Nuove Frontiere nella Nutrizione Clinica
(Levico Terme, TN, 13-14 Aprile 2012)

Stato redox nel paziente chirurgico/oncologico

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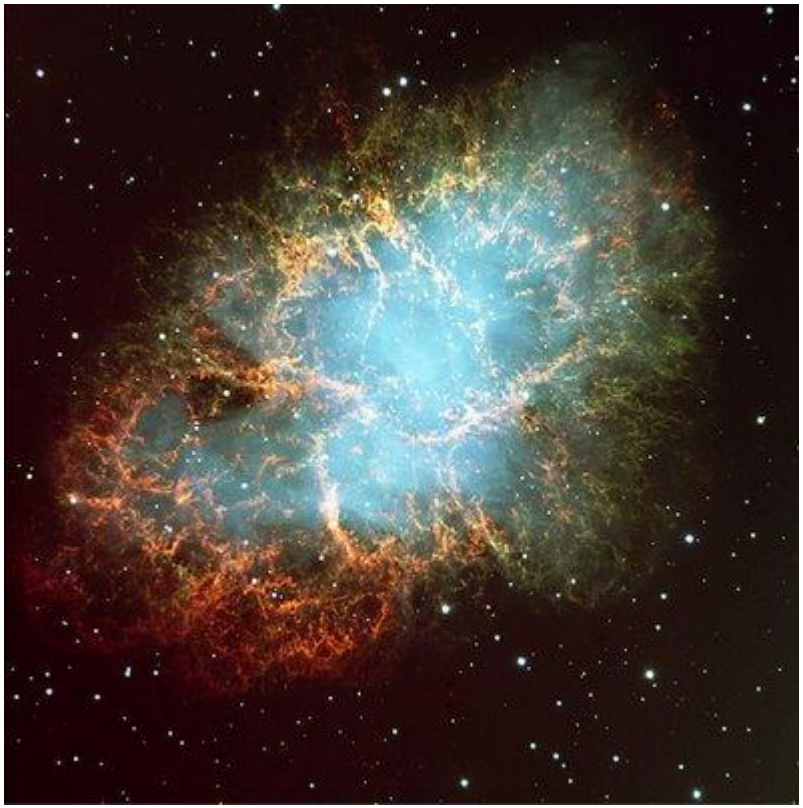
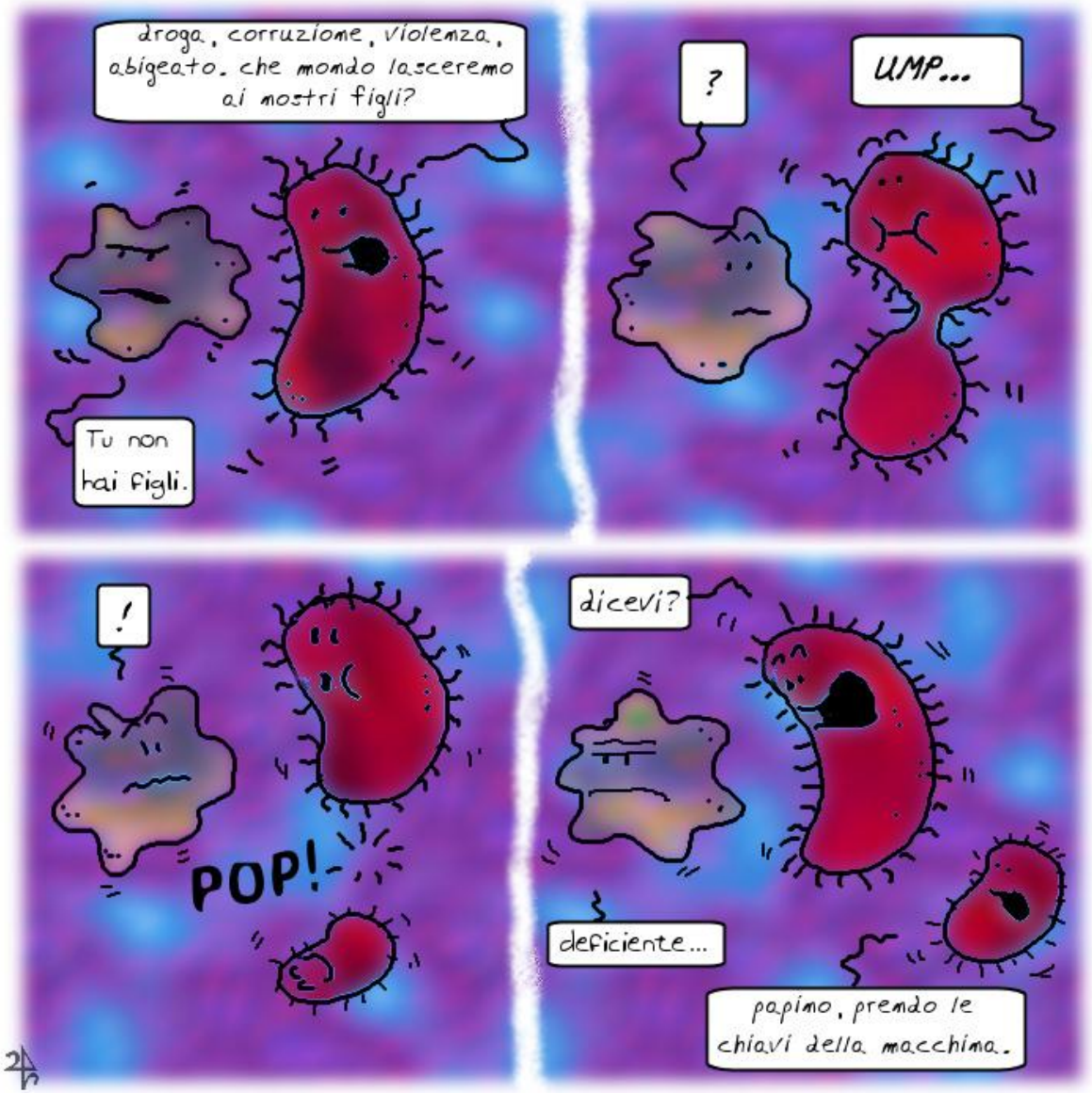


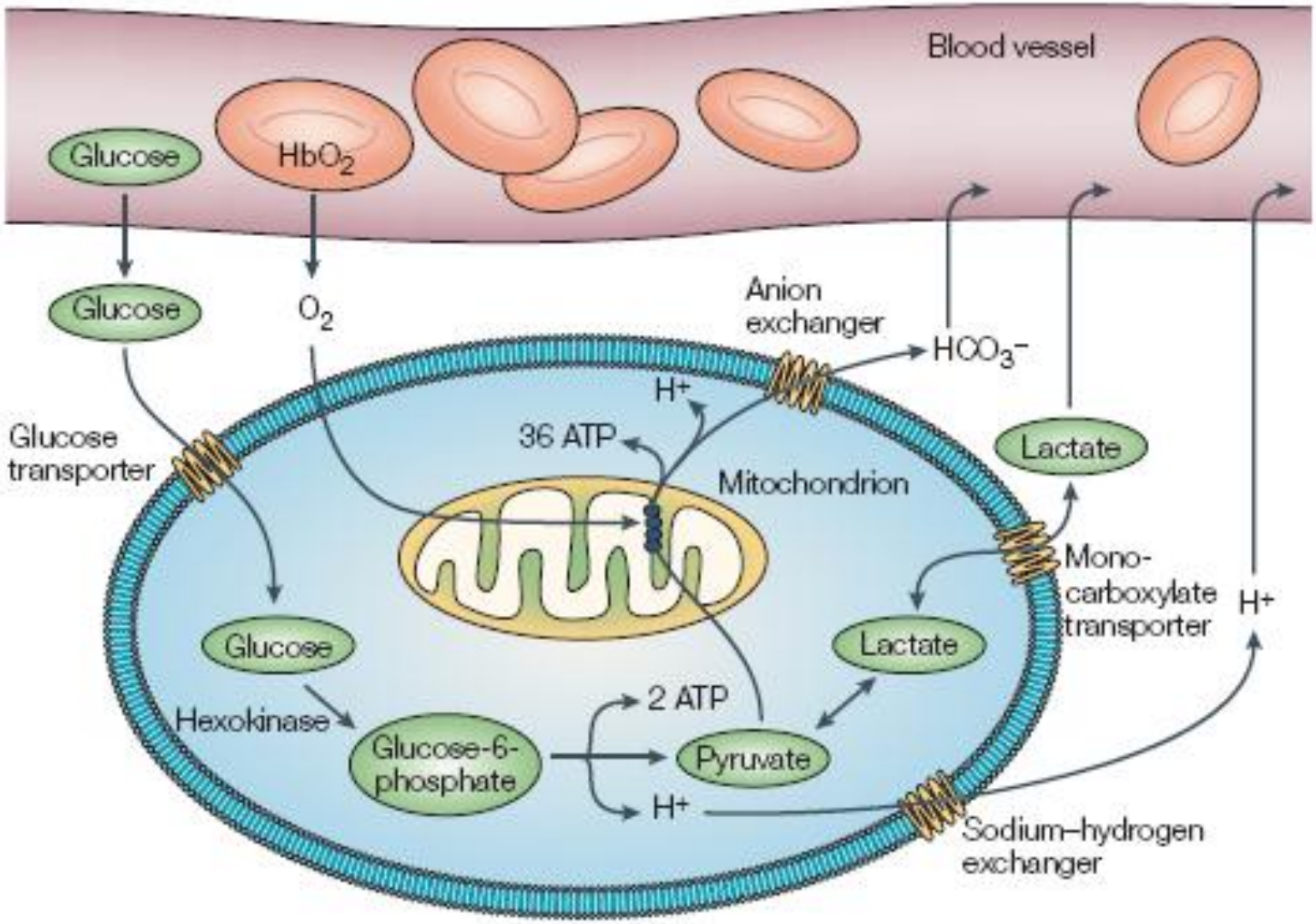
competition
fitness
communication
cooperation
specialization

Evolve!

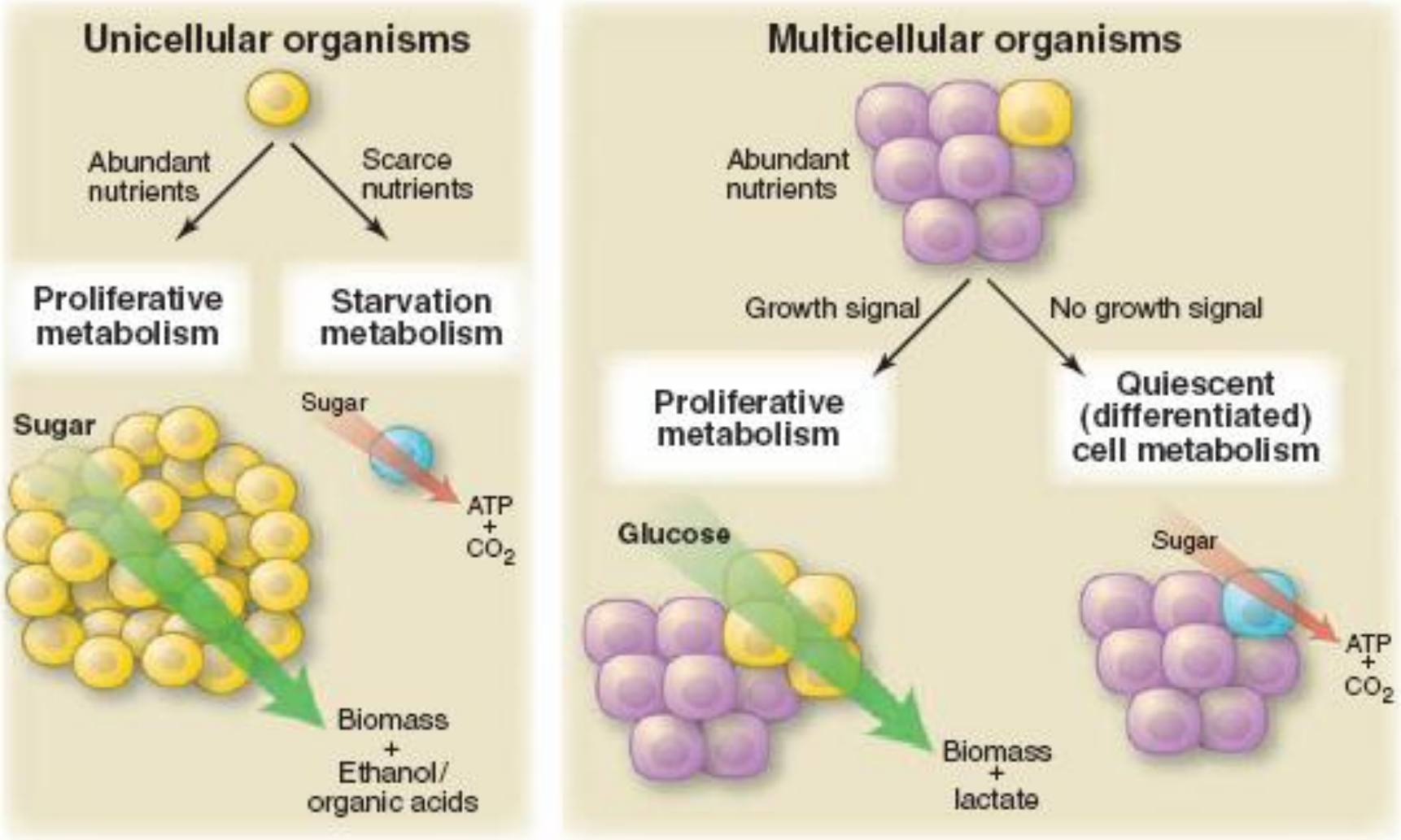
WILL WRIGHT'S GRAND UNIFIED THEORY.

A lot can happen in a billion years, but look closely and you'll see the same dynamic at work in every system, and at every scale. Whether the name of the game is microbiology or geopolitics, it all boils down to the delicate balance between competition and cooperation. ■ ■ ■

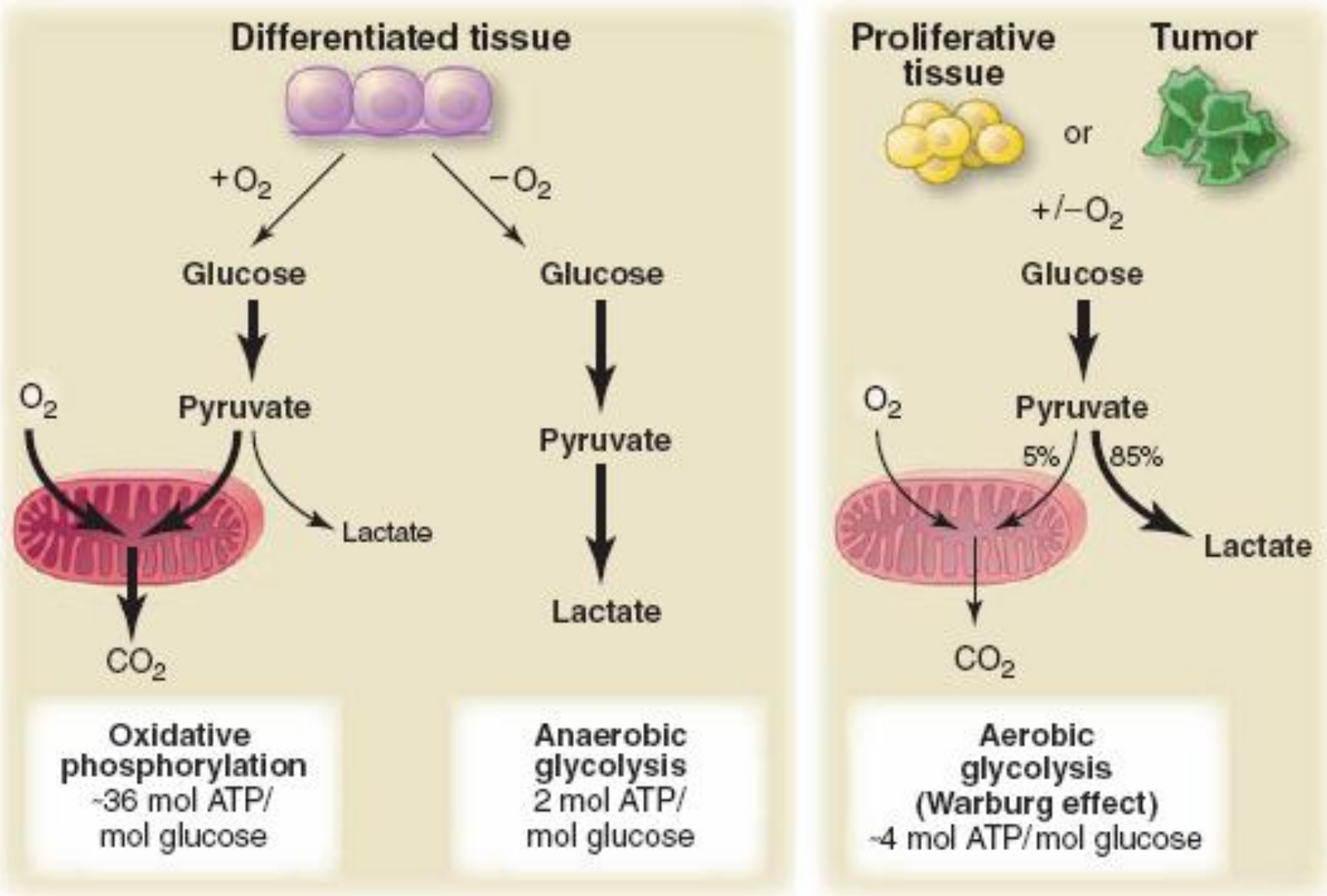

droga, corruzione, violenza, abigeato. che mondo lasceremo ai nostri figli?
Tu non hai figli.
?
UMP...
!
POP!
dicevi?
deficiente...
papino, prendo le chiavi della macchina.



Gatenby RA & Gillies RJ. Nat Rev Cancer 2004; 4:891-899



Vander Heiden MG et al. Science 2009; 324:1029-1033



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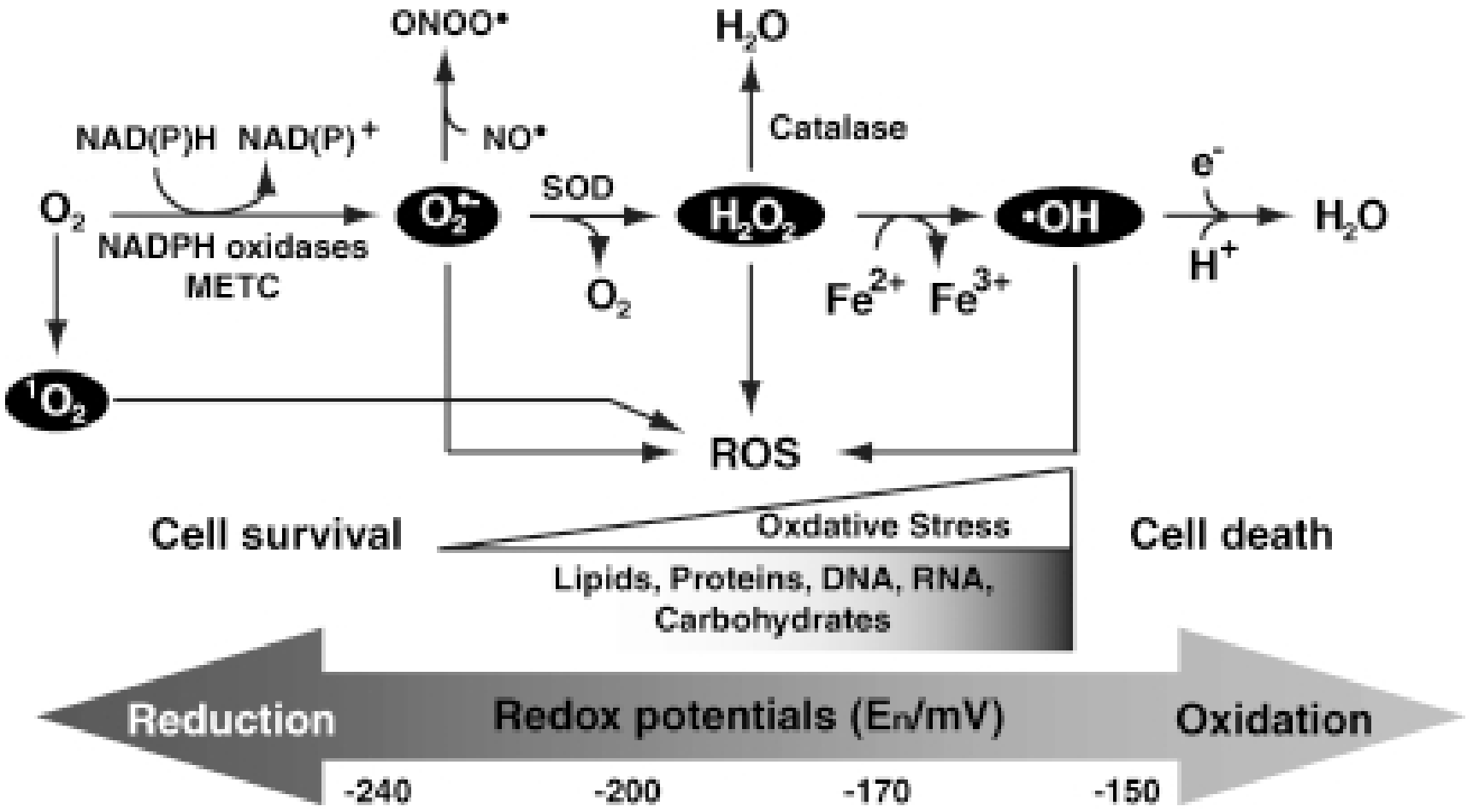
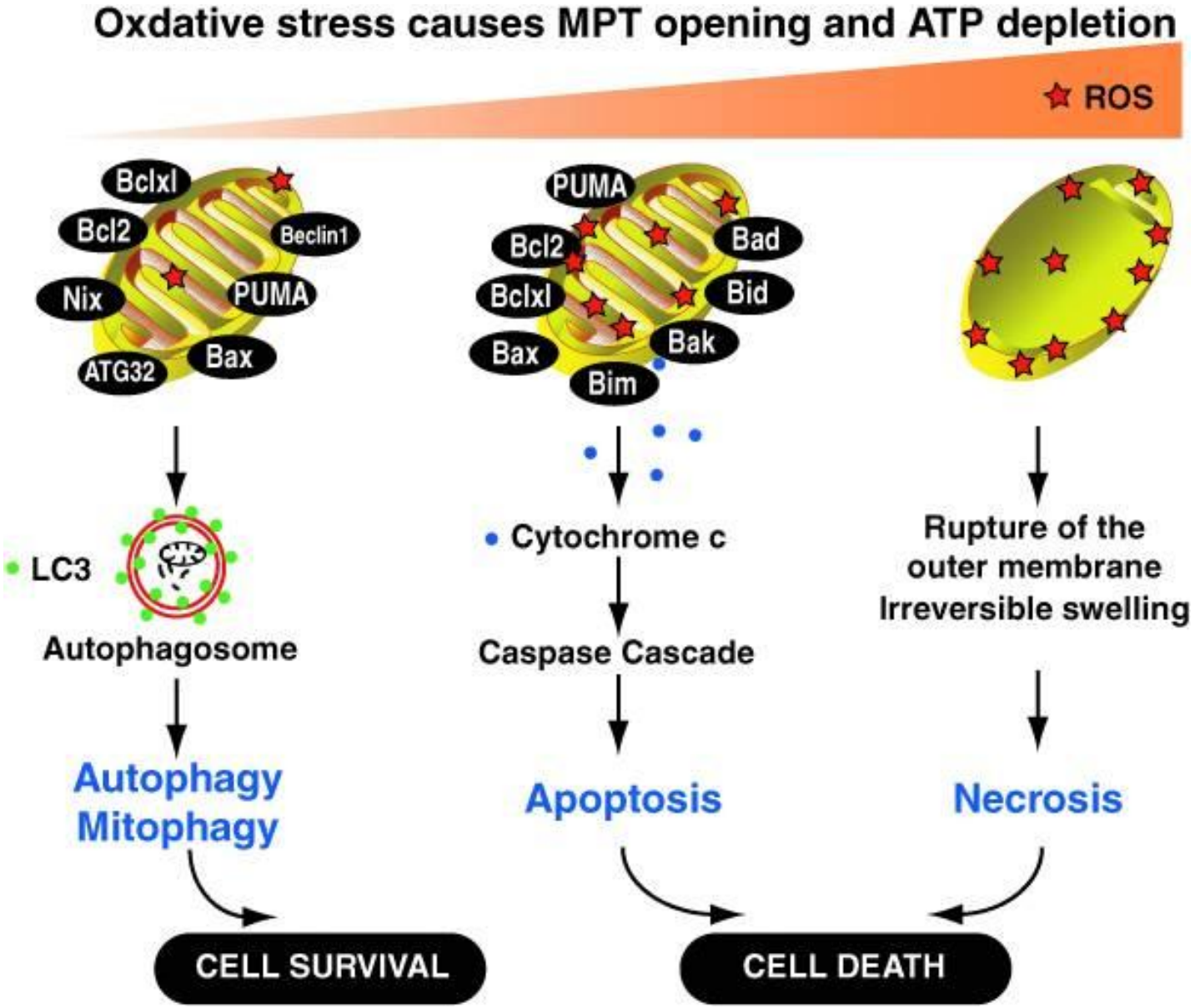


Tang D et al. Antioxid Redox Signal 2011; 14:1315-35



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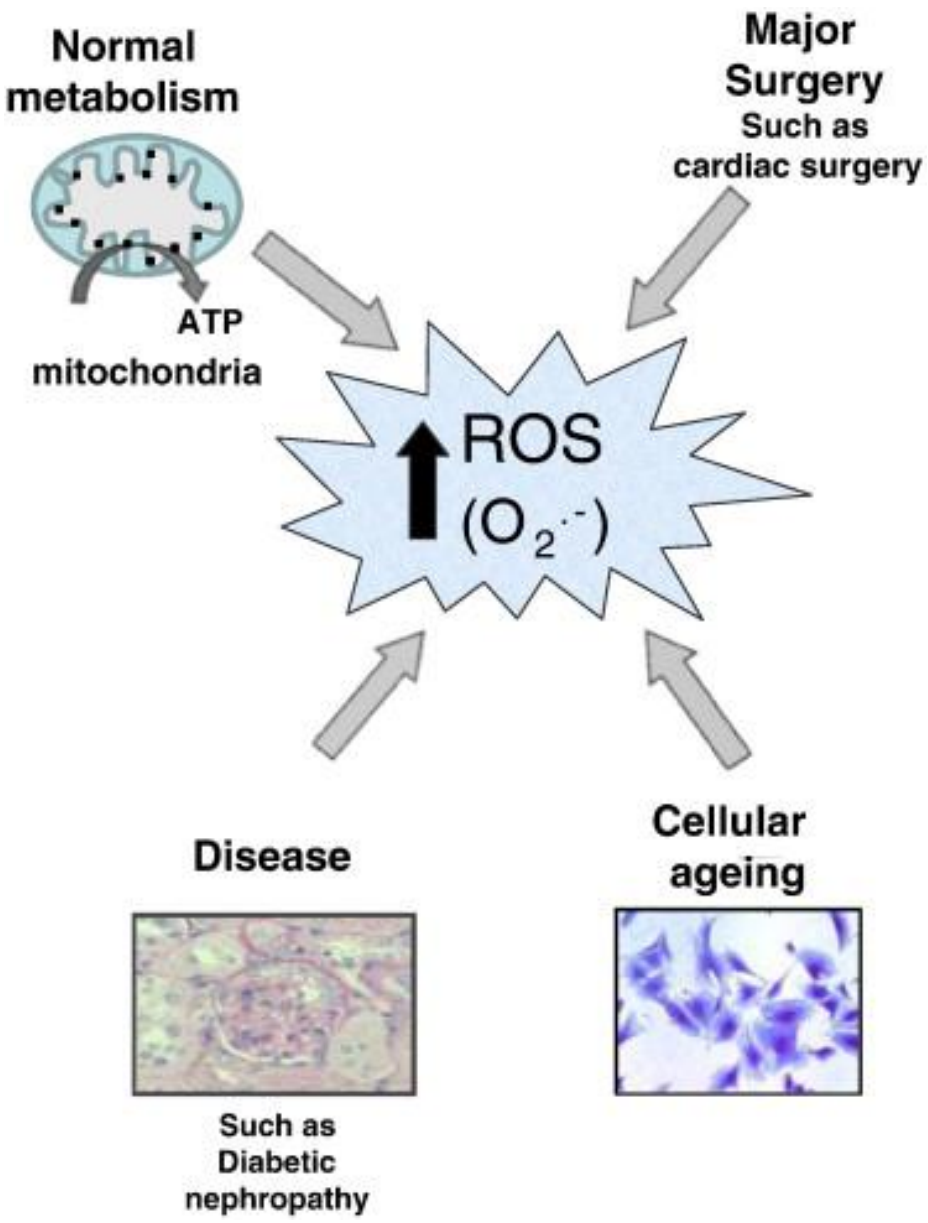
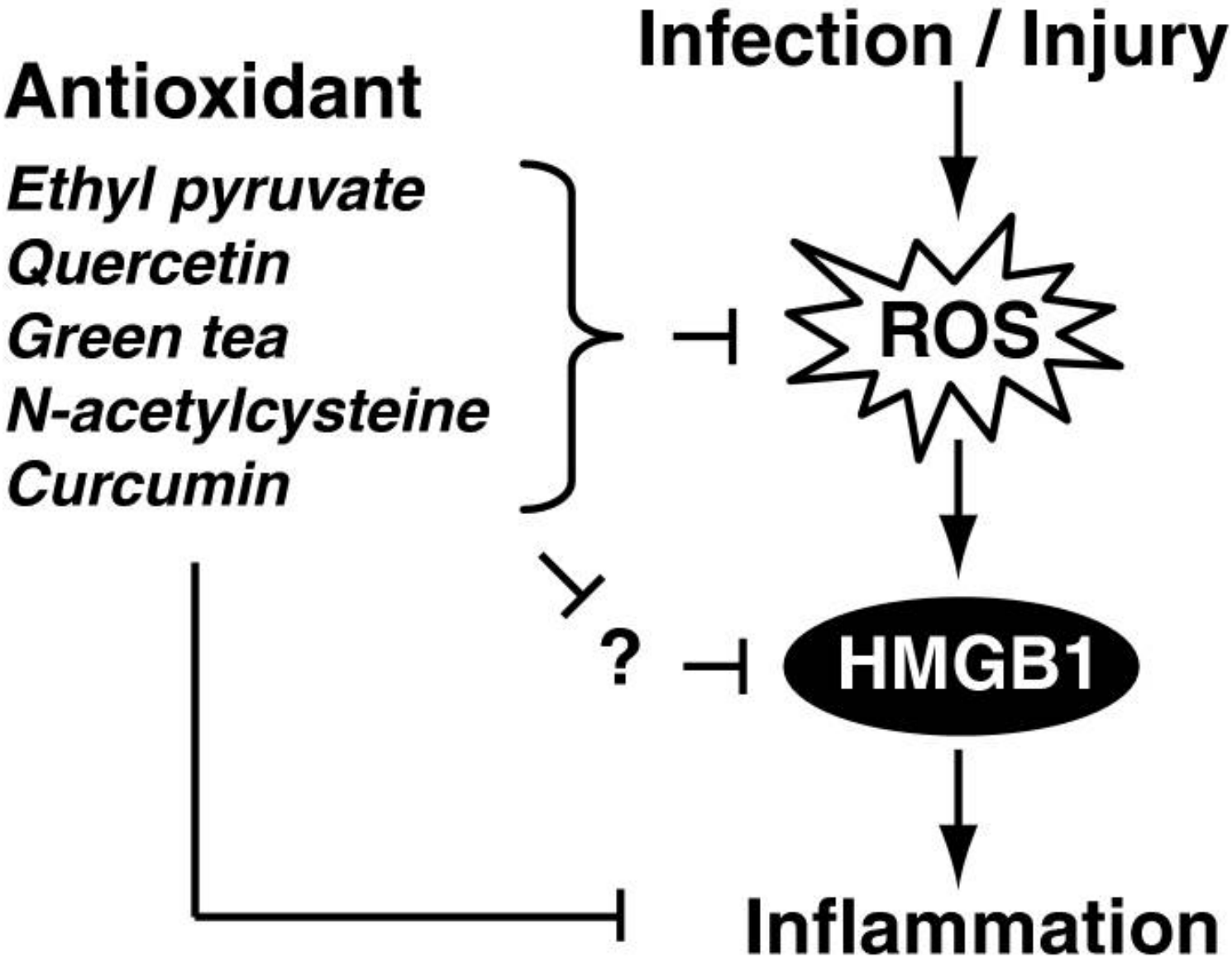


Rosenfeldt F et al. Exp Gerontol 2012 (epub ahead of print)



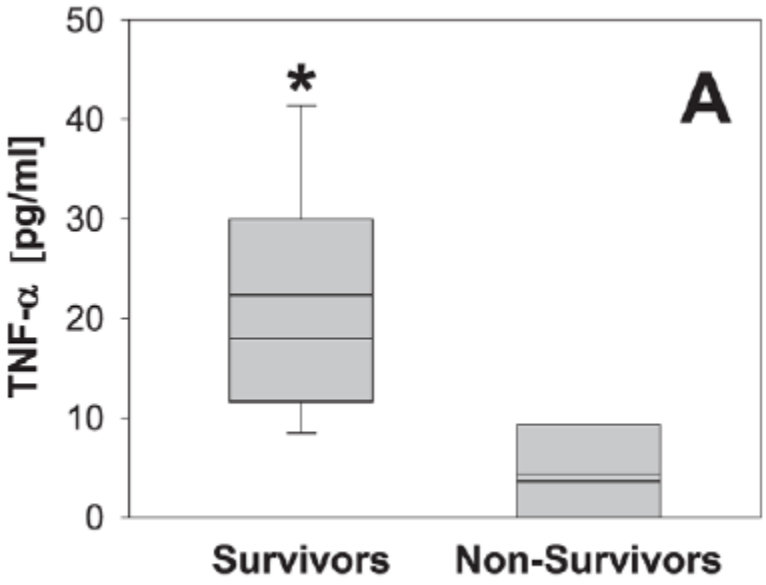
Tang D et al. Antioxid Redox Signal 2011; 14:1315-35

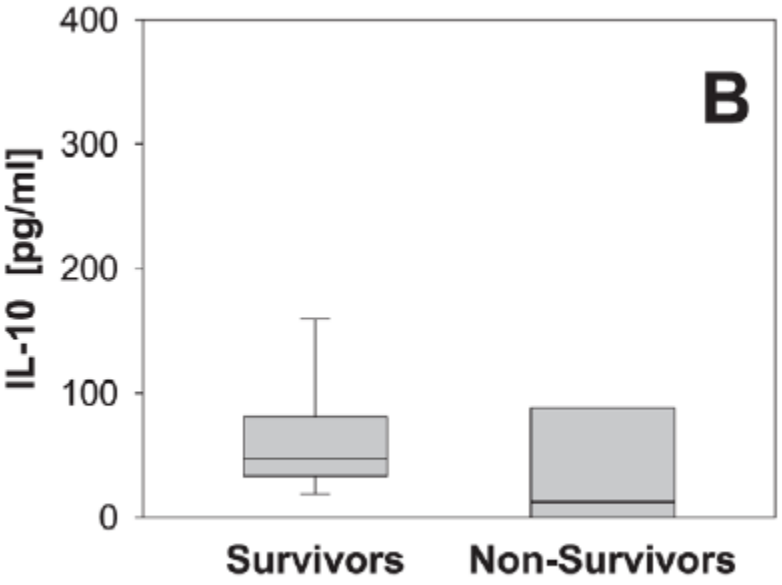
An Adequately Robust Early TNF-α Response Is a Hallmark of Survival Following Trauma/Hemorrhage

Rajaie Namas[1], Ali Ghuma[1], Andres Torres[1], Patricio Polanco[1], Hernando Gomez[1], Derek Barclay[1], Lisa Gordon[1], Sven Zenker[2,3¤], Hyung Kook Kim[2], Linda Hermus[1], Ruben Zamora[1], Matthew R. Rosengart[1], Gilles Clermont[2,3], Andrew Peitzman[1], Timothy R. Billiar[1,3], Juan Ochoa[1,3], Michael R. Pinsky[2,3], Juan Carlos Puyana[1,2,3], Yoram Vodovotz[1,3]*

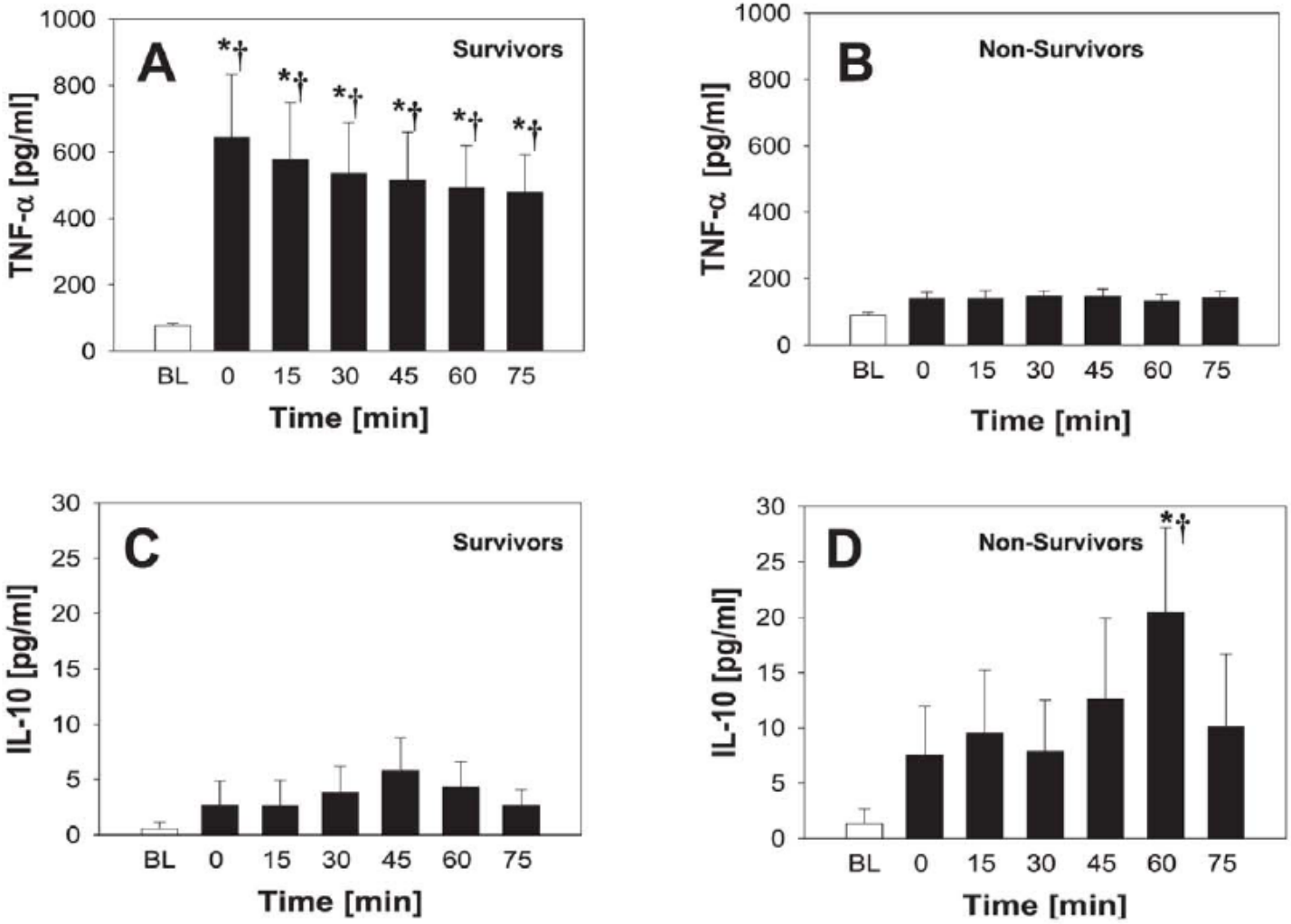
1 Department of Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **2** Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, **3** Center for Inflammation and Regenerative Modeling, McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America

PLoS ONE 4(12): e8406, 2009



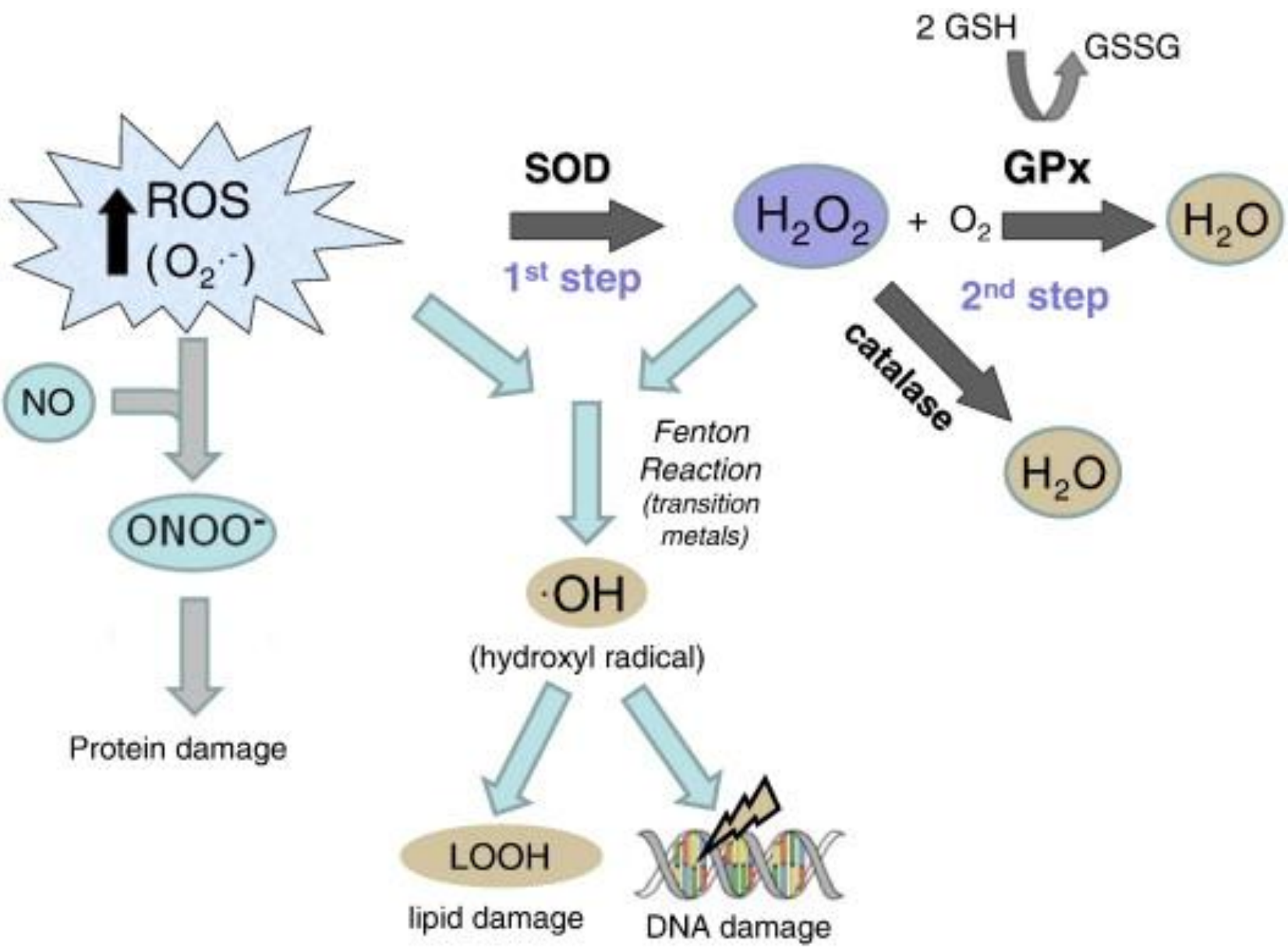


Human trauma patients



Porcine model of haemorrhagic shock

PLoS ONE 4(12): e8406, 2009



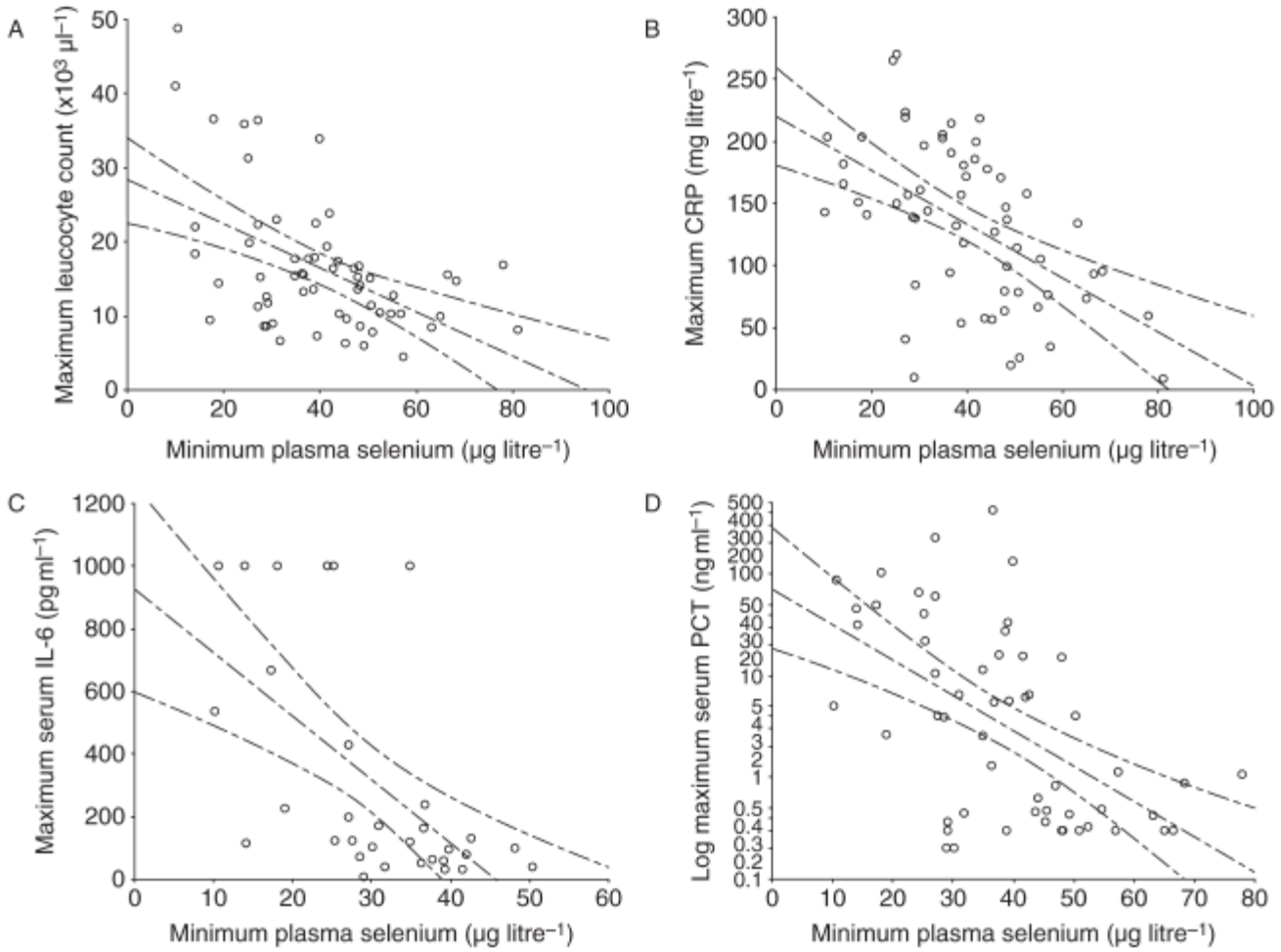
Rosenfeldt F et al. Exp Gerontol 2012 (epub ahead of print)

Table 1
Enzymatic and non-enzymatic antioxidants.

Enzymatic antioxidants	Non-enzymatic antioxidants	
	Lipophilic	Hydrophilic
Superoxide dismutase	Vitamin E	Vitamin C
Glutathione peroxidase	Ubiquinol (Coenzyme Q_{10})	Albumin
Catalase	Flavinoids	Uric acid
Peroxiredoxin		
Glutathione peroxidase		
Ascorbate peroxidase		

Rosenfeldt F et al. Exp Gerontol 2012 (epub ahead of print)

Time course and relationship between plasma selenium concentrations, systemic inflammatory response, sepsis, and multiorgan failure



Sakr Y et al. Br J Anaesth 2007; 98:775-784

Research

Influence of early antioxidant supplements on clinical evolution and organ function in critically ill cardiac surgery, major trauma, and subarachnoid hemorrhage patients

Mette M Berger[1], Ludivine Soguel[1], Alan Shenkin[2], Jean-Pierre Revelly[1], Christophe Pinget[3], Malcolm Baines[2] and René L Chioléro[1]

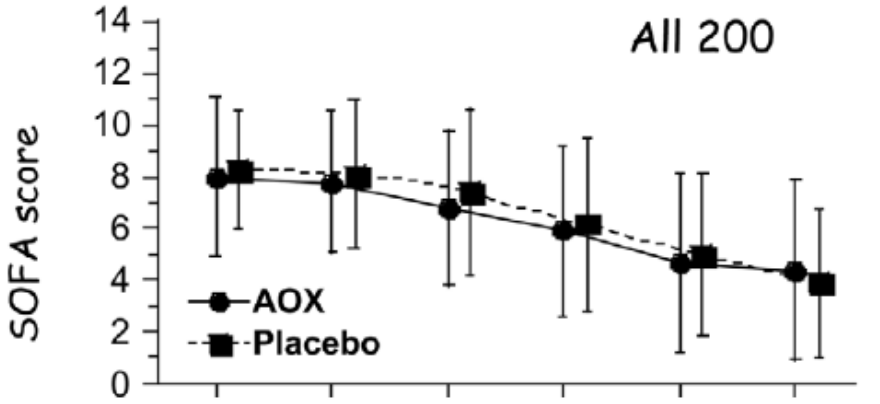
Table 1

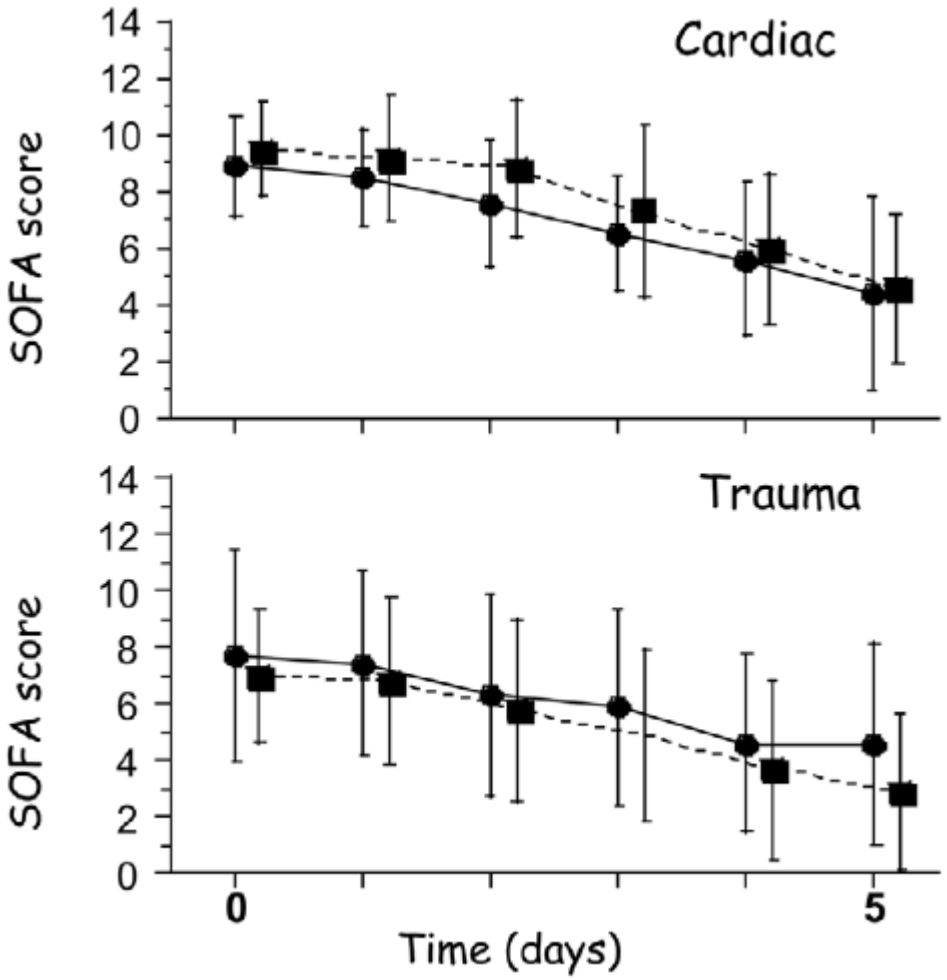
Total antioxidant micronutrient doses in supplements during the first 5 days

Micronutrient	Days 1 and 2	Days 3–5
Zinc, mg	60	30
Selenium, µg	540.4	270.2
Vitamin C, mg	2,700[a]	1,600[a]
Vitamin B_1, mg	305[a]	102.5
Vitamin E enteral, mg	600	300
Vitamin E iv, mg	12.8	6.4

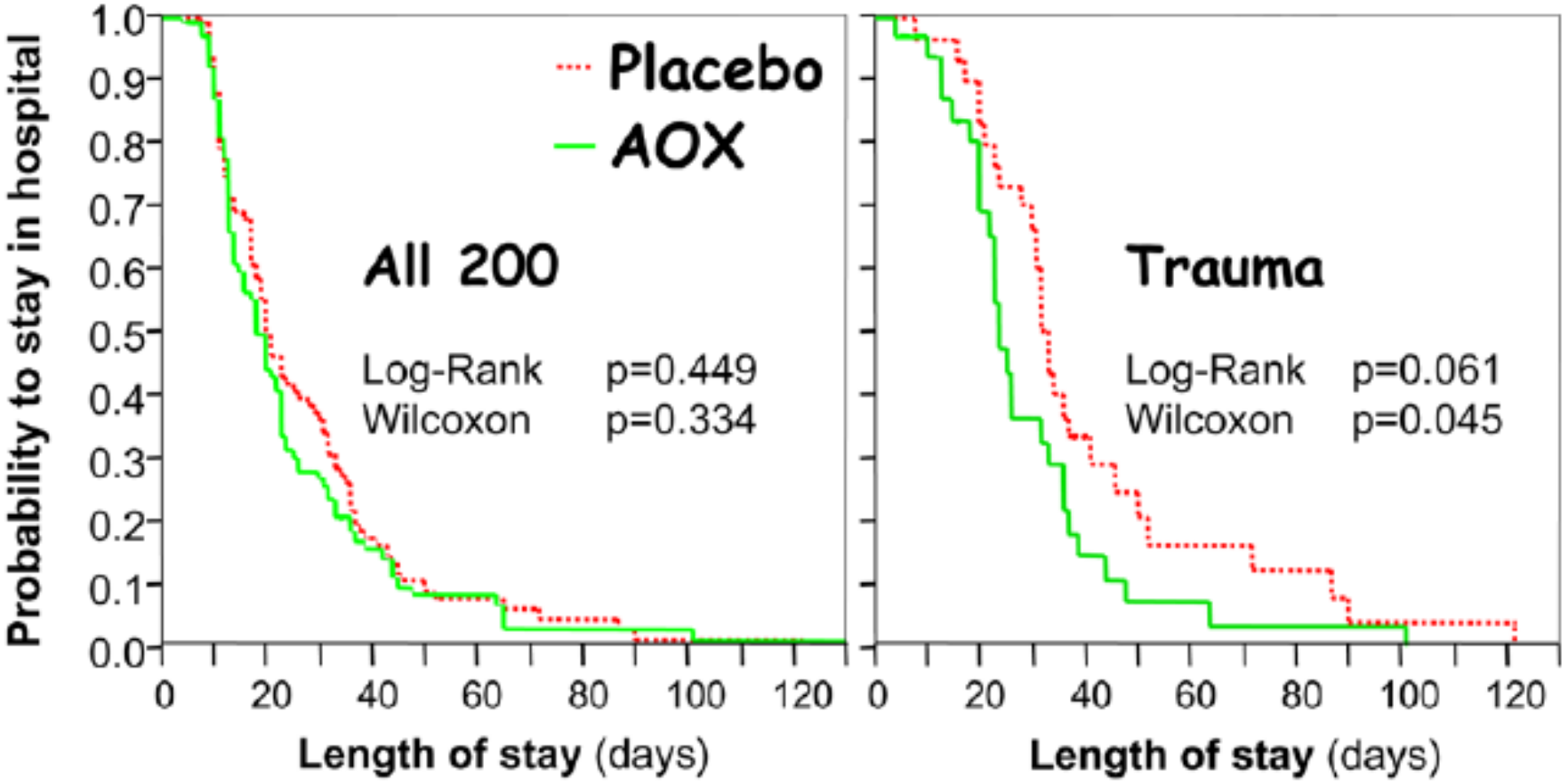
[a]Includes the standard supplementation policy that was provided to both groups (500 mg vitamin C/day for 5 days and 100 mg vitamin B_1/day for 3 days). iv, intravenously.

Figure 2

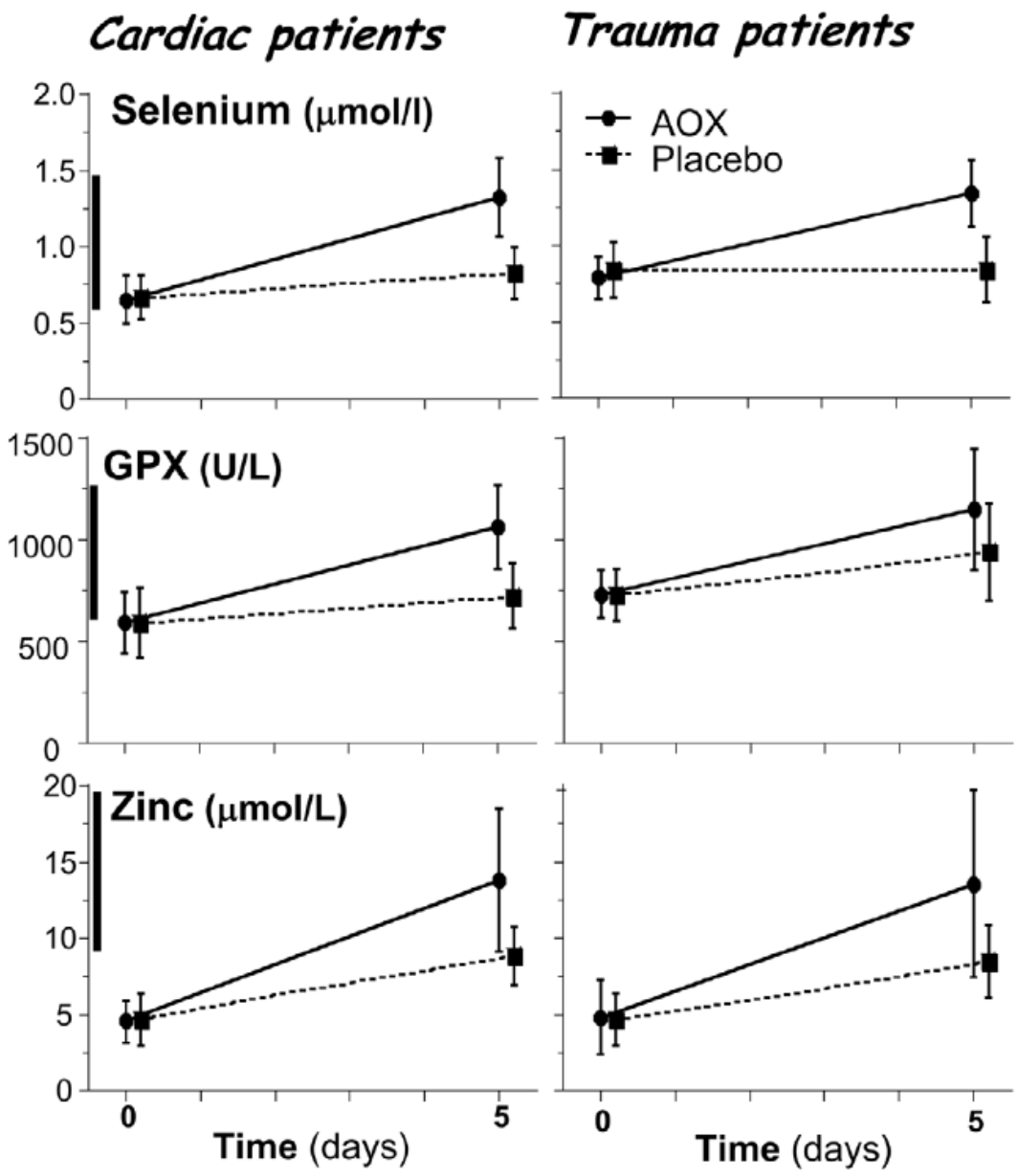




Berger MM et al. Crit Care 2008; 12:R101



Berger MM et al. Crit Care 2008; 12:R101



Berger MM et al. Crit Care 2008; 12:R101

Perioperative metabolic therapy improves redox status and outcomes in cardiac surgery patients: A randomised trial

Jee-Yoong Leong, MBBS[a], Juliana van der Merwe, RN[a], Salvatore Pepe, PhD[a], Michael Bailey, PhD[b], Anthony Perkins, PhD[c], Robyn Lymbury, PhD[c], Donald Esmore, FRACS[a], Silvana Marasco, MS[a] and Franklin Rosenfeldt, MD, FRACS[a,b,*]

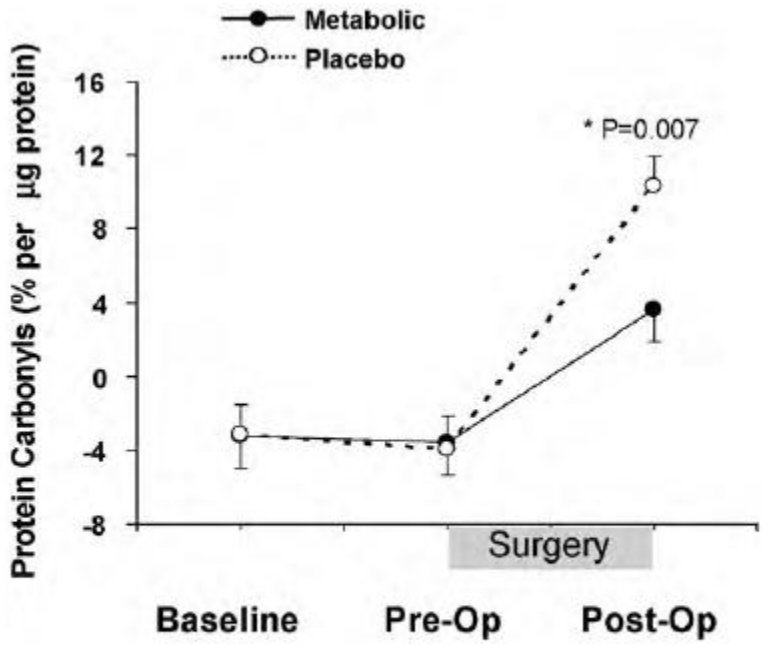


Figure 1. *Protein carbonyls measured at pre-admission clinic (Baseline), immediately before surgery (Pre-Op), and 6 h postoperatively (Post-Op), *metabolic vs placebo at same time point.*

Table 1. *Components of Metabolic Therapy.*

Coenzyme Q_{10}	100 mg tds
Magnesium orotate	400 mg tds
Lipoic acid	100 mg tds
Omega-3 fatty acids	300 mg (in 1 g of fish oil) tds
Selenium	200 µg daily

Heart Lung Circ 2010; 19:584-591

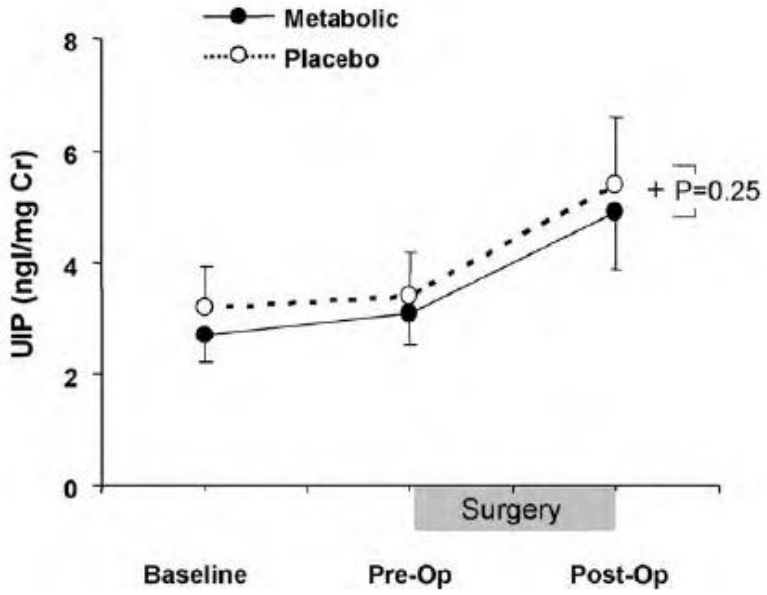


Figure 2. *Urinary isoprostane levels measured at pre-admission clinic (Baseline), immediately before surgery (Pre-Op), and 6 h postoperatively (Post-Op). +overall group effect.*

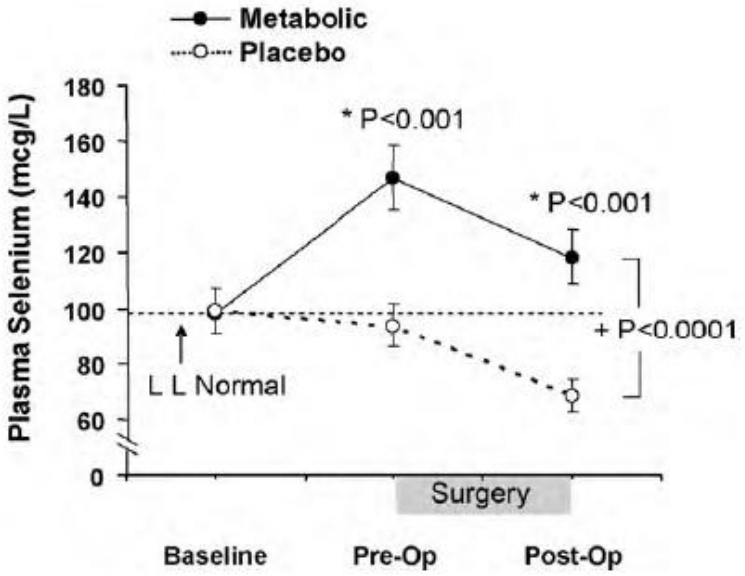
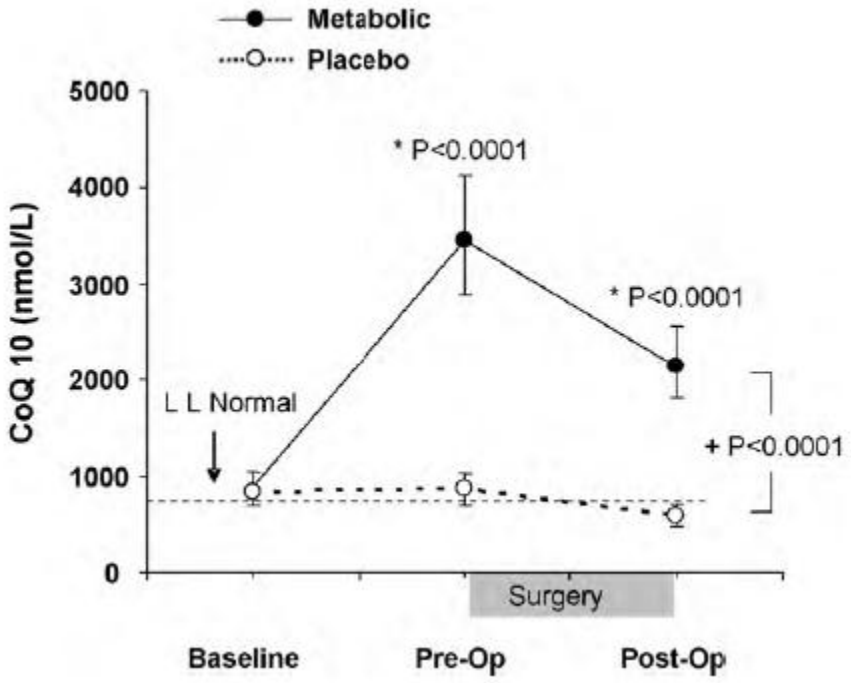
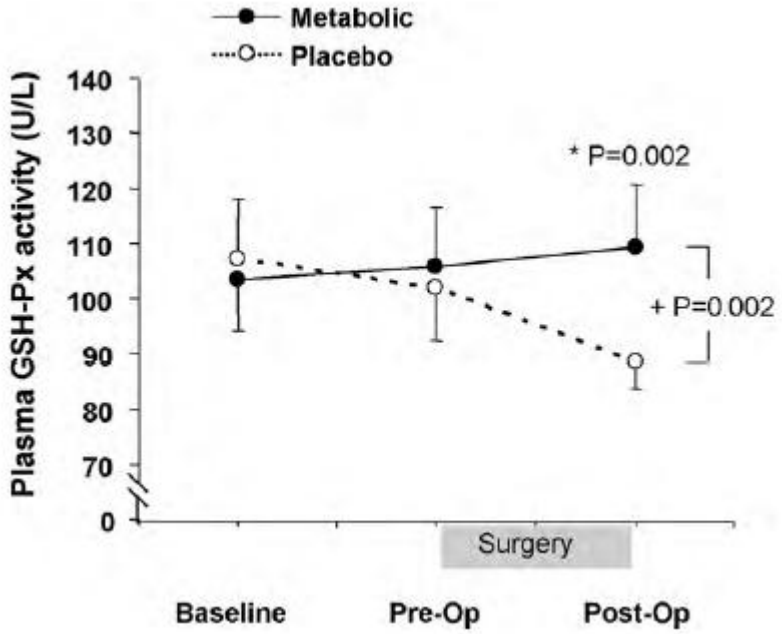


Figure 4. *Plasma selenium measured at pre-admission clinic (Baseline), immediately before surgery (Pre-Op), and 6 h postoperatively (Post-Op). *metabolic vs placebo at same time interval; +repeated measures ANOVA; LL Normal, lower limit of normal.*

Leong J-Y et al. Heart Lung Circ 2010; 19:584-591





Leong J-Y et al. Heart Lung Circ 2010; 19:584-591

Table 5. *Clinical Endpoints and Postoperative Complications.*

	Metabolic	Placebo	*P*-value
Univariate analysis			
All patients (n = 117)			
Troponin at 24 h (μg/L)	1.3 (1.0–1.7)	2.3 (1.8–3.0)	0.002
Length of stay (days)	6.6 (5.7–7.7)	8.3 (7.1–9.7)	0.04
Atrial fibrillation (%)	25% (15/60)	33% (19/57)	0.32
CABG alone (n = 71)			
Troponin at 24 h (μg/L)	1.0 (0.7–1.3)	1.6 (1.1–2.3)	0.036
Length of stay (days)	6.4 (5.5–7.5)	8.3 (6.8–10.1)	0.046
Atrial fibrillation (%)	21% (9/43)	43% (12/28)	0.048
Valve (n = 46)			
Troponin at 24 h (μg/L)	2.7 (1.7–4.2)	3.4 (2.5–4.7)	0.39
Length of stay (days)	7.2 (5.1–10.1)	8.3 (6.4–10.8)	0.50
Atrial fibrillation (%)	35% (6/17)	24% (7/29)	0.42
Multivariate analysis			
CABG alone (n = 71)			
Troponin at 24 h (μg/L)	1.0 (0.7–1.3)	1.6 (1.1–2.3)	0.036
Length of stay (days)	6.4 (5.5–7.5)	8.3 (6.8–10.1)	0.046
Valve (n = 46)			
Troponin at 24 h (μg/L)	2.7 (1.7–4.2)	3.4 (2.5–4.7)	0.39
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Atrial fibrillation (%)	35% (6/17)	24% (7/29)	0.42

Leong J-Y et al. Heart Lung Circ 2010; 19:584-591

N-acetylcysteine supplementation for the prevention of atrial fibrillation after cardiac surgery: a meta-analysis of eight randomized controlled trials

Atrial fibrillation

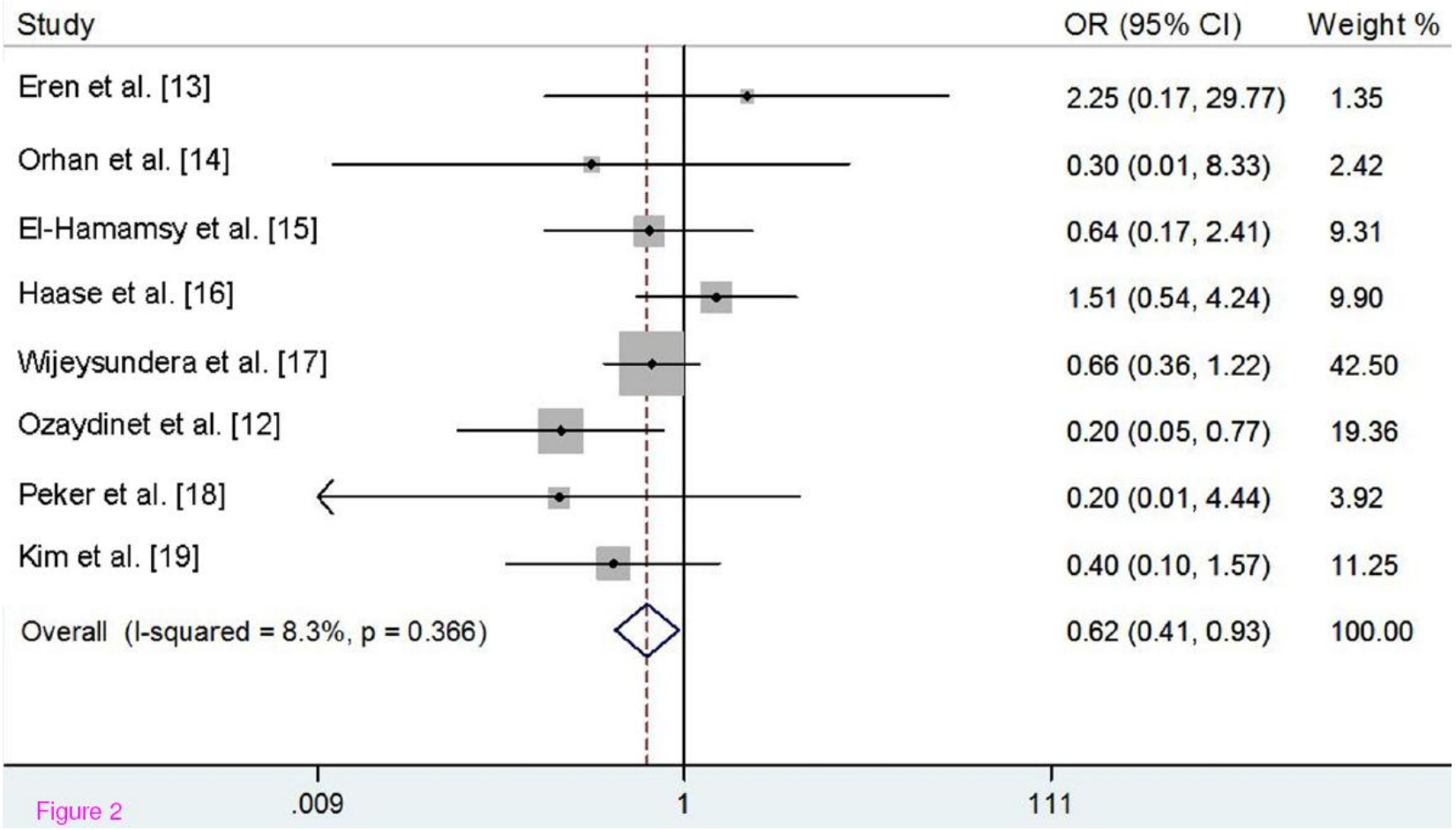


Figure 2

Gu WJ et al. BMC Cardiovasc Disord 2012; 12:10

Length of stay

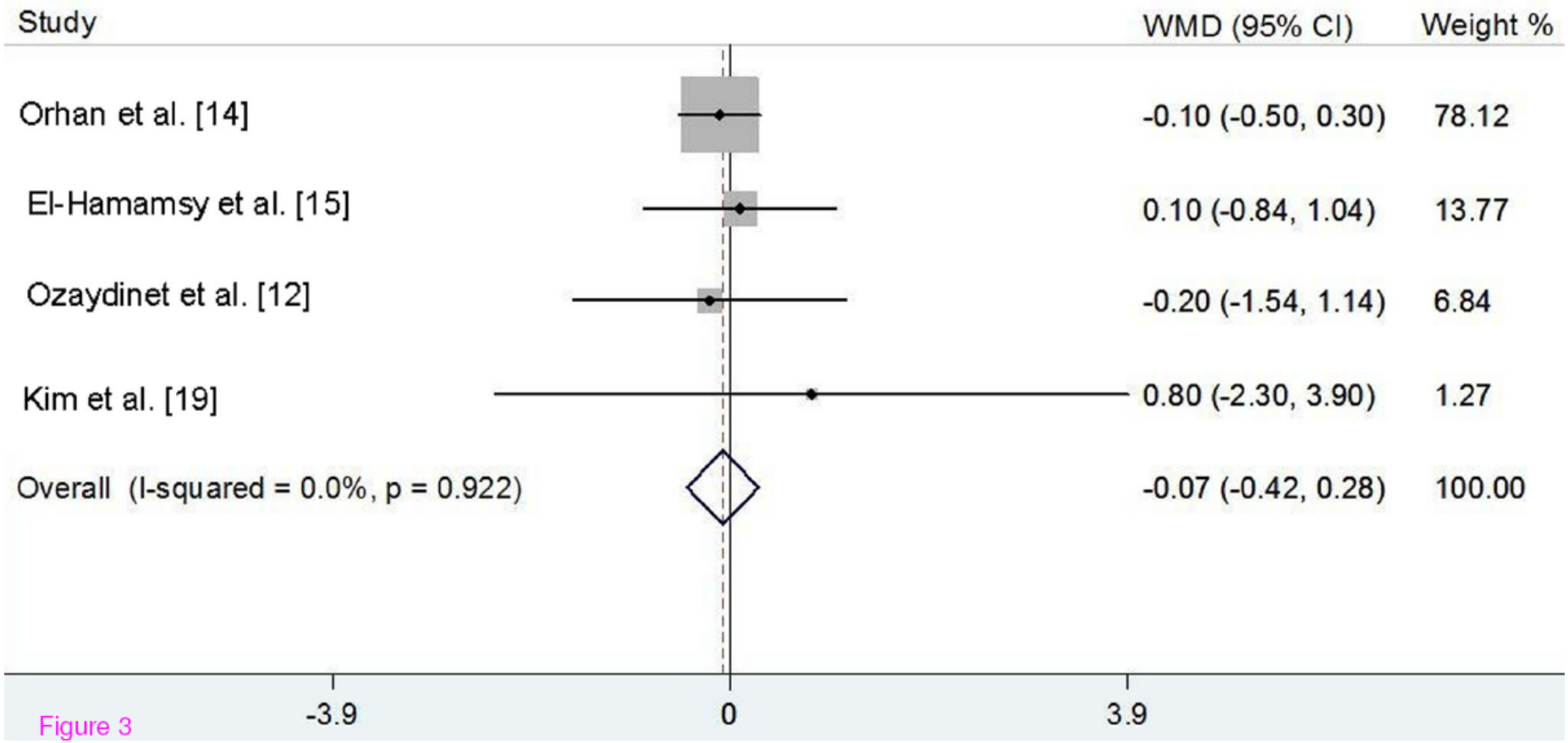


Figure 3

Gli effetti non anestetici del propofol (adattato da Vasileiou I et al, 2009).

- Effetti antiemetici
- Miglioramento della differenziazione delle cellule T verso il tipo di cellule Th1
- Effetti analgesici
- Effetti ansiolitici
- Protezione contro lo stress ossidativo
- Amnesia
- Neuroprotezione
- Inibizione dell'aggregazione piastrinica
- Stimolazione dell’attività dell’ossido nitrico
- Cardioprotezione (cardiac sarcolemmal KATP)

Comparison of the Effects of Propofol and Midazolam on Inflammation and Oxidase Stress in Children with Congenital Heart Disease Undergoing Cardiac Surgery

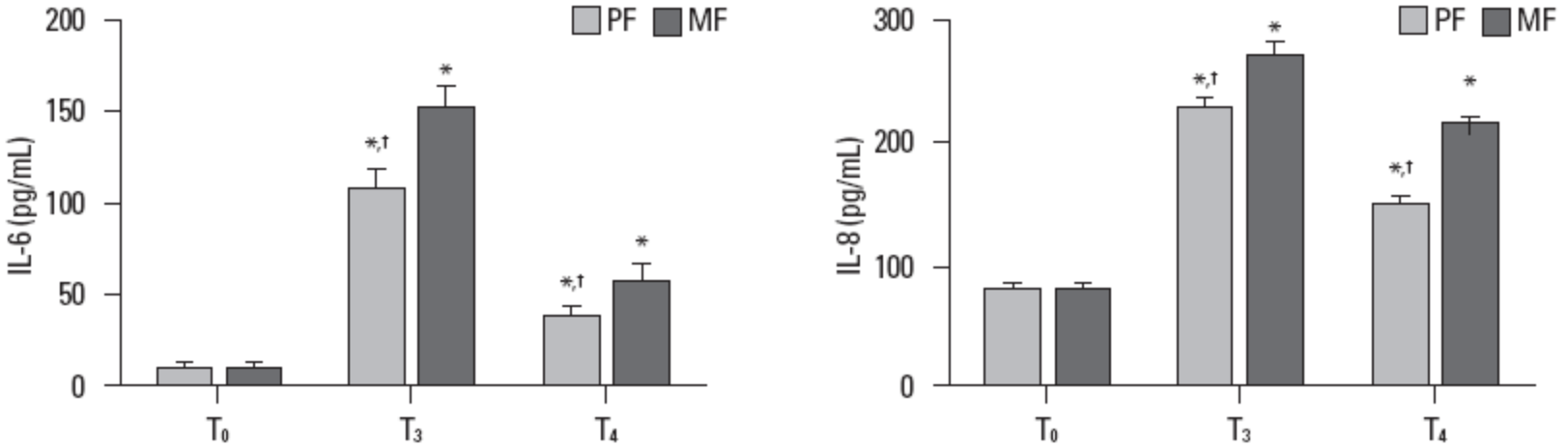
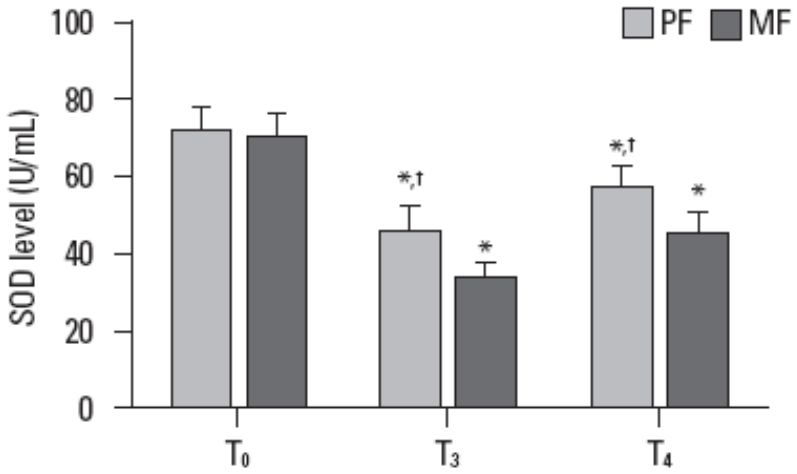


Fig. 1. Comparison of the effects of propofol and midazolam on serum IL-6 and IL-8 levels. Data are shown as mean ± SD. $^{*}p < 0.05$ vs. T_0. $^{\dagger}p < 0.05$ vs. group MF. IL-6, interleukin 6; PF, propofol combined with low dose fentanyl; MF, midazolam combined with low dose fentanyl.

Xia W-F et al. Yonsei Med J 2011; 52:326-332



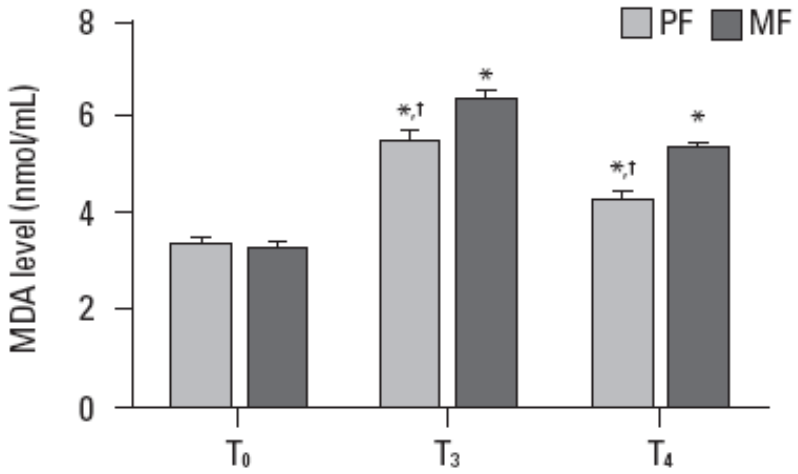
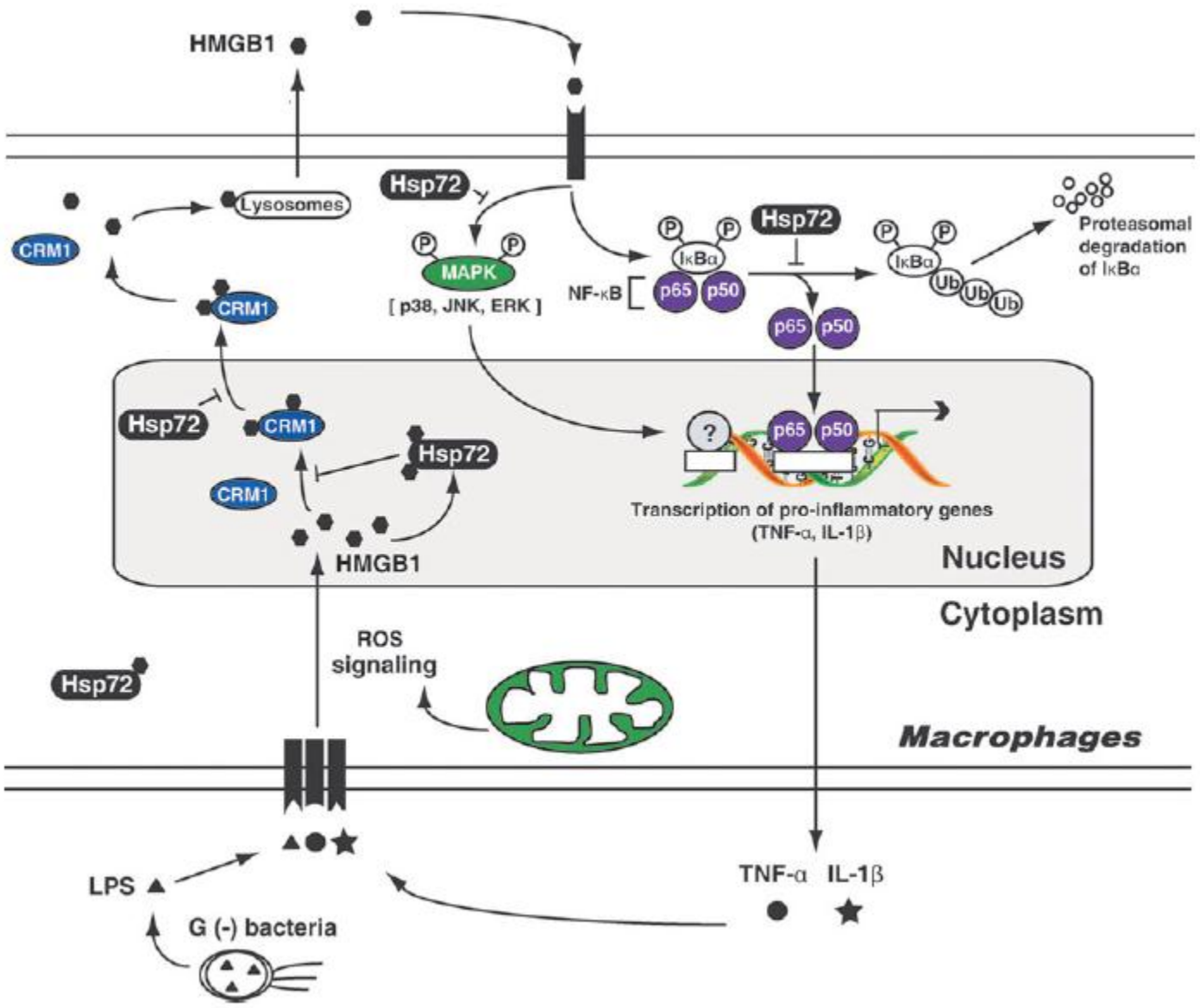


Fig. 2. Comparison of the effects of propofol and midazolam on serum SOD and MDA levels. Data are shown as mean ± SD. *$p < 0.05$ vs. T_0. †$p < 0.05$ vs. group MF. SOD, superoxide dismutase; MDA, malondialdehyde; PF, propofol combined with low dose fentanyl; MF, midazolam combined with low dose fentanyl.



Tang D et al. Antioxid Redox Signal 2011; 14:1315-35


Cancer cachexia

Decreased NADPH oxidase expression and antioxidant activity in cachectic skeletal muscle

Table 2 Gene expression in skeletal muscle of mice with cancer and cancer cachexia

	Cancer	Cachexia
Gene expression (AU)		
NOX2	11.8±2.3	5.0±1.1*
p22phox	88.7±2.9	75.5±10.5
p40phox	21.4±2.8	7.9±1.6*
p47phox	5.7±1.2	7.3±1.4
p67phox	367±92.7	15.6±3.3*
NOX4	4.3±0.6	8.5±2.7
Rac1	3.6±1.1	7.5±1.6
SOD1	350±36.5	120±37.8*
SOD2	122±8.0	59.4±5.4*
SOD3	2.6±0.3	1.8±0.3
Gpx	23.5±2.3	12.8±1.2*
Catalase	49.3±7.3	43.2±5.6

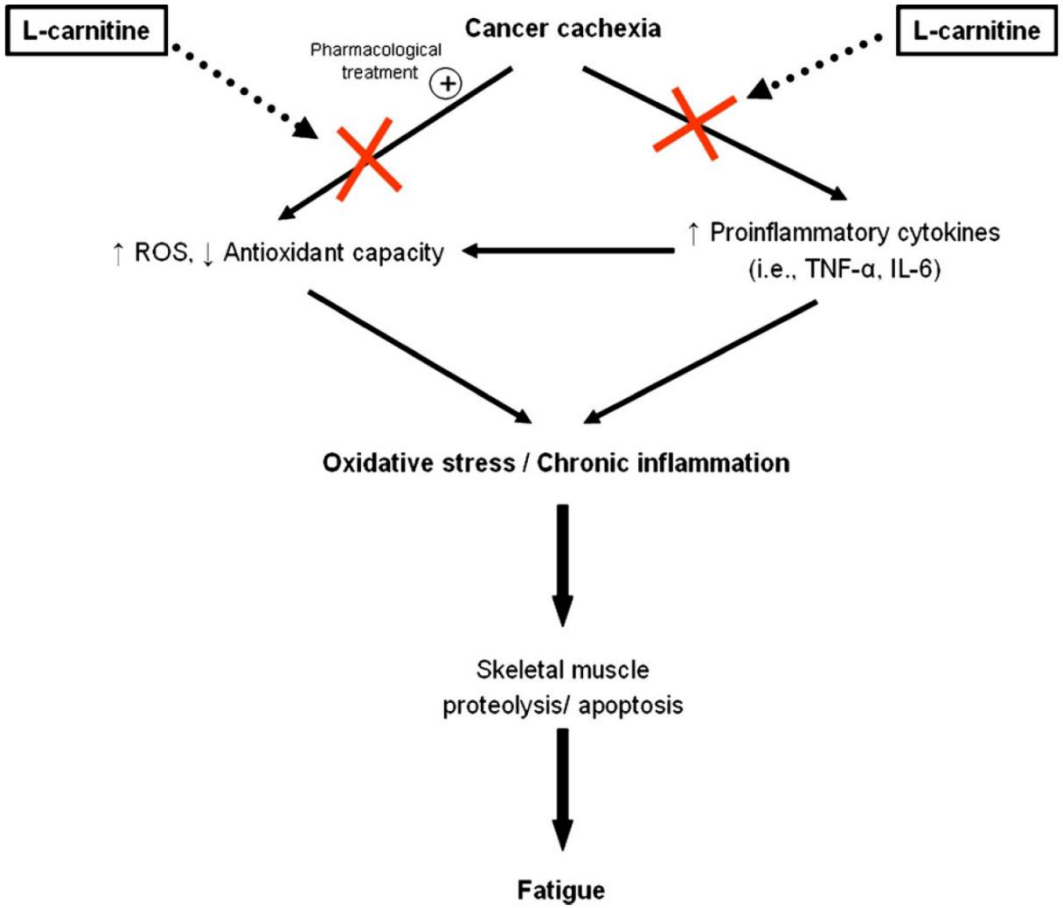
The values represent the mean±SEM

*$P<0.003$, statistically significant differences

Sullivan-Gunn MJ et al. J Cachexia Sarcopenia Muscle 2011; 2:181-188

L-carnitine and cancer cachexia: Clinical and experimental aspects

Renata Silvério · Alessandro Laviano · Filippo Rossi Fanelli · Marília Seelaender



J Cachexia Sarcopenia Muscle 2011; 2:37-44

L-Carnitine induces recovery of liver lipid metabolism in cancer cachexia

Renata Silvério · Alessandro Laviano · Filippo Rossi Fanelli · Marília Seelaender

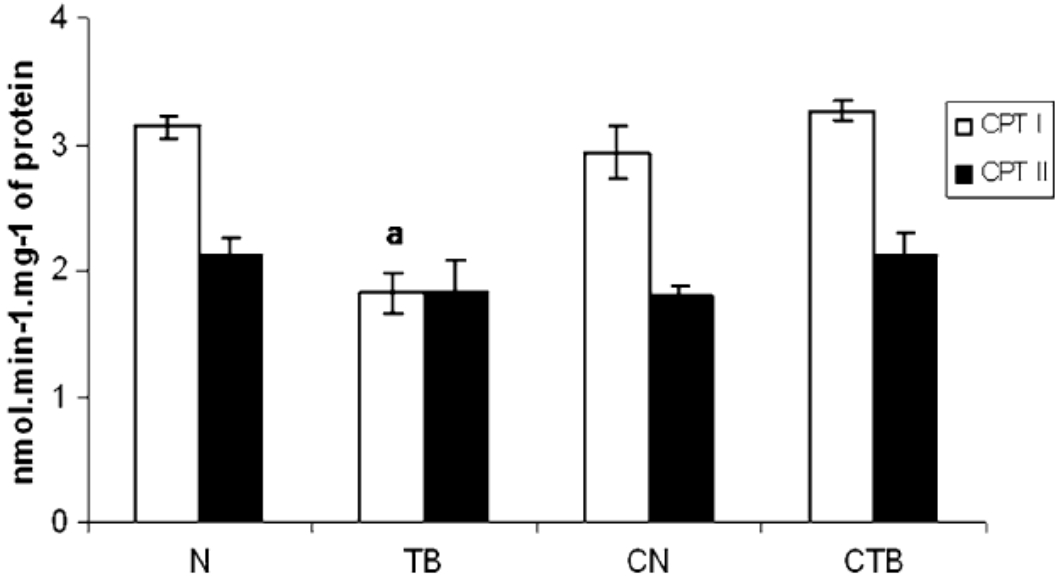
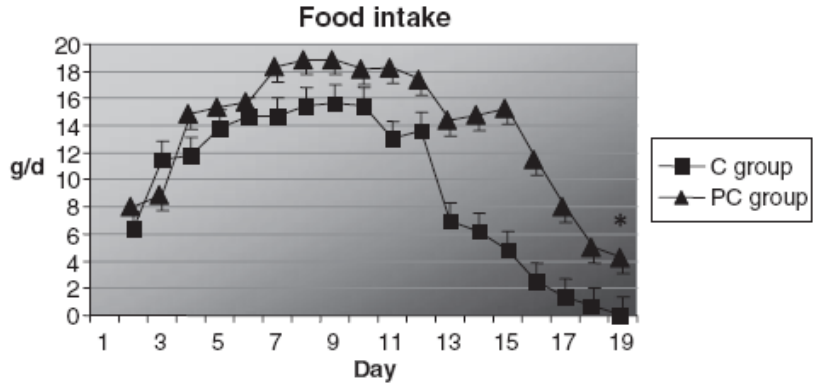


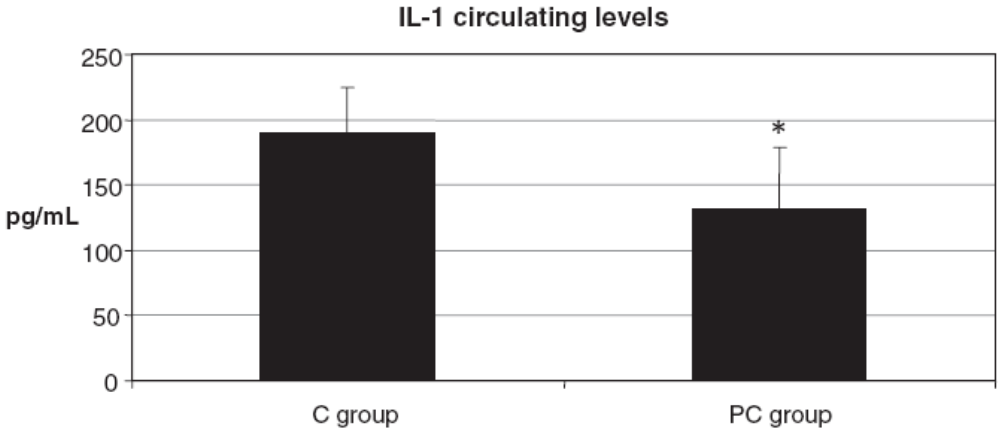
Fig. 2 Maximal activity of liver carnitine palmitoyltransferases I and II. Control (*N*), control supplemented with L-carnitine (CN), tumour bearing (*TB*) and tumour-bearing supplemented with L-carnitine (*CTB*). Data are mean ± SE ($n = 4$). $^{a}p < 0.01$ for comparison with all groups

Amino Acids 2011 (epub ahead of print)

Carnitine Administration Reduces Cytokine Levels, Improves Food Intake, and Ameliorates Body Composition in Tumor-Bearing Rats

Alessandro Laviano,[1] Alessio Molfino,[1,2] Marilia Seelaender,[3] Teresa Frascaria,[1] Giuseppe Bertini,[4] Cesarina Ramaccini,[1] Maria Rosa Bollea,[2] Gennaro Citro,[4] and Filippo Rossi Fanelli[1]





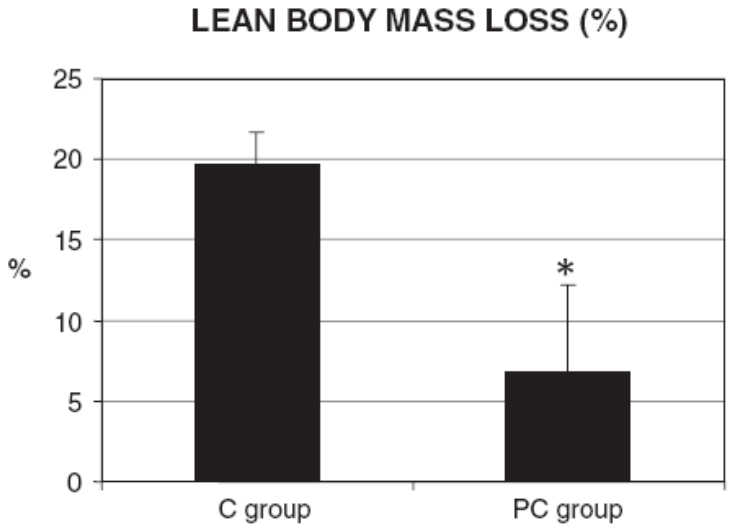


Figure 2. Lean body mass reduction on day 19 in L-propionylcarnitine rats (PC group) and in controls (C group) (*$p < .01$).

Cancer Investigation 2011; 29:696-700

Table 4. Annualized mean net costs of care in 2010 US dollars*

	Annual costs in US 2010 dollars							
	Age <65				Age ≥65			
			Last year of life				Last year of life	
Sex and site	Initial	Continuing	Cancer death	Other cause	Initial	Continuing	Cancer death	Other cause
Female								
Bladder	25694	3710	118047	10005	21412	3710	78698	10005
Brain	129802	8803	211337	39893	108168	8803	140891	39893
Breast	27693	2207	94284	748	23078	2207	62856	748
Cervix	54209	1425	117830	7949	45174	1425	78553	7949
Colorectal	61593	3159	126778	14641	51327	3159	84519	14641
Esophagus	95439	6853	156417	41051	79532	6853	104278	41051
Head and neck	50376	4826	129903	10064	41980	4826	86602	10064
Kidney	46077	6255	110765	24607	38397	6255	73843	24607
Leukemia	39800	8537	195196	31517	33167	8537	130131	31517
Lung	72639	8130	138785	18897	60533	8130	92524	18897
Lymphoma	69457	8622	164763	20462	57881	8622	109842	20462
Melanoma	6057	915	85175	252	5047	915	56784	252
Other	40173	5859	95782	21721	40173	5859	95782	21721
Ovary	98788	8296	149573	12257	82324	8296	99715	12257
Pancreas	112154	8672	164911	40538	93462	8672	109941	40538
Stomach	85291	3977	155636	29172	71076	3977	103758	29172
Uterus	32129	1535	105262	4437	26775	1535	70175	4437

EDITORIAL

nature medicine

Cancer drugs: remedy required

Cancer drugs often impair quality of life and fail to extend patient survival. Mandating increased efficacy and promoting efforts to target tumor metastasis may improve outcomes for patients with cancer.

Nat Med 2011; 17: 231

Fasting Cycles Retard Growth of Tumors and Sensitize a Range of Cancer Cell Types to Chemotherapy

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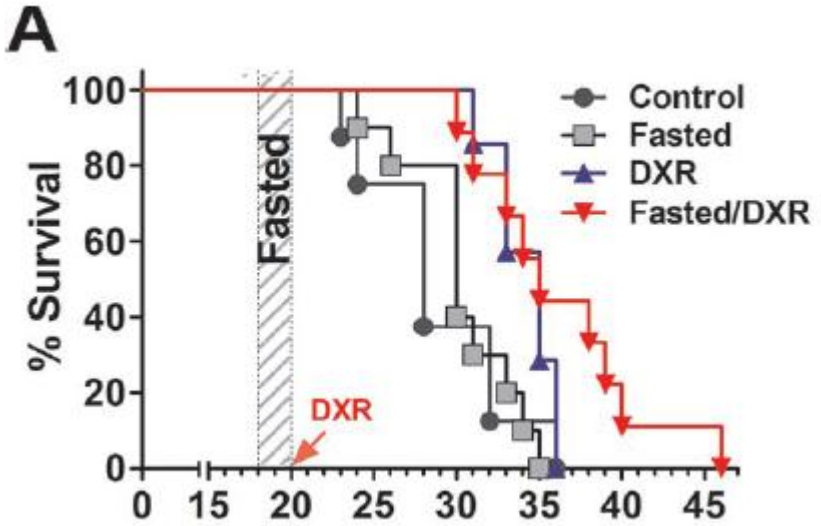

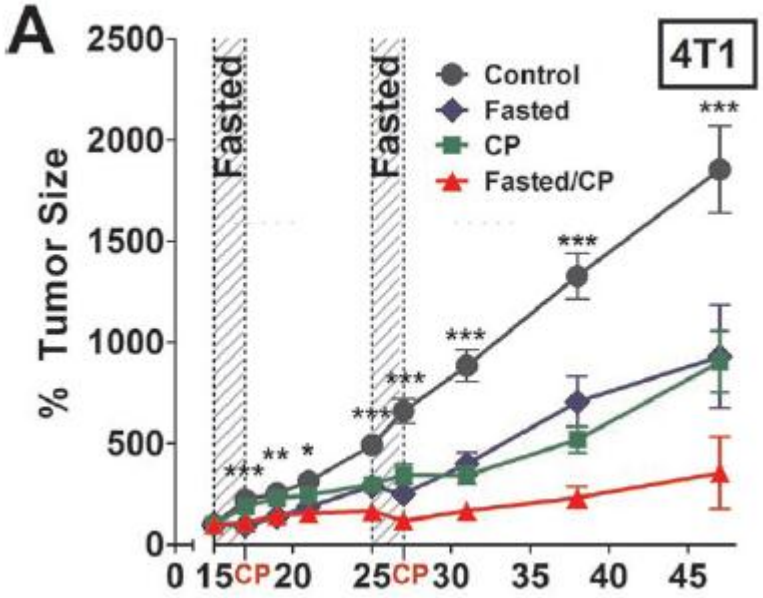

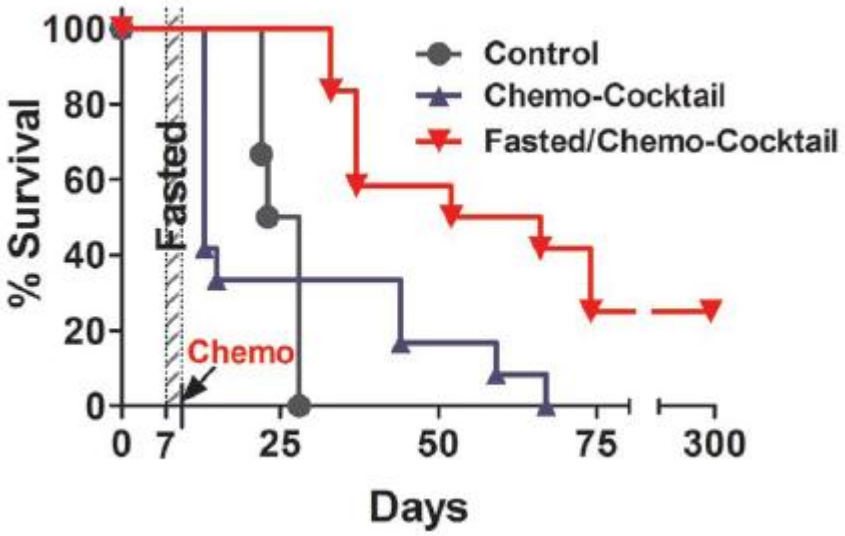

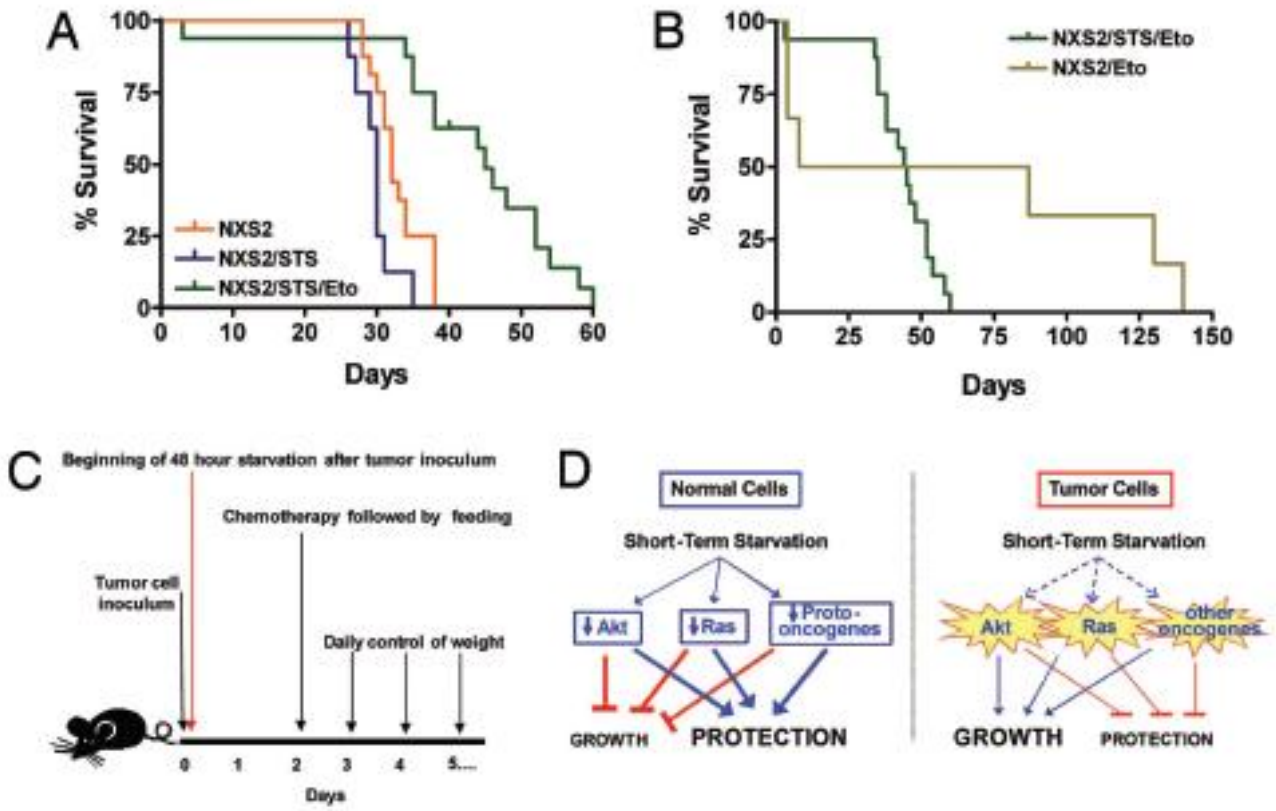

Raffaghello L et al. PNAS 2008; 105:8215-20

Conclusioni

- Lo stress ossidativo è una conseguenza ineluttabile della evoluzione della vita sul pianeta Terra.
- Livelli moderati di stress ossidativo promuovono risposte metaboliche protettive in risposta al trauma.
- Aumento dello stress = aumento morbidità/mortalità
- La supplementazione con antiossidanti in pazienti chirurgici ha dato risultati contrastanti.
- In oncologia, lo stress ossidativo contribuisce allo sviluppo di cachessia.
- La tossicità da stress ossidativo iatrogeno potrebbe essere ridotta sfruttando la DSR delle cellule normali rispetto a quelle neoplastiche.