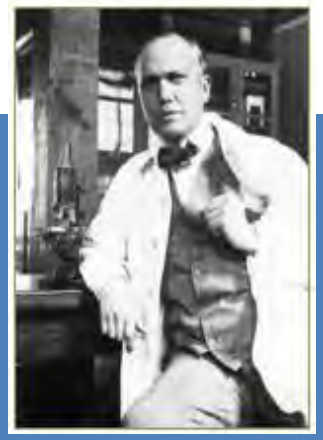
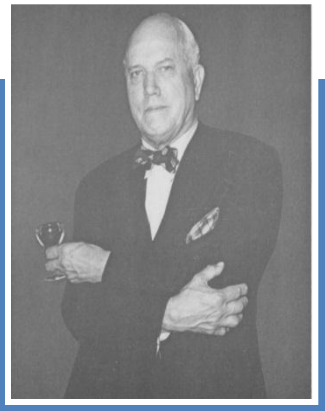
Vitamin E: A long overdue review

By Chee Wai FONG (PhD)
Head of Research & Development
Davos Life Science Pte Ltd (Singapore)

Discovery of Vitamin E





Herbert McLean Evans
(September 23, 1882–March 6, 1971)
was a U.S. anatomist and embryologist.

He was born in Modesto, California.

In 1908, he obtained his medical degree from Johns Hopkins University, eventually becoming its associate professor of anatomy.

Evans moved back to California in 1915 and was made professor of anatomy at the University of California, in Berkeley, California, and held that position until his death.

Recommended daily intake (RDI)

22.5 IU or 15 mg

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Myth 1: There is only one form of Vitamin E

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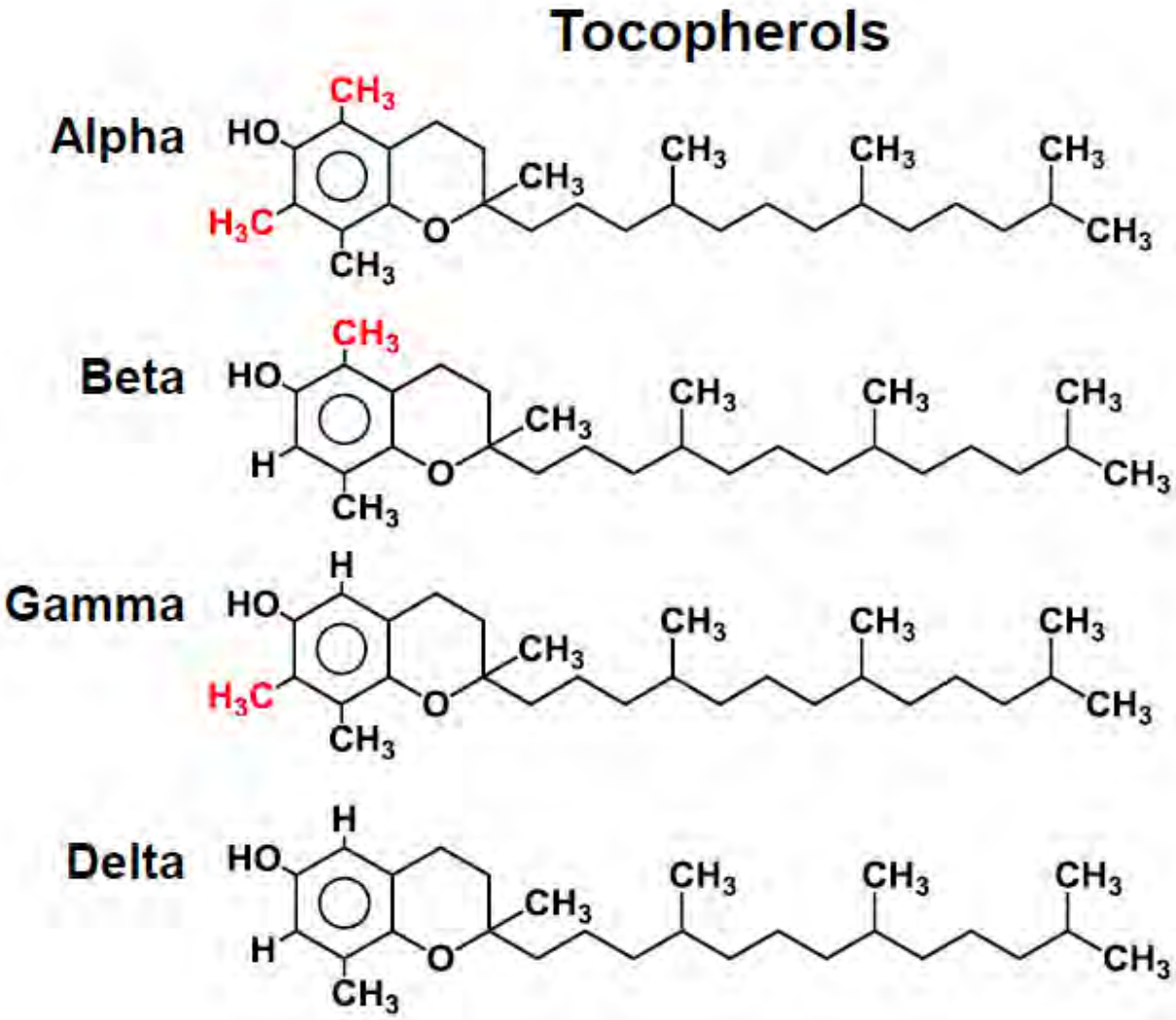
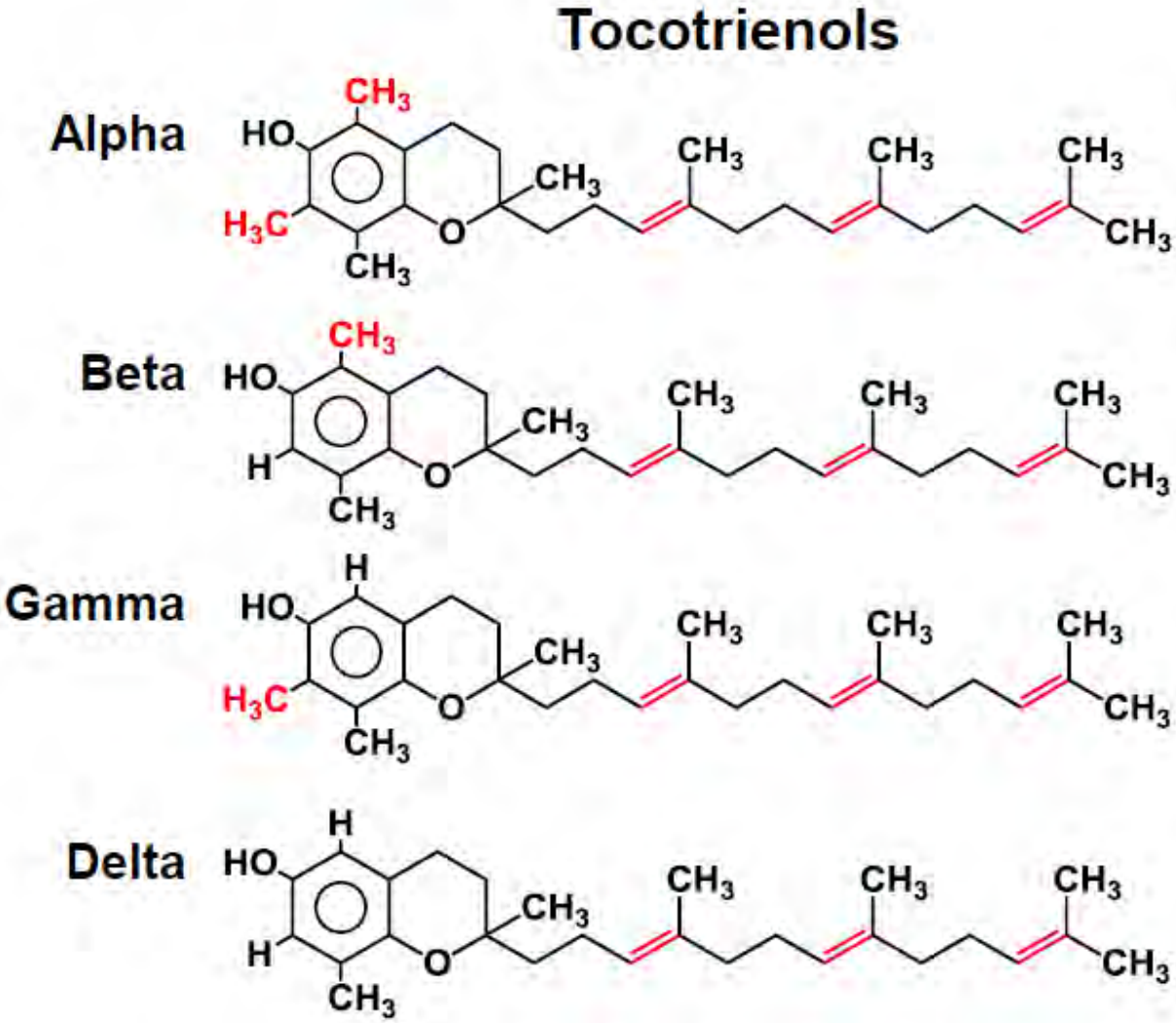


Tocopherols vs Tocotrienols



IU Definition of Vitamin E

The International Unit (IU) of vitamin E is the activity of 1 mg of dl-alpha-tocopheryl acetate. This is the average quantity that, administered orally, prevents resorption-gestation in 50% of female rats ed of vitamin E

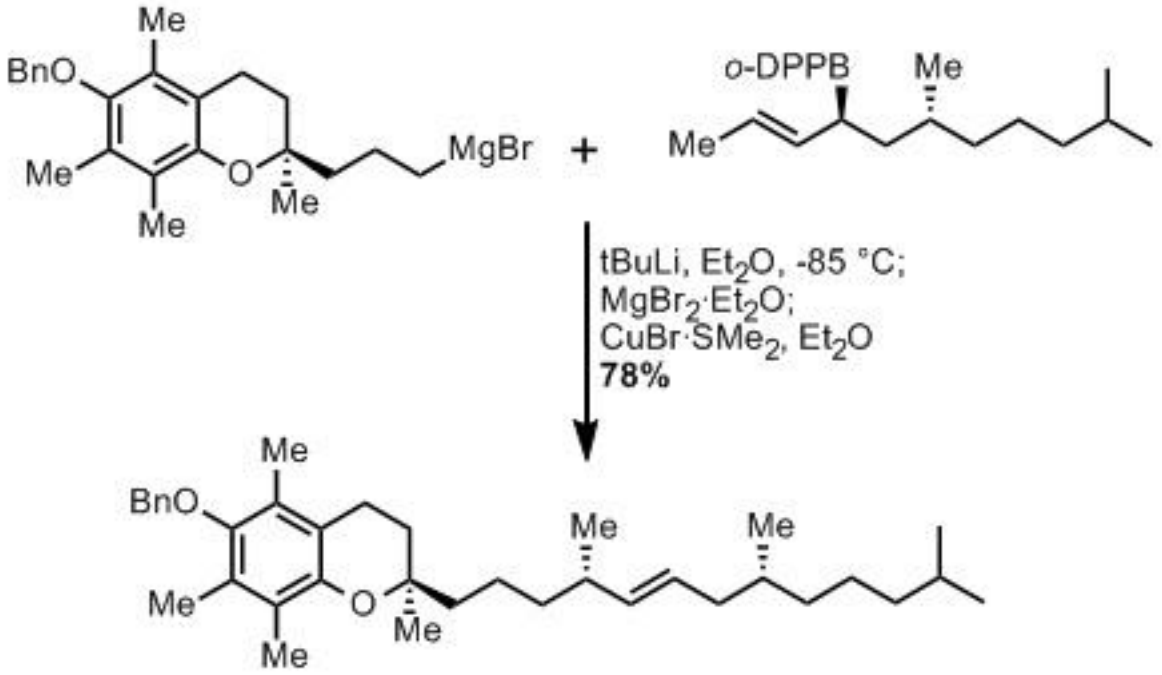
Relative biological activities of vitamin E at resorption-gestation test:

		ity
d-alpha-tocopherol (RRR)		1.49 IU
d-beta-tocopherol (RR	-50%	0.75 IU
d-gamma-tocoph	1-11%	0.25 IU
d-delta-toc	1-3%	0.1 IU
d-alpha-	29-30%	0.45 IU
d-beta-to	5%	0.1 IU
d-gamma-t ienol	Not known	NA
d-delta-tocotrienol	Not known	NA

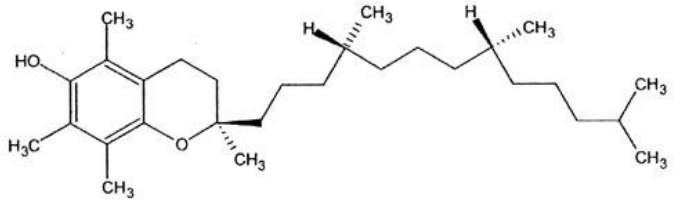
Outdated definition of Vitamin E as purely essential for fertility

Ball, 1988; Kamal-Eldin and Appelqvist, 1996

Myth 2: Synthetic vs Natural

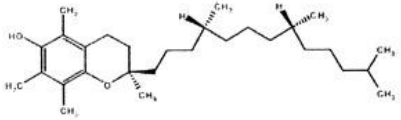


Natural Vitamin E (RRR-α-tocopherol; d-α-tocopherol)

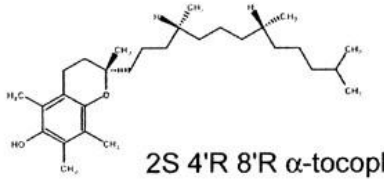


2R 4'R 8'R α-tocopherol

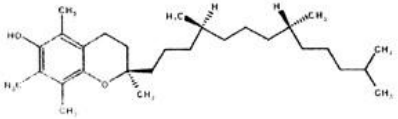
Synthetic Vitamin E (*all-rac*-α-tocopherol; dl-α-tocopherol)



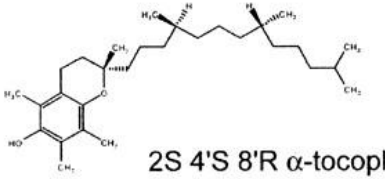
2R 4'R 8'R α-tocopherol



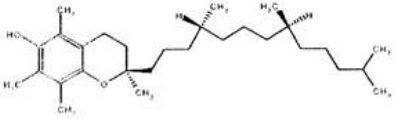
2S 4'R 8'R α-tocopherol



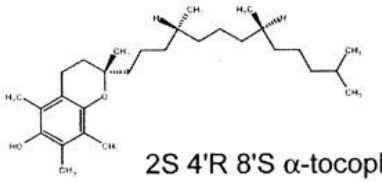
2R 4'S 8'R α-tocopherol



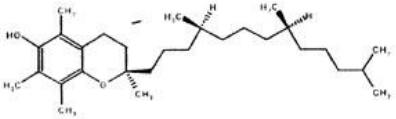
2S 4'S 8'R α-tocopherol



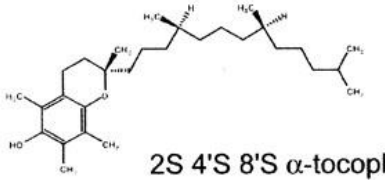
2R 4'R 8'S α-tocopherol



2S 4'R 8'S α-tocopherol



2R 4'S 8'S α-tocopherol



2S 4'S 8'S α-tocopherol

International Unit of Synthetic vs Natural Vitamin E

dl-alpha-tocopheryl acetate	1.00 IU
dl-alpha-tocopherol	1.10 IU
d-alpha-tocopheryl acetate	1.36 IU
d-alpha-tocopherol	1.49 IU

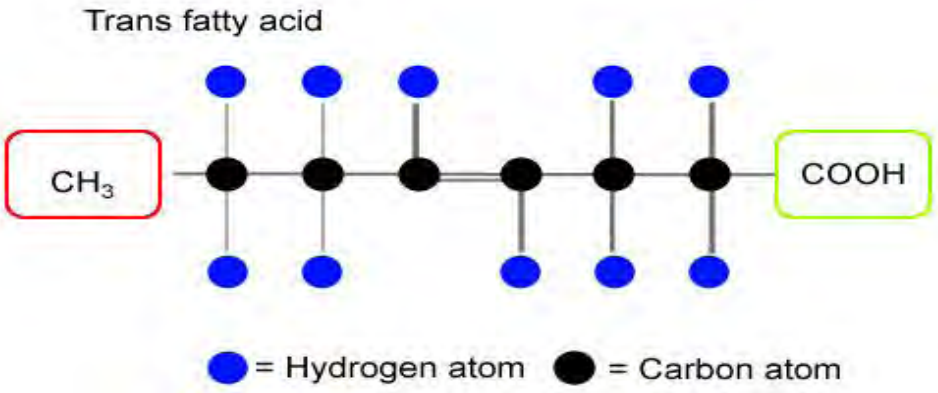
Bieri and McKenna, 1981

US$5.99

US$12.99

Have we learnt our lesson from Trans Fat?

- Made by adding hydrogen to vegetable oil through a process called hydrogenation
- Using trans fats in the manufacturing of foods helps foods stay fresh longer, have a longer shelf life and have a less greasy feel
- Long term study shows it raises your "bad" (LDL) cholesterol and lowers your "good" (HDL) cholesterol, increases Triglycerides & **causes inflammation**
- **increase in consumption correlated with the rise of coronary heart disease and other major illnesses including diabetes & Alzheimer's disease**



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Myth 3:
High Antioxidant levels can prevent cancer

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Merging Science with Nature

NON-OBESE (BMI < 30 kg/m²)

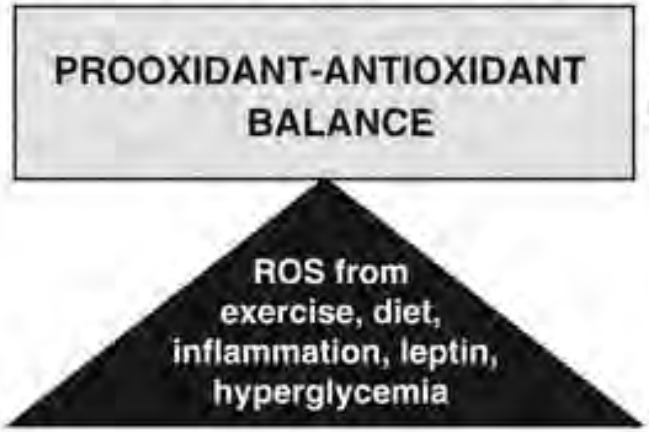
Dietary AOX

↑ Vitamins E and C, α, γ, β carotene, phytochemical, zinc, copper, selenium intake from foods

Enzymatic AOX

↑ SOD, GPX, CAT activities

↑ Blood AOX, TAS and FRAP



↓ Levels of lipid and protein oxidation

OBESE (BMI ≥ 30 kg/m²)

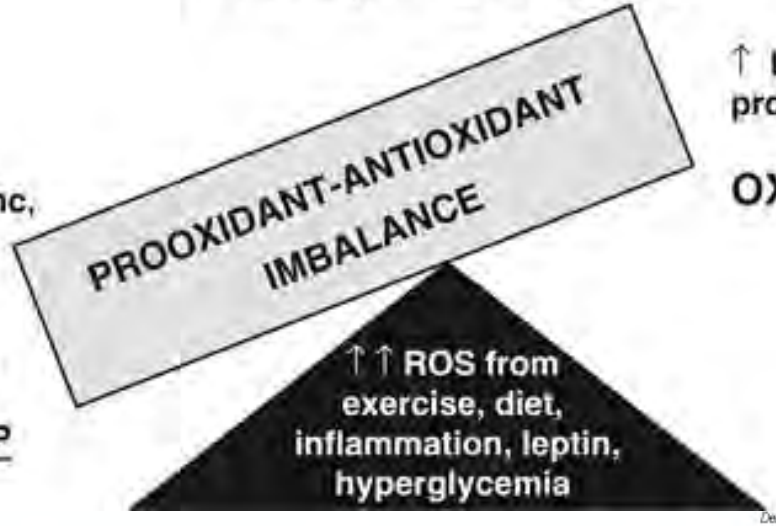
AOX Deficit

↓ Vitamins E and C, α, γ, β–carotene, phytochemical, zinc, copper, selenium intake

Enzymatic AOX

↓ SOD, GPX, CAT depletion

↓ Blood AOX, TAS and FRAP



↑ Levels of lipid and protein oxidation

OXIDATIVE STRESS

Table 1: Tocopherol Clinical trials

Study	Study cohort	Intervention	Effect of αTP versus placebo
ATBC (Finland: 1985-1993)	n=30k male smokers, 50-69y (5-8y)	αTP (50 mg); βcarotene (20 mg); both; placebo (2 x 2)	• Null (lung, pancreas, colon/rectum, urothelium, kidney, stomach, oral/pharynx, larynx, esophagus cancer) • **lower prostate cancer incidence** (RR=0.64, lack of trend & inconclusive) • **reduced VEGF-D** levels in serum Men with higher serum αTP (13-14 mg/L): • **lower total mortality** (RR=0.82); **cancer mortality** (RR=0.79); **CVD mortality** (RR=0.81), (p for trend<00001) • also positively correlated with γTP levels and other lifestyle factors
Linxian (China: 1986-1991)	n=30k, 40-69y, malnourished & at risk for stomach & esophagus cancer (6y)	A (Vit A, Zn), B (Vit B), C (Vit C, Mb), D (αTP, Se, βcarotene). Combi of 2, ABCD or placebo	• Null (esophagus, lung, liver cancer incidence) Group D (**αTP**, **Se**, βcarotene): • **lower** overall (RR= 0.91, p<0.05) and cancer (RR=0.87, p<0.05) **mortality** • **lower gastric cancer incidence** (RR=0.81, p<0.05) • effects were *predominantly* in adults <55y at start of study • **lower esophageal cancer mortality** in adults <55y (RR=0.83, p=0.025)
WHS (USA: 1992-2004)	n=40k women ≥45y (10y)	αTP (600 IU); βcarotene (50 mg); Aspirin (100 mg); combi of 2; all 3 or placebo (2 x 2 x 2)	• Null (all cancers, breast, lung, colon cancer) • **lower CVD incidence** (RR=0.76, p=0.03)
HOPE / HOPE-TOO (World: 1993-2003)	n=9k, ≥55y, with CVD or diabetes (4.5y)	αTP (400 IU) or placebo; ACE inhibitor (ramipril) or placebo (2 x 2)	• Null (cardiovascular disease, total cancer incidence and deaths, prostate, oral/pharynx, GI, melanoma skin, breast cancer) • higher risk of heart failure (RR=1.13, p=0.03) • **lower risk of lung cancer** (RR=0.72, p=0.04), unsupported by other larger studies (ATBC, HPS)
HPS (UK: 1994-2001)	n=20k, 40-80y, with CVD or diabetes (5y)	αTP (600 mg), Vit C (250 mg), βcarotene (20 mg); placebo with simvastatin (40 mg) (2 x 2)	• Null (cardiovascular disease, total cancer incidence, lung, stomach, prostate)
SU.VI.MAX (France: 1994-2002)	n=13k, 35-60y (7.5y)	αTP (30 mg), Vit C (120 mg), βcarotene (6 mg), Se (100 ug), Zn (20 mg); placebo	• Null (health-related quality of life, total cancer incidence) • **lower total cancer incidence** (GI, respiratory, skin) in men (RR=0.69, p<0.05) • **lower prostate cancer incidence** in men with normal PSA levels of 3 ug/L (RR=0.52, p<0.05) • 2008: better memory scores

Table 1: Tocopherol Clinical trials

Study	Study cohort	Intervention	Effect of αTP versus placebo
WASC (USA: 1995-2005)	n=7627 females with CVD or risk factors, >40y (9y)	αTP (600 IU); βcarotene (50 mg); Vit C (500 mg); combi of 2; all 3 or placebo (2 x 2 x 2)	• Null (overall cancer incidence or mortality)
PHS II (USA: 1997-2007)	n=14k males >50y (8y)	αTP (400 IU); βcarotene (50 mg); Vit C (500 mg); multivit or placebo (2 x 2 x 2 x2)	• Null (overall cancer incidence or site-specific caners including prostate cancer)
SELECT (USA: 2001-2008)	n=35k males with PSA < 4 ng/ml, >50y (7-12y)	αTP (400 IU); Se (200 ug); both or placebo (2 x 2)	• Null (overall mortality, cancer incidence, colorectal, lung cancer, diabetes and CVD) • **Increased risk of prostate cancer (RR=1.17, p=0.008)**
CHAOS (UK: 1992-1995)	n=2000 patients with atherosclerosis (8y)	αTP (400/800 IU); or placebo	• **Reduced risk of non-fatal myocardial infarction & CVD** (RR=0.53, p=0.005) • Non significant increase in CVD mortality

- No one size fits
- No overall benefit for the general population
- Choosing your target group (age, risk factors, genetic polymorphism etc.)

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Vitamin E and the Risk of Prostate Cancer

The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

Eric A. Klein, MD
Ian M. Thompson Jr, MD
Catherine M. Tangen, DrPH
John J. Crowley, PhD
M. Scott Lucia, MD
Phyllis J. Goodman, MS
Lori M. Minasian, MD
Leslie G. Ford, MD
Howard L. Parnes, MD
J. Michael Gaziano, MD, MPH
Daniel D. Karp, MD
Michael M. Lieber, MD
Philip J. Walther, MD, PhD
Laurence Klotz, MD
J. Kellogg Parsons, MD, MHS
Joseph L. Chin, MD
Amy K. Darke, MS
Scott M. Lippman, MD
Gary E. Goodman, MD
Frank L. Meyskens Jr, MD
Laurence H. Baker, DO

Context The initial report of the Selenium and Vitamin E Cancer Prevention Trial (SELECT) found no reduction in risk of prostate cancer with either selenium or vitamin E supplements but a statistically nonsignificant increase in prostate cancer risk with vitamin E. Longer follow-up and more prostate cancer events provide further insight into the relationship of vitamin E and prostate cancer.

Objective To determine the long-term effect of vitamin E and selenium on risk of prostate cancer in relatively healthy men.

Design, Setting, and Participants A total of 35 533 men from 427 study sites in the United States, Canada, and Puerto Rico were randomized between August 22, 2001, and June 24, 2004. Eligibility criteria included a prostate-specific antigen (PSA) of 4.0 ng/mL or less, a digital rectal examination not suspicious for prostate cancer, and age 50 years or older for black men and 55 years or older for all others. The primary analysis included 34 887 men who were randomly assigned to 1 of 4 treatment groups: 8752 to receive selenium; 8737, vitamin E; 8702, both agents, and 8696, placebo. Analysis reflect the final data collected by the study sites on their participants through July 5, 2011.

Interventions Oral selenium (200 µg/d from *L*-selenomethionine) with matched vitamin E placebo, vitamin E (400 IU/d of all *rac*-α-tocopheryl acetate) with matched selenium placebo, both agents, or both matched placebos for a planned follow-up of a minimum of 7 and maximum of 12 years.

Main Outcome Measures Prostate cancer incidence.

Results This report includes 54 464 additional person-years of follow-up and 521 additional cases of prostate cancer since the primary report. Compared with the placebo (referent group) in which 529 men developed prostate cancer, 620 men in the vitamin E group developed prostate cancer (hazard ratio [HR], 1.17; 99% CI, 1.004-1.36, $P=.008$); as did 575 in the selenium group (HR, 1.09; 99% CI, 0.93-1.27; $P=.18$), and 555 in the selenium plus vitamin E group (HR, 1.05; 99% CI, 0.89-1.22, $P=.46$). Compared with placebo, the absolute increase in risk of prostate cancer per 1000 person-years was 1.6 for vitamin E, 0.8 for selenium, and 0.4 for the combination.

Conclusion Dietary supplementation with vitamin E significantly increased the risk of prostate cancer among healthy men.

LIFETIME RISK OF PROSTATE CANcer in the United States is currently estimated to be 16%.[1] Although most cases are found at

What's wrong with Vitamin E?

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1. Narrow focus only on α-tocopherol

2. α-tocopherol never shown to be anti-tumorigenesis in-vitro or in-vivo; instead γ & δ isomers shown to kill cancer cells in the laboratory

3. Excessively high dose (400IU & above) over long period of time crowds out other tocopherol & tocotrienol isomers

4. Safety of synthetic form of Vitamin E at high doses for prolonged duration unknown

5. Antioxidants alone will not suppress cancer & other conditions

6. **A broad spectrum of tocopherol & tocotrienol essential to overall nutrition health**

Current form of Vitamin E (alpha-Tocopherol)

Functions	Vitamin E	Remarks
Antioxidant	+++	Prevents lipid peroxidation
Fertility	+++	Only requires 22.5 IU
Cancer Prevention	-	High doses increase cancer risk
Metabolic Syndrome	+	Some study shows effective in fatty liver
Brain Health	-	No study
Broad Spectrum	-	Only one form

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What is the underlying cause of disease that antioxidants failed to address?

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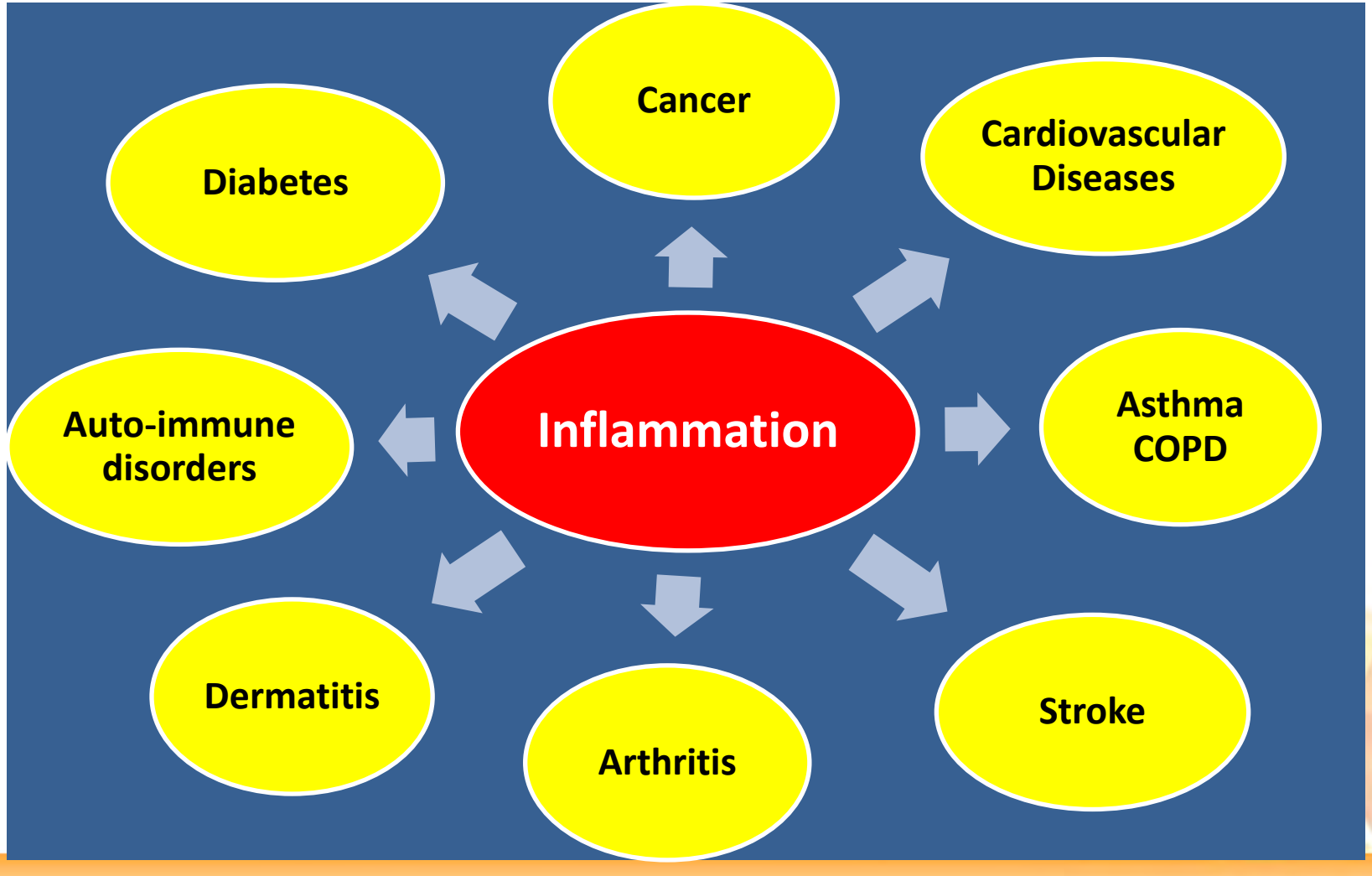
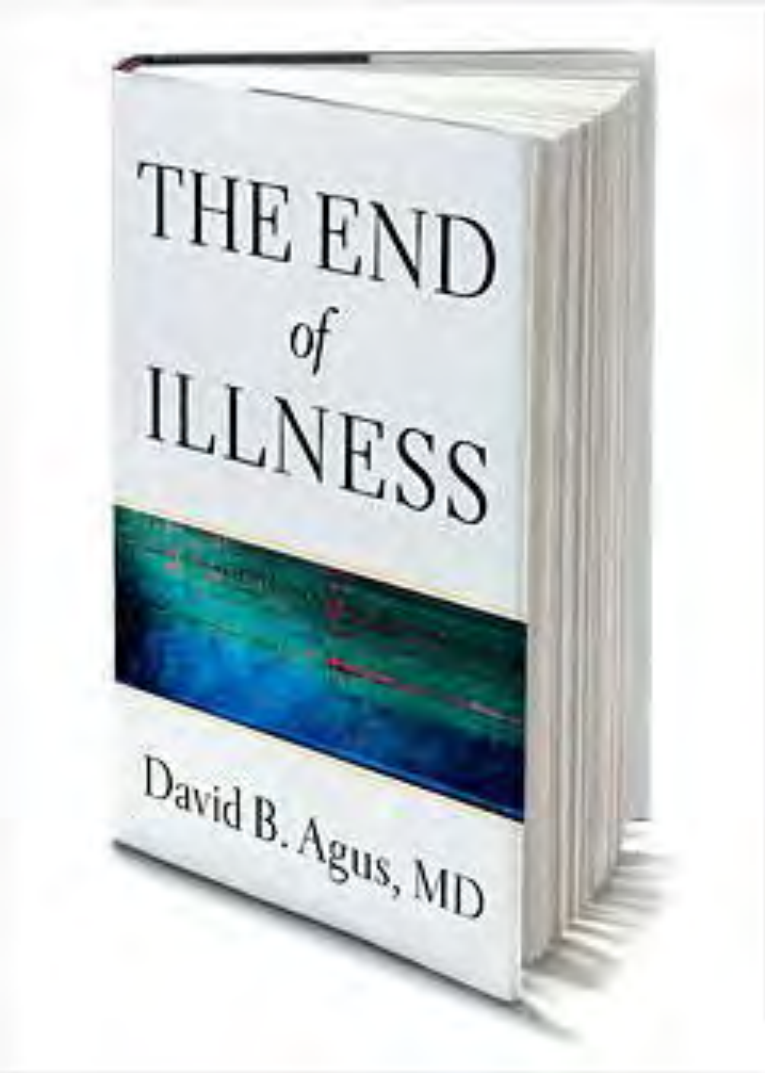
Inflammation
the root of many diseases



Chronic & excessive inflammation is the root cause of many diseases



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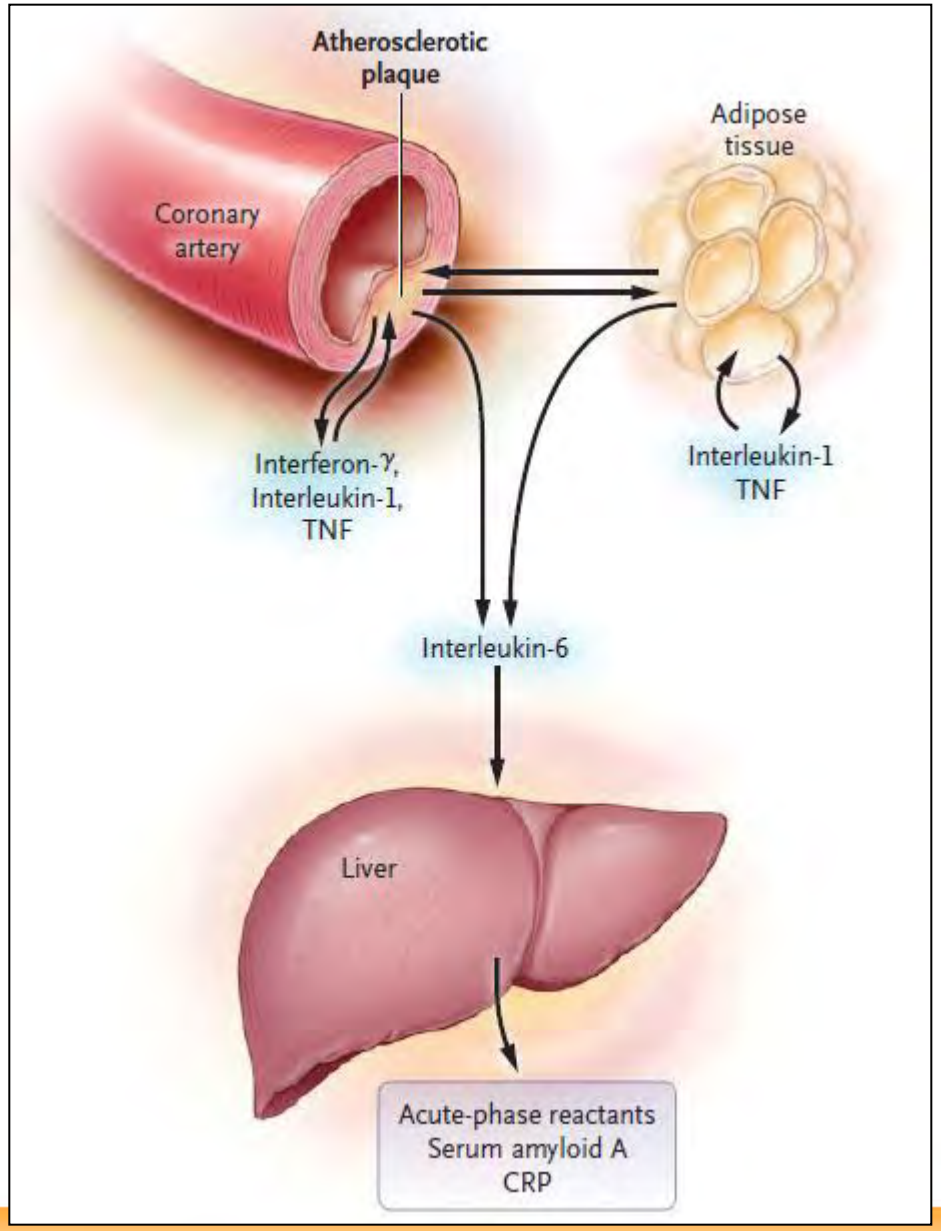
Life style Carcinogens/Risk factors

Cytokine Cascade in Atherosclerosis



N Engl J Med 2005;352:1685-95.

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Type 2 diabetes as an inflammatory disease

Marc Y. Donath and Steven E. Shoelson‡*

Abstract | Components of the immune system are altered in obesity and type 2 diabetes (T2D), with the most apparent changes occurring in adipose tissue, the liver, pancreatic islets, the vasculature and circulating leukocytes. These immunological changes include altered levels of specific cytokines and chemokines, changes in the number and activation state of various leukocyte populations and increased apoptosis and tissue fibrosis. Together, these changes suggest that inflammation participates in the pathogenesis of T2D. Preliminary results from clinical trials with salicylates and interleukin-1 antagonists support this notion and have opened the door for immunomodulatory strategies for the treatment of T2D that simultaneously lower blood glucose levels and potentially reduce the severity and prevalence of the associated complications of this disease.

Nature Reviews Feb 2011 (Vol 11)

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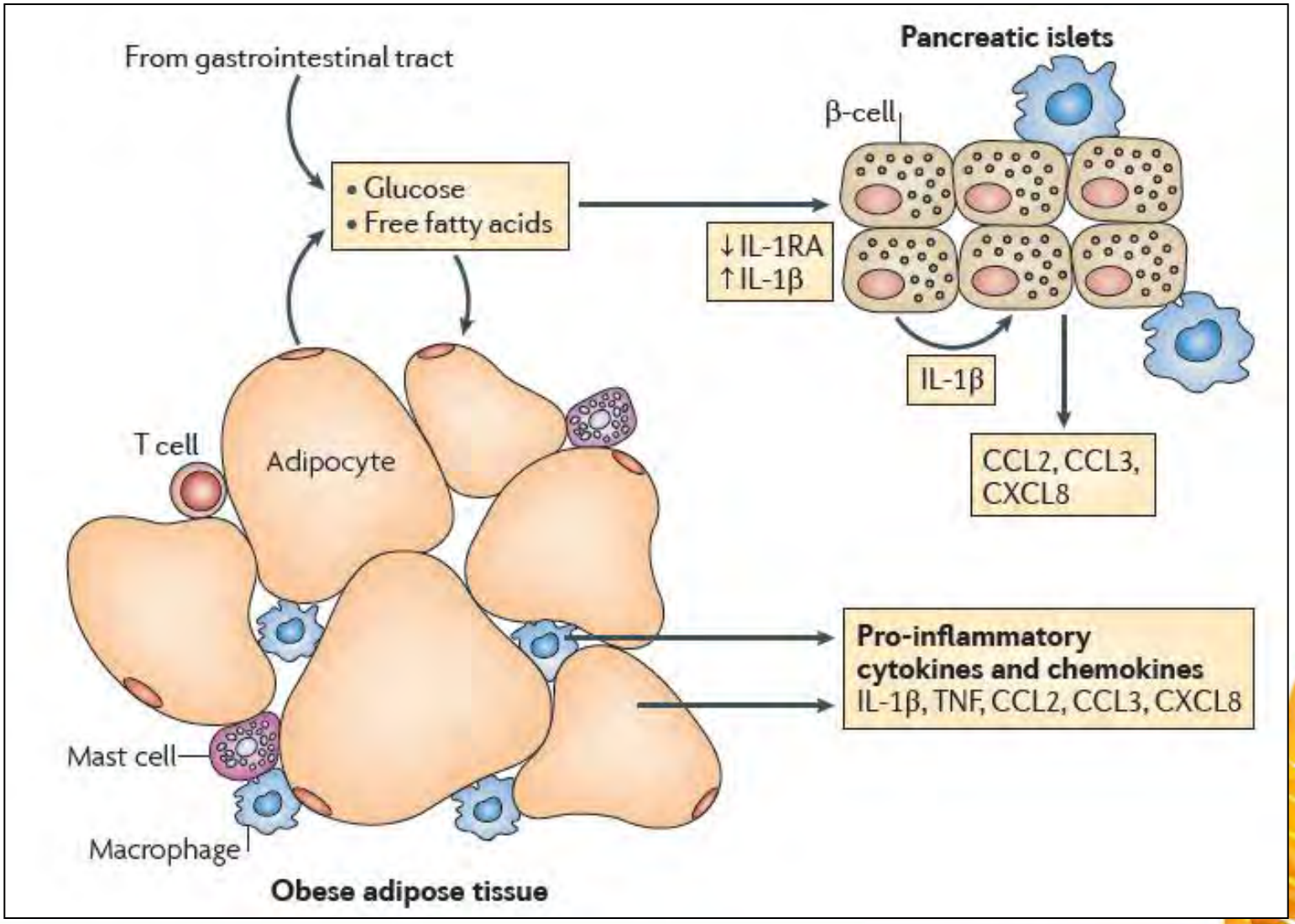
Development of Inflammation in Type 2 Diabetes



Anti-inflammatory Treatment for Diabetes

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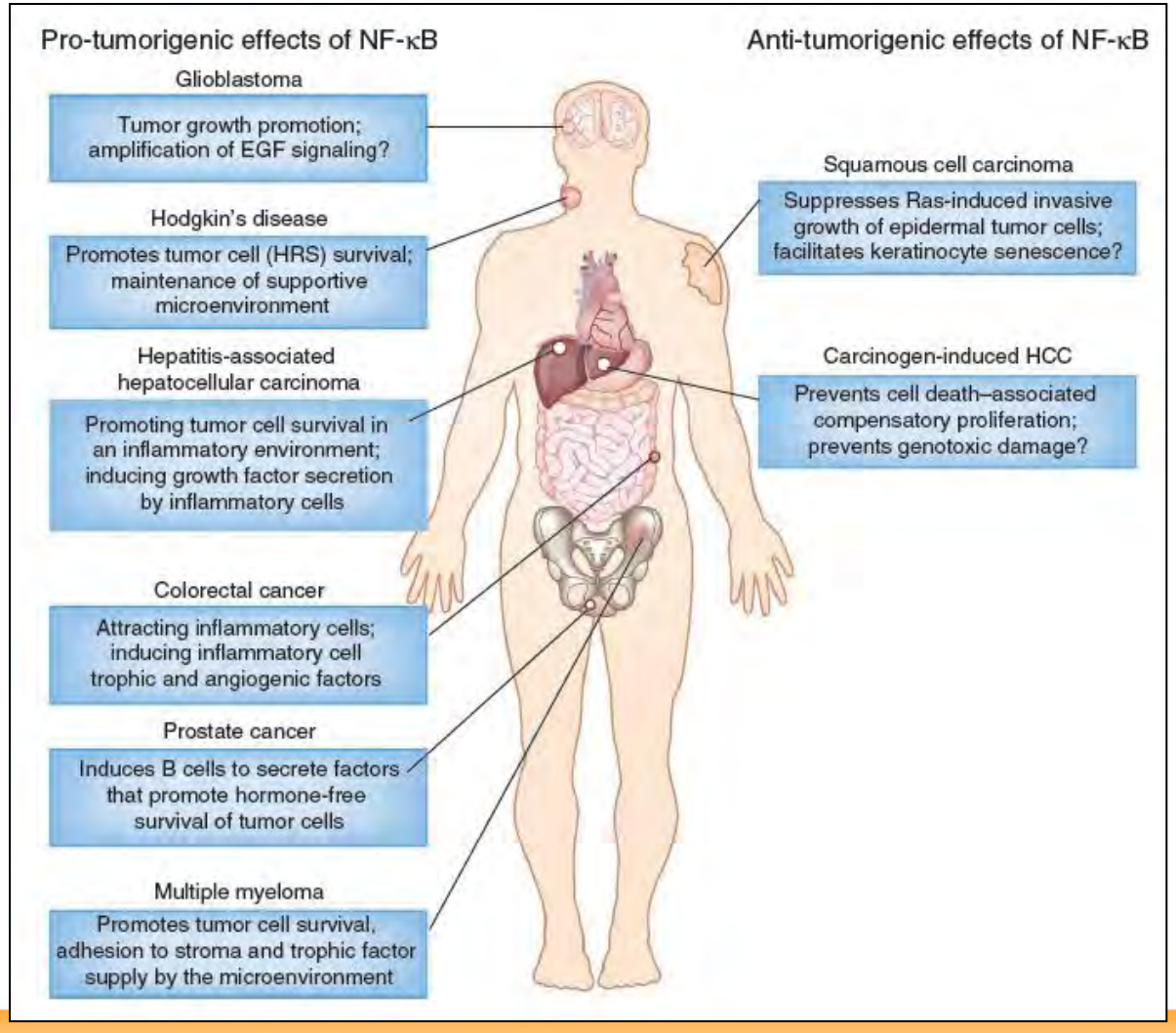
Table 2 | **Clinical studies using anti-inflammatory approaches to treat type 2 diabetes or prediabetes**

Mechanism	Drug	Trial Phase	Number of subjects	Treatment duration (weeks)	Main findings
IL-1 receptor blockade	Anakinra (Kineret; Amgen/Biovitrum)	II	69	13	↓ Glycated haemoglobin, ↓ CRP, ↑ insulin production
IKKβ–NF-κB inhibition	Salsalate	II	20	4	↓ FBG, ↓ CRP, ↑ insulin sensitivity, ↑ adiponectin
IKKβ–NF-κB inhibition	Salsalate	II	16	2–4	↓ FBG, ↓ FFA, ↓ triglycerides, ↓ CRP, ↑ adiponectin
IKKβ–NF-κB inhibition	Salsalate	II	40	1	↓ FBG, ↑ insulin
IKKβ–NF-κB inhibition	Salsalate	IIb	104	12	↓ Glycated haemoglobin, ↓ FBG, ↓ triglycerides, ↑ adiponectin
IL-1β-specific antibody	XOMA 052 (Xoma)	I	98	Single injection	↓ Glycated haemoglobin, ↓ CRP, ↑ insulin production
IL-1 receptor blockade	Anakinra (Kineret; Amgen/Biovitrum)	II	12	4	Ongoing, closed for recruitment
IL-1β-specific antibody	ACZ885 (canakinumab; Novartis)	II	231	Unknown	Ongoing, closed for recruitment
IL-1β-specific antibody	ACZ885 (canakinumab; Novartis)	II	140	48	Ongoing
IL-1β-specific antibody	ACZ885 (canakinumab; Novartis)	II	232	4	Ongoing, closed for recruitment

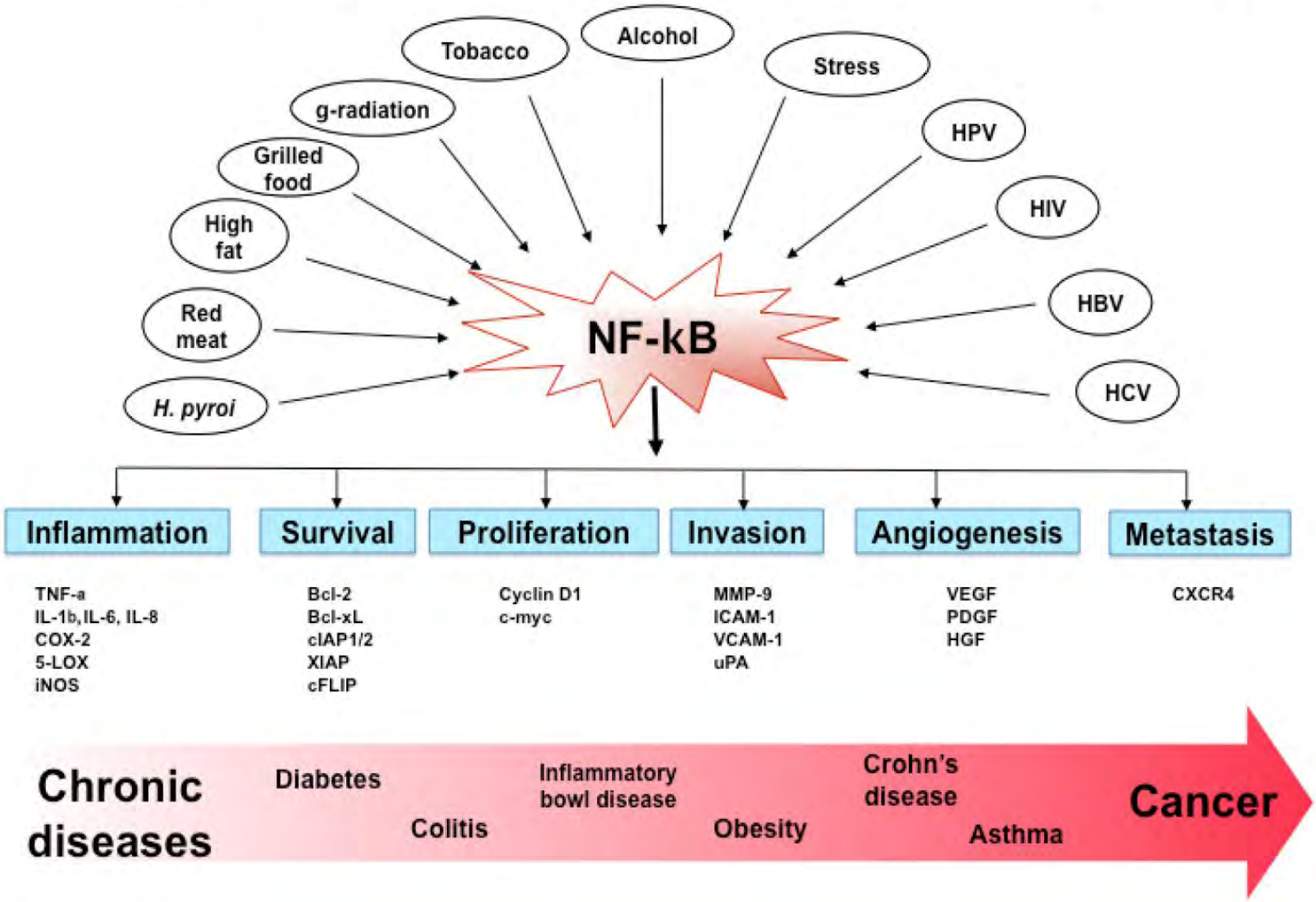
nature immunology NATURE IMMUNOLOGY VOLUME 12 NUMBER 8 AUGUST 2011

Inflammation meets cancer, with NF-κB as the matchmaker

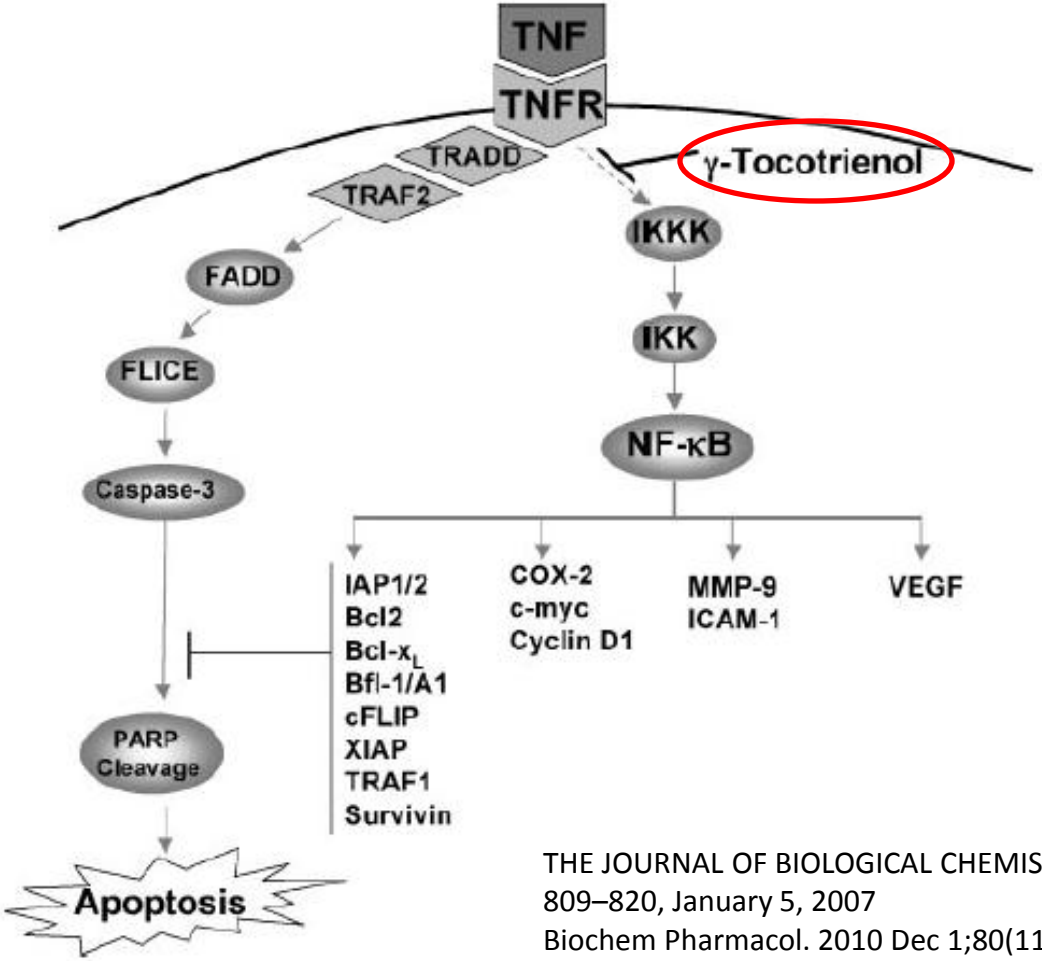
Yinon Ben-Neriah[1] & Michael Karin[2]



Inflammation is a fundamental protective response that sometimes goes awry and becomes a major cofactor in the pathogenesis of many chronic human diseases, including cancer


Tobacco
Alcohol
Stress
g-radiation
HPV
Grilled food
HIV
High fat
HBV
Red meat
NF-kB
H. pyroi
HCV
Inflammation
Survival
Proliferation
Invasion
Angiogenesis
Metastasis
TNF-a
IL-1b, IL-6, IL-8
COX-2
5-LOX
iNOS
Bcl-2
Bcl-xL
cIAP1/2
XIAP
cFLIP
Cyclin D1
c-myc
MMP-9
ICAM-1
VCAM-1
uPA
VEGF
PDGF
HGF
CXCR4
Chronic diseases
Diabetes
Colitis
Inflammatory bowl disease
Obesity
Crohn's disease
Asthma
Cancer

Tocotrienol Exerts Anti-inflammatory Response by Regulating NF-κB & Inflammatory Cytokines



↓ IL6
↓ IL8
↓ TNF-α
↓ IL1
↑ IL12
↑ IFN-γ

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 282, NO. 1, pp. 809–820, January 5, 2007

Biochem Pharmacol. 2010 Dec 1;80(11):1613-31. Epub 2010 Aug 7. Review

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Evidence that Tocotrienol is an effective anti-inflammatory agent

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Lindsay Brown
University of Southern Queensland, Australia

Delta-Tocotrienol in a Rat Model of Metabolic Syndrome

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Tocotrienol can suppress harmful effects of metabolic syndrome

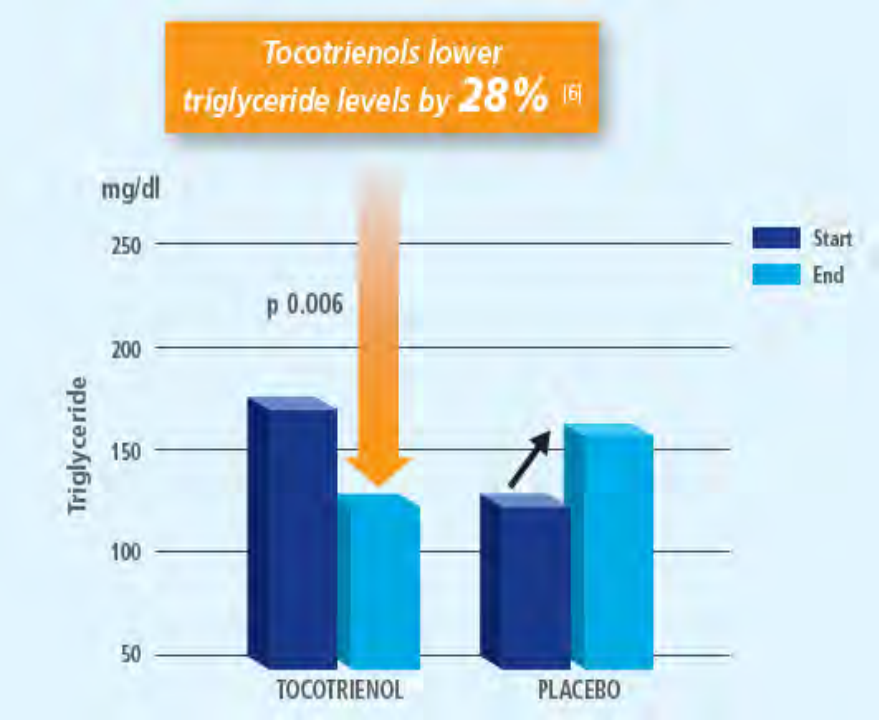
In high carbohydrate, high fat fed rats, δ-tocotrienol attenuated:

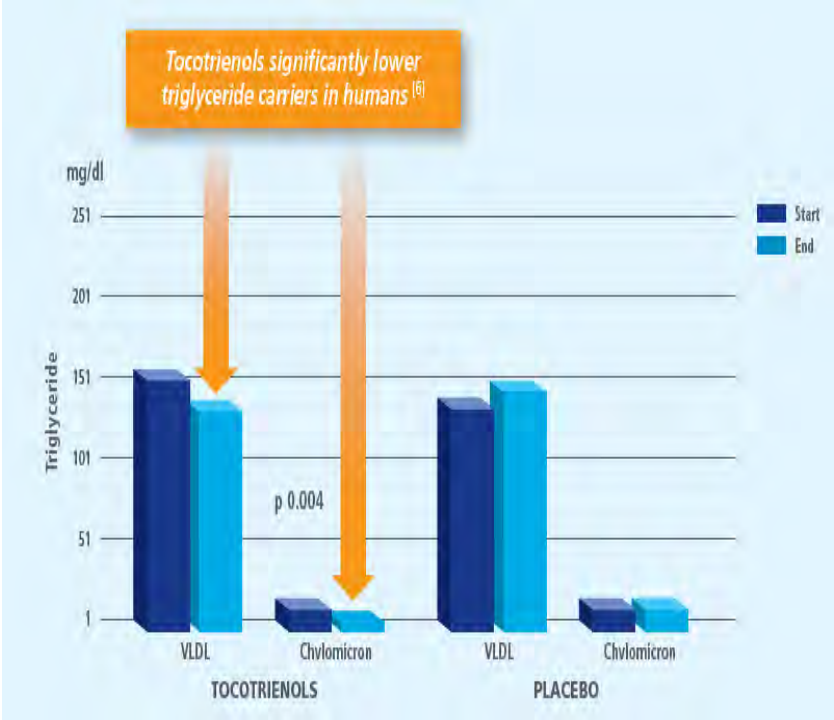
- **Hypertension**
- **Inflammation and fibrosis in the left ventricle and liver**
- **Abdominal fat deposition and dyslipidaemia**
- **Impaired glucose tolerance**

suggesting that inhibition of inflammation is the key target for this compound in metabolic syndrome.

DavosLife Study: Gamma Delta Tocotrienols Reduce Triglyceride Hepatic Synthesis & Secretion

Tocotrienol-treated subjects showed decreasing trends in average weight, body fat mass, body fat percentage and waist measurement.

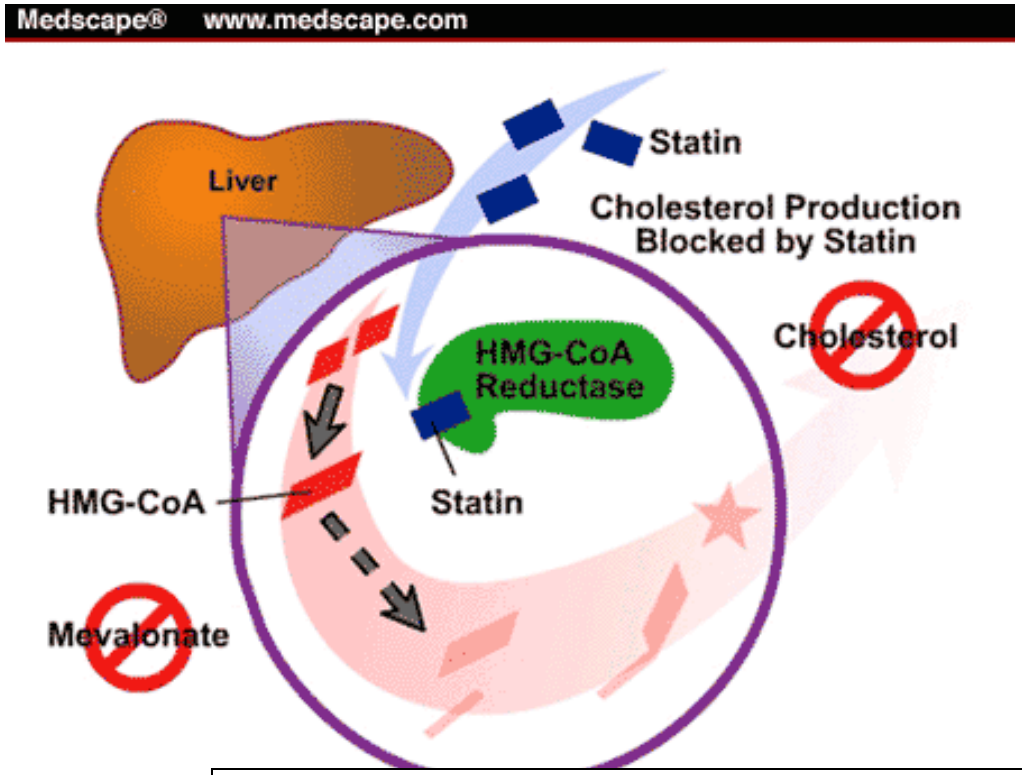




Zaiden N, Yap W, Ong S, Xu C, Teo V, Chang C, Zhang X, Nesaretnam K, Shiba S and Yap Y: Gamma Delta Tocotrienols Reduce Hepatic Triglyceride Synthesis and VLDL Secretion. J Atheroscler Thromb.

Mechanism of Tocotrienol on Lipid Regulation

Natural e3
DavosLife Tocotrienols



γ-T3 reduces HMG-CoA levels post-transcriptionally

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Tocotrienols Regulate Cholesterol Production in Mammalian Cells by Post-transcriptional Suppression of 3-Hydroxy-3-methylglutaryl-Coenzyme A Reductase*

(Received for publication, November 6, 1992, and in revised form, February 1, 1993)

Rex A. Parker‡, Bradley C. Pearce§, Ronald W. Clark, David A. Gordon, and J. J. Kim Wright§

From the Department of Metabolic Diseases, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, New Jersey 08543 and the §Division of Central Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, Connecticut 06492

Upcoming clinical trial using Natural e^3 Effect of Tocotrienol on Serum Lipids in Hypercholesterolemic Subjects Taking Statin

Principal Investigator: Dr David Heber
Director, UCLA Center for Human Nutrition

Study Design:

- 3 arm study of patients, who are on statin medication, but unable to achieve target cholesterol levels
- Statin together with Placebo, 60 mg or 120 mg Natural e^3 γ/δ-tocotrienols.
- Total of 99 patients to be enrolled

Mokenge Malafa
Moffitt Cancer Center
US Florida

Delta-Tocotrienol in Subjects with Resectable Pancreatic Exocrine Neoplasia

Natural e3
DavosLife Tocotrienols

DAVOS
LIFE SCIENCE
Derived from Nature, Driven by Science

Phase I Clinical Trial using Natural e^3 Delta Tocotrienol in Pancreatic Cancer

MOFFITT CANCER CENTER

In collaboration with Moffitt Cancer Center & Research Institute (Florida, USA), oral treatment with Natural e3 in patients with resectable pancreatic cancer showed that:

Tocotrienol increases cancer cell death in human pancreatic tumours

Tocotrienol increases expression of p27 an important protein in cell cycle regulation

Springett G NA, Centeno B, Helm J, Hutchinson T, Jump H, Lush R, Sebti S, Malafa MP. , A phase I dose-escalation study of the safety, PK, and PD of vitamin E δ-tocotrienol administered to subjects with resectable pancreatic exocrine neoplasia. Paper presented at: , in The 102nd Annual Meeting of the American Association of Cancer Research (AACR). 2011: Florida, USA.

Natural e^3 DavosLife Tocotrienols

DAVOS LIFE SCIENCE

Merging Science with Nature

Clinical Trial on:

Natural Tocotrienol Against Ischemic Stroke Event

Subjects: 210 patients with Hyperlipidemic between 40 and 70 years of age currently taking statins with LDL>130mg/dL; TG>150mg/dL; HDL<40mg/dL

- Placebo pills, Tocotrienol pills (400 or 800mg)
- Low-dose 81 mg aspirin (commonly used for secondary prevent stroke),
- Tocotrienol and aspirin

- Duration: 6 months

- Primary Endpoint: to determine the effects of orally supplemented Tocotrienol on platelet function and cholesterol

- Lead Investigator: Chandan K Sen & others from Ohio State University, April 2012

Top US selling drugs in 2010

Rank	Product	Manufacturer	Indications	
1	Lipitor	Pfizer	Cholesterol lowering	Lipid Control
2	Nexium	AstraZeneca	Gastric ulcer & reflux	
3	Plavix	Bristol-Myers Squibb	Oral anti-platelet: reduce blood clot from stent & stroke	
4	Advair Diskus	GlaxoSmithKline	Asthma (steroid + bronchodilator)	Inflammation
5	Abilify	Otsuka	Antidepressant, bipolar disorder	
6	Seroquel	AstraZeneca	Antidepressant, bipolar disorder	
7	Singulair	Merck	Asthma	Inflammation
8	Crestor	AstraZeneca	Cholesterol lowering	Lipid Control
9	Actos	Takeda	Anti-diabetic	Inflammation
10	Epogen	Amgen	Anemia – increase red blood cells	
11	Remicade	Centocor Ortho Biotech	Anti-inflammatory: UC, RA, Crohn's disease	Inflammation
12	Enbrel	Amgen	Anti-inflammatory: autoimmune, psoriasis	Inflammation
13	Cymbalta	Lilly	Antidepressant,	
14	Avastin	Genentech	Anti-angiogenic & anti-cancer: colorectal, lung, breast, kidney & glioblastomas	Cancer
15	OxyContin	Purdue	Analgesic, pain relief	
16	Neulasta	Amgen	Prevents neutropenia during chemotherapy	
17	Zyprexa	Lilly	Anti-psychotic: schizophrenia & bipolar disorder (manic depression)	
18	Humira	Abbott	Anti-inflammatory: rheumatoid arthritis, psoriatic arthritis, Crohn's disease etc	Inflammation
19	Lexapro	Forest	Antidepressant: major depressive disorder	
20	Rituxan	Genentech	Anti-inflammatory & anti-cancer: rheumatoid arthritis, leukemias and lymphomas	Cancer Inflammation

Benefits of Natural e^3

Natural e^3

Alpha Tocopherol

Antioxidants

Tocotrienols

Anti-inflammation

Comparison of Natural e^3 with Vitamin E

Functions	Vitamin E	Natural e3
Antioxidant	+++	+++
Fertility	+++	+++
Cancer Prevention	-	++
Metabolic Syndrome	+	+++
Brain Health	-	++
Broad Spectrum	-	+++ (5 isomers)

Sources of Tocotrienol

Natural e3
DavosLife Tocotrienols

Red annatto

Palm oil
940 mg/kg

Barley
910 mg/kg

Rice bran
465 mg/kg

Grape seed oil
380 mg/kg

Oat
210 mg/kg

Hazelnut
209 mg/kg

Maize
200 mg/kg

Wheat germ oil
189 mg/kg

Olive oil
180 mg/kg

Buckthorn Berry
130 mg/kg

Rye
92 mg/kg

Flax seed oil
25.1 mg/kg

Poppy seed oil
20.5 mg/kg

Safflower oil
11.8 mg/kg

KLK Plantations - *RSPO*

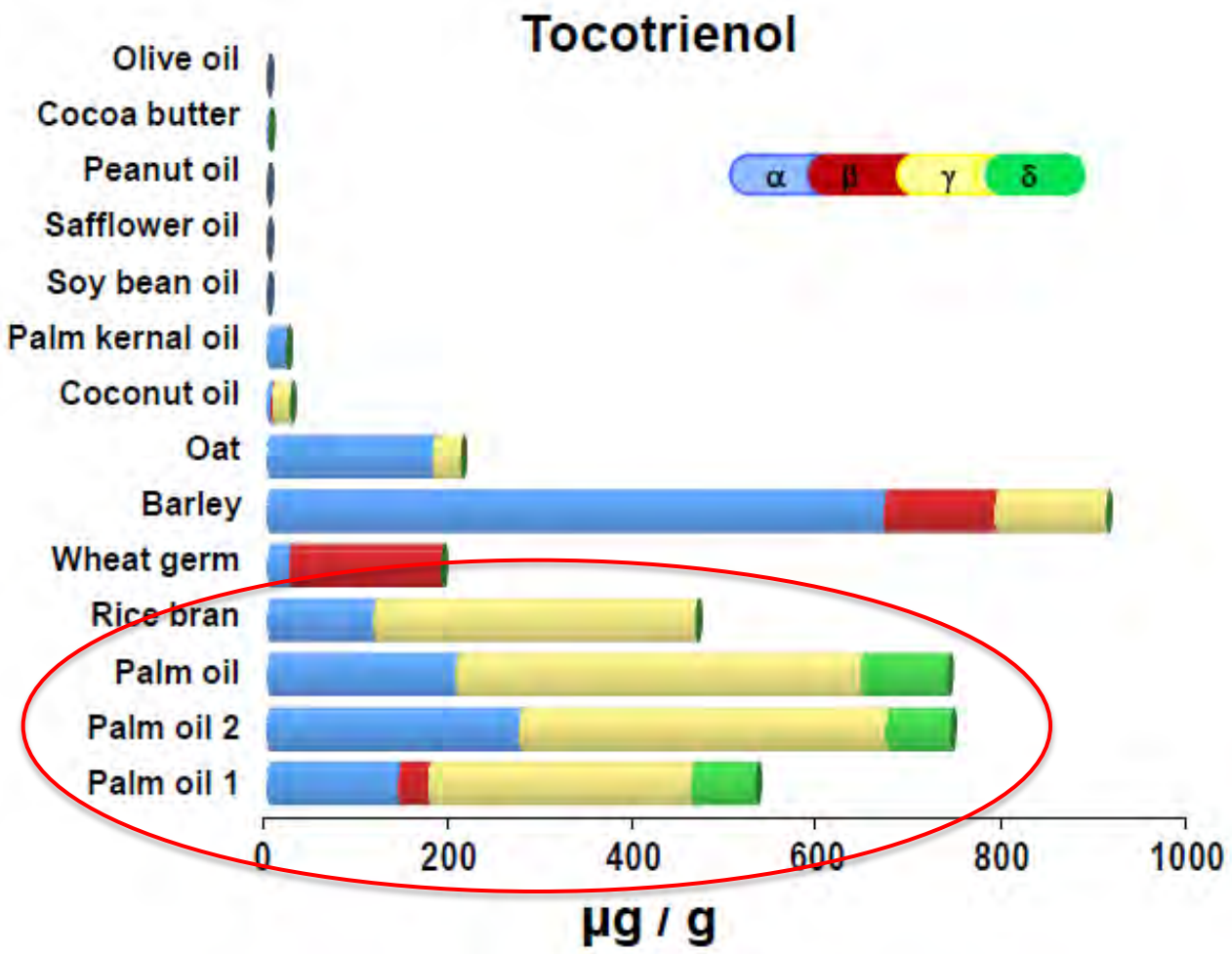
RSPO
Roundtable on Sustainable Palm Oil

- Sabah, Malaysia plantations are fully certified
- Peninsula Malaysia plantations certification is due by 2013
- Indonesian plantations are planned to be certified by 2014

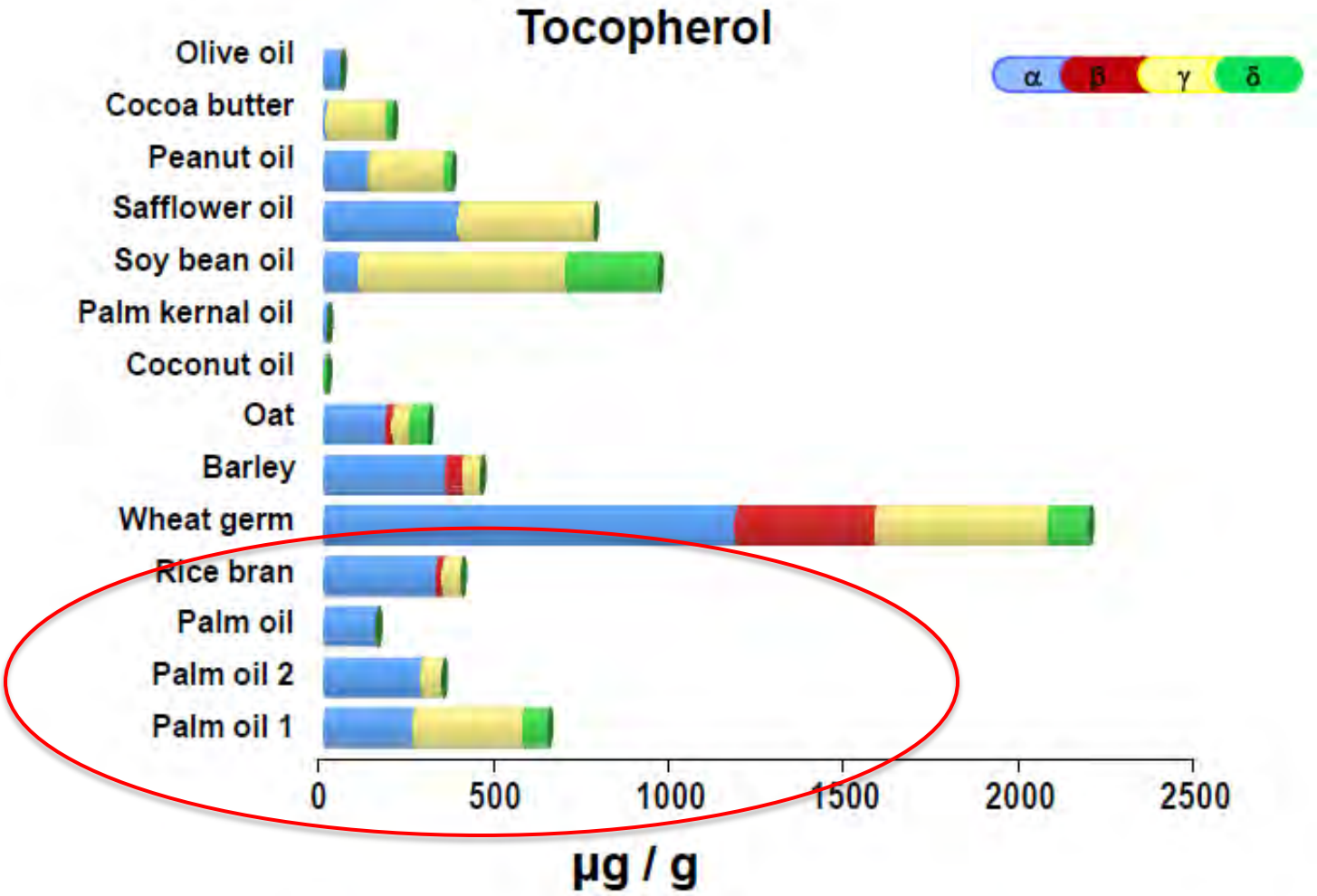


DAVOS LIFE SCIENCE
Merging Science with Nature

Natural e³
Palm-derived Tocotrienol



Natural e³ contains 25% of alpha-Tocopherol



Natural e³ Product Range

GRAS Affirmed

World Leader in Quality

DAVOS LIFE SCIENCE

Merging Science with Nature

Broad Applications

Natural e3
DavosLife Tocotrienols

Multi-functional ingredient with scientifically proven health benefits

Cosmetics and Personal Care Products

Functional Food & Beverages

Nutraceutical

FDA NOW FDA GRAS APPROVED

DAVOS LIFE SCIENCE
Merging Science with Nature

Natural e^3 Food Applications

Anything that is currently using Vitamin E!

DAVOS LIFE SCIENCE

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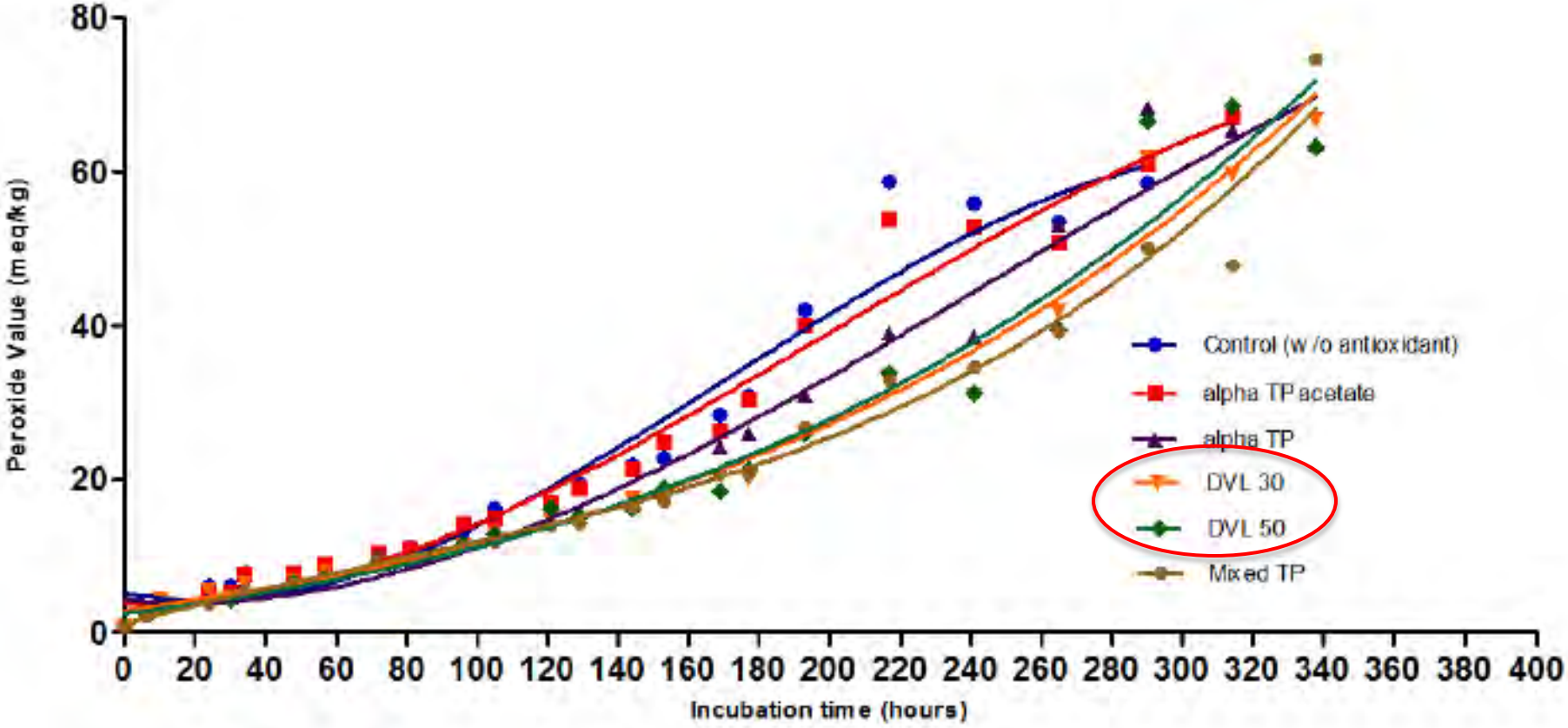
Natural e^3 is a good preservative for Omega-3 fish oil



Natural e^3
DavosLife Tocotrienols

DAVOS
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Derived from Nature, Driven by Science

Davos – Reliable Supplier

Natural e3
DavosLife Tocotrienols

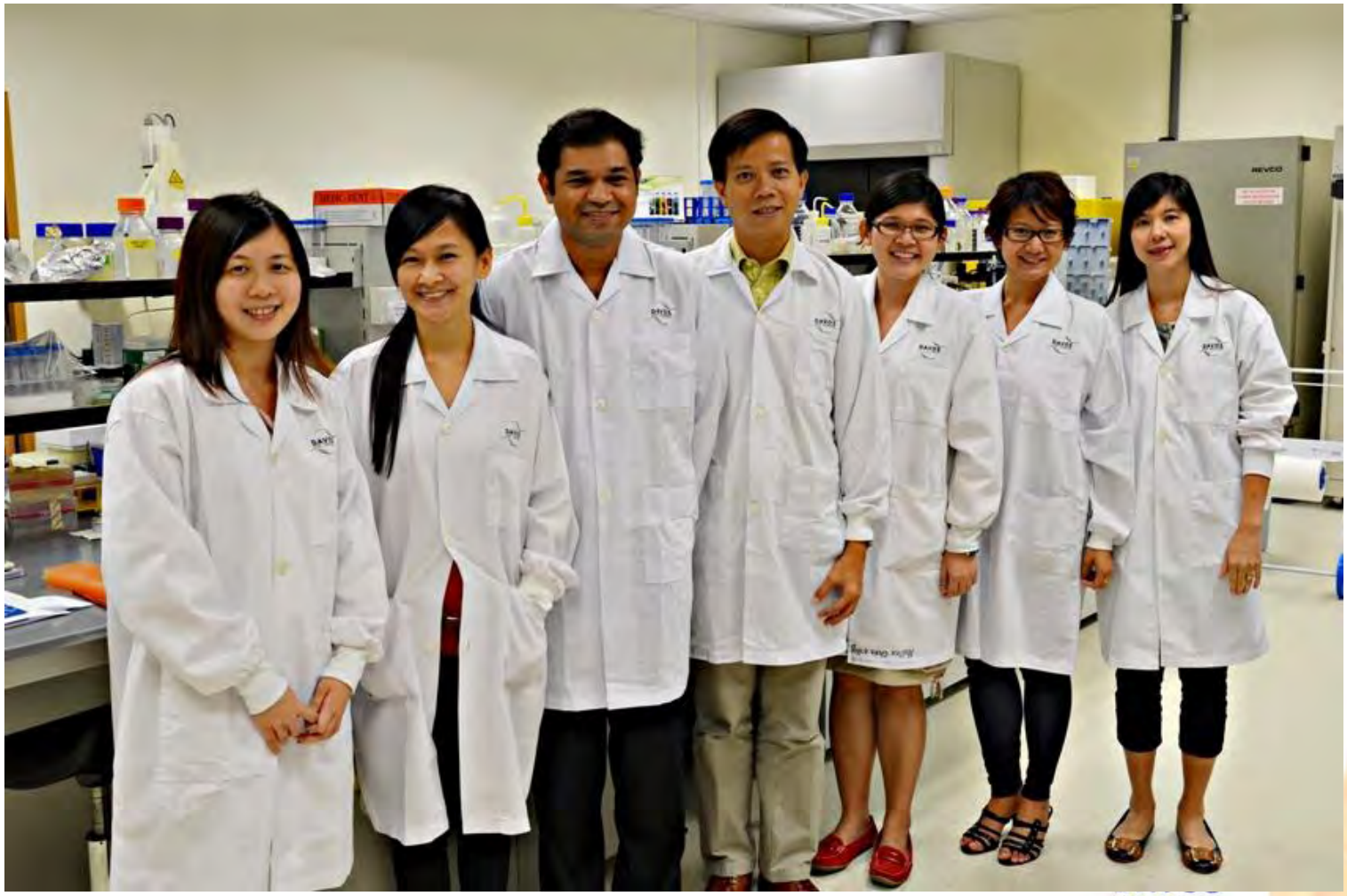
- World's largest tocotrienol manufacturing and R&D facility
- Reliable supplier
  - Integrated supply chain with feedstock fully traceable to parent company's plantations (RSPO-certified)
  - State-of-the-art proprietary molecular distillation process – no front-end biodiesel process required unlike competitors
- Highest purities of up to 97% (Sigma Aldrich tocotrienol isomers supplied by DavosLife)
- Original published research by DavosLife Scientists

Frost and Sullivan 2010 Asia Pacific Excellence in Research Award in the Natural Vitamin E Market

DAVOS
LIFE SCIENCE
Merging Science with Nature

Strong R&D Team

Natural e3
DavosLife Tocotrienols



LIFE SCIENCE
Merging Science with Nature

Derived from Nature, Driven by Science

Natural e3
DavosLife Tocotrienols






DavosLife Tocotrienols

Providing Science-Driven Solutions for Your Evolving Needs

DAVOS

Derived from Nature, Driven by Science

Natural e3
DavosLife Tocotrienols

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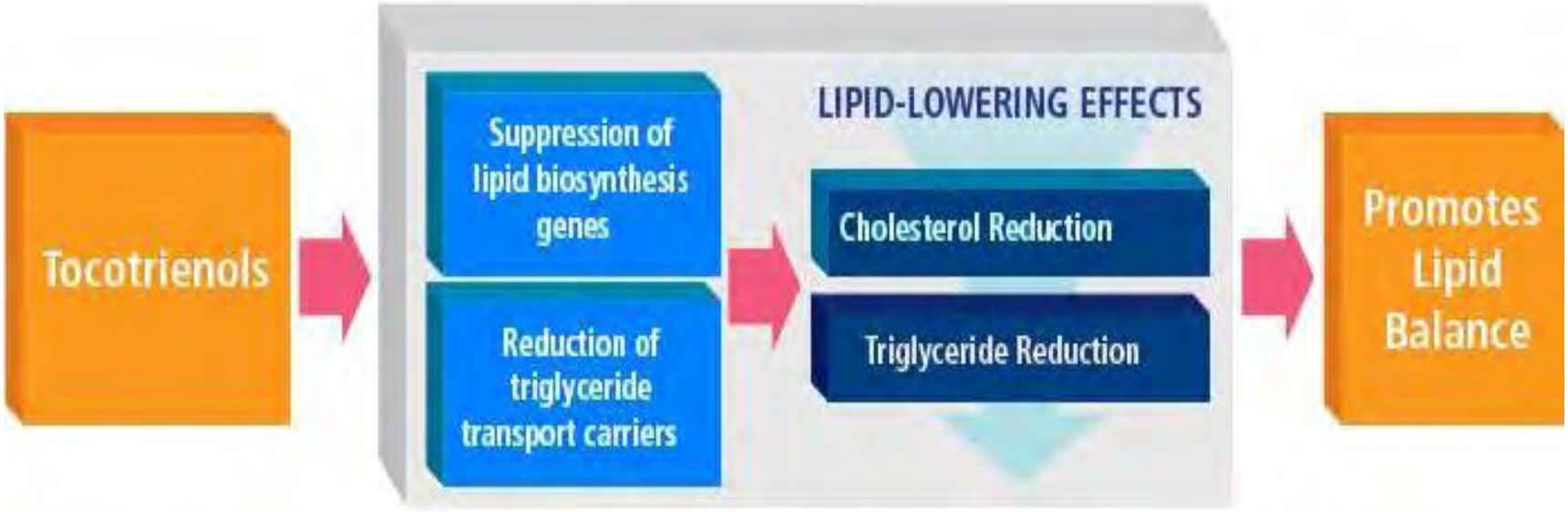
Tocotrienols: Lipid-Balancing Action



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