antioxidants that prevent lipid peroxides and reverse the inhibitory effect of oxidative stress on cell proliferation. (1)

- Vitamina E** Chain breaking lipid soluble antioxidant  
Prevent lipid peroxidation of PUFA  
Enhance the cytotoxicity effects of several anticancer agents
- Vitamin C** Water soluble antioxidants  
Prevent lipid peroxidation  
Enhance the cytotoxicity effects of several anticancer agents
- Beta-carotene** Lipid soluble antioxidants  
Enhance the cytotoxicity effects of several anticancer agents
- Coenzyme Q10** Lipid soluble antioxidant  
Scavenge lipid radical within biological membrane  
Play an important role in preventing lipid peroxidation damage of mitochondria membrane
- Superoxide Dismutase SOD** – A key important antioxidant enzyme that also prevent or reduce lipid peroxidation

# The benefit of antioxidant in cancer Therapy

(Oncol Feb. 2002 vol.16-2)

## **Antioxidants provide therapeutic advantages by enhancing antineoplastic agents**

- Reduce or prevent from excessive ROS activity and therefore from damaging effects to normal cells.
- Reduce or prevent lipid peroxidation (increase the proliferation rate of cancer cells).
- Inhibit COX 2 activity – inhibit angiogenesis – (decrease tumor resistance).
- Selectively induce apoptosis over necrosis.
- Stimulate or restore the immune system – enhance immunologic elimination of cancer cells.
- Prevent oxidation of phagocytosis – Prevent from infection.

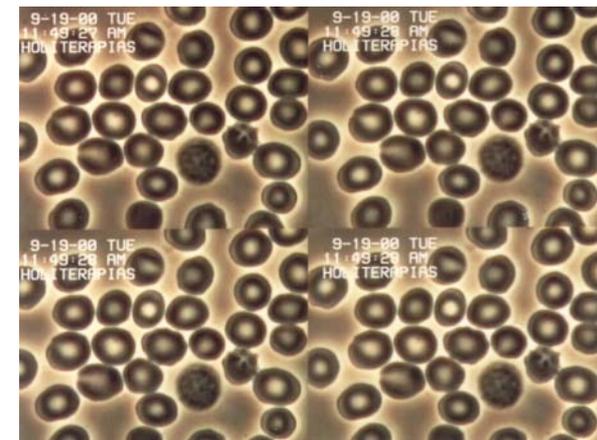
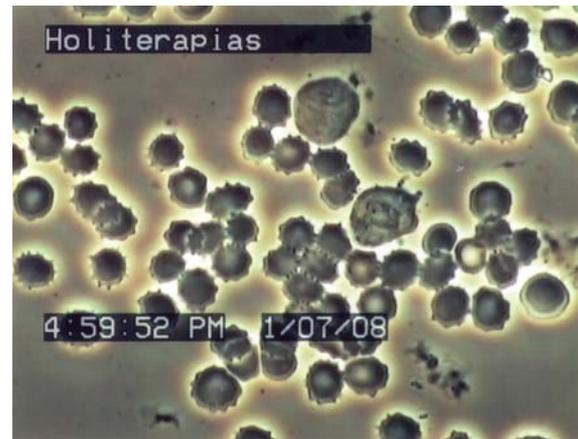
**Interfere with signal transduction regulation at different levels in a way to activate tumor suppressor genes.**

# Oxidative Stress Assessment

**Oxidative stress can be from middle strong or very strong condition.**

The technic:           Peripheral blood analysis (HRBM)  
                              Multi-phase optical microscopic system with high definition (40 x 18.000)

Target:    High free radicals activity results on significative morphofunctional alteration of red blood cells indicating oxidative status and antioxidant defenses for the whole organism (1)



Serge Jurasunas – Holiterapias 2008

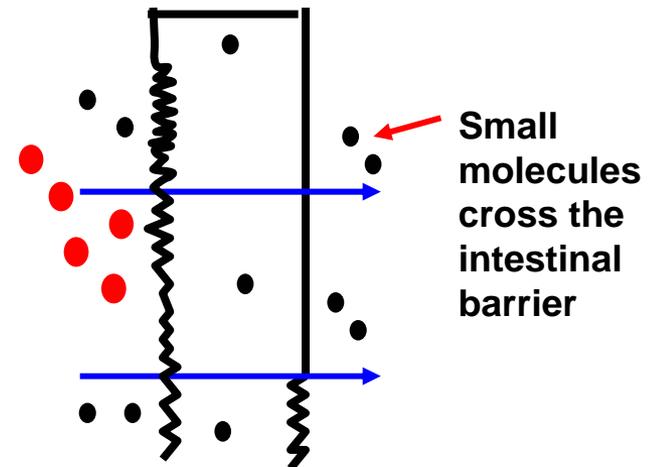
# A new antioxidant therapy – Anoxe

## Targeting of cancer inflammatory mediators

**The compound:** Low molecular weight antioxidant compound having a SOD molecule like activity. Dietetic supplementation made from small molecules extracted from modified selected vegetables, herbs and seeds rich in antioxidants and with no toxicity.

**Presentation:** granule sachets of 3g for oral intake to preserve the fully active antioxidants enzyme.

**Characteristics:** The compound is quickly absorbed by the body and highly effective against ROS activity and lipid peroxide.



# Anoxe – Low molecular antioxidant compound SOD like activity – 7.3 x 1,000 unit/g

Plants/herbs	Active Ingredients Full spectrum of antioxidant	Pharmacological effects
<p><b><u>Vegetable basis</u></b></p> <p>Soya bean Japanese darkon raddish Rice bran Green tea Wheat germ Yuzu orange Hatomugi Sesame seed</p>	<p>Vitamin A.C.E. Beta-carotene Catalase Glutathione Riboflavine Polyphenols Flavonoids Tannins Catechins</p>	<p>Decrease ROS activity. Strong anti-inflammatory property. In vitro – inhibit COX1-COX2 activity Strong oxido-reduction property. In vitro decrease Tyrosinase activity. May inhibit NF.KB</p>
	<p>Balance Antioxidants in blood circulation. Very strong antioxidant property.</p>	<p>Prevent or decrease lipid peroxidation. Antibacterien. Protect RBC – WBC from oxidation.</p>
<p>Modified to extract low molecular antioxidants fully active</p>	<p>Very quick absorption into the body</p>	<p>Anti-bacterial/fungal activity Strength immune function.</p>

# Effects of Anoxe over lipid peroxides in presence of DHA and measured with TBA

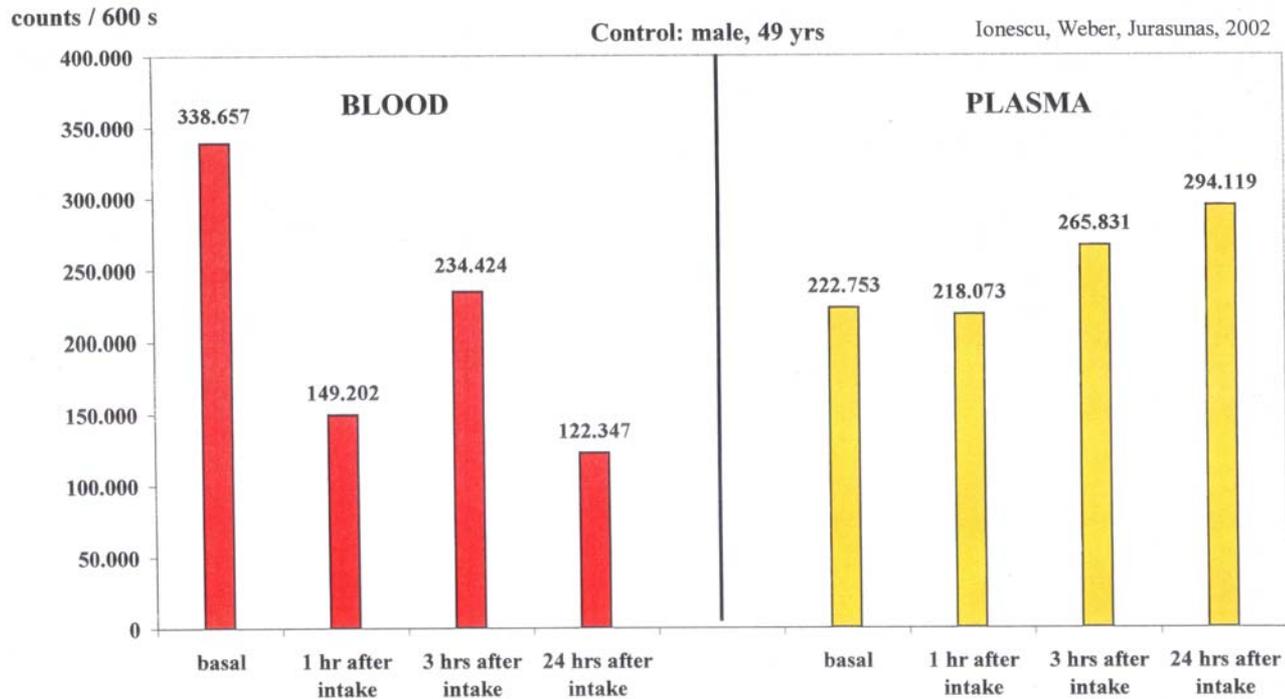
Scale of 100 units of peroxides produced by DHA alone

*Index of lipid peroxides produced*

	Polyunsaturated	100
Very effective	Anoxe	39
	Vitamin E	83
	Untreated ingredients of Anoxe	85
	S.O.D. enzyme	94
	Catalase enzyme	105
	Vitamin C	136

# Evaluation of Anoxe free radical quenching activity *in vivo*

Fig. 4 Effects of Anoxe intake (15 g / 250 ml H<sub>2</sub>O) on free radical generation in blood and plasma, in vivo



The single administration of 250ml of a 6% Anoxe solution resulted in a clear-cut reduction of the photon counts (free radical levels in whole blood at 1,3 and 24 hours, after intake, in all tested samples.

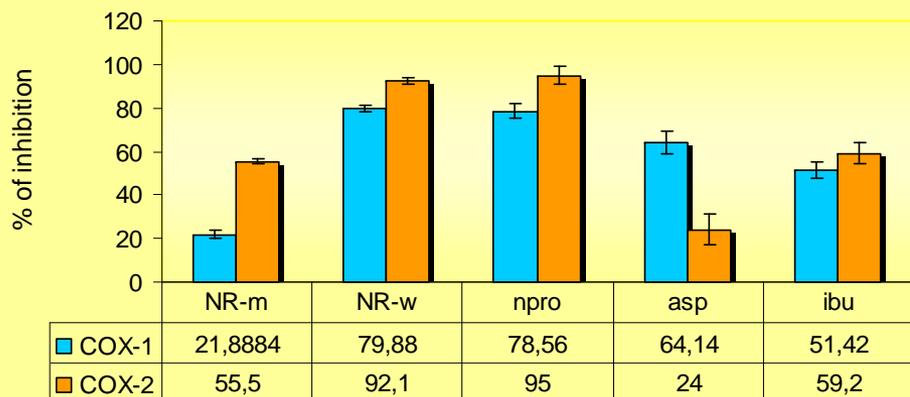
The most significant ROS-inhibition was registered at 1 hour and 24 hours, after 15g Anoxe intake.

# Anti-inflammatory and COX-2 inhibitory property of Anoxe

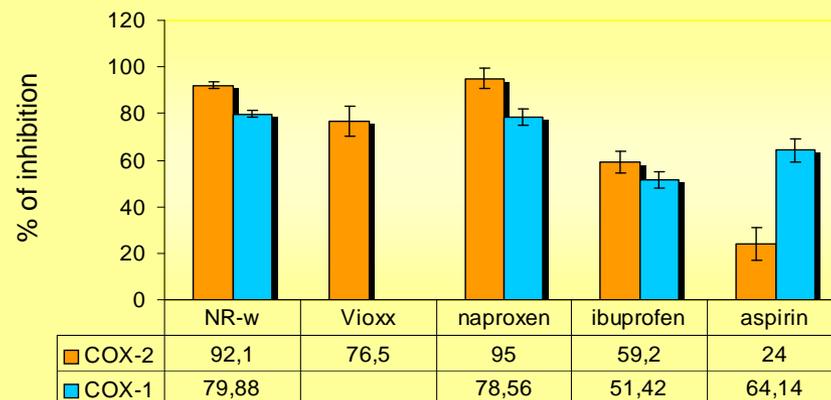
Bioactive Natural Products Laboratory

National Food Safety and Toxicology Center – Michigan State Univ. - USA

Anti-inflammatory activities of NR-m & NR-w



NR-w COX-1 and COX-2 inhibitory activity



## Conclusion:

**Anoxe is an innovative biological compound with bioavailability**

- Reduce and neutralize excessive ROS activity.
- Significant anti-inflammatory activities.
- As inhibitor of COX2 may be considered as a novel agent to inhibit angiogenesis.
- Boost the immune system activity
- Potential clinical application to protect normal cells from damaging effects of chemotherapy and enhance the effectiveness of chemotherapy.

# H.R.B.M. – 6,000 x

F. 80 years

– Rheumatoid arthritis – degeneration of the aortic valve – Bad physical condition

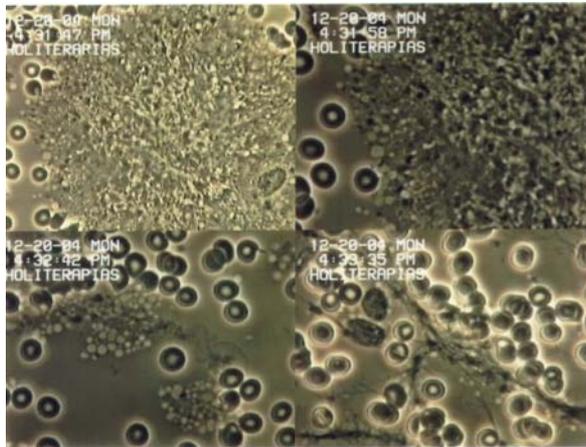


Photo 1

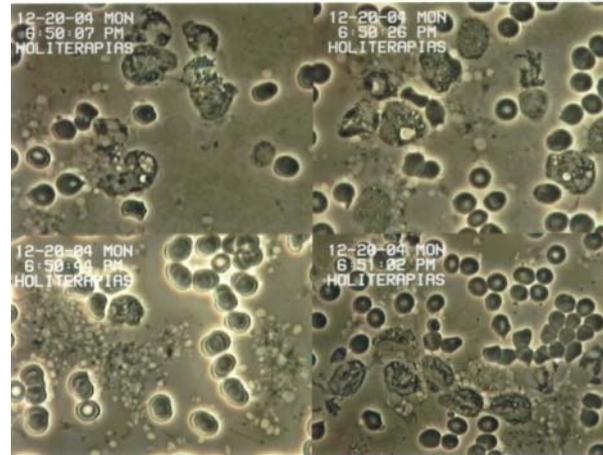


Photo 2

Dosage:  
18g per day  
during 15 days

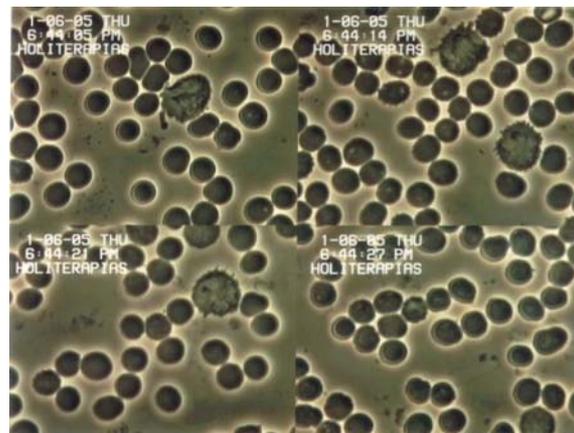


Photo 3

A 100% change in the blood status increased immune function.  
Normalization of phagocytosis.  
Elimination of large colonies of yeast form – like candida.

# Case 13125

F. 42 years old – cancer of colon

1 – Blood examined 3 days after chemotherapy session – 1st consultation  
– adverse effects.



Photo 1



Photo 2

Dosage:  
18g per day



Photo 3

After one month:

2 - Blood examined one week after a chemotherapy session but the patient follow as support the antioxidant therapy. Significant result with less adverse effects.

## Case 602

F. 68 years old – uterus carcinoma - chemotherapy

High oxidative stress

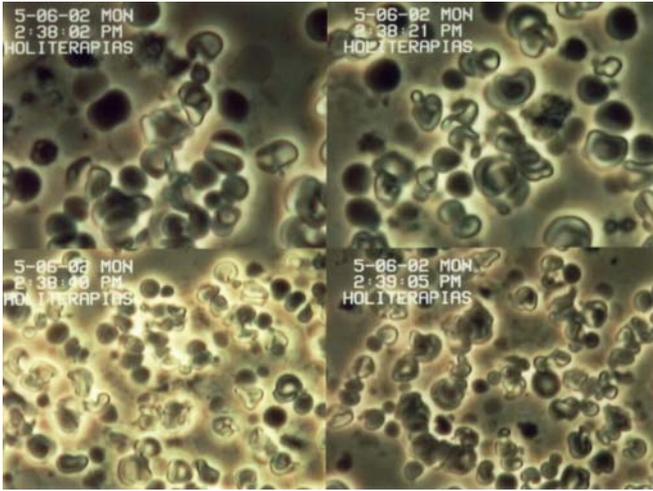


Photo 1

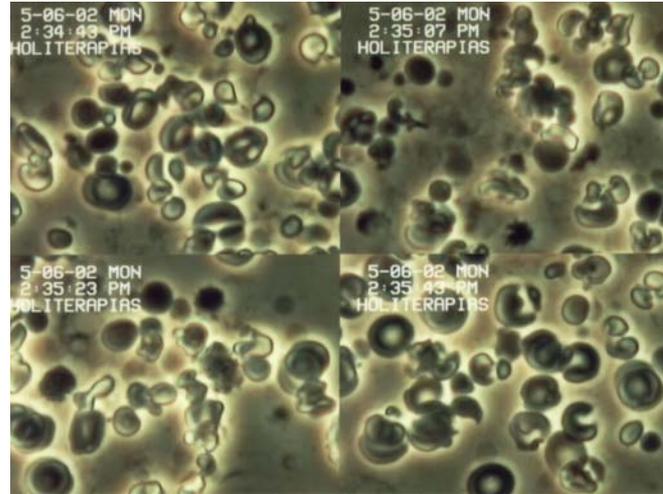


Photo 2

Dosage:  
18g per day  
no specific diet  
during 7 days

After 7 days  
100% modification of  
the red cells status.

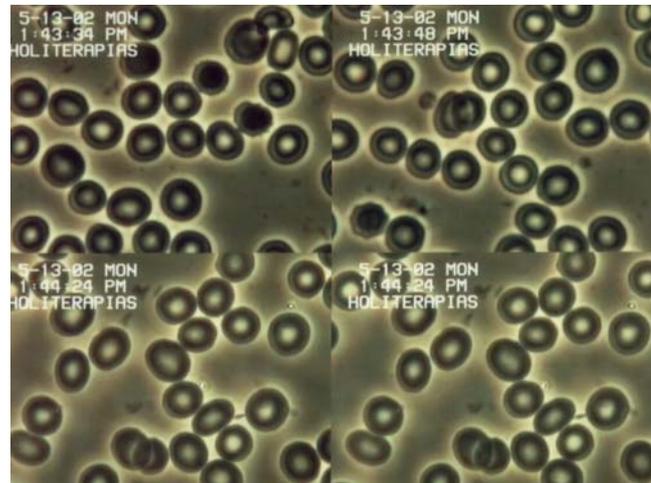


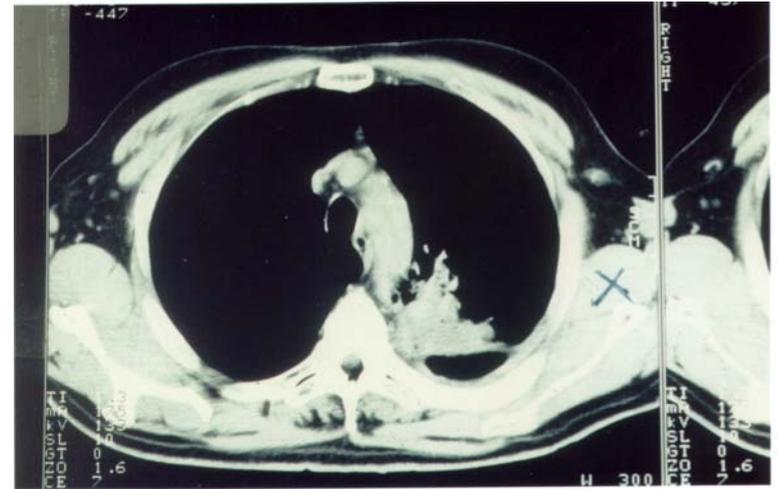
Photo 3

Balanced antioxidants status

# Effects of Anoxe – A low molecular antioxidant compound on a resistant tumor to radiation therapy

M. 42 years – lymphoma treated with chemotherapy.

Recurrency with a large tumor localized in the bronchial area resistant to new radiation therapy.



Before treatment



After treatment

40 days using the low molecular antioxidant compound Anoxe (together with radiation) at 24g per day.

Shown a significative reduction of the tumor size.

# Colorectal Cancer

## F-55 years

### Standard Therapy

May 2005  
CA 19.9 – 26 u/ml  
CEA .....

One year

Poor quality of life  
Strong adverse effects

June 2006  
CA 19.9 – 1000 u/ml  
CEA 69.7ng/ml

Liver metastases

Beginning of July 2006

The difference

Increasing Quality of Life

End of July 2006

Antigene CA 19.9 – 834 u/ml  
Tumor marker CEA – 60 ng/ml

Anoxe  
L.C.E.

CA 19.9 – 498 u/ml  
CEA 46.6 ng/ml

## References (cyclooxygenase 2)

1 – Dandekar D.S., Lokeshmar B.L. – Inhibition of cyclooxygenase (COX 2) – expression by Tet inducible COX 2 antisense cDNA in hormone – refractory prostate cancer significantly slows tumor growth and improve efficacy of chemotherapy drugs – Clin Cancer Res. 2004 (10) 8037-47.

**2 – Fugita H., Koshida K., Keller Et et al. – cyclooxygenase 2 promotes prostate cancer progression: prostate 2002: 53-232-40.**

3 – Raju U., Ariga H., Dittman K., Nakata E., Ang K.K., Milas L. – Inhibitor of DNA repair as a mechanism of enhanced radioresponse of head and neck carcinoma cells by a selective cyclooxygenase 2 – Inhibitor Celecoxib – Int J Radiat Oncol Bio Phys 2005-63-520-28.

**Masferrer J.L., Leaky K.M., Kobi A.T. et al – Antiangiogenic and antitumor activities of cyclooxygenase 2 – inhibitors. Cancer Res. 2000 – 60-1306 – 11.**

Gasparini G., Logo R., Sarmiento R. and Morobito A. – COX 2 inhibitors in cancer therapy. Lancet Oncol. Vol.4 – 6006-7

**Hida T., Koza Ki K., Muramatsu H. et al – Cyclooxygenase 2 – inhibitor induce apoptosis and enhances cytotoxicity of various anticancer agents in non-small-cell lung cancer cells lines. Clin Cancer Res. 2000-6-2006 - 11**

# References (chemotherapy)

- 1 – Shacker E. – Williams J.A., Hunson et al: oxidative stress interfere with cancer chemotherapy – Inhibition of lymphoma cell apoptosis and phagocytosis.  
Blood – July 1 – 96 (1) 96 (1) 307-313.
- 2 – Wegl N.I., Hofman G.D., Wipkrink – Bakler A., Lentjes E., GWM, Berger H.M. et al – Cisplatin combination chemotherapy induces a fall in plasma antioxidants of cancer patients.  
Ann Oncol. 9 – 1331, 1337 – 1998.
- 3 – Ritcher C. et al – Cellular ATP is na important determinant for apoptic cell death.  
FEBS, Letter 1996 – 1378-107-110.
- 4 – Modica, Napolitano J., Singh K. – Mitochondria as targets for detection and treatment of cancer in Review in Molecular Medicine.  
London – Cambridge University Press.
- 5 – Clems M.R. et al – Plasma vitamin E and betacarotene concentration during radio/chemotherapy preceding bone marrow transplantation.  
Ann J. Clini Nut. 1990 Febr 51 (2) 2169.
- 6 – Toyokami S., Okamada K., Yocho J. and Hiaitt – Persistent oxidative stress in cancer.  
FEBS 1995 – 358-1-3.
- 7 – Conklin K. A. Chemotherapy – associated oxidative stress.  
Int Cancer Ther. 2004 (4) 294-299.
- 8- Brown N. S. and Bicknell R. – Hypoxia and oxidative stress in breast cancer – Oxidative stress its effects on the growth, metastasic potential and response to therapy of breast cancer.  
Breast Cancer Res. 3 – 2001 – 323, 327

## References (lipid peroxidation)

**Bartoli G.M. and Galleoti T. – Growth related lipid peroxidation in tumor microsomal membrane and mitochondria – Biochim.**

**Biophys Acta 574, 537, 541 – 1979.**

Chajes V., Sattler W., Stranzl A., and Kostner G.M. – Influences of n3 fatty acids on the growth of human breast cancer cells in vitro – relationship to peroxides and vitamin E.

Breast Cancer Res. Treat. 34 – 199, 212 – 1995.

Gonzalez M.J., Schemmel R.A., Gray J.I., Dugan L., Sheffield L.G. et al: Effects of dietary fat on growth of MCF-7 and MDA – MB23/ human breast carcinoma in athymic nude mice: relationship between carcinogenesis 12 – 1231, 1235 – 1991.

Gonzalez M.J., Schemmel R.A., Gray J.L., Dugan L. and Welsh – Dietary fish oil inhibit human breast carcinoma growth: a function of increased lipid peroxidation. Lipids 28 – 827-832 – 1993.

**Sangeetha D., Das Un., Karathar P., Surayprobla P. – Increase in free radical generation and lipid peroxidation following chemotherapy in patients with cancer.**

**Free Radic Biol-Med 1990-8, 15, 19**

**Khantzode SS, Muddeshmar M.G., Khantzode S.D., Dakkale G.N., - Antioxidant enzymes and lipid peroxidation in different stages of breast cancer.**

**Free Radic Res. 2004 – 38, 81, 85.**

## References (antioxidants)

**Prasad K.N. et al – High doses of multiple antioxidant vitamins – essential ingredients in improving the efficacy of standard cancer therapy. J.Am. Coll Nutr. 1999 – Feb 18 (1) 1325.**

**Coklin K.A. – Dietary antioxidants during cancer chemotherapy: impact on chemotherapy effectiveness and development of side effects. Nutr.Cancer 2000-37-18.**

Greenberg et al – Modulation of Redox, signal transduction pathways in the treatment of cancer: Therapeutic use of antioxidants.  
Antioxidant Redox Signalling 2001 – n°3 – P350-54

Schwartz J.L. – The dual roles of nutrients as antioxidants and prooxidants: Their effects on tumor cell growth.  
J.Nutr. 1996 Ap 126(4) Suppl 1221 – S.75.

Chinery R. et al – Antioxidants enhance the cytotoxicity of chemotherapeutic agents in colorectal cancer a P53 – independent induction of P21 WAF1/C1P1 via C/EBF Beta Nat Med. 1997 Nov.3 (11) 1233-41.

**Carole Nico et al – Superoxide dismutase (SOD) mimics control tumor Growth by modulating endogenous production of reactive oxygen Species (ROS).  
3th International Seminar on SOD. 2004 – June 10-11 – Institute Pasteur – Paris - France**

# Thank you for your attention

## For more information:

- Measuring oxidative stress level with the technique of FORM test (Free Oxygen Radical Monitor) in cancer disease – Balancing antioxidant levels with the compound Anoxe (Publication available on request).
- Therapeutic application of a new molecular antioxidant compound (Anoxe) in ROS activities.
- Int. Symposium on ROS/RNS, diagnostic, preventive and therapy application St. Petersburg 2002-8-11 July – Russia.
- My journey to Anoxe – (A cancer therapy revolution in Europe – By Serge Jurasunas and Mike Culbert.
- Mitochondria and Cancer by Serge Jurasunas – Townsend Letter August/Sept.2008 – (USA)

## Holiterapias Institute

Rua da Misericórdia, 137 – 1º - Lisbon – Portugal  
Phone 00351 21 3471117 Fax: 00351 21 3471119

Email: [info@sergejurasunas.com](mailto:info@sergejurasunas.com)

[www.sergejurasunas.com](http://www.sergejurasunas.com)