Corso di 2° livello per l'organizzazione e la gestione di un ambulatorio degli stili di vita

STILE DI VITA: ATTIVITÀ MOTORIA, ALIMENTAZIONE, INTERVENTI DIETETICO NUTRIZIONALI

NUTRACEUTICA E NUTRIGENOMICA

3° modulo

08 / 09 novembre - 2014

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Dipartimento di Sanità Pubblica Veterinaria e Sicurezza Alimentare

Istituto Superiore di Sanità

SIMPeSV
Società Italiana di Medicina di Prevenzione e degli Stili di Vita

Articolazione del Corso

- **Parte generale-** *definizioni, diagramma di flusso della ricerca in nutrigenomica-*
- **Studi clinici-** *Studi di intervento, lo studio PREDIMED-*
- **Ricerca biomolecolare-** *Meccanismi di azione molecolare di componenti nutraceutici*

Obiettivi del corso

Fornire strumenti utili a

- **Aumentare la conoscenza** dei principi di base della nutraceutica e della nutrigenomica e del complesso processo di studio e ricerca necessario a supportare qualsiasi nuova evidenza
- **Accrescere la capacità** di giudicare con competenza e senso critico i tanti messaggi, spesso privi di solide basi scientifiche, quotidianamente indirizzati ai cittadini così da indirizzare correttamente le loro scelte nutrizionali.

Nutrizione **Farmaceutica**

Nutraceutica

studio di alimenti che hanno una funzione benefica sulla salute umana.

“ Un alimento può essere definito ‘ funzionale’ se è dimostrata in maniera soddisfacente la sua capacità di influenzare positivamente una o più funzioni fondamentali dell’organismo, al di là degli effetti strettamente nutrizionali, in modo che determini un miglioramento dello stato di salute e di benessere e/o una riduzione del rischio di malattia.
Gli alimenti funzionali devono rimanere alimenti e devono dimostrare i loro effetti in concentrazioni comparabili a quelle normalmente assunte con la dieta:
non sono pillole né capsule ma parti di un normale regime dietetico.»

The European Commission's Concerted Action on Functional Food Science in Europe (FuFoSE), coordinated by International Life Science Institute (ILSI) Europe

« Alimenti nei quali alcuni componenti sono stati aggiunti, eliminati o modificati»

Scientific concept of functional foods in Europe Consensus document
The British Journal of Nutrition, 81 (1999), pp. S1–S27

Nutraceutico= componente bioattivo contenuto in un alimento funzionale con proprietà curative di comprovata efficacia

- micronutrienti (vitamine e acidi grassi)
- non nutrienti (fitocomposti e probiotici)

Table 1

Functional foods classification, some sources, and examples of bioactive substances.

Functional food	Bioactive component (nutraceutic)		Source (s)
Micronutrients	Vitamins	Retinol (vitamin A) α-tocopherol (vitamin E) Calciferol (vitamin D3)	Walnuts, almonds, hazelnuts, spinach, fish oil
	Polyunsaturated fatty acids (PUFAs)	Omega 3 Fatty acids: eicosapentaenoic acid (EPA) docosahexaenoic acid (DHA)	Salmon, tuna and others fish oils
Nonnutrients Phytochemicals	Carotenoids	Beta-carotene luteín, zeaxanthin lycopene	Carrots, pumpkin, collards, kale, spinach, tomatoes, watermelon
	Phenolic acid derivatives	Caffeic acid Ferulic acid Gallic acid Curcumin	Coffee, pears, apples, corn, curcumin, vanilla
	Flavonoids	Flavonols (quercetin) Isoflavones Coumarins Anthocyanidines Stilbenes (resveratrol)	Berries, cherries, red grapes, tea, cocoa, apples, citrus fruits, onion, broccoli, cranberries, strawberries, soybeans
	Sulfides/thiols	Diallyl sulfide S-allyl cysteine sulfoxide 1,2-viniyldithiin	Garlic, onions, banana, cruciferous vegetables
	Dietary fiber (prebiotic)	Fructooligosaccharides Neoglicans	Whole grains, onions, chicory, agave, some fruits
Probiotics	PUFAs induction	*Saccharomyces cerevisiae* (var. *boulardii*) Bifidobacteria and *Lactobacillus* genus *Escherichia coli* strain Nissle1917 (EcN) Compound VSL3	Certain yogurts and other cultured dairy and no-dairy applications

- Increased consumption of fruit and vegetables for the primary prevention of cardiovascular diseases. **Cochrane Database Syst Rev. 2013.**
- Health benefits of fruit and vegetables. **Adv Nutr. 2012;** 3:506-16
- Population-level changes to promote cardiovascular health(on behalf of the PEP section of the EACPR). **Eur J Prev Cardiol. 2013**; 20(3):409-21
- Intake of fruit, berries, and vegetables and risk of type 2 diabetes in Finnish men: the Kuopio Ischaemic Heart Disease Risk Factor Study. **Am J Clin Nutr. 2014** doi: 10.3945/ajcn.113.069641.
- Systematic review and meta-analysis of school-based interventions to improve daily fruit and vegetable intake in children aged 5 to 12 y. **Am J Clin Nutr. 2012**;96(4):889-901.
- Health effects of mixed fruit and vegetable concentrates: a systematic review of the clinical investigations. **J Am Coll Nutr. 2011**; 30(5):285-94.
- Conformity to traditional Mediterranean diet and cancer incidence: the Greek EPIC cohort. **Br J Cancer 2008**; 99:191-5

Public Health Nutr. 2013 Nov 29:1-14. [Epub ahead of print]

Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score.

Sofi F[1], Macchi C[2], Abbate R[1], Gensini GF[1], Casini A[1].

Author information

Abstract

OBJECTIVE: To update previous meta-analyses of cohort studies that investigated the association between the Mediterranean diet and health status and to utilize data coming from all of the cohort studies for proposing a literature-based adherence score to the Mediterranean diet.

DESIGN: We conducted a comprehensive literature search through all electronic databases up to June 2013.

SETTING: Cohort prospective studies investigating adherence to the Mediterranean diet and health outcomes. Cut-off values of food groups used to compute the adherence score were obtained.

SUBJECTS: The updated search was performed in an overall population of 4 172 412 subjects, with eighteen recent studies that were not present in the previous meta-analyses.

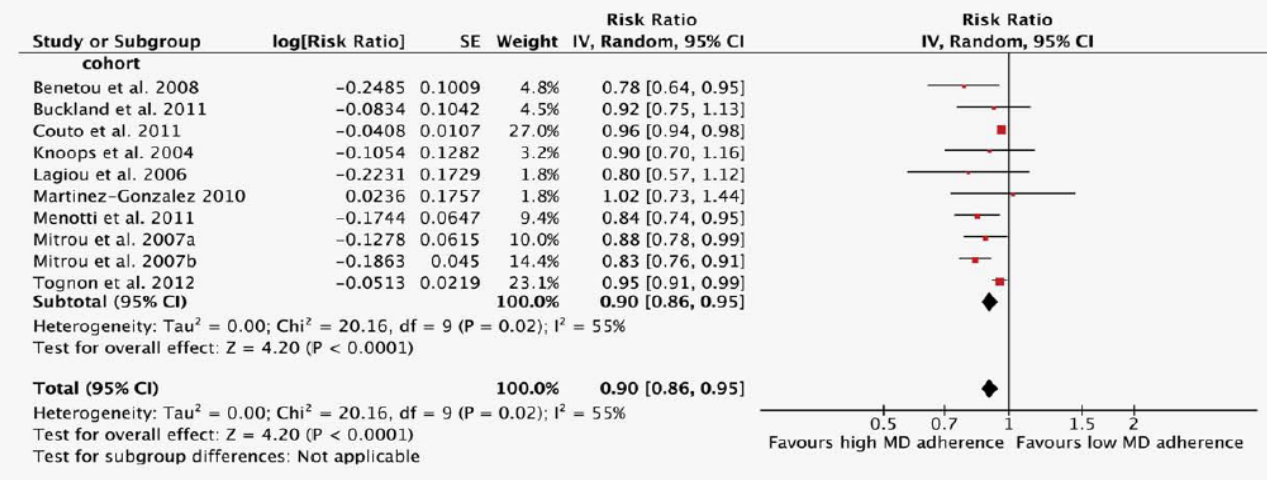
RESULTS: A 2-point increase in adherence score to the Mediterranean diet was reported to determine an 8 % reduction of overall mortality (relative risk = 0·92; 95 % CI 0·91, 0·93), a 10 % reduced risk of CVD (relative risk = 0·90; 95 % CI 0·87, 0·92) and a 4 % reduction of neoplastic disease (relative risk = 0·96; 95 % CI 0·95, 0·97). We utilized data coming from all cohort studies available in the literature for proposing a literature-based adherence score. Such a score ranges from 0 (minimal adherence) to 18 (maximal adherence) points and includes three different categories of consumption for each food group composing the Mediterranean diet.

CONCLUSIONS: The Mediterranean diet was found to be a healthy dietary pattern in terms of morbidity and mortality. By using data from the cohort studies we proposed a literature-based adherence score that can represent an easy tool for the estimation of adherence to the Mediterranean diet also at the individual level.

International Journal of Cancer
Early View, Article first published online: 11 MAR 2014
Abstract | Full Article (HTML) | Enhanced Article (HTML) | References
Supporting Information | Cited By
Wiley Online Library

Adherence to Mediterranean diet and risk of cancer: A systematic review and meta-analysis of observational studies

Lukas Schwingshackl and Georg Hoffmann



What's new?

Adherence to a "Mediterranean Diet" is associated with **significant improvements in health** status, including a **lower overall risk of cancer**, **especially colorectal and aerodigestive cancers**.

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J Alzheimers Dis. 2014;39(2):271-82. doi: 10.3233/JAD-130830.

Association of mediterranean diet with mild cognitive impairment and Alzheimer's disease: a systematic review and meta-analysis.

Singh B[1], Parsaik AK[2], Mielke MM[3], Erwin PJ[4], Knopman DS[2], Petersen RC[5], Roberts RO[5].

Author information

Abstract

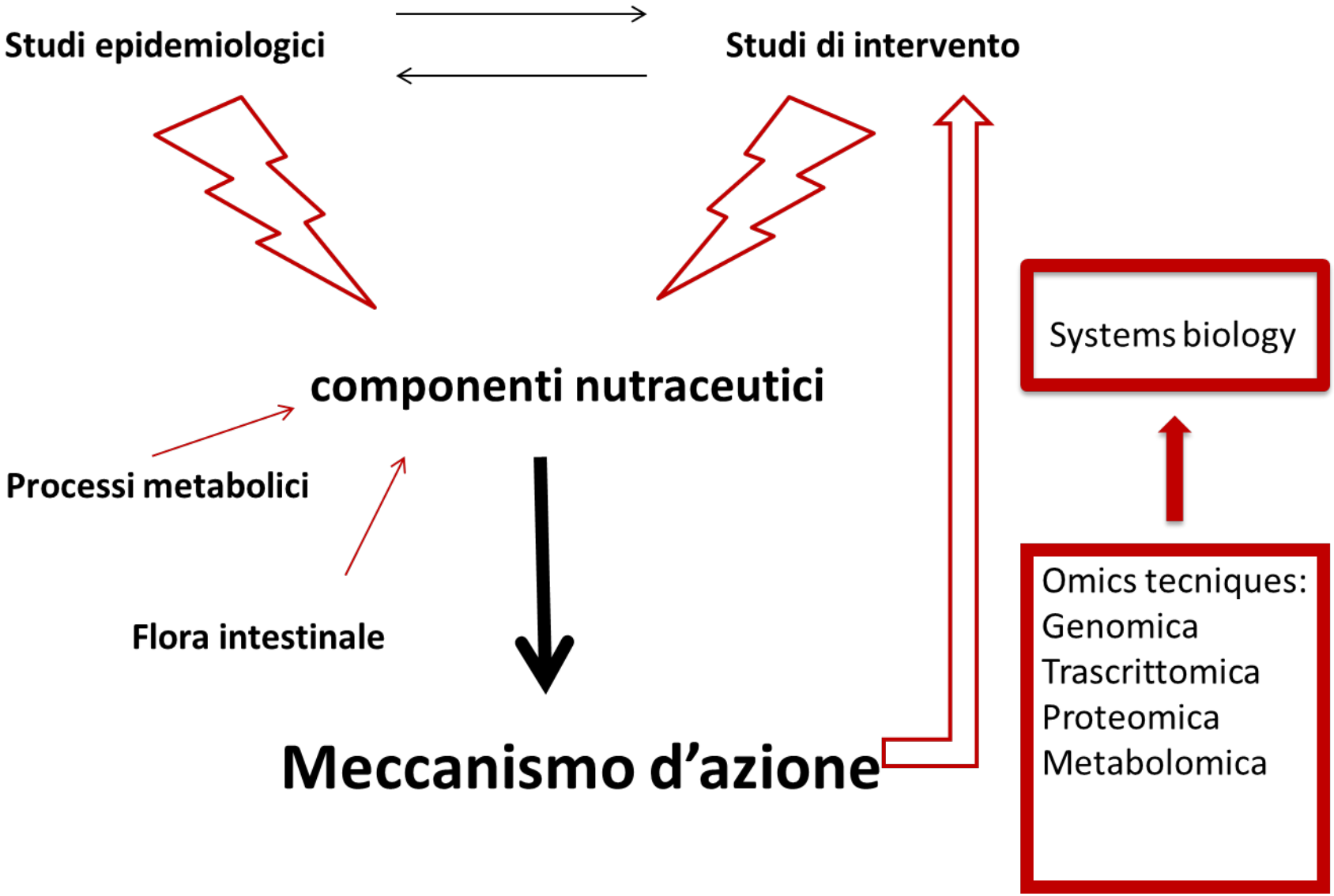
BACKGROUND/OBJECTIVE: To conduct a systematic review of all studies to determine whether there is an association between the Mediterranean diet (MeDi) and cognitive impairment.

METHODS: We conducted a comprehensive search of the major databases and hand-searched proceedings of major neurology, psychiatry, and dementia conferences through November 2012. Prospective cohort studies examining the MeDi with longitudinal follow-up of at least 1 year and reporting cognitive outcomes (mild cognitive impairment [MCI] or Alzheimer's disease [AD]) were included. The effect size was estimated as hazard-ratio (HR) with 95% confidence intervals (CIs) using the random-effects model. Heterogeneity was assessed using Cochran's Q-test and I2-statistic.

RESULTS: Out of the 664 studies screened, five studies met eligibility criteria. Higher adherence to the MeDi was associated with reduced risk of MCI and AD. The subjects in the highest MeDi tertile had 33% less risk (adjusted HR = 0.67; 95% CI, 0.55-0.81; $p < 0.0001$) of cognitive impairment (MCI or AD) as compared to the lowest MeDi score tertile. Among cognitively normal individuals, higher adherence to the MeDi was associated with a reduced risk of MCI (HR = 0.73; 95% CI, 0.56-0.96; $p = 0.02$) and AD (HR = 0.64; 95% CI, 0.46-0.89; $p = 0.007$). There was no significant heterogeneity in the analyses.

CONCLUSIONS: While the overall number of studies is small, pooled results suggest that a higher adherence to the MeDi is associated with a reduced risk of developing MCI and AD, and a reduced risk of progressing from MCI to AD. Further prospective-cohort studies with longer follow-up and randomized controlled trials are warranted to consolidate the evidence. Systematic review registration number: PROSPERO 2013: CRD42013003868.

KEYWORDS: Alzheimer's disease; Mediterranean diet; meta-analysis; mild cognitive impairment; systematic review


Studi epidemiologici
Studi di intervento
componenti nutraceutici
Processi metabolici
Flora intestinale
Meccanismo d'azione
Systems biology
Omics tecniques:
Genomica
Trascrittomica
Proteomica
Metabolomica

- Può l'espressione genica in risposta a processi metabolici influenzare lo stato di salute di un individuo?

- La relazione tra risposta metabolica e espressione genica può essere il risultato delle interazioni fra genotipo e nutrienti/ambiente?

- La comprensione di queste interazioni può portare alla prescrizione di diete specifiche per ogni individuo?

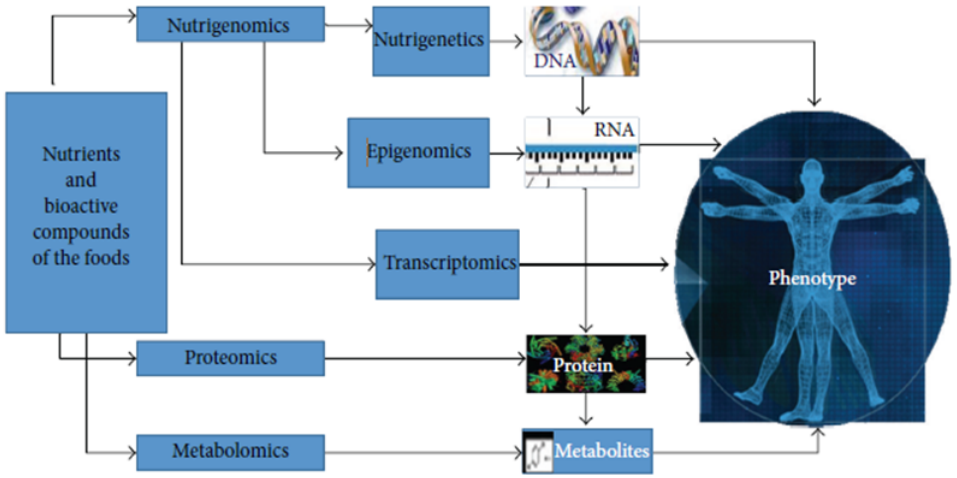
Nutrigenomica

Studia i meccanismi con i quali gli alimenti funzionali possono influenzare

l'espressione genica

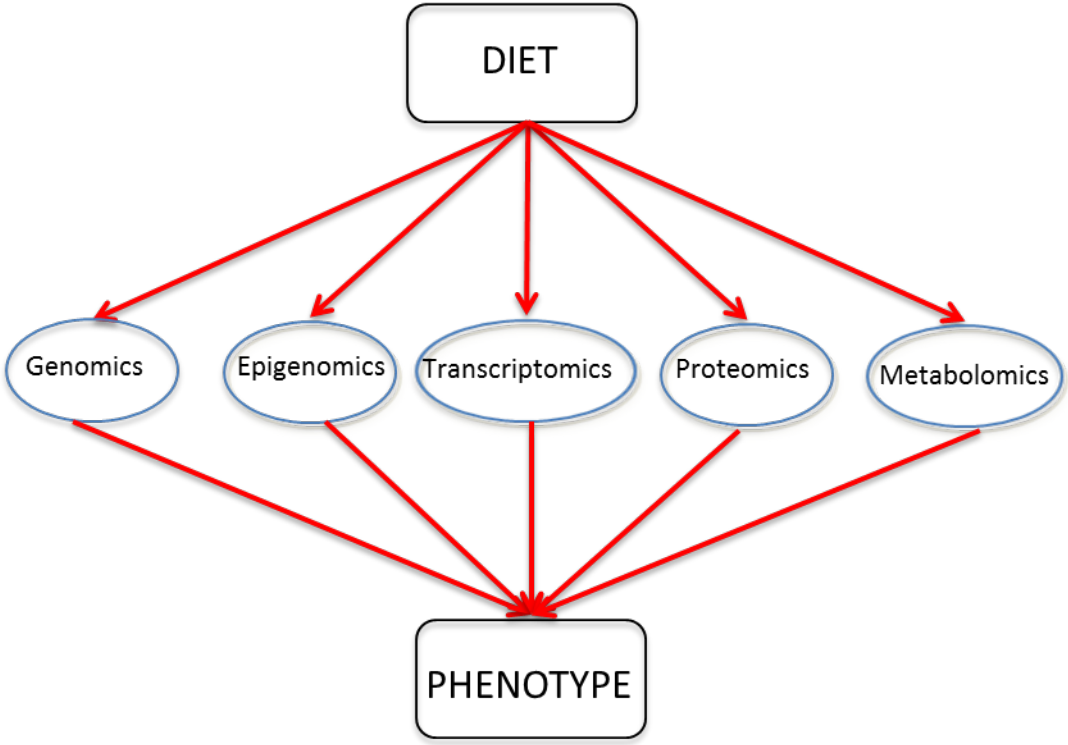
- **il transcrittoma → profilo degli RNA**
- **il proteoma → profilo delle proteine**
- **il metaboloma → profilo dei metaboliti**

Obiettivo finale: comprendere come il cibo interferisce con il codice genetico e come l'organismo risponde a queste interferenze modificando il fenotipo.



J Nutr Metab

FIGURE 1: "Omics" sciences used in understanding the relationship between nutrition versus health versus disease (source: [4], with modifications; [9] with modifications).


DIET
Genomics
Epigenomics
Transcriptomics
Proteomics
Metabolomics
PHENOTYPE

Studi Nutrigenomici

- **Correlare modifiche dell'espressione genica a risultati sistemici**
- **Mettere insieme i risultati delle diverse tecniche «omiche» con lo studio classico dei biomarcatori**

Visione olistica di come la dieta può influenzare i nostri geni

Evidence-based medicine → High level of scientific evidence

↓

Nutritional recommendation

Randomized, controlled double-bind, clinical intervention trials (level I of evidence)

Large cohort studies (level II of evidence)

The NEW ENGLAND JOURNAL of MEDICINE

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Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D., Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D., Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D., José Lapetra, M.D., Ph.D., Rosa Maria Lamuela-Raventos, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D., for the PREDIMED Study Investigators*

Table 1. Summary of Dietary Recommendations to Participants in the Mediterranean-Diet Groups and the Control-Diet Group.

Food	Goal
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day
Low-fat diet (control)	
Recommended	
Low-fat dairy products	≥3 servings/day
Bread, potatoes, pasta, rice	≥3 servings/day
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Lean fish and seafood	≥3 servings/wk
Discouraged	
Vegetable oils (including olive oil)	≤2 tbsp/day
Commercial bakery goods, sweets, and pastries§	≤1 serving/wk
Nuts and fried snacks	≤1 serving /wk
Red and processed fatty meats	≤1 serving/wk
Visible fat in meats and soups¶	Always remove
Fatty fish, seafood canned in oil	≤1 serving/wk
Spread fats	≤1 serving/wk
Sofrito‡	≤2 servings/wk

PREDIMED trial (Prevención con Dieta Mediterránea)

Studio a bracci paralleli, multicentrico, randomizzato

7447 soggetti (donne e uomini; 55-80 anni)

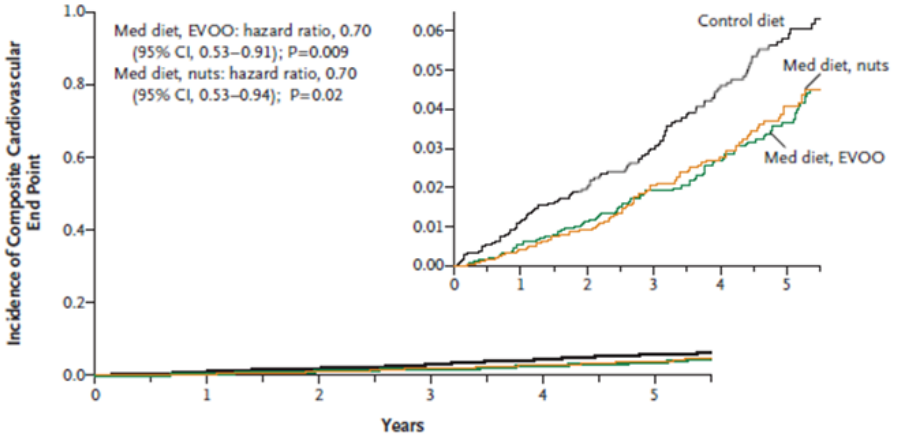
- No CVD al momento dell'arruolamento
- T2D o almeno 3 fattori di rischio (fumo, ipertensione, alto c-LDL, basso c-HDL, sovrappeso/obesità)

- Dieta mediterranea **+ EVOO** (30gr/die)

- Dieta mediterranea + **noci/mandorle/nocciole** (30 gr/die)

- Dieta di controllo (**low fat**)

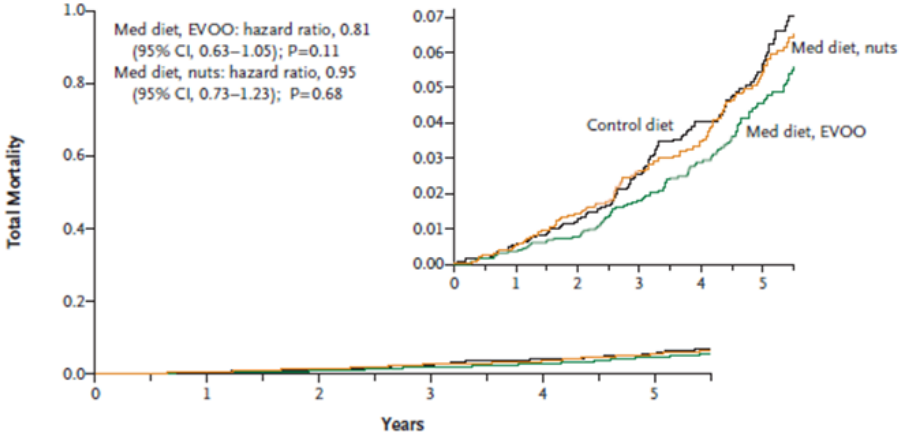
A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)



No. at Risk

Control diet	2450	2268	2020	1583	1268	946
Med diet, EVOO	2543	2486	2320	1987	1687	1310
Med diet, nuts	2454	2343	2093	1657	1389	1031

B Total Mortality



No. at Risk

Control diet	2450	2268	2026	1585	1272	948
Med diet, EVOO	2543	2485	2322	1988	1690	1308
Med diet, nuts	2454	2345	2097	1662	1395	1037

Figure 1. Kaplan–Meier Estimates of the Incidence of Outcome Events in the Total Study Population.

Panel A shows the incidence of the primary end point (a composite of acute myocardial infarction, stroke, and death from cardiovascular causes), and Panel B shows total mortality. Hazard ratios were stratified according to center (Cox model with robust variance estimators). CI denotes confidence interval, EVOO extra-virgin olive oil, and Med Mediterranean.

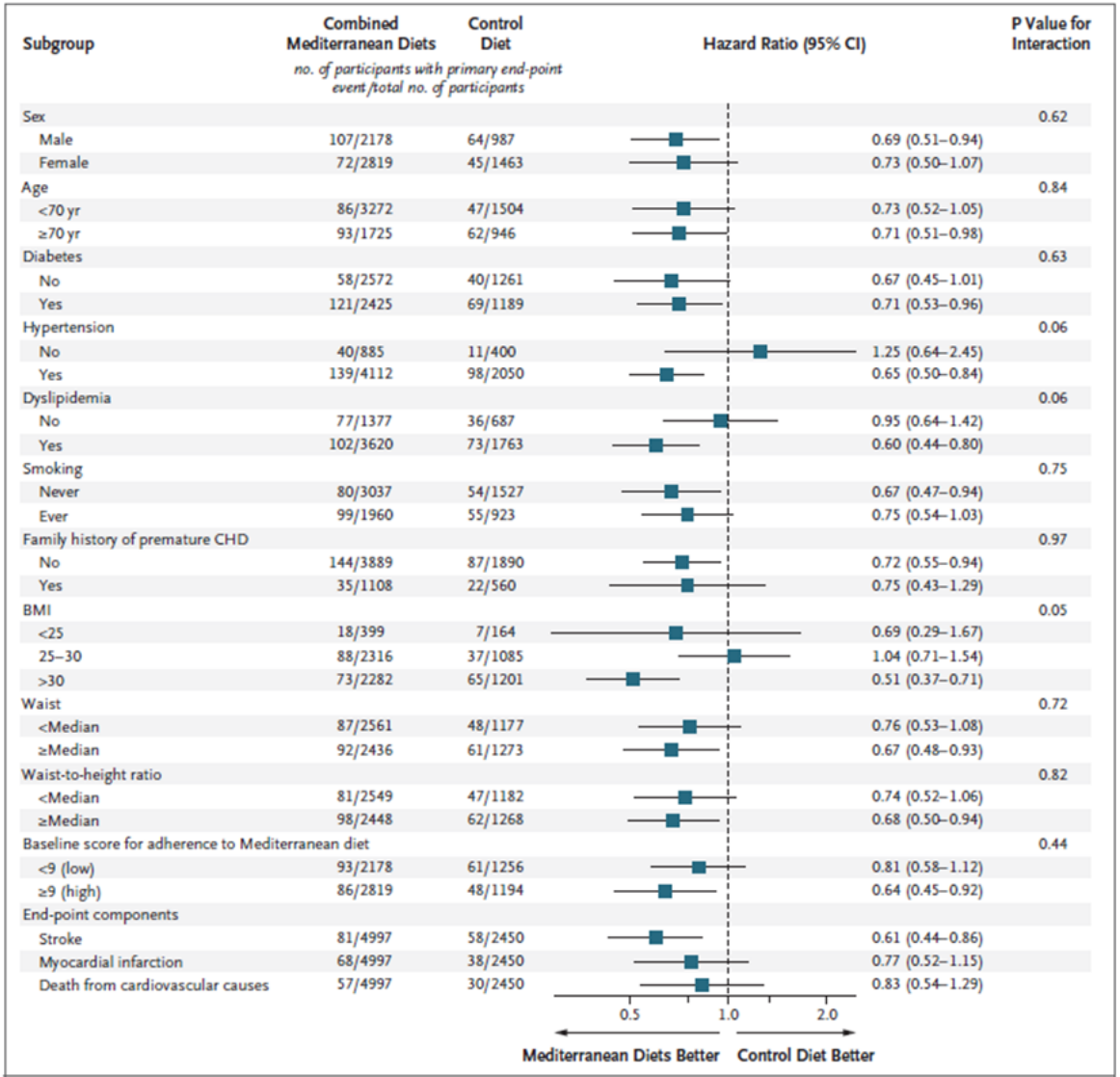


Figure 2. Results of Subgroup Analyses.

Shown are adjusted hazard ratios for the primary end point within specific subgroups. Squares denote hazard ratios; horizontal lines represent 95% confidence intervals. Hazard ratios indicate the relative risk in both intervention groups merged together (vs. the control group) within each stratum. Hazard ratios were stratified according to recruiting center and were adjusted for sex, age (continuous variable), family history of premature coronary heart disease (CHD) (yes or no), smoking (never smoked, former smoker, or current smoker), body-mass index (BMI) (continuous variable), waist-to-height ratio (continuous variable), hypertension at baseline (yes or no), dyslipidemia at baseline (yes or no), and diabetes at baseline (yes or no). Scores for adherence to the Mediterranean diet range from 0 to 14, with higher scores indicating greater adherence.

Display Settings: Abstract

Send to:

BMC Med. 2014 May 13;12(1):78. doi: 10.1186/1741-7015-12-78.

Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study.

Guasch-Ferré M, Hu FB, Martínez-González MA, Fitó M, Bulló M, Estruch R, Ros E, Corella D, Recondo J, Gómez-Gracia E, Fiol M, Lapetra J, Serra-Majem L, Muñoz MA, Pintó X, Lamuela-Raventós RM, Basora J, Buil-Cosiales P, Sorlí JV, Ruiz-Gutiérrez V, Martínez JA, Salas-Salvadó J[1].

Author information

Abstract

BACKGROUND: It is unknown whether individuals at high cardiovascular risk sustain a benefit in cardiovascular disease from increased olive oil consumption. The aim was to assess the association between total olive oil intake, its varieties (extra virgin and common olive oil) and the risk of cardiovascular disease and mortality in a Mediterranean population at high cardiovascular risk.

METHODS: We included 7,216 men and women at high cardiovascular risk, aged 55 to 80 years, from the PREvención con DIeta MEDiterránea (PREDIMED) study, a multicenter, randomized, controlled, clinical trial. Participants were randomized to one of three interventions: Mediterranean Diets supplemented with nuts or extra-virgin olive oil, or a control low-fat diet. The present analysis was conducted as an observational prospective cohort study. The median follow-up was 4.8 years. Cardiovascular disease (stroke, myocardial infarction and cardiovascular death) and mortality were ascertained by medical records and National Death Index. Olive oil consumption was evaluated with validated food frequency questionnaires. Multivariate Cox proportional hazards and generalized estimating equations were used to assess the association between baseline and yearly repeated measurements of olive oil intake, cardiovascular disease and mortality.

RESULTS: During follow-up, 277 cardiovascular events and 323 deaths occurred. Participants in the highest energy-adjusted tertile of baseline total olive oil and extra-virgin olive oil consumption had 35% (HR: 0.65; 95% CI: 0.47 to 0.89) and 39% (HR: 0.61; 95% CI: 0.44 to 0.85) cardiovascular disease risk reduction, respectively, compared to the reference. Higher baseline total olive oil consumption was associated with 48% (HR: 0.52; 95% CI: 0.29 to 0.93) reduced risk of cardiovascular mortality. For each 10 g/d increase in extra-virgin olive oil consumption, cardiovascular disease and mortality risk decreased by 10% and 7%, respectively. No significant associations were found for cancer and all-cause mortality. The associations between cardiovascular events and extra virgin olive oil intake were significant in the Mediterranean diet intervention groups and not in the control group.

CONCLUSIONS: Olive oil consumption, specifically the extra-virgin variety, is associated with reduced risks of cardiovascular disease and mortality in individuals at high cardiovascular risk.

TRIAL REGISTRATION: This study was registered at controlled-trials.com (http://www.controlled-trials.com/ISRCTN35739639). International Standard Randomized Controlled Trial Number (ISRCTN): 35739639. Registration date: 5 October 2005.

- Elevato contenuto di MUFA
- Elevato contenuto di polifenoli

Mol. Nutr. Food Res. 2013, *57*, 760–771

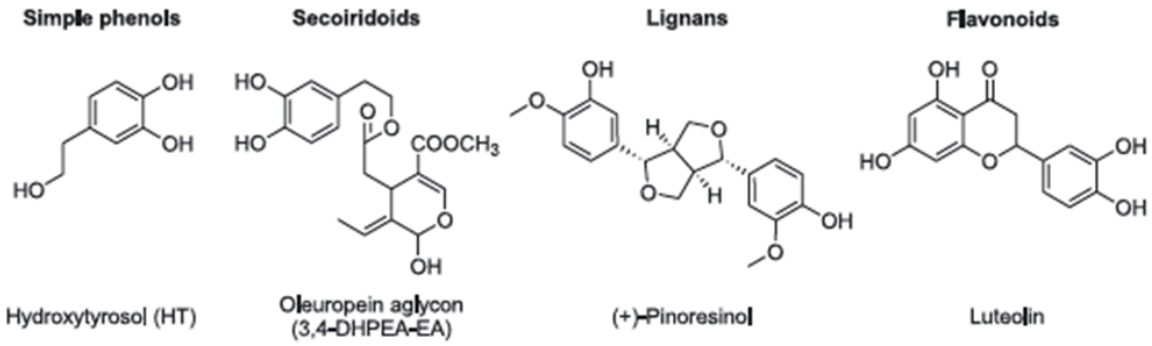
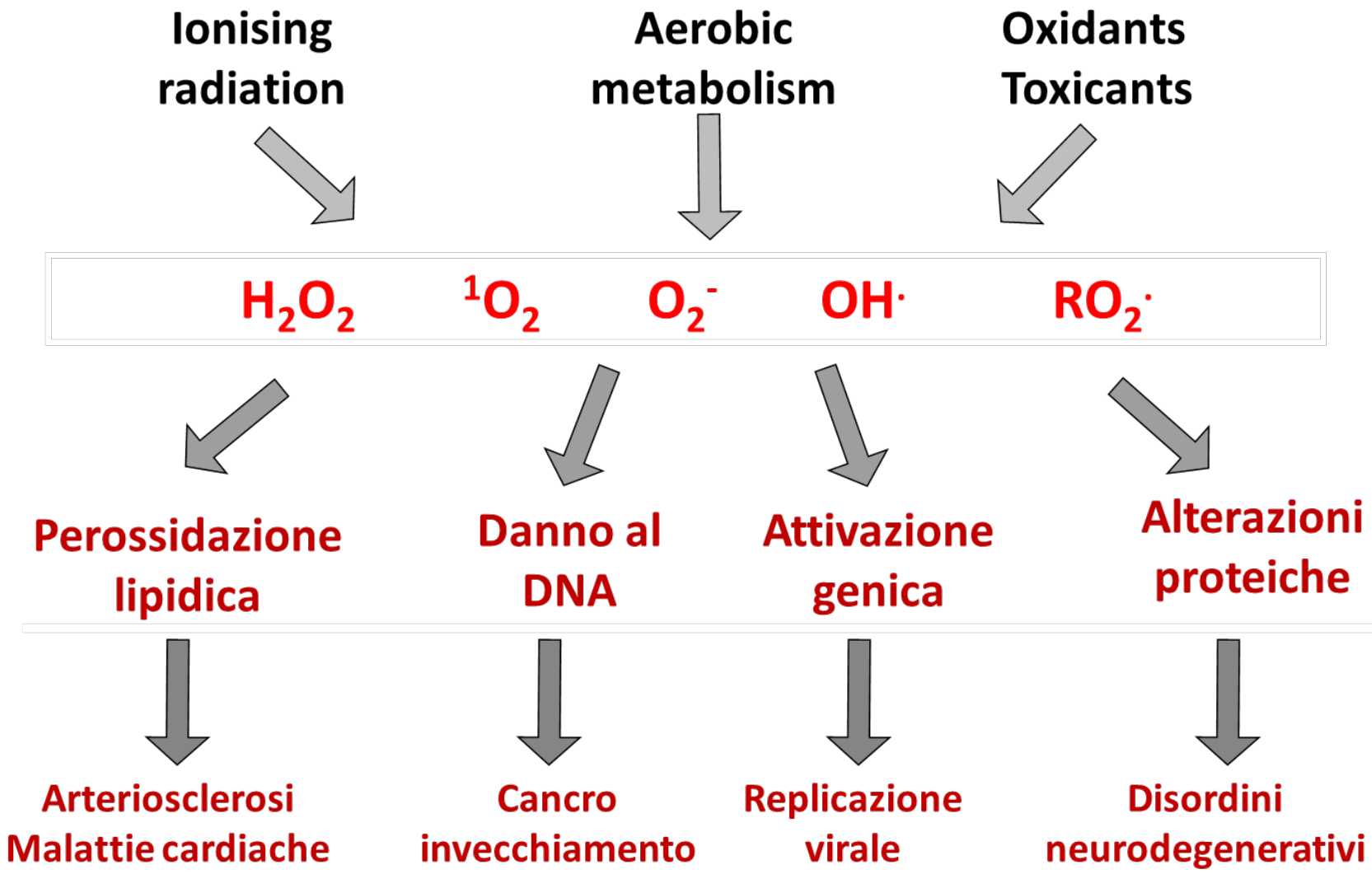


Figure 1. Main classes of OOPC with representative compounds.

Attività antiossidante


Ionising radiation
Aerobic metabolism
Oxidants Toxicants
H_2O_2
$^1O_2$
O_2^-
$OH^\cdot$
$RO_2^\cdot$
Perossidazione lipidica
Danno al DNA
Attivazione genica
Alterazioni proteiche
Arteriosclerosi Malattie cardiache
Cancro invecchiamento
Replicazione virale
Disordini neurodegenerativi

Difese antiossidanti esogene

Vitamine antiossidanti

polifenoli

- Stilbeni

- Acidi Fenolici
  - Acidi idrossicinnamici

  - Acidi idrossibenzoici

- Flavonoidi
  - Isoflavoni

  - Flavonoli

  - Antociani

  - Flavanoni, flavoni

  - Flavanoli
    - Catechine

    - Pro(anto)cianidine

Protective Effect of Oleuropein, an Olive Oil Biophenol, on Low Density Lipoprotein Oxidizability in Rabbits

E. Coni[a,*], R. Di Benedetto[a], M. Di Pasquale[a], R. Masella[b], D. Modesti[b], R. Mattei[c], and E.A. Carlini[c]

[a]Food Department and [b]Metabolism and Pathological Biochemistry Department, Istituto Superiore di Sanità, 00161 Rome, Italy, and [c]Psychobiology Department, Universidade Federal de Saõ Paulo, 04023-062 Saõ Paulo, Brazil

TABLE 1
Nutritional Composition of the Three Diets (% w/w on wet weight)[a]

Component	Diet A	Diet B	Diet C
Experimental data[b]			
Water	12.08 ± 0.34	11.97 ± 0.41	12.07 ± 0.28
Carbohydrates[c]	41.76	36.16	36.29
Protein	13.51 ± 0.78	12.21 ± 0.69	12.18 ± 0.87
Fat	2.13 ± 0.35	11.10 ± 0.27	11.04 ± 0.33
Saturated fatty acids	0.40 ± 0.05	1.76 ± 0.22	1.81 ± 0.32
Monounsaturated fatty acids	1.05 ± 0.16	8.16 ± 0.53	8.09 ± 0.64
Polyunsaturated fatty acids	0.53 ± 0.09	1.06 ± 0.22	1.08 ± 0.19
Cholesterol	$4.0 \cdot 10^{-5}$	$3.3 \cdot 10^{-5}$	$3.3 \cdot 10^{-5}$
Fiber	22.04 ± 0.98	20.11 ± 1.02	19.96 ± 1.21
Minerals	8.42 ± 078	8.39 ± 0.86	8.40 ± 0.66
Vitamin E[d]	0.078 ± 0.021	0.073 ± 0.019	0.074 ± 0.016
Manufacturer's data			
Vitamin integration[e]	0.060	0.058	0.058
Mineral integration	0.028	0.028	0.028

[a]Diet A, standard rabbit food; diet B, standard food modified by the addition of 10% (w/w) extra virgin olive oil; diet C, same as diet B but with 7 mg kg^{-1} oleuropein.
[b]Values are expressed as mean ± SD (n = 5).
[c]Calculated for difference.
[d]Expressed as % α-tocopherol; calculated using activity coefficients for individual tocopherols (51).
[e]The value related to diet A is greater because it provides for higher vitamin E supplementation.

TABLE 2
Biophenol and Vitamin E Contents of the Extra Virgin Olive Oil Added to Diets[a] B and C

Component	mg L^{-1} [b]
Vitamin E[c]	11.9 ± 0.9
Total biophenols[d]	238 ± 54
Oleuropein	2.04 ± 0.78

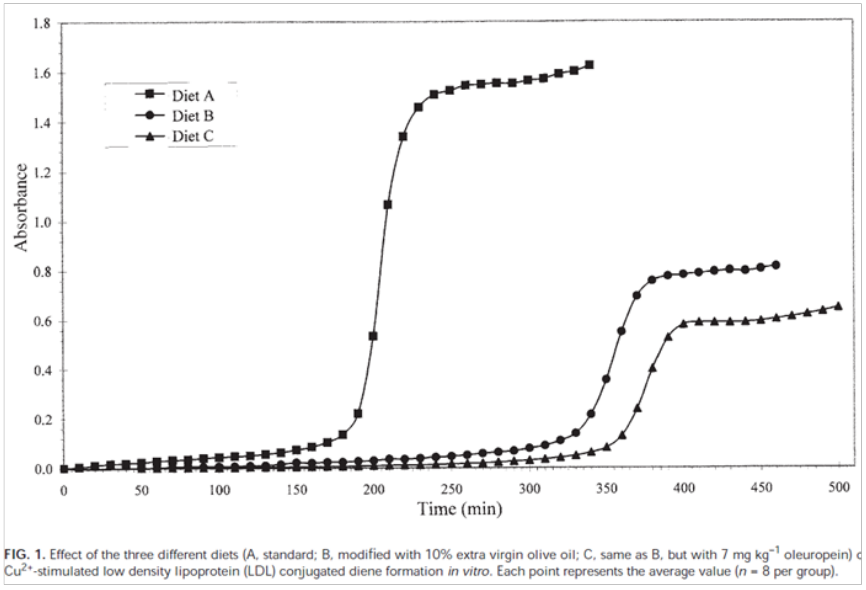


FIG. 1. Effect of the three different diets (A, standard; B, modified with 10% extra virgin olive oil; C, same as B, but with 7 mg kg^{-1} oleuropein) o Cu^{2+}-stimulated low density lipoprotein (LDL) conjugated diene formation *in vitro*. Each point represents the average value (n = 8 per group).

Coni E et al, Lipids 2000

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Effects of Dietary Virgin Olive Oil Phenols on Low Density Lipoprotein Oxidation in Hyperlipidemic Patients

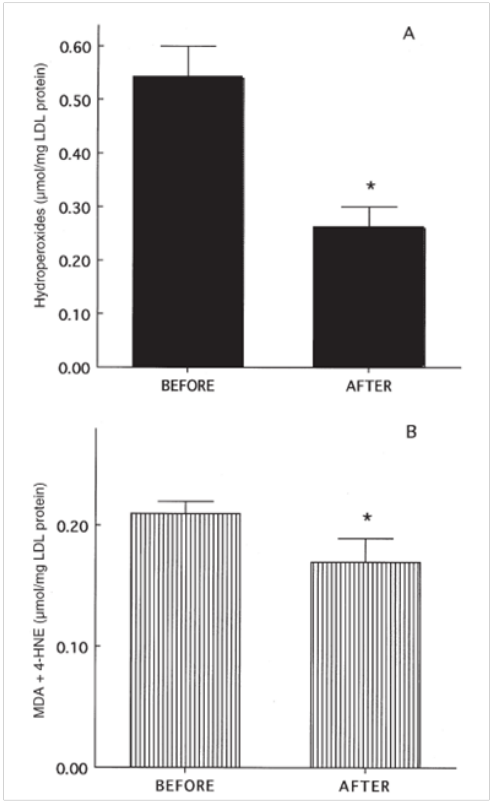
Roberta Masella[a,*], Claudio Giovannini[a], Rosaria Varì[a], Roberta Di Benedetto[b], Ettore Coni[b], Roberto Volpe[c], Nadia Fraone[d], and Antonello Bucci[d]

Departments of [a]Metabolism and Pathological Biochemistry and [b]Food, Istituto Superiore di Sanità, 00161 Rome, Italy, [c]Servizio Prevenzione e Protezione, Consiglio Nazionale delle Ricerche, 00161 Rome, Italy, and [d]Istituto di Terapia Medica Sistematica, University of Rome "La Sapienza," 00161 Rome, Italy

TABLE 3
Percentage of Fatty Acids in LDL[a] Fraction Before and After Extra Virgin Olive Oil Consumption

	Before	After
Palmitic acid, 16:0	24.4 ± 1.6	24.3 ± 1.5
Palmitoleic acid, 16:1	4.4 ± 1.1	3.7 ± 1.0
Stearic acid, 18:0	6.7 ± 1.3	5.8 ± 0.8
Oleic acid, 18:1	27.8 ± 1.0	29.5 ± 0.9
Linoleic acid, 18:2	29.5 ± 0.8	30.0 ± 1.7
Eicosatrienoic acid, 20:3	1.3 ± 0.3	1.5 ± 0.6
Arachidonic acid, 20:4	5.7 ± 0.5	6.2 ± 0.5

[a]Values are the percentage of the total fatty acid content measured before and after extra virgin olive oil consumption. Values are expressed as mean ± SEM. See Table 1 for abbreviation.



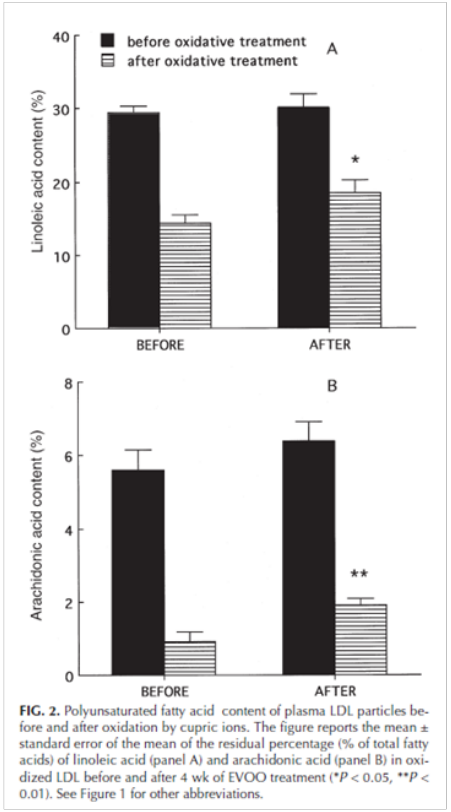


FIG. 2. Polyunsaturated fatty acid content of plasma LDL particles before and after oxidation by cupric ions. The figure reports the mean ± standard error of the mean of the residual percentage (% of total fatty acids) of linoleic acid (panel A) and arachidonic acid (panel B) in oxidized LDL before and after 4 wk of EVOO treatment (*$P < 0.05$, **$P < 0.01$). See Figure 1 for other abbreviations.

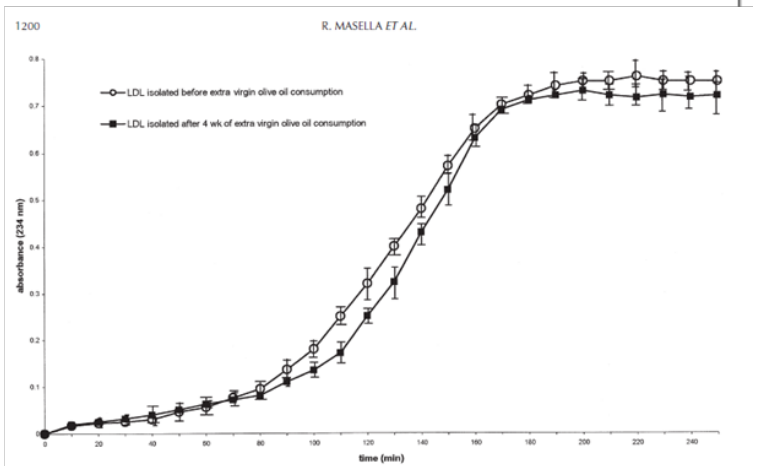


FIG. 3. Effect of dietary EVOO on the length of lag phase of plasma LDL. Mean curves of conjugated diene formation induced by copper in LDL isolated from patients before and after dietary intervention are presented. The change in absorbance at 234 nm was continuously monitored for 4 h. See Figure 1 for abbreviations.

Masella R et al. Lipids, 2001

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I Polifenoli

- **Sono assorbiti in quantità piuttosto bassa ed i loro livelli ematici sono molto più bassi di quelli di vitamine come ascorbato e tocoferoli**

- **Sono modificati durante i processi metabolici**

Polifenoli

Antiossidanti e non solo….

Attività biologiche

Modulatori di → **vie di segnale intracellulare**
attività enzimatiche
recettoriale

Extra Virgin Olive Oil Biophenols Inhibit Cell-Mediated Oxidation of LDL by Increasing the mRNA Transcription of Glutathione-Related Enzymes[1]

R. Masella et al. J. Nutr 134: 785–791, 2004.

- Oleuropeina
- Acido protocatecuico

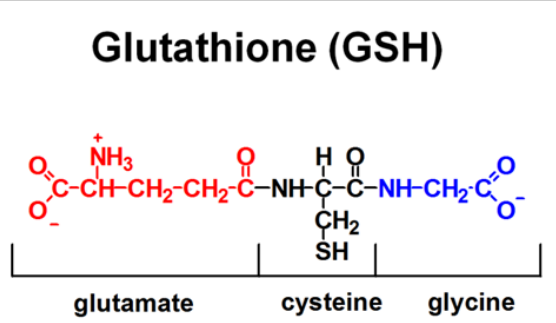
Macrofagi murini J774 A.1

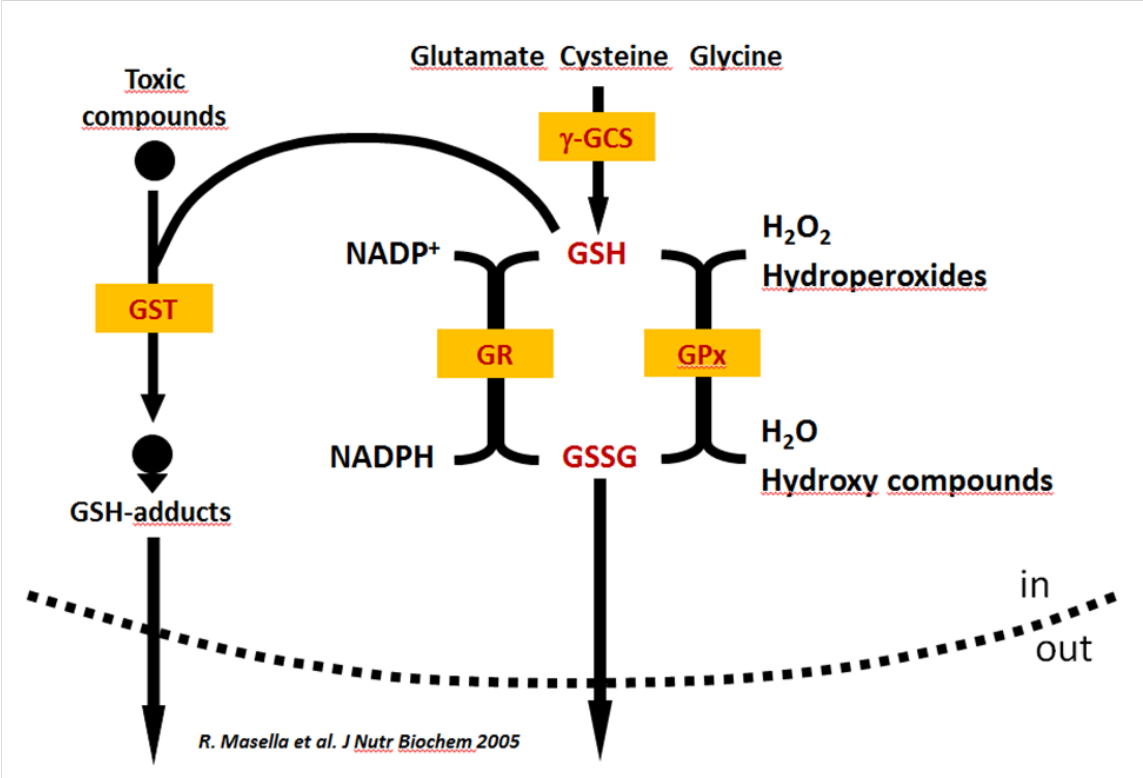
I due polifenoli proteggono le LDL dall'ossidazione anche quando non sono presenti nel mezzo di coltura.

- **Diminuzione di radicali liberi prodotti**
- **Aumento del GSH**

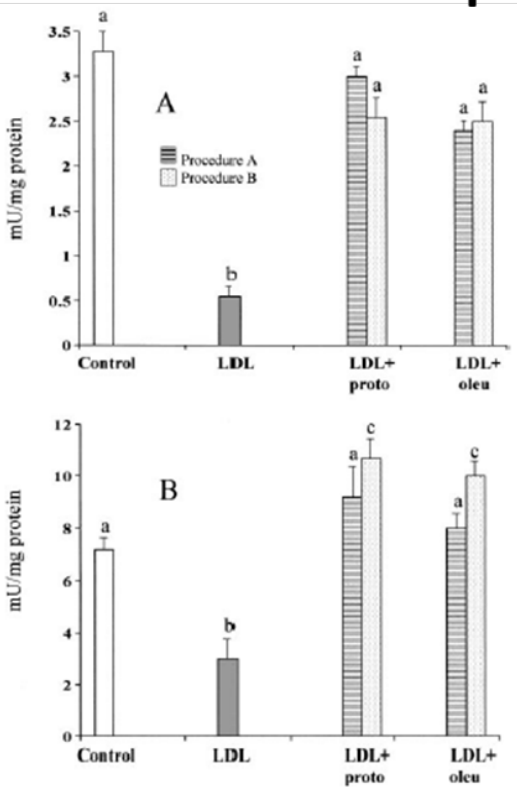
Polifenoli dell'olio di oliva innescano processi cellulari di difesa.

Difese antiossidanti endogene





Espressione di enzimi di fase 2



GR

GPx

FIGURE 2 Biophenols restore GR (*A*) and GPx (*B*) activities in J774 A.1 macrophage-like cells following both procedure A or procedure B. Activities were measured after a 24-h incubation with LDL (0.2 g protein/L). Values are means ± SEM, $n = 4$. Bars without a common letter differ, $P < 0.05$. LDL = cell exposed to LDL; LDL + proto = cell exposed to LDL and protocatechuic acid; LDL + oleu = cell exposed to LDL and oleuropein.

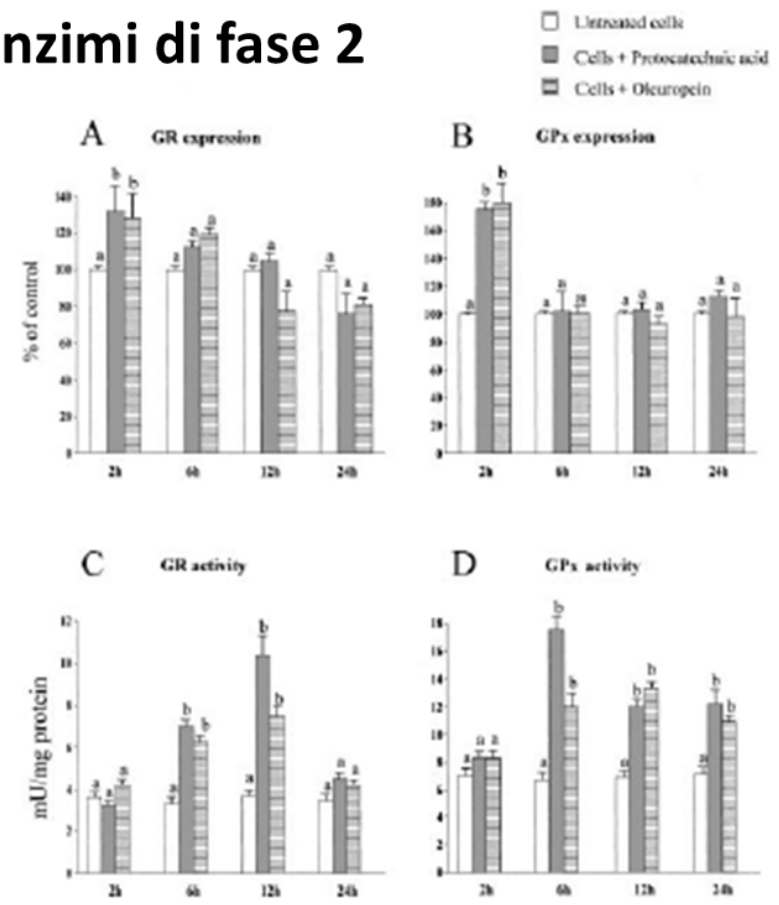
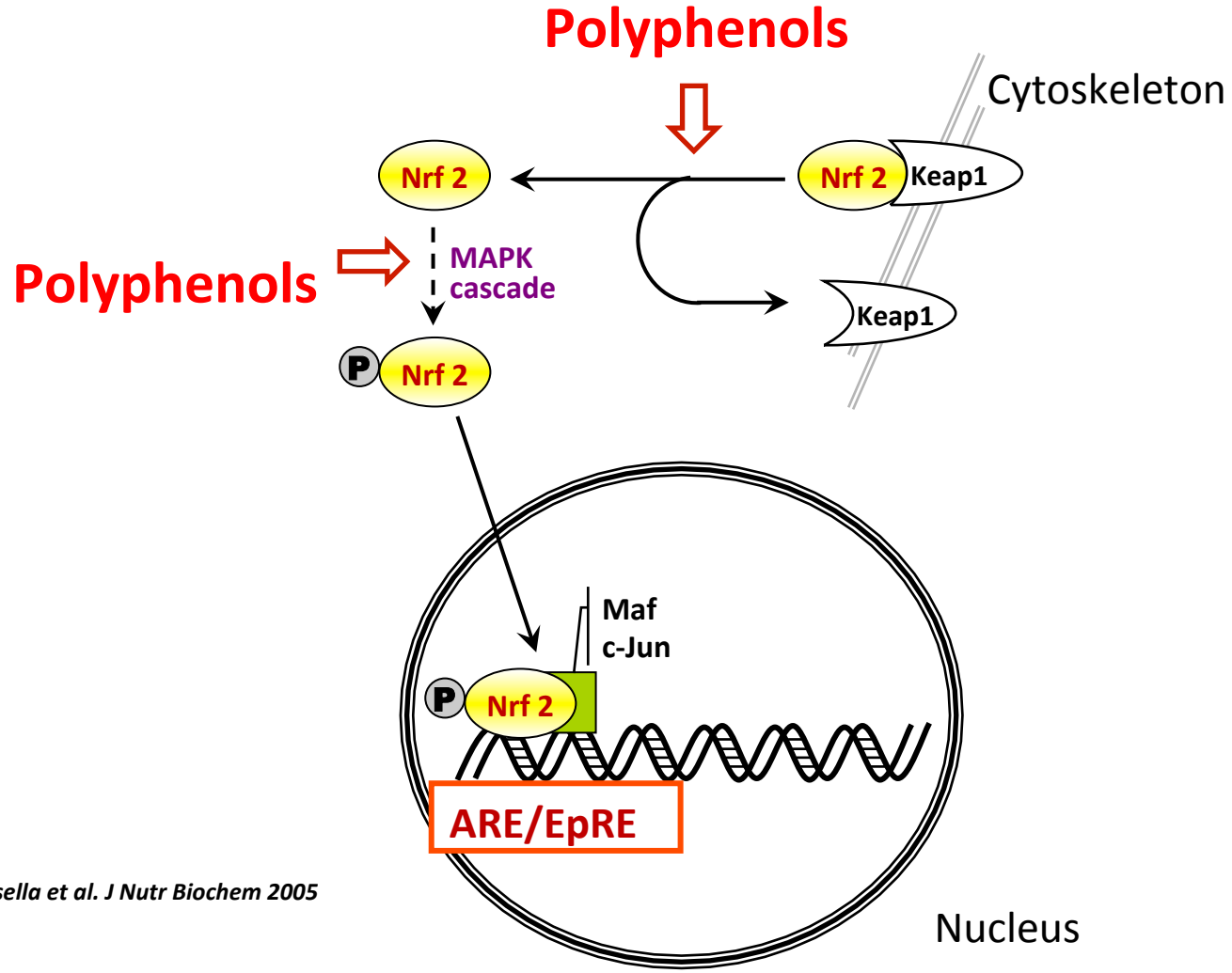
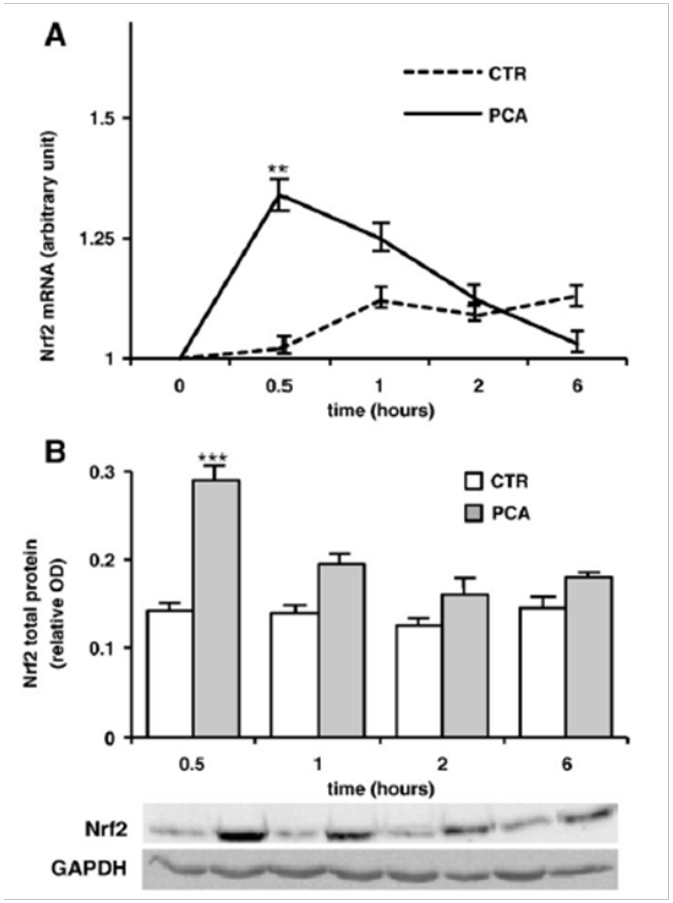


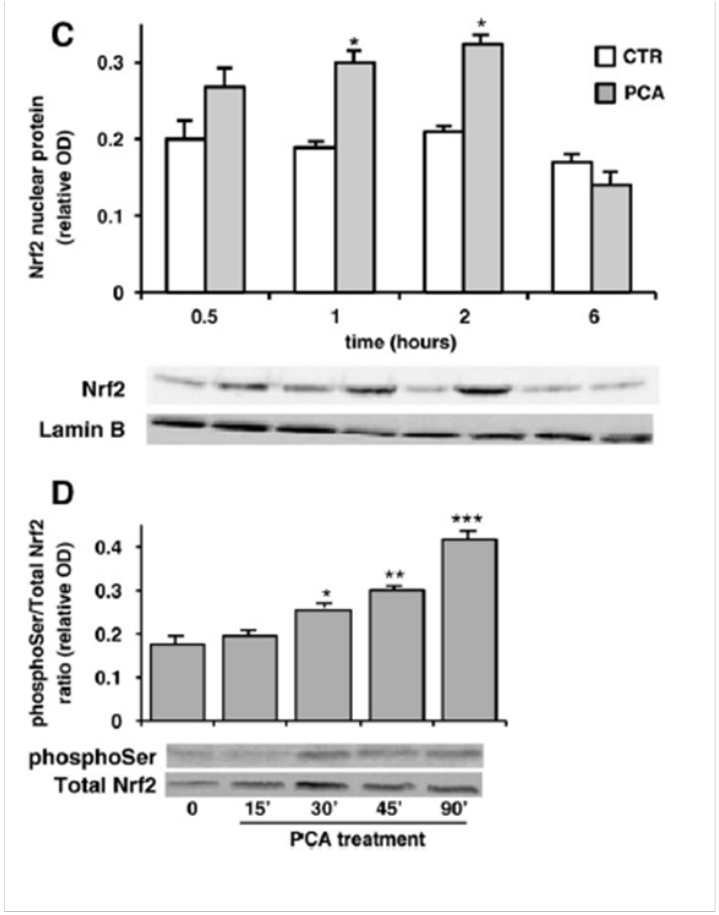
FIGURE 4 Direct effect of the biophenols on DNA transcription of GSH-related enzymes in J774 A.1 cells incubated with protocatechuic acid and oleuropein following procedure B. (*A*) Semiquantitative RT-PCR time-course evaluation of mRNA for GR and GPx. (*B*) Time-course evaluation of GR and GPx activities. Values are means ± SEM, $n = 4$. Bars without a common letter differ, $P < 0.05$.

Meccanismi di regolazione dell'espressione di enzimi di fase 2

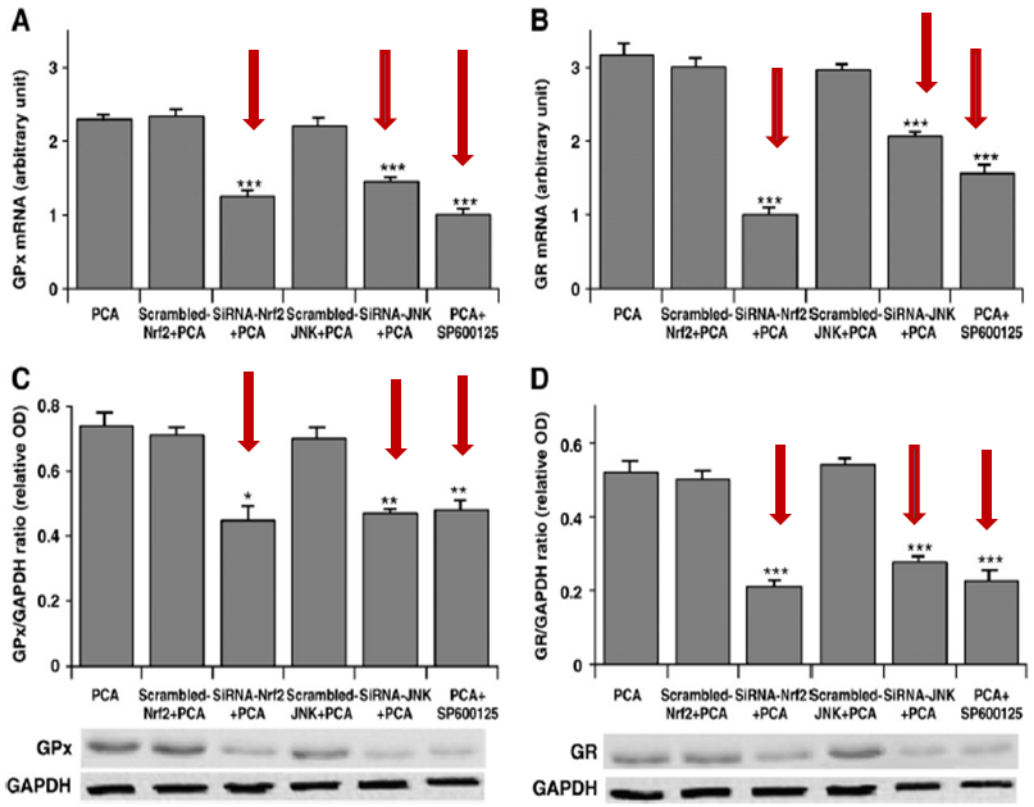


R. Masella et al. J Nutr Biochem 2005





R. Varì et al. J Nutr Biochem, 2011



R. Varì et al. J Nutr Biochem, 2011

Table 1. Randomized, crossover, controlled studies on the antioxidant effect of sustained consumption of phenolic compounds from olive oil on *in vivo* markers of lipid and DNA oxidation

	Olive oil intervention (time)	Daily olive oil dose	Subjects	Washout period	Oxidative markers	Effects
Vissiers *et al.* (2001) [79]	High-phenol vs Low-phenol (3 weeks)	69 g (in sauces, or baked products)	46 healthy (31 women, 15 men)	2 weeks without olives and olive oil	MDA, FRAP LP, PC LDL-resistance[a)] to oxidation	None
Moschandreas *et al.* (2002) [80]	High vs Low phenol (3 weeks)	70 g raw	25 healthy (14 women, 11 men)	2 weeks without olives and olive oil	MDA, FRAP LP, PC LDL resistance[a)] to oxidation	None
Marrugat *et al.* (2004) [66]	Virgin vs Common vs Refined (3 weeks with refined olive oil for cooking)	25 mL (22 g) raw	30 healthy men	2 weeks with refined olive oil for raw and cooking purposes	Plasma oxidized LDL LDL resistance[a)] to oxidation Antobodies against oxidized LDL HDL-cholesterol	Decrease with olive oil phenolics None Increase after virgin olive oil
Weinbrenner *et al.* (2004) [68]	High vs Meium vs Low phenol (4 days with low phenolic olive oil for raw and cooking	25 mL raw	12 healthy men	10 days: low phenol olive oil for raw and cooking; very-low antioxidant diet	Plasma oxidized LDL MDA in urine 8oxodG in urine and lymphoctyes F_2-isoprostanes GSH-Px HDL-cholesterol	Decrease with olive oil phenolics None Increase with olive oil phenolics
Visioli *et al.* (2005) [81]	Virgin vs refined (raw)	40 mL raw	22 lipemic patients (12 men, 10 women)	4 weeks with	Plasma antioxidant capacity F_2-isoprostanes	Increase with olive oil phenolics None
Fitó *et al.* (2005) [82]	Virgin vs Refined (raw) (3 weeks, refined olive oil for cooking)	50 mL, raw	Coronary heart disease patiens (40 men)	2 weeks withrefined olive oil for all purposes	Plasma oxidized LDL, LP GSH-Px	Decrease with olive oil phenolics Increase with olive oil phenolics
Salvini *et al.* (2006) [103]	High vs Low (8 weeks) phenolics	*ad libitum* in substitution of other fats	10 post-menopausal women	2 weeks (usual diet)	Comet assay for DNA oxidation	Decrease with olive oil
Covas *et al.* (2006) [84]	Virgin vs Common vs Refined (3 weks)	25 mL, raw	200 healthy men	2 weeks without olives and olive oil	Plasma oxidized LDL Uninduced dienes Hydroxy fatty acids Antiboides against oxidizee LDL F_2-isoprostans	Decrease with olive oil phenolics None

ELSEVIER Journal of Nutritional Biochemistry 24 (2013) 1334–1339

Olive oil polyphenols enhance the expression of cholesterol efflux related genes *in vivo* in humans. A randomized controlled trial

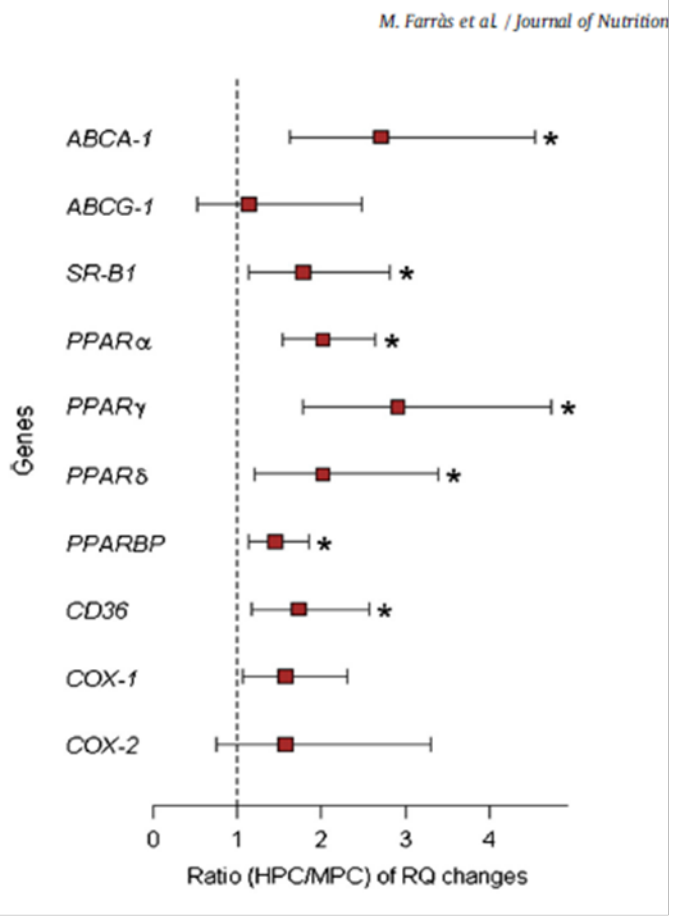
Marta Farràs[a,b], Rosa M. Valls[c], Sara Fernández-Castillejo[c], Montserrat Giralt[c], Rosa Solà[c], Isaac Subirana[d], María-José Motilva[e], Valentini Konstantinidou[c], María-Isabel Covas[a,*,1], Montserrat Fitó[a,*,1]

22 partecipanti ipertesi;
cross-over randomizzato; a doppio cieco.
30 ml di uno dei due olii di oliva :

- **MPC**= a medio contenuto di poilifenoli

- **HPC** = MPC arricchito con un estratto di polifenoli (7 mg /ml di olio)

Dopo 5 h **mRNA** dei geni responsabili del trasporto di colesterolo dalle cellule alle HDL nelle cellule bianche del sangue



The FASEB Journal • Research Communication **24, 2546 –2557 (2010)**

In vivo nutrigenomic effects of virgin olive oil polyphenols within the frame of the Mediterranean diet: a randomized controlled trial

90 Soggetti sani

- TMDVOO extra vergine di oliva ricco in polifenoli
- TMDWOO extravergine di oliva deprivato di polifenoli
- Controllo dieta abituale

cellule bianche del sangue periferico

TABLE 4. *Change in expression of atherosclerosis-related genes after 3 mo of intervention*

Gene symbol	Gene name	Control, n = 20	TMD-global, n = 36	*P* value
Cholesterol, lipid transport, and metabolism				
ABCA1	ATP-binding cassette, subfamily A, member 1	0.320 ± 0.231	0.051 ± 0.159	0.334
ABCG1	ATP-binding cassette, subfamily G, member 1	0.146 ± 0.127	0.064 ± 0.092	0.608
ANXA1	Annexin A1	0.259 ± 0.229	−0.444 ± 0.161	0.160
ARHGAP15	Rho GTPase activating protein 15	0.448 ± 0.175	−0.040 ± 0.126	0.043
ARHGAP19	Rho GTPase activating protein 19	0.400 ± 0.151	0.134 ± 0.112	0.166
ARHGEF6	Rac/Cdc42 guanine nucleotide exchange factor 6	0.460 ± 0.144	0.157 ± 0.106	0.099
CD36	CD36 molecule (thrombospondin receptor)	0.197 ± 0.170	−0.009 ± 0.126	0.342
CETP	Cholesteryl ester transfer protein, plasma	−0.262 ± 0.331	−0.058 ± 0.257	0.631
MSR1	Macrophage scavenger receptor 1	0.542 ± 0.222	0.253 ± 0.157	0.301
PLA2G4B	Phospholipase A2, group IVB	0.148 ± 0.156	0.082 ± 0.109	0.735
SCARB1	Scavenger receptor class B, member 1	−0.025 ± 0.078	0.085 ± 0.056	0.261
Inflammation				
IFNg	Interferon, γ	1.048 ± 0.464	−0.109 ± 0.330	0.049
IL10	Interleukin 10	0.915 ± 0.360	0.609 ± 0.270	0.506
CHUK	Conserved helix-loop-helix ubiquitous kinase	0.325 ± 0.192	0.036 ± 0.140	0.236
ADAM17	ADAM metallopeptidase domain 17 (tumor necrosis factor, α, converting enzyme)	0.290 ± 0.153	0.008 ± 0.112	0.148
ADAMTS1	ADAM metallopeptidase with thrombospondin type 1 motif, 1	0.166 ± 0.208	−0.120 ± 0.150	0.277
IFNA1	Interferon, α 1	0.726 ± 0.356	0.001 ± 0.258	0.117
TNFSF10	Tumor necrosis factor (ligand) superfamily, member 10	0.195 ± 0.219	−0.195 ± 0.156	0.157
TNFSF12_13	Tumor necrosis factor (ligand) superfamily, member 12-member 13	−0.021 ± 0.102	0.133 ± 0.075	0.235
IL6	Interleukin 6	−0.017 ± 0.588	0.356 ± 0.401	0.612
IL7R	Interleukin 7 receptor	0.580 ± 0.182	0.095 ± 0.132	0.037
USP48	Ubiquitin specific peptidase 48	0.380 ± 0.179	0.203 ± 0.131	0.431
MPO	Myeloperoxidase	−0.159 ± 0.121	−0.013 ± 0.090	0.343
RGS2	Regulator of G-protein signaling 2, 24 kDa	0.439 ± 0.268	0.289 ± 0.196	0.656
NFKB2	Nuclear factor of κ light polypeptide gene enhancer in B-cells 2	−0.098 ± 0.082	0.008 ± 0.063	0.315
Nuclear receptors and fatty acids receptors				
NR1H2	Nuclear receptor subfamily 1, group H, member 2	−0.081 ± 0.070	−0.003 ± 0.050	0.369
NR1H3	Nuclear receptor subfamily 1, group H, member 3	0.166 ± 0.108	0.034 ± 0.077	0.331
PPARA	Peroxisome proliferator-activated receptor α	0.088 ± 0.123	0.068 ± 0.092	0.897
PPARBP	PPAR binding protein	0.341 ± 0.160	0.022 ± 0.105	0.084
PPARG	Peroxisome proliferator-activated receptor γ	0.002 ± 0.242	0.235 ± 0.175	0.463
PPARD	Peroxisome proliferator-activated receptor δ	0.066 ± 0.128	0.010 ± 0.096	0.732
Oxidative stress				
LIAS	Lipoic acid synthetase	0.228 ± 0.197	0.188 ± 0.148	0.874
PTGS1	Prostaglandin-endoperoxide synthase 1	−0.176 ± 0.171	−0.170 ± 0.117	0.978
PTGS2	Prostaglandin-endoperoxide synthase 2	0.170 ± 0.545	−0.231 ± 0.379	0.557
OLR1	Oxidized low-density lipoprotein (lectin-like) receptor 1	0.521 ± 0.948	0.113 ± 0.580	0.724
OSBP	Oxysterol binding protein	0.219 ± 0.130	0.035 ± 0.093	0.260
ADRB2	Adrenergic, β-2, receptor, surface	0.225 ± 0.135	−0.138 ± 0.098	0.036
OGT	*O*-linked *N*-acetylglucosamine (GlcNAc) transferase	0.373 ± 0.235	0.014 ± 0.162	0.218
ALDH1A1	Aldehyde dehydrogenase 1 family, member A1	−0.101 ± 0.187	−0.116 ± 0.135	0.949
DNA repair				
CCNG1	Cyclin G1	0.396 ± 0.192	0.004 ± 0.139	0.106
POLK	Polymerase (DNA directed) κ	0.595 ± 0.275	−0.115 ± 0.204	0.045
TP53	Tumor protein p53	−0.071 ± 0.077	−0.048 ± 0.056	0.812
DCLRE1C	DNA cross-link repair 1C	0.406 ± 0.169	0.052 ± 0.123	0.100
ERCC5	Excision repair cross-complementing rodent repair deficiency, complementation group 5	0.401 ± 0.227	0.049 ± 0.169	0.221
XRCC5	X-ray repair complementing defective repair in Chinese hamster cells 5 (double-strand-break rejoining; Ku autoantigen, 80 kDa)	0.267 ± 0.152	0.000 ± 0.111	0.166

Gene expression changes, adjusted by age and sex, are presented as means ± SE of the RQ $\log_2$ ratio (posttreatment *vs.* basal values).

Atherosclerosis 208 (2010) 442–450

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Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Effect of Mediterranean diet on the expression of pro-atherogenic genes in a population at high cardiovascular risk

Vicenta Llorente-Cortés[a], Ramón Estruch[b,c], Mari Pau Mena[b,c], Emilio Ros[b,d], Miguel Angel Martínez González[e], Montserrat Fitó[b,f], Rosa María Lamuela-Raventós[b,g], Lina Badimon[a,b,*]

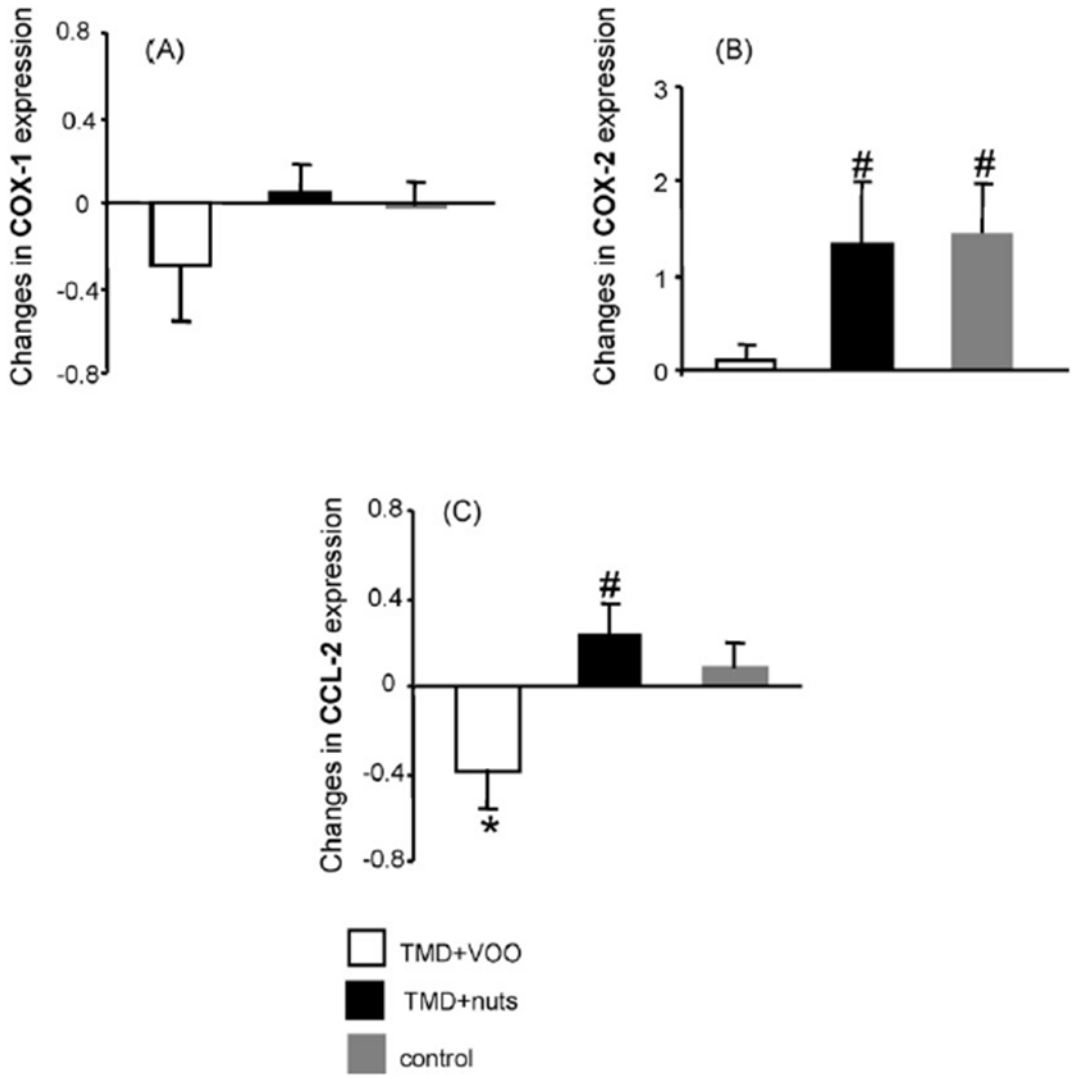
49 soggetti con almeno 2 fattori di rischio per CHD; 3 mesi di intervento: MD + 30gr/die EVOO o 30 gr/die noci/ mandorle/nocciole

Table 2
Changes in weight, adiposity, blood pressure, and other cardiovascular-risk factors[a].

Variable	TMD + VOO	TMD + nuts	Control	*P* time[b]	*P* group[c]	*P* interaction[d]
Weight, kg						
Baseline	73.6 ± 11.6[e]	76.9 ± 6.6	74.9 ± 13.1	0.488	0.761	0.373
Final	74.0 ± 11.1	76.0 ± 6.3	74.6 ± 13.5			
BMI, kg/m^2						
Baseline	28.8 ± 2.7	27.7 ± 2.5	29.9 ± 5.5	0.567	0.175	0.539
Final	28.8 ± 2.5	27.4 ± 2.3	29.9 ± 5.4			
Waist, cm						
Baseline	102 ± 10	101 ± 5	105 ± 16	0.007	0.706	0.533
Final	101 ± 8	98 ± 6[f]	100 ± 10			
Systolic BP, mmHg						
Baseline	153 ± 10	149 ± 18	161 ± 17	0.043	0.006	0.145[g,h]
Final	147 ± 11[f]	142 ± 15[i]	161 ± 11			
Diastolic BP, mmHg						
Baseline	82 ± 9	83 ± 8	87 ± 12	0.021	0.153	0.743
Final	80 ± 9	80 ± 8[f]	86 ± 11			
Glucose, mg/dL						
Baseline	156 ± 59	144 ± 47	156 ± 59	0.018	0.418	0.011[g]
Final	132 ± 40[i]	128 ± 36[f]	165 ± 79			
Cholesterol, mg/dL						
Baseline	231 ± 31	218 ± 23	205 ± 28	0.014	0.472	0.050[g]
Final	208 ± 40[i]	205 ± 18	209 ± 43			
LDL-cholesterol, mg/dL						
Baseline	148 ± 28	143 ± 29	125 ± 29	0.003	0.202	0.207
Final	129 ± 41[i]	135 ± 19	121 ± 31			
HDL-cholesterol, mg/dL						
Baseline	52.3 ± 12.9	48.1 ± 11.1	48.5 ± 9.9	0.154	0.252	0.201
Final	56.2 ± 14.1[f]	48.6 ± 10.0	48.4 ± 10.5			
Triglycerides, mg/dL						
Baseline	147 ± 67	127 ± 78	145 ± 68	0.215	0.275	0.405
Final	126 ± 50	106 ± 38	152 ± 84			
Cholesterol/HDL ratio						
Baseline	4.6 ± 1.0	4.7 ± 1.2	4.1 ± 0.68	0.004	0.682	0.041[g]
Final	3.9 ± 1.1[i]	4.3 ± 0.8[f]	4.1 ± 0.73			

Table 3
Changes in inflammatory, lipoprotein receptor and thrombotic gene expression[a].

Variable	TMD + VOO	TMD + nuts	Control	*P* time[b]	*P* group[c]	*P* interaction[d]
COX-1						
Baseline	1.16 ± 1.03[e]	1.02 ± 0.94	0.73 ± 0.48	0.289	0.676	0.057
Final	0.80 ± 0.68	1.04 ± 6.87	0.82 ± 0.49			
COX-2						
Baseline	1.09 ± 0.81	1.18 ± 0.87	0.88 ± 0.93	0.003	0.532	0.612
Final	1.75 ± 1.29	2.67 ± 1.67[f]	2.20 ± 1.97[g]			
MCP-1						
Baseline	1.07 ± 1.11	0.52 ± 0.56	0.33 ± 0.40	1.000	0.178	0.013
Final	0.67 ± 0.75[f]	0.71 ± 0.36	0.54 ± 0.42			
LDLR						
Baseline	0.68 ± 0.46	0.68 ± 0.51	0.54 ± 0.47	0.001	0.787	0.880
Final	0.92 ± 0.54	0.97 ± 0.44[f]	0.90 ± 0.59[f]			
LRP1						
Baseline	0.96 ± 0.60	0.75 ± 0.51	0.52 ± 0.61	0.001	0.303	0.017[g]
Final	1.06 ± 0.65	1.09 ± 0.51[f]	0.90 ± 0.70[f]			
CD36						
Baseline	0.93 ± 0.57	0.70 ± 0.53	0.61 ± 0.48	0.011	0.210	0.047[h]
Final	0.95 ± 0.49	1.08 ± 0.51[f]	0.69 ± 0.42			
TF						
Baseline	0.68 ± 0.43	0.63 ± 0.55	0.52 ± 0.65	0.064	0.675	0.946
Final	0.86 ± 0.68	0.88 ± 0.72	0.69 ± 0.58			
TFPI						
Baseline	0.99 ± 0.60	0.61 ± 0.47	0.72 ± 0.56	0.789	0.392	0.048[i]
Final	0.80 ± 0.63	0.85 ± 0.50[j]	0.74 ± 0.42			



Camargo *et al. BMC Genomics* 2010, **11**:253
http://www.biomedcentral.com/1471-2164/11/253

BMC Genomics

RESEARCH ARTICLE Open Access

Gene expression changes in mononuclear cells in patients with metabolic syndrome after acute intake of phenol-rich virgin olive oil

Conclusion: This study shows that intake of virgin olive oil based breakfast, which is rich in phenol compounds is able to repress *in vivo* expression of several pro-inflammatory genes, thereby switching activity of peripheral blood mononuclear cells to a less deleterious inflammatory profile. These results provide at least a partial molecular basis for

20 soggetti ; 40 gr olio con pane; dopo 4 ore prelievo;

98 geni modulati da EVOO ad alto contenuto di polifenoli rispetto a EVOO a basso contenuto di polifenoli: **19 iper-espressi**, **79 ipo-espressi**

DOI 10.1002/mnfr.201200613 *Mol. Nutr. Food Res.* 2013, *57*, 772–783

REVIEW

Up-to date knowledge on the in vivo transcriptomic effect of the Mediterranean diet in humans

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[2] Cardiovascular Risk and Nutrition Research Group, Mar Institute of Medical Research (IMIM), CIBER de Fisiopatología de la Obesidad y la Nutrición (CIBEROBN), Barcelona, Spain

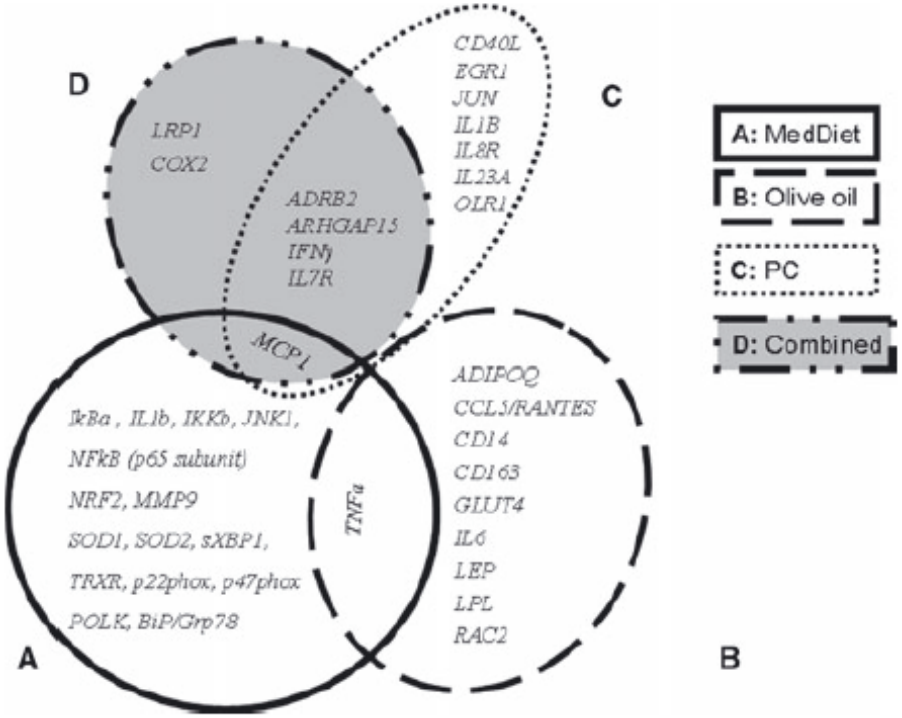

Figure 1. Group of genes differentially expressed, as verified by qRT-PCR, in transcriptomic studies in humans after (A) MedDiet intervention, (B) olive oil (OO) intervention, (C) OO phenolic compounds intervention, and (D) MedDiet and OO combined intervention.

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Table 1. Summary of Dietary Recommendations to Participants in the Mediterranean-Diet Groups and the Control-Diet Group.

Food	Goal
Mediterranean diet	
Recommended	
Olive oil*	≥4 tbsp/day
Tree nuts and peanuts†	≥3 servings/wk
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Fish (especially fatty fish), seafood	≥3 servings/wk
Legumes	≥3 servings/wk
Sofrito‡	≥2 servings/wk
White meat	Instead of red meat
Wine with meals (optionally, only for habitual drinkers)	≥7 glasses/wk
Discouraged	
Soda drinks	<1 drink/day
Commercial bakery goods, sweets, and pastries§	<3 servings/wk
Spread fats	<1 serving/day
Red and processed meats	<1 serving/day
Low-fat diet (control)	
Recommended	
Low-fat dairy products	≥3 servings/day
Bread, potatoes, pasta, rice	≥3 servings/day
Fresh fruits	≥3 servings/day
Vegetables	≥2 servings/day
Lean fish and seafood	≥3 servings/wk
Discouraged	
Vegetable oils (including olive oil)	≤2 tbsp/day
Commercial bakery goods, sweets, and pastries§	≤1 serving/wk
Nuts and fried snacks	≤1 serving /wk
Red and processed fatty meats	≤1 serving/wk
Visible fat in meats and soups¶	Always remove
Fatty fish, seafood canned in oil	≤1 serving/wk
Spread fats	≤1 serving/wk
Sofrito‡	≤2 servings/wk

PREDIMED trial (Prevención con Dieta Mediterránea)

Studio a bracci paralleli, multicentrico, randomizzato

7447 soggetti (donne e uomini; 55-80 anni)

- No CVD al momento dell'arruolamento
- T2D o almeno 3 fattori di rischio (fumo, ipertensione, alto c-LDL, basso c-HDL, sovrappeso/obesità)

- Dieta mediterranea **+ EVOO** (30 gr/die)
- Dieta mediterranea + **noci/mandorle/nocciole** (30 gr/die)
- Dieta di controllo (**low fat**)

J Am Coll Nutr. 2011 Dec;30(6):502-10.

Nut consumption is associated with decreased health risk factors for cardiovascular disease and metabolic syndrome in U.S. adults: NHANES 1999-2004.

O'Neil CE[1], Keast DR, Nicklas TA, Fulgoni VL 3rd.

Author information

Abstract

BACKGROUND: Few recent epidemiologic studies have assessed the effect that nut consumption (including tree nuts and peanuts) has on health risks, including metabolic syndrome (MetS).

OBJECTIVE: This study compared the health risk for cardiovascular disease, type 2 diabetes, and MetS of nut consumers with that of nonconsumers.

DESIGN: Adults 19+ years (n = 13,292) participating in the 1999-2004 National Health and Nutrition Examination Survey were used. Intake from 24-hour recalls was used to determine intake. Nut/tree nut consumers consumed ≥¼; ounce per day. Covariate-adjusted means, standard errors, and prevalence rates were determined for the nut consumption groups.

RESULTS: The prevalence of nut consumers was 18.6% ± 0.7% and 21.0% ± 0.9% in those 19-50 years and 51 years and older, respectively. Nut consumption was associated with a decreased body mass index (27.7 kg/m(2) ± 0.2 vs 28.1 ± 0.1 kg/m(2), $p < 0.05$), waist circumference (95.6 ± 0.4 cm vs 96.4 ± 0.3 cm, $p < 0.05$), and systolic blood pressure (121.9 ± 0.4 mmHg vs 123.20 ± 0.3 mmHg, $p < 0.01$) compared with nonconsumers. Tree nut consumers also had a lower weight (78.8 ± 0.7 kg vs 80.7 ± 0.3 kg, $p < 0.05$). Nut consumers had a lower percentage of two risk factors for MetS: hypertension (31.5% ± 1.0% vs 34.2% ± 0.8%, $p < 0.05$) and low high density lipoprotein-cholesterol (HDL-C) (29.6% ± 1.0% vs 34.8% ± 0.8%, $p < 0.01$). Tree nut consumers had a lower prevalence of four risk factors for MetS: abdominal obesity (43.6% ± 1.6% vs 49.5% ± 0.8%, $p < 0.05$), hypertension (31.4% ± 1.2% vs 33.9% ± 0.8%, $p < 0.05$), low HDL-C (27.9% ± 1.7% vs 34.5% ± 0.8%, $p < 0.01$), high fasting glucose (11.4% ± 1.4% vs 15.0% ± 0.7%, $p < 0.05$), and a lower prevalence of MetS (21.2% ± 2.1% vs 26.6% ± 0.7%, $p < 0.05$).

CONCLUSION: Nut/tree nut consumption was associated with a decreased prevalence of selected risk factors for cardiovascular disease, type 2 diabetes, and MetS.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Association of Nut Consumption with Total and Cause-Specific Mortality

Ying Bao, M.D., Sc.D., Jiali Han, Ph.D., Frank B. Hu, M.D., Ph.D., Edward L. Giovannucci, M.D., Sc.D., Meir J. Stampfer, M.D., Dr.P.H., Walter C. Willett, M.D., Dr.P.H., and Charles S. Fuchs, M.D., M.P.H.

369; 2013

Associazione tra consumo di frutta secca oleosa e mortalità totale e causa-specifica in 76,464 donne arruolate nel Nurses' Health Study (1980–2010) e 42,498 uomini arruolati nel Health Professionals Follow-up Study (1986–2010).

Table 1. Characteristics of Person-Years According to Frequency of Nut Consumption.*

Characteristic	Frequency of Nut Consumption					
	Never	Less Than Once per Week	Once per Week	Two to Four Times per Week	Five or Six Times per Week	Seven or More Times per Week
Age (yr)	57.5±11.4	60.1±10.9	60.8±10.9	62.0±10.8	62.7±11.1	61.8±11.5
Body-mass index	26.0±5.1	26.1±5.0	25.9±4.6	25.6±4.4	25.2±4.2	24.9±4.1
Physical activity (metabolic equivalents/wk)	19.2±28.9	20.4±27.5	25.2±32.5	28.5±34.9	31.3±38.4	34.3±42.3
Current smoker (%)	17.3	13.6	10.8	9.9	9.9	9.8
Underwent physical examination for screening purposes (%)	51.1	60.6	60.3	61.2	57.7	54.7
Currently uses multivitamins (%)	41.9	48.9	51.3	54.3	55.2	52.9
Alcohol intake (g/day)	6.0±11.1	6.4±10.9	8.2±12.4	9.5±13.5	11.0±15.2	11.3±15.6
Red or processed meat intake (servings/day)	1.3±0.9	1.4±0.8	1.4±0.9	1.3±0.9	1.3±0.9	1.2±1.0
Fruit intake (servings/day)	2.1±1.4	2.1±1.2	2.3±1.3	2.5±1.4	2.8±1.6	2.9±1.7
Vegetable intake (servings/day)	2.4±1.4	2.6±1.3	2.9±1.4	3.2±1.5	3.4±1.6	3.4±1.8

* Plus–minus values are means ±SD. All variables except age are age-standardized. Separate results for women and men are shown in Table S3 in the Supplementary Appendix. Frequency of nut consumption pertains to one serving of nuts, defined as 28 g.

Table 1. Hazard ratios for deaths compared with participants who did not eat nuts (17)

	Multivariable-adjusted HRs (95% CI)	Frequency of nut consumption	P_{trend}*
Total mortality			<.001
	0.93 (0.90 to 0.96)	< 1 per week	
	0.89 (0.86 to 0.93)	1 per week	
	0.87 (0.83 to 0.90)	2 to 4 times per week	
	0.85 (0.79 to 0.91)	5 or 6 times per week	
	0.80 (0.73 to 0.86)	7 or more times per week	
Cardiovascular disease			<.001
	0.84 (0.78 to 0.90)	< 1 per week	
	0.83 (0.76 to 0.89)	1 per week	
	0.79 (0.73 to 0.86)	2 to 4 times per week	
	0.75 (0.62 to 0.84)	5 or more times per week	
Heart disease			<.001
	0.84 (0.77 to 0.91)	< 1 per week	
	0.78 (0.71 to 0.86)	1 per week	
	0.75 (0.68 to 0.82)	2 to 4 times per week	
	0.71 (0.63 to 0.81)	5 or more times per week	
Cancer			.03
	0.93 (0.88 to 0.98)	< 1 per week	
	0.93 (0.87 to 1.00)	1 per week	
	0.92 (0.85 to 0.98)	2 to 4 times per week	
	0.89 (0.81 to 0.99)	5 or more times per week	

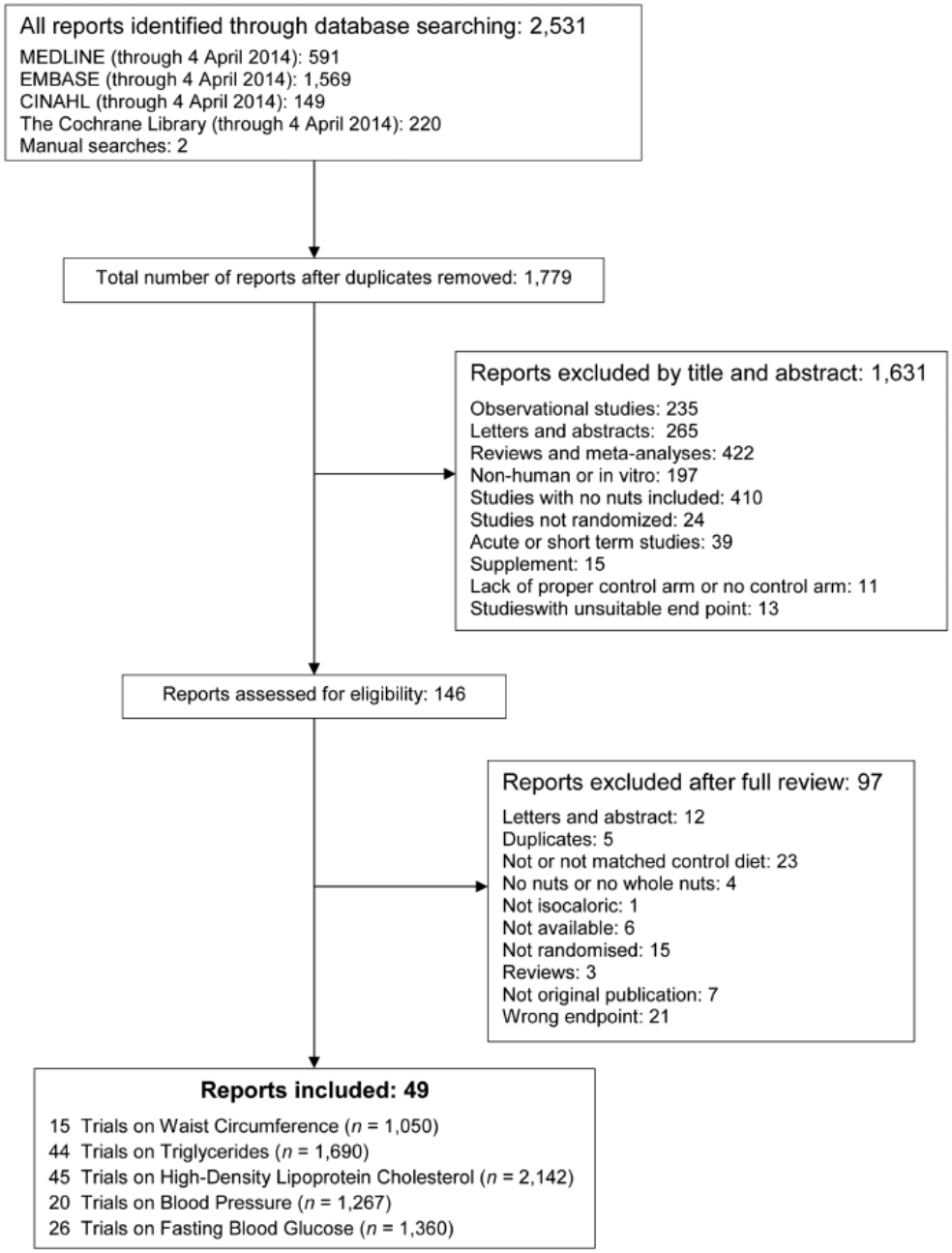
* Statistical tests were two-sided, and *P* values were calculated with the use of the Wald test. HR = hazard ratio.

BMJ Open

Effect of tree nuts on metabolic syndrome criteria: a systematic review and meta-analysis of randomised controlled trials

Sonia Blanco Mejia,[1,2] Cyril W C Kendall,[1,2,3] Effie Viguiliouk,[1,2] Livia S Augustin,[1,2] Vanessa Ha,[1,2] Adrian I Cozma,[1,2] Arash Mirrahimi,[1,2,4] Adriana Maroleanu,[2] Laura Chiavaroli,[1,2] Lawrence A Leiter,[1,2,5,6,7] Russell J de Souza,[1,2,8] David J A Jenkins,[1,2,5,6,7] John L Sievenpiper[2,5,6,9]

BMJ Open 2014;4:e004660. doi:10.1136/bmjopen-2013-004660



~50 g/day follow-up of 8 weeks

↓ TRIGLICERIDI

↓ GLICEMIA

= Circonferenza vita
BMI
HDL-C
Pressione sanguigna

Association of Nut and Seed Intake with Colorectal Cancer Risk in the European Prospective Investigation into Cancer and Nutrition

Mazda Jenab, Pietro Ferrari, Nadia Slimani, et al.

Cancer Epidemiol Biomarkers Prev 2004;13:1595-1603.

European Prospective Investigation into Cancer and Nutrition EPIC study, studio prospettico condotto in 10 paesi europei fra cui l'Italia

478,040 soggetti (141,988 uomini e 336,052 donne) con un totale di 855 cancri del colon e 474 cancri del retto

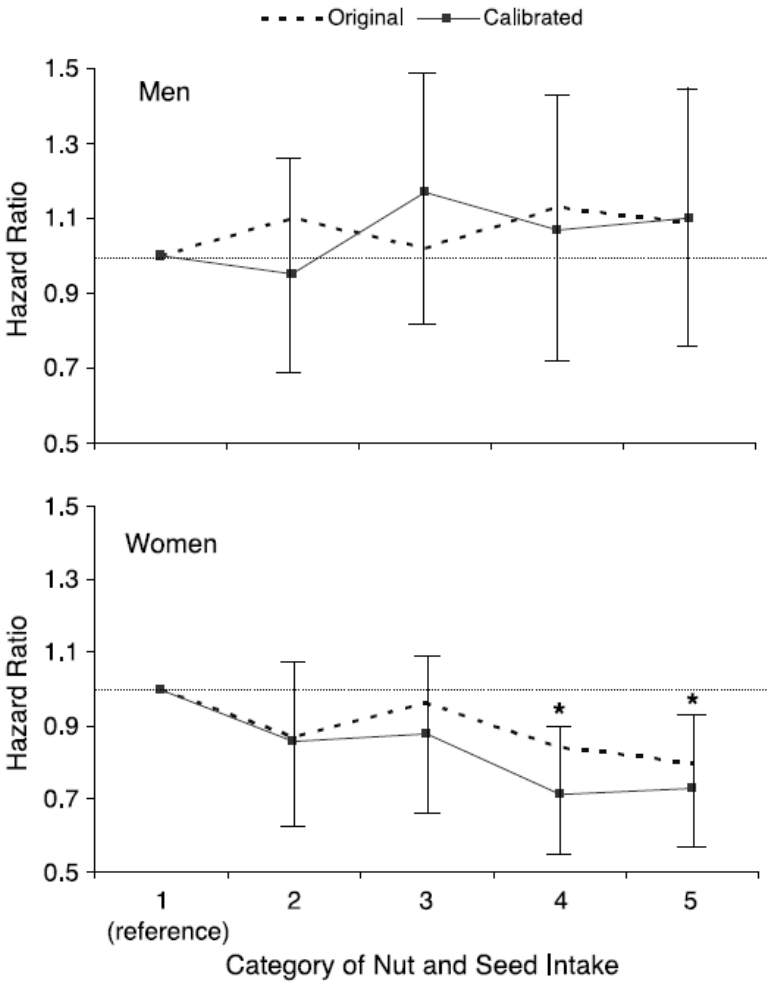


Figure 1. HRs for the risk of CRC in men and women associated with intake of nuts and seeds, original versus calibrated data. *Dotted line,* original HRs for noncalibrated dietary data and CRC risk, which are given and described in Table 3. *Solid line,* calibrated HRs with 95% CIs (*bars*). Calibrated HRs were

Frutta secca

	Nocciole	Noci	Pinoli	Arachidi	Mandorle	Pistacchi
Energia	655 Kcal	**689 Kcal**	595 Kcal	598 Kcal	603 Kcal	608 Kcal
Parte edibile	42 %	39 %	**100 %**	65 %	24 %	50 %
Acqua	4,5 g	3,5 g	4,3 g	2,3 g	**5,1 g**	3,9 g
Carboidrati	6,1 g	5,1 g	4,0 g	**8,5 g**	4,6 g	8,1 g
Grassi	64,1 g	**68,1 g**	50,3 g	50,0 g	55,3 g	56,1 g
Proteine	13,8 g	14,3 g	**31,9 g**	29,0 g	22,0 g	18,1 g
Fibre	8,1 g	6,2 g	4,5 g	10,9 g	**12,7 g**	10,6 g
vitamina E	15,00 mg	4,0 mg	-	-	**26,0 mg**	4,0 mg
Ferro	3,3 mg	2,4 mg	2,0 mg	3,5 mg	3,0 mg	**7,3 mg**
Calcio	150 mg	61 mg	40 mg	64 mg	**240 mg**	131 mg
Fosforo	322 mg	300 mg	466 mg	283 mg	**550 mg**	500 mg
Potassio	466 mg	603 mg		680 mg	780 mg	**972 mg**

- Acidi grassi insaturi n-3 e n-6 nel rapporto ottimale
- Arginina
- Acido folico
- Vitamine del gruppo B

Acidi grassi polinsaturi

Proteine vegetali

Fibre

Fitocomposti

Migliorare metabolismo lipidico

Diminuire il carico glicemico della dieta

Diminuire i processi infiammatori

OPEN ACCESS Freely available online

PLOS ONE

The Effects of the Mediterranean Diet on Biomarkers of Vascular Wall Inflammation and Plaque Vulnerability in Subjects with High Risk for Cardiovascular Disease. A Randomized Trial

Rosa Casas[1,2], Emilio Sacanella[1,2]*, Mireia Urpí-Sardà[1,3], Gemma Chiva-Blanch[1,2], Emilio Ros[2,4], Miguel-Angel Martínez-González[2,5], Maria-Isabel Covas[2,6], Rosa Mª Lamuela-Raventos[2,3], Jordi Salas-Salvadó[2,7], Miquel Fiol[2,8], Fernando Arós[2,9], Ramon Estruch[1,2]

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Abstract

Background: Adherence to the Mediterranean diet (MD) is associated with reduced morbidity and mortality due to cardiovascular disease. However, how the MD exerts its effects is not fully known.

Aim: To assess the 12-month effects of two enhanced MDs compared to a low-fat diet on inflammatory biomarkers related to atherosclerosis and plaque vulnerability in a subcohort of the PREDIMED (Prevención con Dieta Mediterránea) study.

Methods: A total of 164 participants at high risk for cardiovascular disease were randomized into three diet groups: MD supplemented with 50 mL/d of extra virgin olive oil (MD+EVOO) or 30 g/d of nuts (MD+Nuts) and a low-fat diet. Changes in classical cardiovascular risk factors, inflammatory biomarkers of atherosclerosis and plaque vulnerability were measured after 12 months of intervention.

Results: Compared to participants in the low-fat diet group, those receiving MD+EVOO and MD+Nuts showed a higher decrease in systolic (6 mmHg) and diastolic (3 mmHg) blood pressure (P = 0.02; both), as well as a reduction of 10% and 8% in LDL-cholesterol (P = 0.04), respectively. Patients in the MD+Nuts group showed a significant reduction of 34% in CD40 expression on monocyte surface compared to low-fat diet patients (P = 0.03). In addition, inflammatory biomarkers related

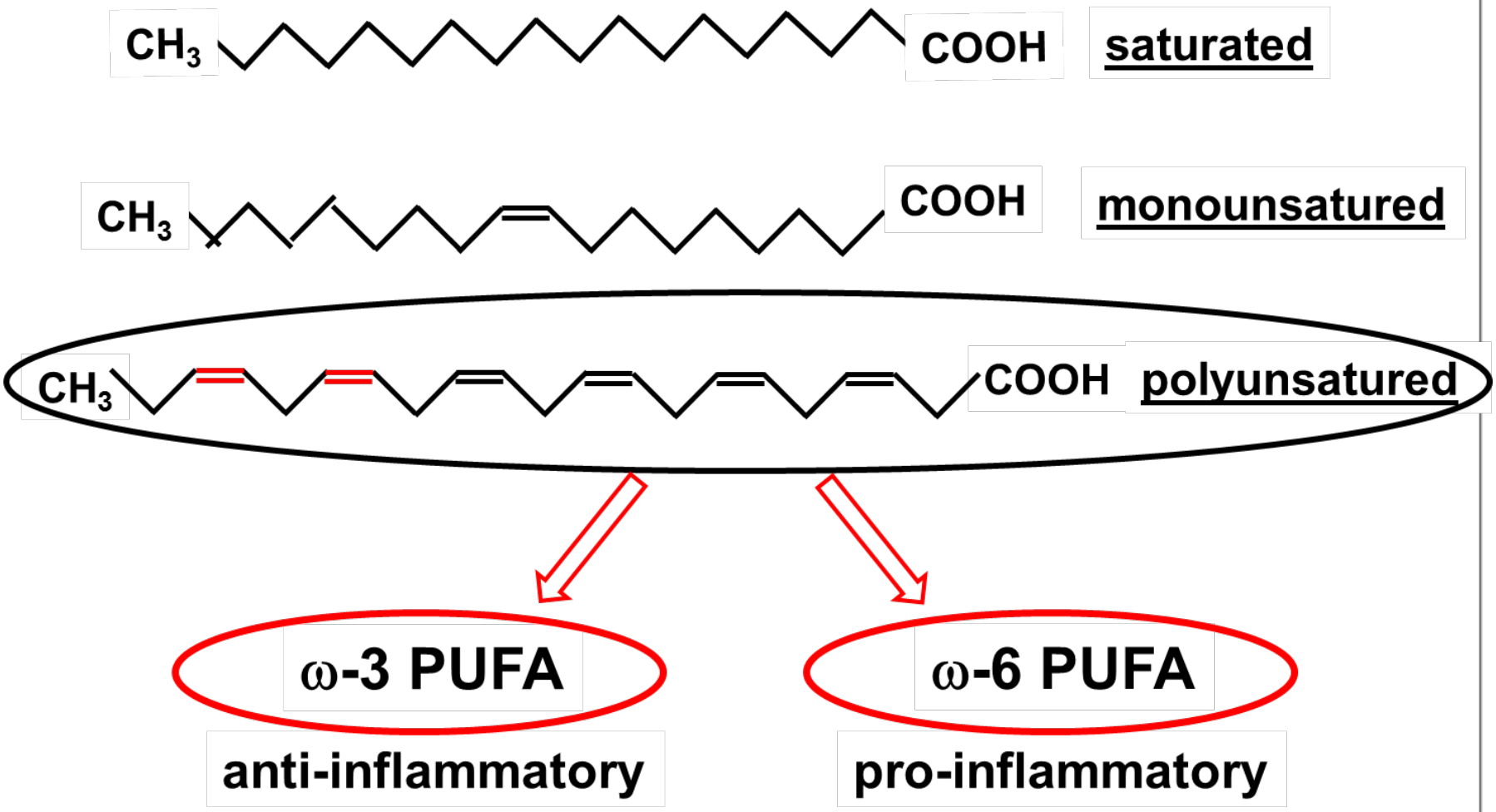
Table 3. Changes in adhesion molecule expression in circulating T- lymphocytes and monocytes.

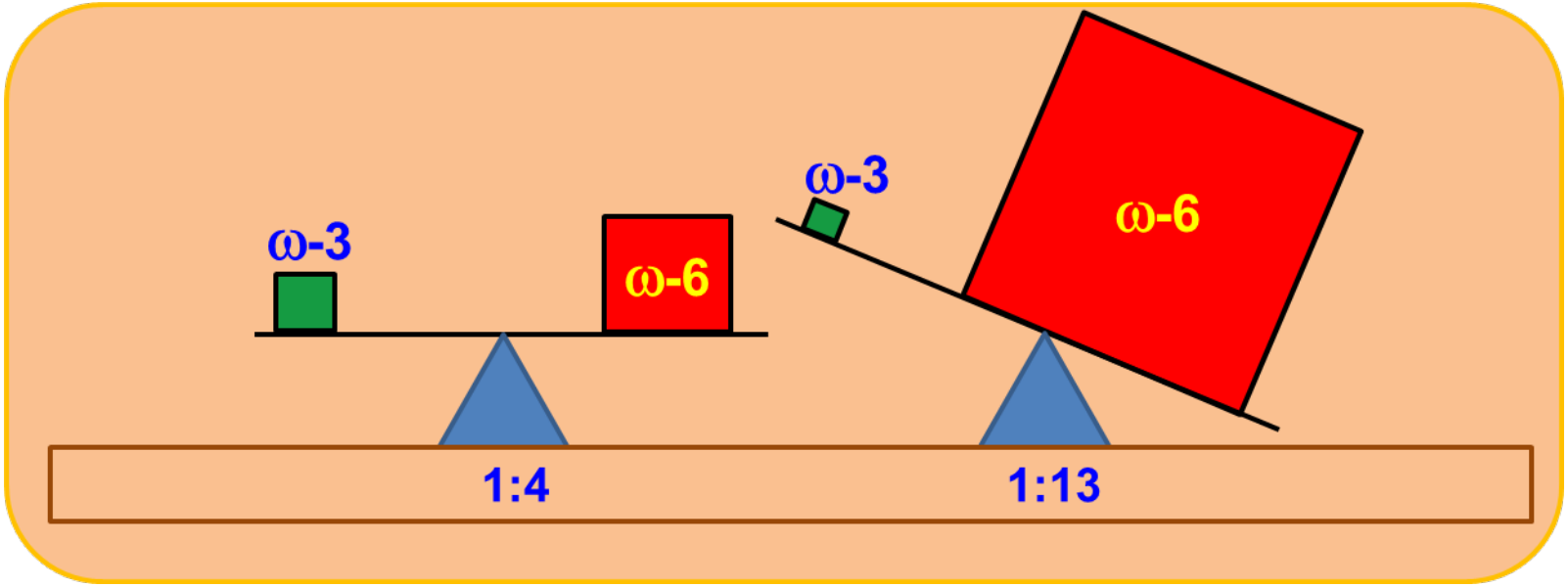
		MD+EVOO (n = 55)		MD+Nuts (n = 55)		Low-fat diet (n = 54)		
		Mean	P[3]	Mean	P[3]	Mean	P[3]	Pint[4]
T-LYMPHOCYTES								
CD11a	Baseline[1]	132±4.7		137±5.2		121±5.2		0.26
	1y.[1]	107±5.3		107±6.0		103±6.0		
	Mean changes[2]	−24.4 (−36.0 to −13.0)	<0.001	−29.9 (−43.1 to −16.7)	<0.001	−18.3 (−31.2 to −5.2)	0.006	
CD49d	Baseline	48.3±1.1		39.0±1.1		34.8±1.1		0.33
	1y.	36.7±1.1		41.0±1.1		39.9±1.1		
	Mean changes	−11.7 (−16.1 to −7.2)	0.004	2.0 (−0.7 to 4.7)	0.54	5.1 (3.1 to 7.1)	0.14	
CD40	Baseline	47.5±1.1		55.3±1.1		44.2±1.1		0.20
	1y.	36.7±1.1		42.0±1.1		38.6±1.1		
	Mean changes	−11.0 (−12.6 to −9.3)	0.001	−13.5 (−15.5 to −11.4)	0.001	−5.6 (−6.5 to −4.8)	0.09	
MONOCYTES								
CD11a	Baseline	85.0±4.2		80.1±4.4		71.8±4.2		0.41
	1y.	57.3±2.0		56.8±2.1		53.9±2.1		
	Mean changes	−27.7 (−36.1 to −19.5)	<0.001	−23.3 (−32.0 to −14.6)	<0.001	−24.9 (−33.3 to −6.6)	<0.001	
CD11b	Baseline	44.7±2.1		47.3±2.2		43.9±2.2		0.38
	1y.	34.6±1.3		36.5±1.3		35.1±1.3		
	Mean changes	−10.1 (−14.6 to −5.5)	<0.001	−10.8 (−15.6 to −6.1)	<0.001	−8.8 (−13.6 to −4.1)	<0.001	
CD49d	Baseline	35.2±1.1		39.0±1.1		35.0±1.1		0.50
	1y.	27.2±1.1		29.2±1.1		30.7±1.1		
	Mean changes	−8.0 (−9.4 to −6.5)	<0.001	−9.8 (−11.6 to −8.1)	<0.001	−4.3 (−5.3 to −3.2)	0.06	
CD40	Baseline	36.1±2.9		46.5±2.9		35.2±2.9		0.03
	1y.	26.3±1.9		30.9±1.9		31.1±1.9		
	Mean changes	−9.8 (−15.0 to −4.6)[b]	<0.001	−15.6 (−20.9 to −10.2)[a,b]	<0.001	−4.1 (−9.4 to 1.2)	0.13	

Data analyzed by repeated-measures 2-factor ANOVA (simple-effect analysis by Bonferroni's multiple contrast).
[1]Values are mean ± SD.
[2]Mean differences (95% CI).
[3]P: Significant differences (P<0.05) between before and after the intervention.
[4]Pint: comparison between measures obtained before and after intervention and among the 3 diet groups, P<0.05.
[a]MD+EVOO or MD+nuts vs. low fat-diet and [b]MD+EVOO vs. MD+nuts are significantly different, P<0.05. EVOO, extra virgin olive oil; MD+EVOO, Mediterranean diet supplemented with extra virgin olive oil; MD+Nuts, Mediterranean diet supplemented with nuts.
doi:10.1371/journal.pone.0100084.t003

Table 4. Changes in the expression of circulating markers of plaque instability and other inflammatory biomarkers.

		MD+EVOO (n = 55)		MD+Nuts (n = 55)		Low-fat diet (n = 54)		
		Mean	P[3]	Mean	P[3]	Mean	P[3]	P int[4]
sVCAM (ng/mL)	Baseline[1]	872±47.0		935±49.2		776±48.6		0.30
	1 y.[1]	734±44.9		727±47.1		720±46.5		
	Mean changes[2]	−138 (−251 to −25.2)	0.02	−208 (−327 to −89.6)	0.001	−55.6 (−173 to 61.5)	0.35	
sICAM (ng/mL)	Baseline	437±27.3		394±23.3		369±24.0		0.04
	1 y.	217±22.0		364±18.8		431±19.2		
	Mean changes	−220 (−273 to −166)[b]	<0.001	−30.3 (−76.1 to 15.5)[b]	0.20	62.3 (15.5 to 109)[b]	0.01	
sE-SEL (ng/mL)	Baseline	28.6±2.5		33.0±2.6		32.3±2.6		0.55
	1 y.	26.9±2.4		28.3±2.5		30.1±2.5		
	Mean changes	−1.7 (−4.5 to 1.2)	0.26	−4.7 (−7.7 to −1.7)	0.003	−2.2 (−5.3 to 0.9)	0.16	
sP-SEL (ng/mL)	Baseline	91.4±9.3		87.6±9.4		50.0±10.5		0.04
	1 y.	66.5±8.3		70.8±8.4		51.1±9.3		
	Mean changes	−25.0 (−32.3 to −17.6)[a]	<0.001	−16.8 (−24.3 to −9.4)[a]	<0.001	1.1 (−7.1 to 9.4)	0.78	
IL-6 (pg/mL)	Baseline	0.7±0.1		0.9±0.1		0.7±0.1		0.04
	1 y.	0.4±0.1		0.5±0.1		1.0±0.1		
	Mean changes	−0.3 (−0.9 to 0.3)[a]	<0.001	−0.4 (−1.0 to 0.2)[a]	<0.001	0.3 (−1.1 to 1.7)	<0.001	
CRP (mg/mL)	Baseline	3.8±1.1		3.5±1.1		3.6±1.1		0.04
	1 y.	1.9±1.1		2.1±1.1		3.3±1.1		
	Mean changes	−1.9 (−2.4 to −1.6)[a]	<0.001	−1.4 (−2.1 to −0.7)[a]	<0.001	−0.3 (−1.3 to 0.8)	0.46	
IL-18 (pg/mL)	Baseline	139±14.3		131±14.5		103±14.6		0.18
	1 y.	137±13.1		112±13.2		101±13.4		
	Mean changes	−1.8 (−13.8 to 10.2)	0.76	−18.6 (6.4 to 30.7)	0.003	−1.3 (−13.5 to 11.0)	0.84	
IL-10 (pg/mL)	Baseline	1.4±1.1		1.3±1.1		1.2±1.1		0.40
	1 y.	1.5±1.1		1.4±1.1		1.3±1.1		
	Mean changes	0.05 (−0.2 to 0.3)	0.62	0.05 (−0.2 to 0.3)	0.60	0.1 (−0.1 to 0.3)	0.29	
IL-18/IL-10 ratio	Baseline	31.9±4.0		17.0±4.1		20.6±4.0		0.02
	1 y.	17.2±3.4		7.9±3.5		19.0±3.4		
	Mean changes	−14.7 (−23.1 to −6.2)	<0.001	−9.1 (−18.0 to −0.3)	0.04	−1.6 (−10.1 to 6.9)	0.71	
MMP-9 (ng/mL)	Baseline	7.7±1.2		7.9±1.2		6.2±1.2		0.78
	1 y.	10.0±1.2		10.4±1.2		10.5±1.2		
	Mean changes	2.3 (0.9 to 3.8)	0.13	2.5 (1.1 to 3.8)	0.11	4.3 (1.2 to 7.3)	0.003	
TIMP-1 (ng/mL)	Baseline	143±6.7		146±7.3		144±7.2		0.94
	1 y.	146±7.4		144±8.2		152±8.2		
	Mean changes	2.7 (−8.7 to 14.0)	0.64	−2.4 (−14.9 to 10.1)	0.71	7.5 (−4.7 to 19.8)	0.23	
MMP-9/TIMP-1 ratio	Baseline	0.06±1.2		0.06±1.2		0.04±1.2		0.60

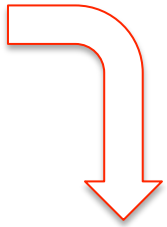

CH3
COOH
saturated
CH3
COOH
monounsatured
CH3
COOH
polyunsatured
ω-3 PUFA
anti-inflammatory
ω-6 PUFA
pro-inflammatory



Source INRAN 2012

L'infiammazione

- Aumento del rischio di malattia
- Influenza della dieta



Acidi grassi

Precursori di mediatori lipidici che hanno un ruolo fondamentale nei processi infiammatori

Obesità

Acidi grassi della dieta

Infiammazione cronica a basso livello

Malattie croniche-degenerative

L'obesità rappresenta uno dei maggiori fattori di rischio per malattie cronico-degenerative

- 44% di T2D
- 23% di CVD
- 7 - 41% di tumori (11% of CRC in Europa)

sono attribuibili ad obesità

WHO 2013

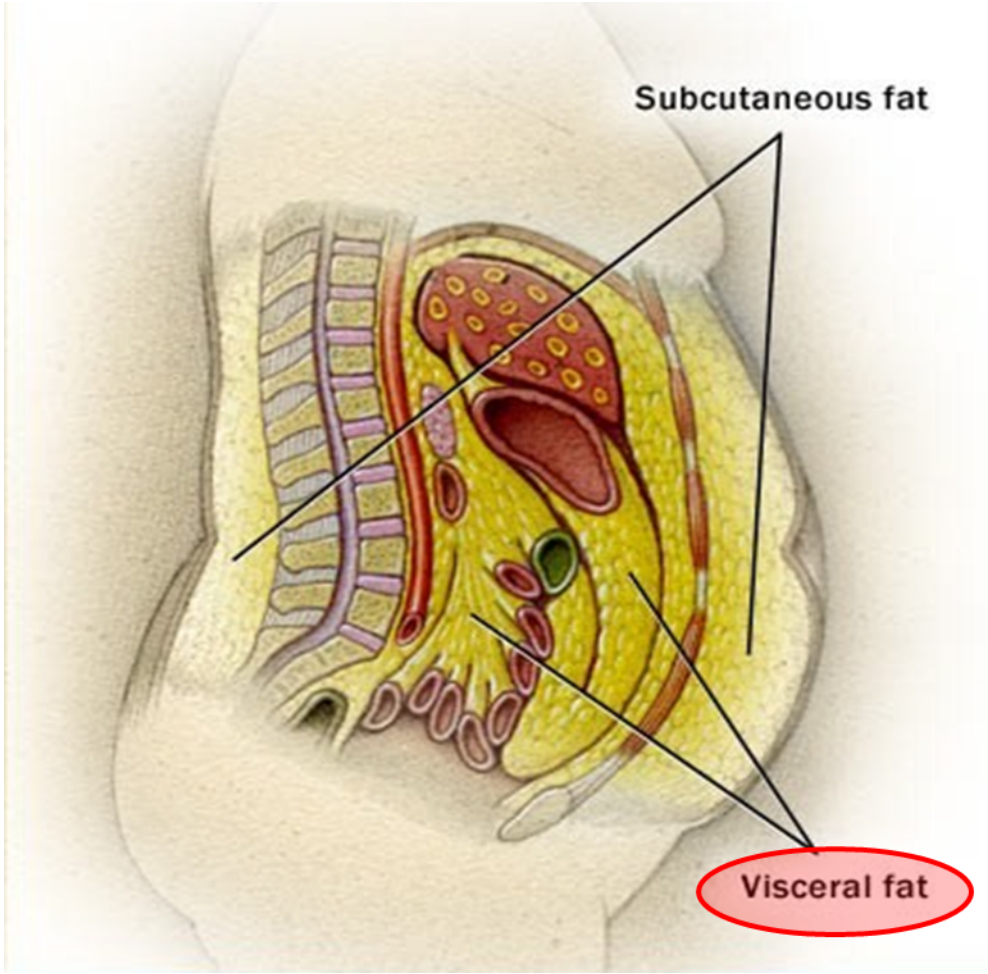
BMI (body mass index) e cancro del colon

Negli uomini ogni 5 unità di aumento del BMI aumenta

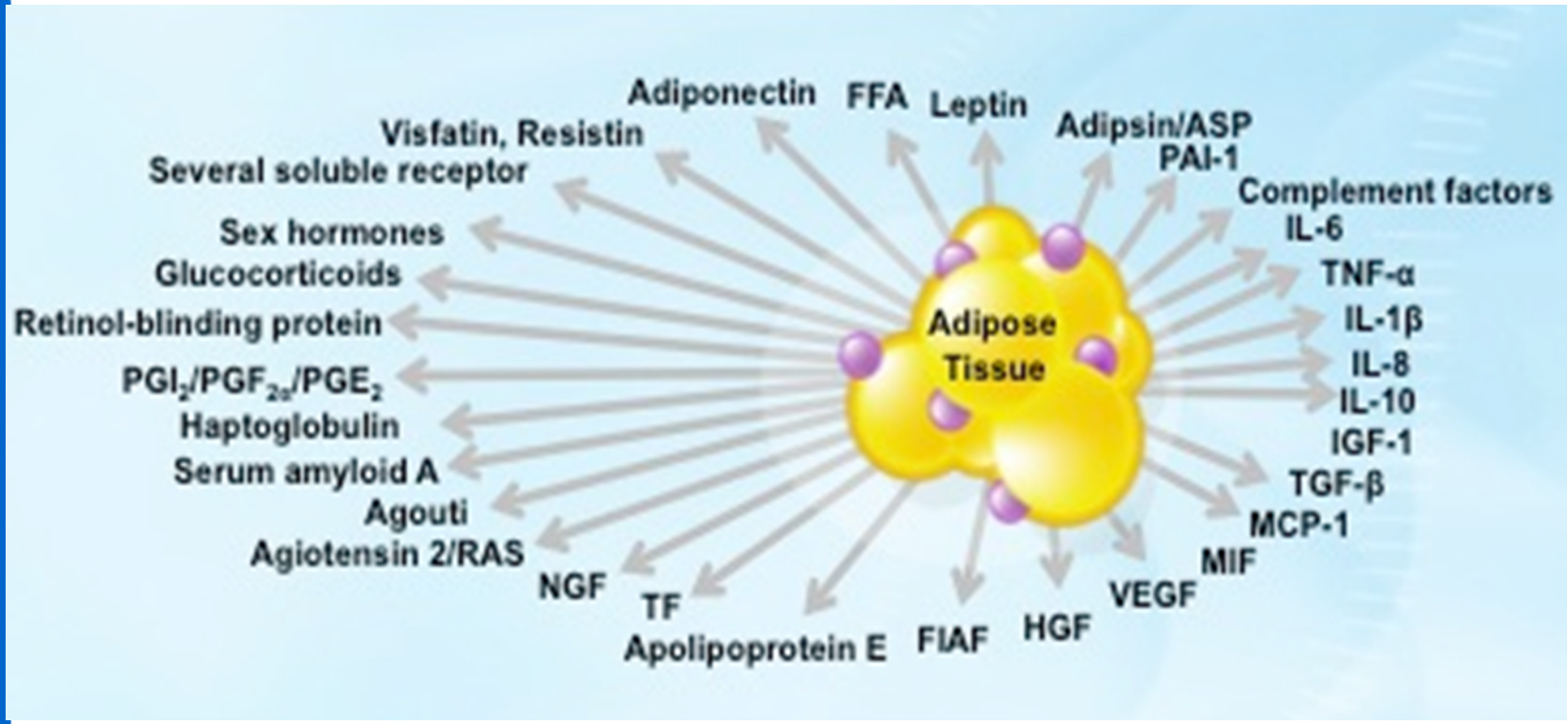
del 25% il rischio di CRC

Am J Epidem 2011; 174(10): 1127-1139

BMI + colorectal cancer nel 2014 = 97 pubblicazioni



Ipotesi: vista la vicinanza anatomica tra grasso viscerale e intestino, i prodotti infiammatori secreti dal tessuto adiposo viscerale possono facilmente esercitare la loro azione



Il tessuto adiposo è un organo endocrino molto attivo

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PLOS | ONE

ω3-PUFAs Exert Anti-Inflammatory Activity in Visceral Adipocytes from Colorectal Cancer Patients

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Abstract

Objective: The aim of this study was to correlate specific fatty acid profiles of visceral white adipose tissue (WAT) with inflammatory signatures potentially associated with colorectal cancer (CRC).

Methods: Human adipocytes were isolated from biopsies of visceral WAT from 24 subjects subdivided in four groups: normal-weight (BMI 22.0-24.9 Kg/m^2) and over-weight/obese (BMI 26.0-40.0 Kg/m^2), affected or not by CRC. To define whether obesity and/or CRC affect the inflammatory status of WAT, the activation of the pro-inflammatory STAT3 and the anti-inflammatory PPARγ transcription factors as well as the expression of adiponectin were analyzed by immunoblotting in adipocytes isolated from each group of subjects. Furthermore, to evaluate whether differences in inflammatory WAT environment correlate with specific fatty acid profiles, gas-chromatographic analysis was carried out on WAT collected from all subject categories. Finally, the effect of the ω3 docosahexaenoic acid treatment on the balance between pro- and anti-inflammatory factors in adipocytes was also evaluated.

Results: We provide the first evidence for the existence of a pro-inflammatory environment in WAT of CRC patients, as assessed by the up-regulation of STAT3, and the concomitant decrease of PPARγ and adiponectin with respect to healthy subjects. WAT inflammatory status was independent of obesity degree but correlated with a decreased ω3-/ω6-polyunsaturated fatty acid ratio. These observations suggested that qualitative changes, other than quantitative ones, in WAT fatty acid may influence tissue dysfunctions potentially linked to inflammatory conditions. This hypothesis was further supported by the finding that adipocyte treatment with docosahexaenoic acid restored the equilibrium between STAT3 and PPARγ.

Conclusion: Our results suggest that adipocyte dysfunctions occur in CRC patients creating a pro-inflammatory environment that might influence cancer development. Furthermore, the protective potential of docosahexaenoic acid in re-establishing the equilibrium between pro- and anti-inflammatory factors might represent a useful tool for preventive and therapeutic strategies.

Citation: D'Archivio M, Scazzocchio B, Giammarioli S, Fiani ML, Varì R, et al. (2013) ω3-PUFAs Exert Anti-Inflammatory Activity in Visceral Adipocytes from Colorectal Cancer Patients. PLoS ONE 8(10): e77432. doi:10.1371/journal.pone.0077432

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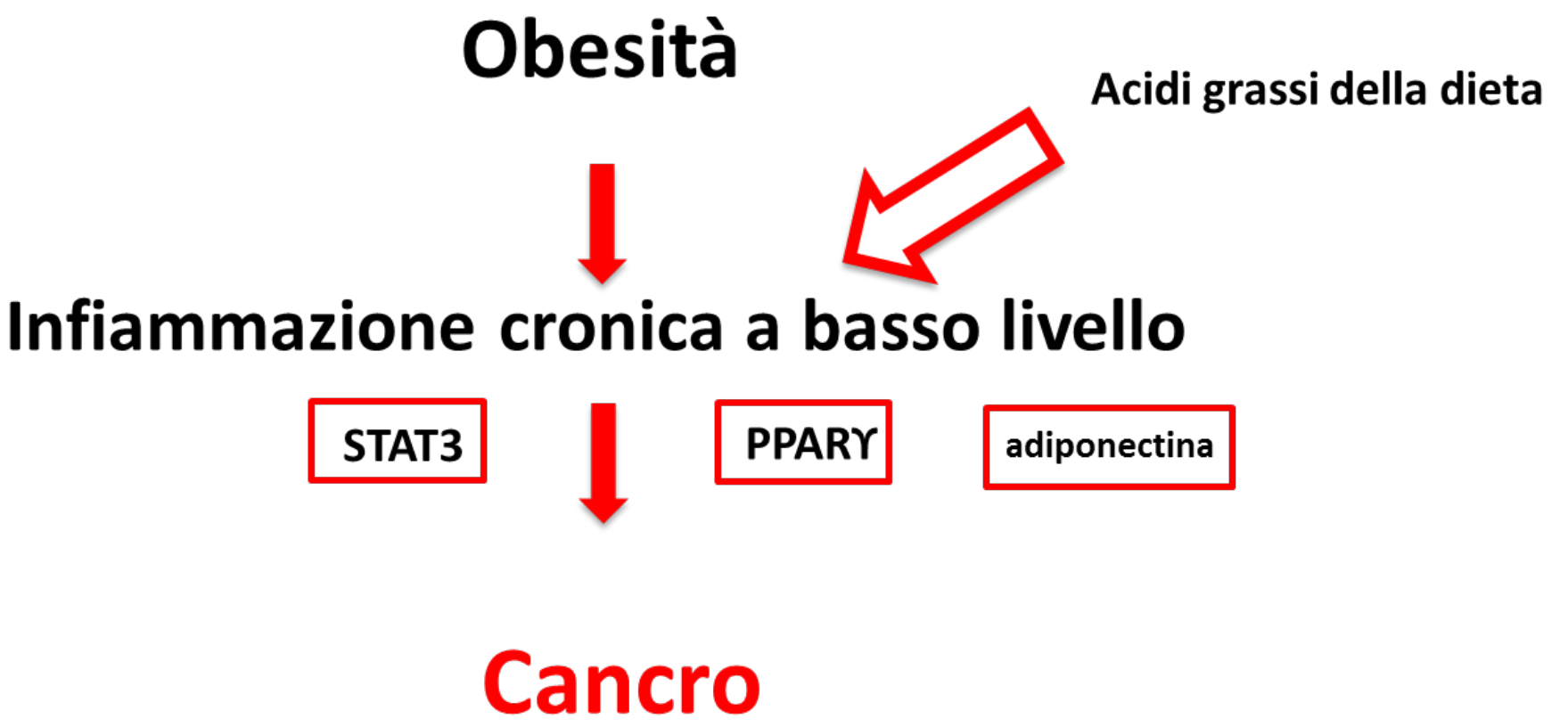
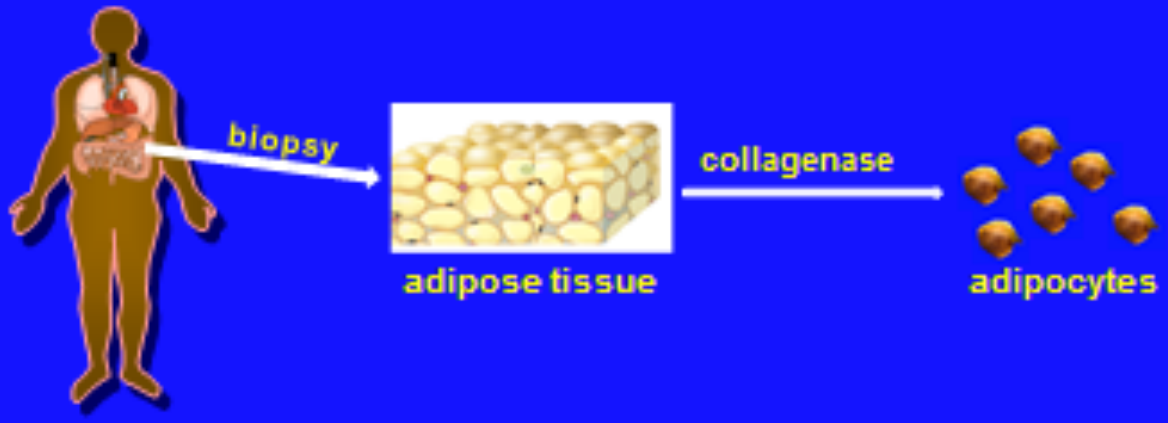
Scopo dello studio

- **Determinare se il tessuto adiposo viscerale di pazienti affetti da cancro mostrasse segni di infiammazione**

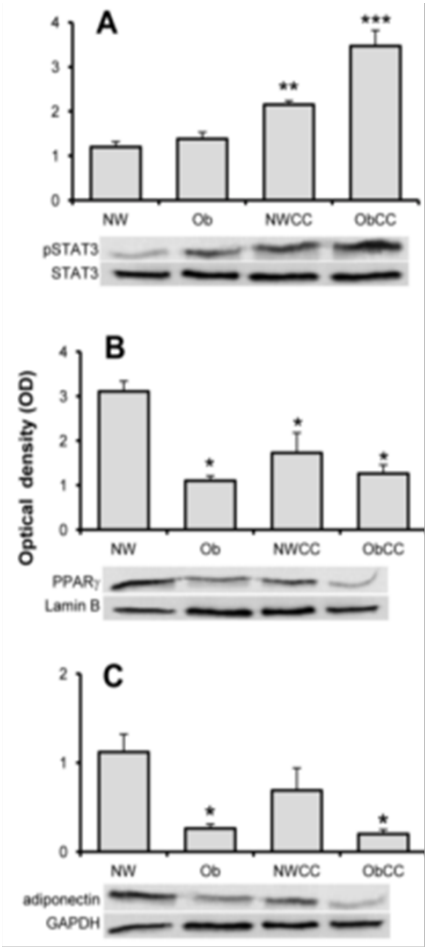
- **Definire se la potenziale infiammazione potesse essere correlata a modifiche quantitative o qualitative della composizione in acidi grassi del tessuto adiposo**


Obesità
Acidi grassi della dieta
Infiammazione cronica a basso livello
STAT3
PPARγ
adiponectina
Cancro

Visceral adipose tissue biopsies from patients with or without CRC



1. Normal weight without CRC
2. Overweight/obese without CRC
3. Normal weight with CRC
4. Overweight/obese with CRC



D'Archivio M et al. PlosOne 2013, 8

Il tessuto adiposo dei pazienti con cancro del colon mostra segni di infiammazione a livello molecolare

⇩

L'obesità esacerba questa condizione

L'infiammazione è presente anche nei non-obesi affetti da tumore

⇩

Indipendente dalla quantità di grasso

Può dipendere dalla sua qualità?

	NW	Ob	NWCC	ObCC
Saturated FAs (%)	30±3	32±4	31±3	30±3
Monounsaturated FAs (%)	59±4	54±5	58±3	55±6
ω3-PUFAs (%)	0.8±0.1	0.7±0.2	0.7±0.2	0.9±0.2
ω6-PUFAs (%)	10.6±1.1	12.8±1.4	10.6±0.2	$14.0\pm1.2^{*\#}$

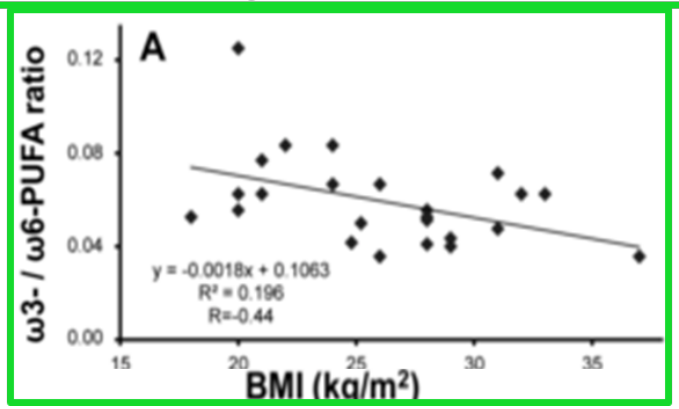
D'Archivio et al. PLoS One. 2013 ;8(10):e77432

	NW	Ob	NWCC	ObCC
ω3-/ω6-PUFA ratio	0.08±0.009	0.056±0.008*	0.065±0.006*	0.059±0.006*

Decreased ω3/ω6 ratio in adipose tissue of all obese patients

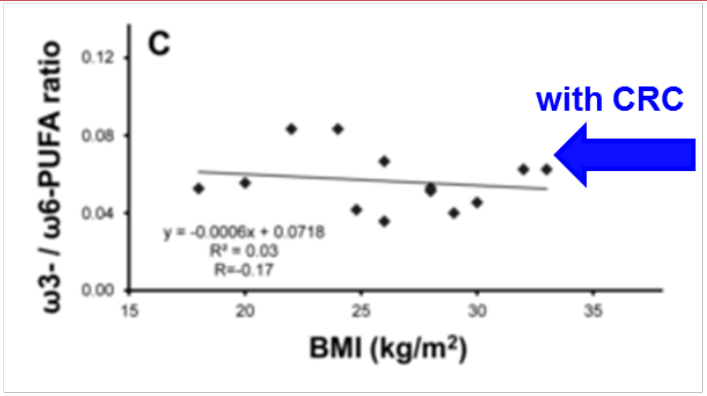
BMI inversely correlated with ω3/ω6 ratio (with increasing BMI, ω3/ω6 ratio decreases)

confirm the link between obesity and a particular fatty acid composition



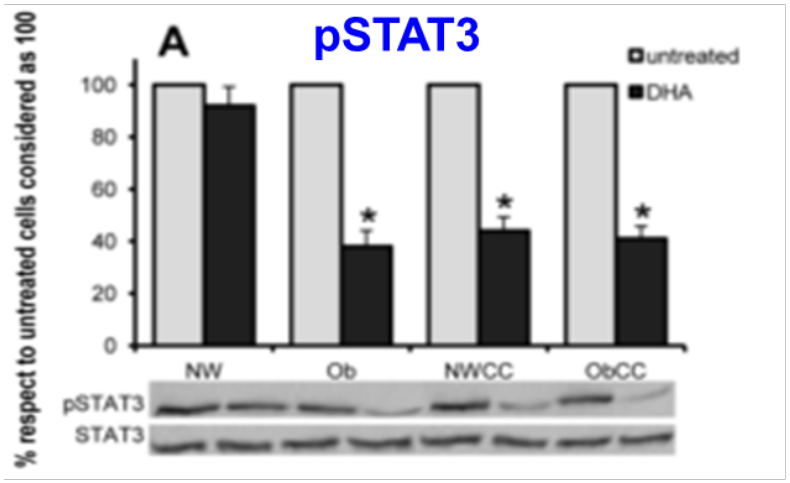
Decreased ω3/ω6 ratio in adipose tissue of normal weight CRC

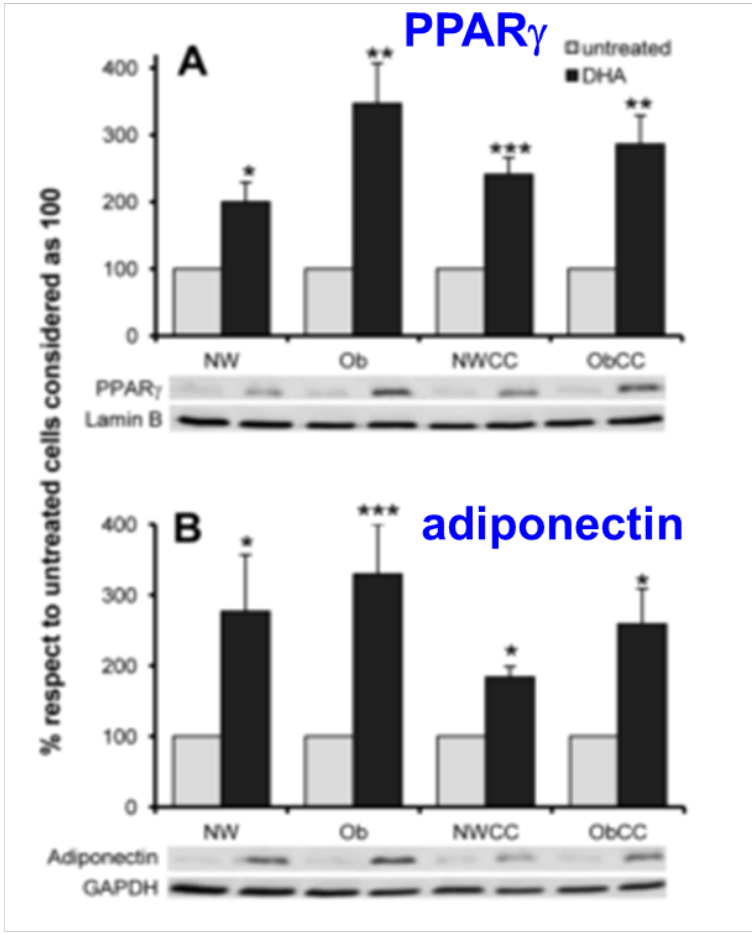
independent of increased fat mass



Modifiche nel rapporto ω3/ω6 può avere un ruolo nell'innescare processi infiammatori nel tessuto adiposo

E' possibile contrastare l'infiammazione trattando gli adipociti viscerali con acidi grassi ω3 ?





DHA counteracted STAT3 activation and increased PPARγ and adiponectin expressions

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SciVerse ScienceDirect
Journal of Nutritional Biochemistry 23 (2012) 616–621
Journal of Nutritional Biochemistry

Modulation of blood cell gene expression by DHA supplementation in hypertriglyceridemic men☆,☆☆,★

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Table 1
Selected genes regulated by DHA supplementation[a]

Gene name	Gene symbol	Fold of	*P* values
Up-regulated by DHA			
Protein serine/threonine kinases			
Mitogen-activated protein kinase kinase kinase 3	MAP3K3	1.79	.0089
Protein kinase N2	PKN2	1.78	.022
Mitogen-activated protein kinase 14	MAPK14	1.76	.022
Serine/threonine kinase 38	STK38	1.73	.014
Mitogen-activated protein kinase 1	MAPK1	1.56	.03
Transcription regulator or activator/nucleotide binding			
CUGBP, Elav-like family member 2	CELF2	2.02	.0064
Cell division cycle and apoptosis regulator 1	CCAR1	1.84	.0015
Transcription factor CP2	TFCP2	1.78	.0035
CUGBP, Elav-like family member 1	CELF1	1.72	.001
Enzymes			
Phosphorylase, glycogen, liver	PYGL	1.75	.038
Protein phosphatase 1, regulatory (inhibitor) subunit 12 B	PPP1R12B	1.69	.039
Other			
Interferon (alpha, beta and omega) receptor 2	IFNAR2	1.74	.006
Enoyl coenzyme A hydratase domain containing 1	ECHDC1	1.69	.0022
Transforming growth factor, beta receptor	TGFBR1	1.64	.0069
Cathepsin S	CTSS	1.63	.0014
Down-regulated by DHA			
Lipoprotein receptor			
Oxidized low-density lipoprotein (lectin-like) receptor 1	OLR1	−2.84	.0046
Low-density lipoprotein receptor	LDLR	−1.64	.041
Transcription factors/regulator of transcription			
Peroxisome proliferator-activated receptor gamma	PPARG	−2.3	.035
SKI-like oncogene	SKIL	−1.91	.0028
Peroxisome proliferator-activated receptor delta	PPARD	−1.8	.013
Activating transcription factor 5	ATF5	−1.57	.048
Aryl hydrocarbon receptor	AHR	−1.53	.024
Other			
Prostaglandin E synthase	PTGES	−2.1	.014
Cytochrome p450, family 51, subfamily A, polypeptide 1	CYP51A1	−1.8	.05
Nuclear receptor interacting protein 3	NRIP3	−1.64	.024
Fatty acid desaturase 1	FADS1	−1.63	.0268
Syndecan 2	SDC2	−1.63	.028
Cathepsin L	CTSL1	−1.59	.0014
Heparin-binding EGF-like growth factor	HBEGF	−1.54	.0165

[a] Numbers represent folds of the control value. Positive numbers represent increase; negative numbers represent decrease.

Pazienti con leggera ipertrigliceridemia divisi in due gruppi:

- 7.5 g/die DHA (3g) in capsule
- 7.5 g/die EVOO in capsule.

Prelievo basale e dopo 90 giorni di intervento

SIMPeSV Società Italiana di Medicina di Prevenzione e degli Stili di Vita
FIMMG

Conclusioni

- I componenti della dieta possono interagire con il genoma influenzando le attività cellulari

- Individuare e definire il meccanismo d'azione molecolare dei singoli componenti bioattivi degli alimenti funzionali richiede un complesso processo di studio e ricerca che comprende studi epidemiologici, trial clinici e studi sperimentali

Grazie per l'attenzione