Microbiota e Dieta Mediterranea

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UNIVERSITA' degli STUDI di ROMA
TOR VERGATA

Ruolo del microbiota nei fenotipi dell'obesità

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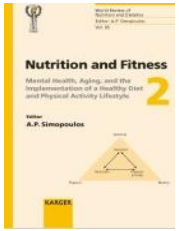
Simopoulos AP (ed): Nutrition and Fitness: Mental Health, Aging, and the Implementation of a Healthy Diet and Physical Activity Lifestyle.
World Rev Nutr Diet. Basel, Karger, 2005, vol 95, pp 115-121



The Nicotera Diet: The Reference Italian Mediterranean Diet

Flaminio Fidanza[a], Adalberta Alberti[a], Daniela Fruttini[b]

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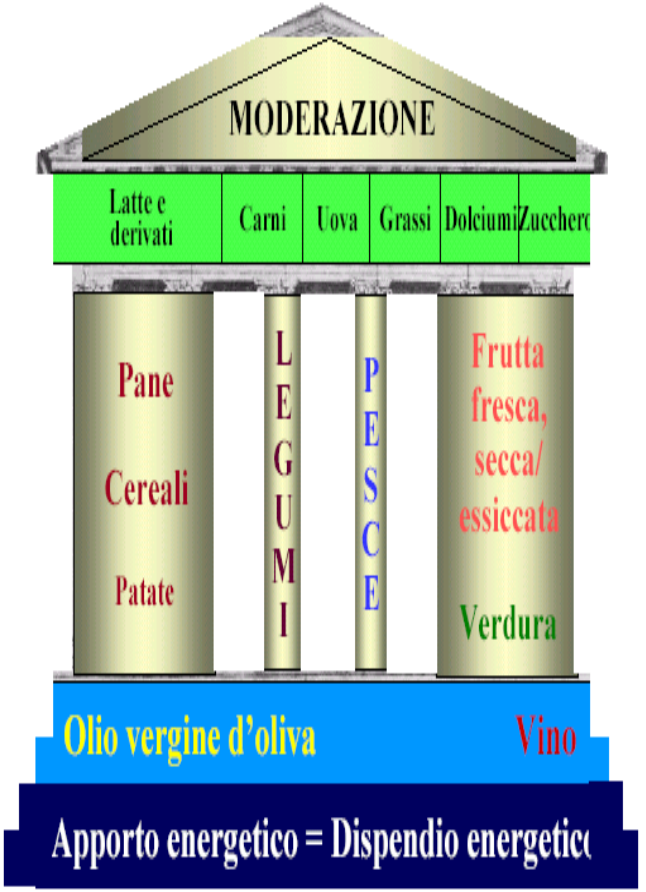
Nicotera, a small town in the Calabria Region in Southern Italy, was the third Italian rural area of the Seven Countries Study (SCS) examined in the fall of 1957 as a pilot study. Because both due to shortage of funds and similarity with the two rural areas of Greece, this study was not followed longitudinally.

Nicotera, selected for the quite high olive oil and legumes consumption, is perched on a spot of the Poro Mountain overlooking the Tyrrhenian Sea about 60 km north of Reggio Calabria near the toe of Italy. The main farm products were olives, grapes, figs, oranges, tomatoes, pulses, wheat, bergamot for the perfume trade, and for local use, a little meat and poultry. In the hamlet of Nicotera Marina few families were engaged in fishing. There was no manufacturing industry. The population was relatively poor in comparison to the two rural areas of Italy in the SCS, but there was a migration of persons under the age of 40. Besides the main center of Nicotera and the hamlet of Nicotera Marina there were three more detached hamlets: Comerconi, Badia, and Preitoni. The total population of the entire survey area was 9,043 inhabitants at the time of the survey. About 80% of the people lived in the centers and went out daily to work in their small fields often as far as several kilometers away. Both men and women were engaged in moderate physical activity and only men in some cases in rather heavy physical work. Because of its geography (altitude 0–641 m) and road conditions, transportation was mainly by mule. The prevalence of myocardial infarction in men aged 45–64 years was very low (4 cases out of 598 examined in 1957), and hypertension, overweight and obesity were uncommon. Similar findings were observed in the cohort of men from Corfu (Greece) examined in 1960.



The 7 Seven Countries Study

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Italy

Italy played a central role not only in the SCS but also in the pilot studies leading up to it. In 1957, a preliminary field survey was carried out in Nicotera, a small village in Calabria in the south of Italy. Two rural cohorts and a railroad cohort with different diets were enrolled in the Study. Italian colleagues later joined the FINE study and the HALE project.

European Journal of Clinical Nutrition (1999) 53, 854-860

http://www.stockton-press.co.uk/ejcn

Dietary studies on two rural Italian population groups of the Seven Countries Study. 3. Trend of food and nutrient intake from 1960 to 1991

A Alberti-Fidanza[1]*, F Fidanza[1], MP Chiuchiù[1], G Verducci[1] and D Fruttini[1]

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Discussion

As we have shown previously each Mediterranean country has its own Reference Mediterranean Diet (Alberti-Fidanza, 1990; Fidanza, 1991b). For Italy we have suggested as the Reference Mediterranean Diet that of the subjects from Nicotera, in 1960, a rather poor rural area in the south, perched on a spur overlooking the Tyrrhenian Sea about 60 km north of Reggio Calabria near the toe of Italy. The main farm products, obtained after heavy manual work, were olives, grapes, figs, oranges, tomatoes, pulses, wheat and for local use a little meat and poultry. In the hamlet of Nicotera Marina a few families were engaged in fishing. At that time Nicotera was one of the rural Italian areas of the Seven Countries Study, but because of shortage of money and similarity with the two rural areas of Greece, the longitudinal study was not carried out.

Seven Countries Study - Revisione

	EUROPA MEDITERRANEA	EUROPA NON MEDITERRANEA
15° ANNO (1973-76)		
Uomini a rischio	3506	2701
Tutte le cause	1612	2078
CHD	284	655
25° ANNO (1983-86)		
Uomini a rischio	3598	2884
Tutte le cause	4299	5550
CHD	978	1947

Tassi Di Mortalità Per 10000 Individui Standardizzati Per L'età Al Quindicesimo E Venticinquesimo Anno Di Riesame Per Tutte Le Cause E Per Cardiopatia Coronarica (Chd)

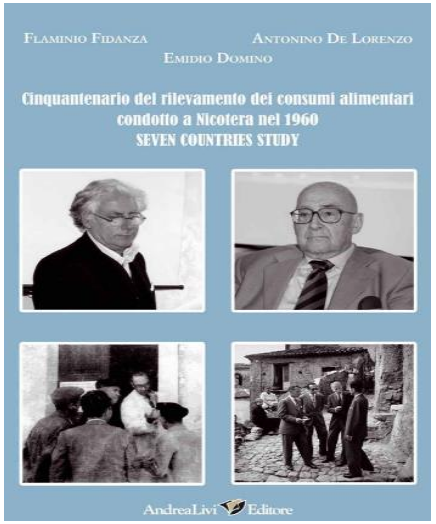
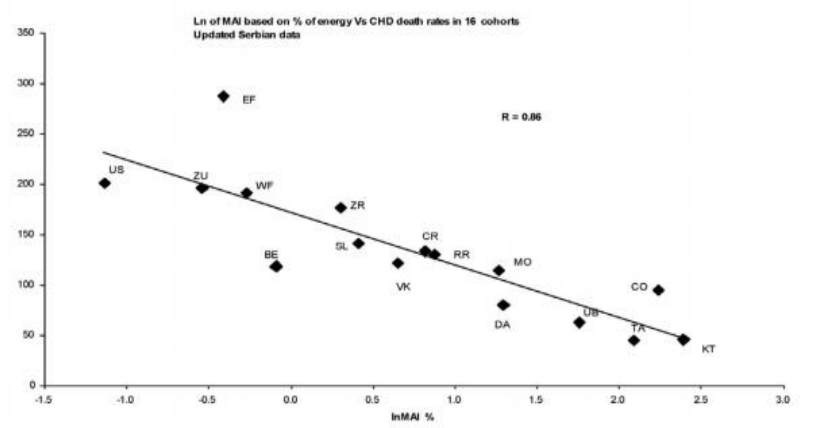


FIG. 1 - CORRELAZIONE DEL LOGARITMO NATURALE DEL MAI DELLE DIETE DELLE 16 COORTI DEL SEVEN COUNTRIES STUDY (ln MAI dopo esclusione della birra e dei superalcolici) CON IL TASSO DI MORTALITÀ PER CARDIOPATIA CRONARICA AL 25° ANNO DI RIESAME



I simboli sono: US-ferrovieri USA; EF-Finlandia orientale; WF-Finlandia occidentale; ZU-Zutphen, Olanda; CR-Crevalcore, Italia; MO-Montegiorgio, Italia; RR-ferrovieri di Roma, Italia; D-Dalmazia, Croazia-ex Jugoslavia; SL-Slavonia, Croazia, ex Jugoslavia; VK-Velika Krsna, Serbia, ex Jugoslavia; ZR-Zrenianin, Serbia, ex Jugoslavia; BE-Belgrado, Serbia, ex Jugoslavia; KT-Creta, Grecia; CO-Corfù, Grecia; TA-Tanushimaru, Giappone; UB-Ushibuka, Giappone.

Acta Diabetol. 2013 Jun;50(3):409-16. doi: 10.1007/s00592-012-0445-7. Epub 2012 Nov 28.

Body composition changes and cardiometabolic benefits of a balanced Italian Mediterranean Diet in obese patients with metabolic syndrome.

Di Daniele N, Petramala L, Di Renzo L, Sarlo F, Della Rocca DG, Rizzo M, Fondacaro V, Iacopino L, Pepine CJ, De Lorenzo A.

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Abstract

Metabolic syndrome (MS) is a cluster of metabolic alteration associated with a higher risk of cardiovascular disease and overall mortality than the single alterations alone. The Italian Mediterranean Diet (IMD) can exert a positive effect on cardiovascular risk and related morbidity and mortality. The aim was to evaluate the benefits of dietary intervention based on a typical IMD on body composition, cardiometabolic changes and reduction in cardiovascular disease in patients with MS. Eighty White Italian subjects with MS were prescribed a balanced hypocaloric IMD. We investigated dietary habits and impact of the diet on health status, blood biochemical markers, anthropometric measurements and body composition during a 6-month follow-up period. Body composition, fat mass and distribution were assessed by Dual X-ray absorptiometry. Adherence to the IMD led to a decrease in body weight (102.59 ± 16.82 to 92.39 ± 15.94 kg, $p < 0.001$), body mass index (BMI) (38.57 ± 6.94 to 35.10 ± 6.76, <0.001) and waist circumference (112.23 ± 12.55 vs 92.42 ± 18.17 cm, $p < 0.001$). A significant loss of total body fat especially in waist region was observed. The MS was resolved in 52 % of the patients. Significant improvements in systolic and diastolic blood pressure and fasting glucose occurred. Low-density lipoprotein cholesterol was reduced from 128.74 ± 33.18 to 108.76 ± 38.61 mg/dl ($p < 0.001$), triglycerides from 169.81 ± 80.80 to 131.02 ± 63.88 mg/dl ($p < 0.001$). The present results suggest that a dietary intervention based on a typical IMD effectively promotes weight loss and reduces the growing burden of cardiovascular risk factors that typifies patients with MS.

Table 3 Body composition measured by DXA in study subjects at baseline and after 6 months of dietary intervention

Parameters	Baseline	At 6 months	*p* value
Total body fat			
%	42.5 ± 7.5	39.8 ± 8.5	<0.001
Kg	42.1 ± 12.9	36.9 ± 11.3	<0.001
Total body lean			
%	58.4 ± 9.8	61.1 ± 10.3	<0.001
Kg	54.9 ± 14.6	52.9 ± 11.5	0.088
Android body fat			
%	52.5 ± 5.6	48.9 ± 7.1	<0.001
Kg	4.5 ± 1.5	3.8 ± 1.3	<0.001
Trunk body fat			
%	46.2 ± 5.7	43.5 ± 6.8	<0.001
Kg	43.1 ± 11.2	36.8 ± 11.4	<0.001

Parameters are expressed as mean ± SD

Table 4 Metabolic syndrome parameters and atherogenic lipid indices at baseline and 6 months of dietary intervention

Parameters	Baseline	At 6 months	*p* value
SBP (mmHg)	135.2 ± 14.6	123.72 ± 11.9	<0.001
DBP (mmHg)	85.7 ± 10.1	76.01 ± 7.6	<0.001
Fasting glucose (mg/dl)	113.6 ± 21.4	100.65 ± 16.9	<0.001
Total-C (mg/dl)	205.7 ± 33.5	180.18 ± 38.1	<0.001
HDL-C (mg/dl)	45.9 ± 10	47.97 ± 14	0.339
LDL-C (mg/dl)	128.7 ± 33.2	108.76 ± 38.6	<0.001
Triglycerides (mg/dl)	169.8 ± 80.8	131.02 ± 63.9	<0.001
Total-C/HDL-C	4.6 ± 1.6	4.05 ± 1.4	0.003
LDL-C/HDL-C	2.9 ± 1.1	2.50 ± 1.1	0.002
Log TG/HDL-C	0.5 ± 0.2	0.42 ± 0.3	0.001

Parameters are expressed as mean ± SD

NS not significant, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *Total-C* total cholesterol, *HDL-C* HDL cholesterol, *LDL-C* LDL cholesterol

European Review for Medical and Pharmacological Sciences 2013; 17: 2555-2565

Body composition phenotype: Italian Mediterranean Diet and C677T MTHFR gene polymorphism interaction

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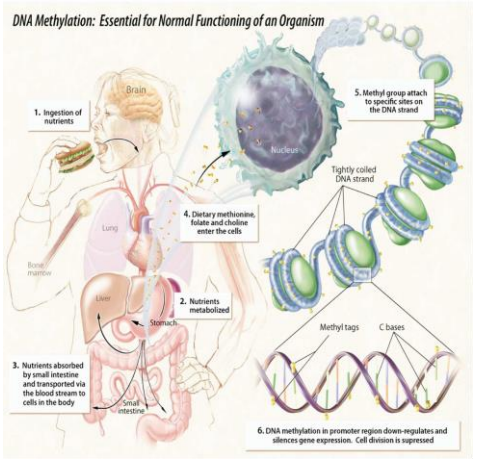

Table III. Anthropometric parameters and tHcy levels at baseline and week 12 after nutritional intervention, according to genotypes[1].

Parameters	Baseline			Week 12		
	Total (n=56)	T (–) (n=39)	T (+) (n=17)	Total (n=56)	T (–) (n=39)	T(+) (n=17)
Sex (F/M)	37/19	27/12	10/7	37/19	27/12	10/7
Weight (kg)	95.92 ± 16.36	99.23 ± 14.28	104.39 ± 18.04[3]	87.26 ± 15.91[7]	83.68 ± 13.92[7]	95.49 ± 17.52[3,7]
BMI (kg/m^2)	36.59 ± 5.81	35.57 ± 5.50	38.91 ± 6.02[2]	33.26 ± 5.56[7]	32.24 ± 5.13[7]	35.60 ± 5.93[2,7]
Waist (cm)	105.29 ± 12.65	102.02 ± 11.58	112.59 ± 12.15[3]	98.03 ± 12.90[7]	95.19 ± 12.15[7]	104.79 ± 11.99[3,7]
Abdomen (cm)	115.49 ± 11.77	112.61 ± 10.85	121.93 ± 11.46[3]	108.47 ± 12.07[7]	105.73 ± 11.17[7]	115.47 ± 11.57[3,7]
Hip (cm)	116.78 ± 10.35	115.28 ± 10.70	120.12 ± 8.92[4]	110.71 ± 9.67[7]	109.03 ± 9.48[7]	114.94 ± 8.88[2,7]
Waist/Hip	0.90 ± 0.10	0.89 ± 0.10	0.94 ± 0.08[2]	0.89 ± 0.09[7]	0.87 ± 0.09[5]	0.91 ± 0.07[6]
tHcy (µmol/l)	22.15 ± 5.10	18.0 ± 4.50	26.30 ± 5.60[2]	20.85 ± 5.70	17.8 ± 6.15	23.90 ± 5.30[2,7]

[1]All values are mean ± SD. [2]Reflects the significance of the differences between genotypes at baseline and week 12 determined with an independent t test ($p \leq 0.05$). [3]Reflects the significance of the differences between genotypes at baseline and week 12 determined with an independent *t* test ($p \leq 0.01$). [4]Reflects the significance of the differences between genotypes at baseline and week 12 determined with an independent t test ($p \leq 0.001$). [5]Reflects the significance of the differences between baseline and week 12 determined with a paired t test ($p \leq 0.05$). [6]Reflects the significance of the differences between baseline and week 12 determined with a paired t test ($p \leq 0.01$). [7]Reflects the significance of the differences between baseline and week 12 determined with a paired t test ($p \leq 0.001$).

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 5), pp: 8947-8979

Review

Impact of Mediterranean diet on metabolic syndrome, cancer and longevity

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Keywords: *Mediterranean diet, public health, obesity, cancer, antioxidant*

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Table 3: Nutritional factors and targets

Nutritional factors	Targets
Total Fat	15-30%
Saturated fatty acids	<10%
Polinsatured fatty acids (PUFA)	6-10%
Polinsatured fatty acids n 3 (PUFA)	5-8%
Polinsatured fatty acids n 6 (PUFA)	1-2%
Trans fatty acids	<1%
Monoinsatured fatty acids (MUFA)	*
Total Carbohydrates	55-75%
Carbohydrates simple	<10%
Proteins	10-15%
Cholesterol	<300 mg/day
Sodium Chloride	<5 g/day (<2 g/day)
Vegetables and Fruits	≥ 400 g/day
Flavonois	> 50 mg/kg
Total dietary fiber	> 25-30 g/day
Non-starch polysaccharides	> 20 g/day
Mediterranean Adequacy Index (MAI)	>6,5

Legend Table 3:

PUFA: Polinsatured fatty acids
MUFA: Monoinsatured fatty acids
MAI: Mediterranean Adequacy Index

Ranges of values for the nutritional targets in the general population according to Mediterranean Diet.
*** This value is calculated as total fat - (satured fatty acids + polynsatured fatty acids + trans fatty acids)**

Università di Roma Tor Vergata

Indices calculated using a ration between components - MAI

It is based on two assumptions:

1. If the energy consumption of a population substantially changes over time, the consumption of each food group must be expressed as a percentage of total consumption.
2. To assess how food changes over time it is necessary to define «national reference diet» → Nicotera in 1960

Nicotera: Calabrian mountain rural area remaining Tyrrhenian Sea.

It is defined as the third Italian rural area in the Seven Countries Study.

ased on 18 food components, divided in two groups:

YPICALLY MEDITERRANEAN (10):

fruit, vegetables, legumes, cereals, bread, potatoes, fish, red wine and vegetable oils

NOT TYPICALLY MEDITERRANEAN (8):

meat, milk, cheese, eggs, animal fats and margarine, sugary drinks, cakes, biscuits and sugar.

MAI costruction:

a. **Total energy calculation (%)** provided by both food groups

b. **Final score**: total energy ratio% of the TIPICALLY MEDITERRANEAN group and NOT TYPICALLY MEDITERRANEAN

MAI USA	MAI CREVALCORE	MAI MONTEGIORGIO	MAI POLLICA	MAI NICOTERA
0,8-0,9	2,4	5,6	5,6-6,3	7,2-10

The Nicotera Diet: The Reference Italian Mediterranean Diet

Flaminio Fidanza[a], Adalberta Alberti[b], Daniela Fruttini[b]

The Mediterranean Adequacy Index: Further confirming results of validity

Adalberta Alberti[a,*], Daniela Fruttini[b], Flaminio Fidanza[a]

Indice di Adeguatezza Mediterraneo (IAM)

$$IAM = \frac{\%\ \text{energia da CARBOIDRATI (gr. 1) + PROTETTIVI (gr. 2)}}{\%\ \text{energia da DERIVATI ANIMALI (gr. 3)+DOLCI (gr. 4)}}$$

Carboidrati (gruppo1): *pane, cereali, legumi, patate*
Protettivi (gruppo 2): *vegetali, frutta, pesce, vino rosso, olio d'oliva*
(Gruppi di alimenti appartenenti alla dieta mediterranea)

Derivati animali (gruppo 3): *latte, formaggio, carne, uova, grassi animali e margarina*
Dolci (gruppo 4): *bevande dolci, biscotti/torte, zucchero*
(Gruppi di alimenti non appartenenti alla dieta mediterranea)

Alberti et all. Eur J Clin Nutr 1999

PATTO in cucina Magazine per la salute

Prodotti Agroalimentari Tradizionali Tipici Originali per la salute.

Periodico telematico dedicato alla divulgazione del patrimonio scientifico, culturale e artistico della tradizione italiana in ambito nutrizionale.

Cuore

MAI e poi MAI...

di Laura Di Renzo | 10 ottobre 2016

L'Indice di Adeguatezza Mediterranea (MAI) ci permette di verificare la corrispondenza della nostra alimentazione alla Dieta Mediterranea. Valori di MAI

Home About

Calcolatore di Indice di Adeguatezza Mediterranea (MAI)

Con questo strumento è possibile calcolare il MAI di ricette composte da numero qualsiasi di alimenti. E' anche possibile inserire tutti gli alimenti che compongono un intero pasto.

Per ognuno degli alimenti da introdurre si inizia a digitare il nome dell'alimento nell'apposita casella: il sistema proporrà in tempo reale una lista di alimenti compatibili. E' assolutamente necessario scegliere una delle opzioni predefinite proposte dal sistema. Si inseriscono poi i grammi relativi all'alimento scelto. La procedura viene ripetuta per ogni alimento. Per inserire più di 10 alimenti utilizzare il tasto "Aggiungi Alimento".

La tua ricetta

Nome ricetta/pasto

Alimento 1 Grammi

Alimento 2 Grammi

Alimento 3 Grammi

Alimento 4 Grammi

Alimento 5 Grammi

Alimento 6 Grammi

Alimento 7 Grammi

Alimento 8 Grammi

Alimento 9 Grammi

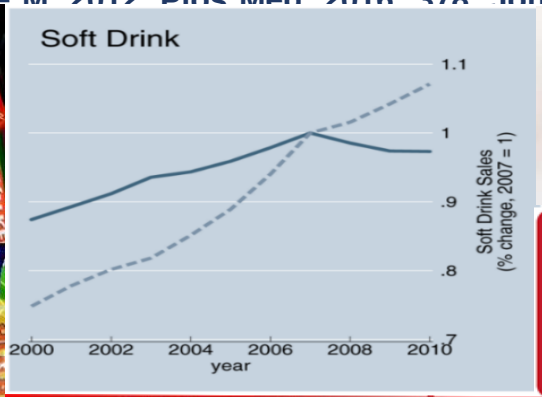
Alimento 10 Grammi

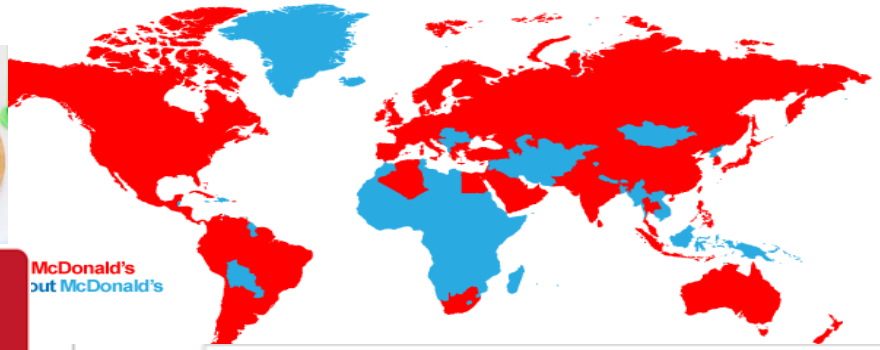
Aggiungi Alimento

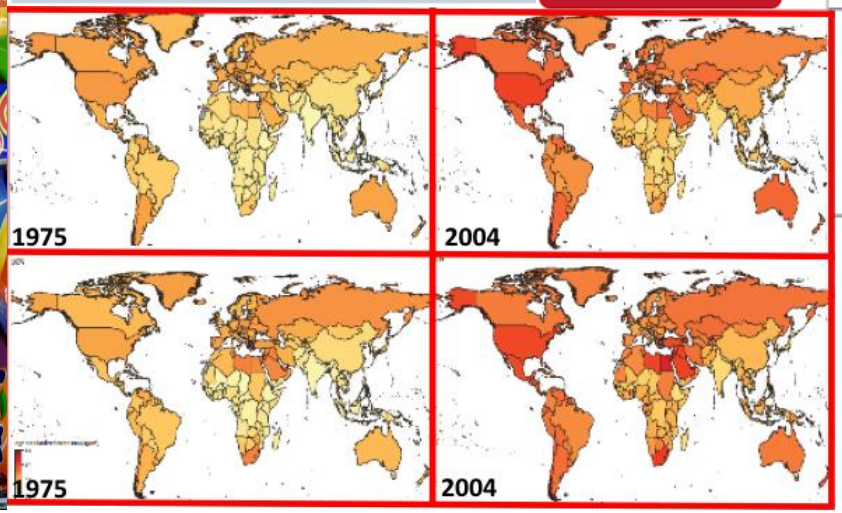
Calcola MAI

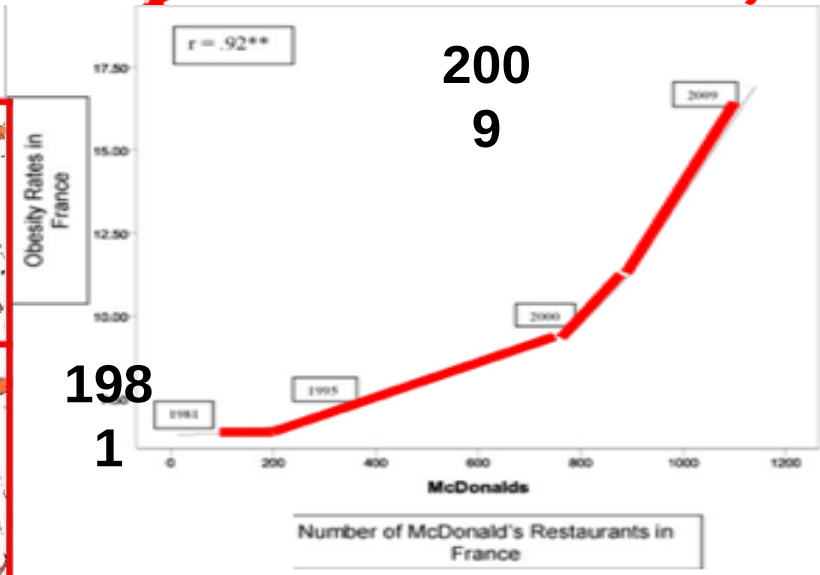
START POINT: BMI in crescita e Junk Food

Rif bibl. : 1NCD RisC, 20016.The Lancet, 2016; 366.
Stuckler D, Nestle M. 2012. Plos Med. 2016. 378. Johnson





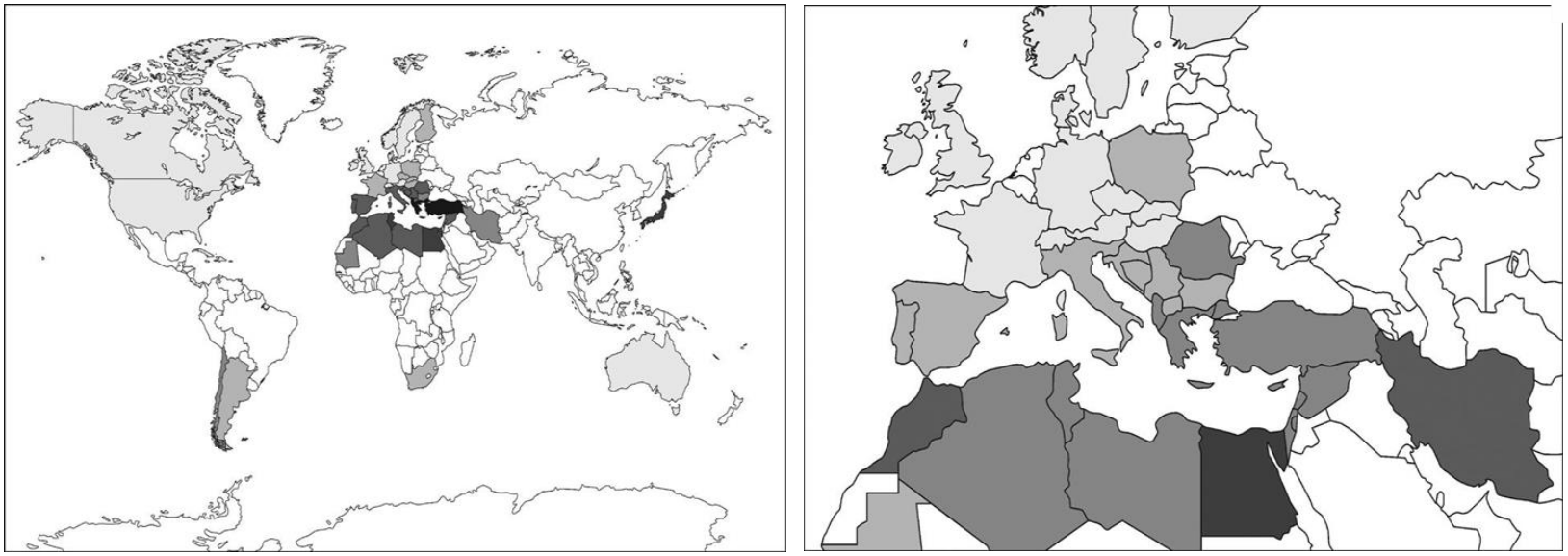




200
9

198
1

Dietary pattern changes



Map of the adherence to the Mediterranean dietary pattern, comparing Mediterranean adequacy index value
(□, 0·00–0·99; □, 1·00–1·99; □, 2·00–2·99; □, 3·00–3·99; □, 4·00–4·99; □, 5·00–5·99)

1961-1965

MAI Worldwide: 2.86
MAI Mediterranean Countries: 3.44
MAI Italy: 3.30

2000-2003

MAI Worldwide: 2.03
MAI Mediterranean Countries : 1.98
MAI Italy: 1.62

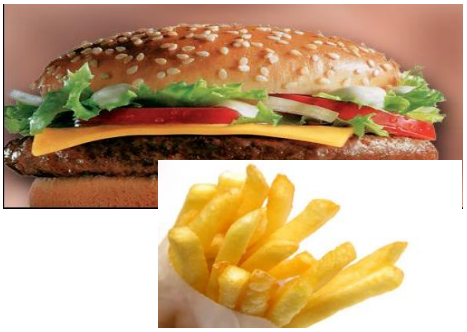
In 40 anni l'indice si è ridotto di -1.68

Da Silva et al., Public Health Nutr

Mediterranean meal versus Western meal effects on postprandial ox-LDL, oxidative and inflammatory gene expression in healthy subjects: a randomized controlled trial for nutrigenomic approach in cardiometabolic risk

De Lorenzo A, Bernardini S, Gualtieri P, Cabibbo A, Perrone MA, Giambini I, Di Renzo L

Acta Diabetol (2017) 54: 141. doi:10.1007/s00592-016-0917-2



vs

Baseline vs Mediterraneo

↓ **IRAK1** – chinasi 1 recettore interleuchina 1 associato
L'IRAK1 è parzialmente responsabile dell'eliminazione del fattore di trascrizione NF-kappa B indotta da IL1.

Baseline vs McD

↑ **IRAK1 –** chinasi 1 recettore interleuchina 1 associato
↑ **DUOX2 –** tiroide ossidasi 2
DUOX2 genera perossido di idrogeno.

Nutritional quality indices		
	Pasto McD	Pasto Mediterraneo
AI	1,97	0,17
TI	1,73	0,32

McD vs Mediterraneo

↓**CCL5** – chemochina ligando 5
↓ **DUOX2 –** tiroide ossidasi 2

Indici nutrizionali di un pasto

tipico americano
Valore di 100g

Ingredienti:
Hamburger 40g
Panino 26g
Maionese 5g
Cetrioli 4g
Lattuga 2g
Formaggio Fuso 13g
Cipolle 5g
Olio EVO 5g

kcal	238,6
Proteine(g)	14,9
Carboidrati(g)	13,0
Lipidi(g)	14,5
INQ proteine	2,1
INQ Carboidrati	0,3
INQ lipidi	2,0
CSI	6,7
AGEs (KU/100g)	7801
H_2O (litri)	795
CO2 Keq	1,86

(fino alla distribuzione)

tipico mediterraneo
Valore di 100g

Ingredienti:
Pasta 55g
Fagioli 40g
Olio EVO 5g

kcal	334,5
Proteine(g)	11,8
Carboidrati(g)	54,8
Lipidi(g)	9,1
INQ proteine	1,2
INQ Carboidrati	1,0
INQ lipidi	0,9
CSI	2,0
AGEs (KU/100g)	754
H_2O (litri)	98
CO_2 Keq	0,17

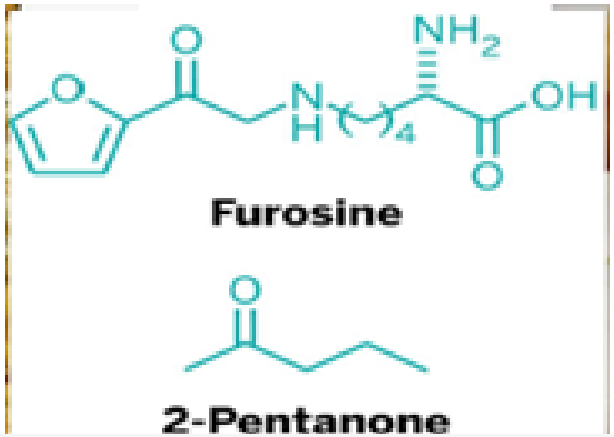
(fino alla distribuzione)

EFFETTI DELLE ALTE TEMPERATURE SUI PROCESSI DI ESSICCAZIONE DELLA PASTA

La legge italiana fissa in 8,6 mg/100 g di proteine il limite di furosina presente nel latte crudo e pastorizzato, ed in 12 mg/100 g di proteine il limite per i formaggi freschi a pasta filata.

Tempi di essiccazione delle paste lunghe in rapporto all'evoluzione tecnologica		
Anno di riferimento	Tipo di essiccazione	Tempo di essiccazione
1880	Essicazione naturale	8/10 gg (estate) 20/30 gg (inverno)
1903	Essicazione meccanica	3/5 gg
1950	Bassa temperatura (< 60°C)	24/36 ore
1970	Alta temperatura (> 65°C)	12/15 ore
1990	Alta temperatura (> 85°C)	4/6 ore
2000	Altissima temperatura (da 90°C a 110°C)	2/3 ore

Tipo di essiccazione	Valori di furosina mg/110 g di proteine
Lavorazione artigianale: basse temperature	107 - 186
Grandi marchi e supermercati: alte temperature	226 - 304
Grandi marchi e supermercati: altissime temperature	345- 506



La furosina (o *ε-furoilmetil - lisina*)

PRESENZA DI GLIFOSATO E DEL SUO METABOLITA "AMPA"	(MG/KG)	FORMATO
DIVELLA	0.110	Spaghetti
Barilla	0.102	Spaghetti
Garofalo	0.062	Spaghetti
DE CECCO	0.052	Spaghetti

PRESENZA DI GLIFOSATO E DEL SUO METABOLITA "AMPA"	(MG/KG)	FORMATO
Voiello	0.050	Spaghetti
granoro Dedicato filiera 100% PUGLIA	0.039	Spaghetti
La Molisana	0.033	Spaghetti
coop	0.013	Spaghetti

Tipologia	Denominazic	Micotossina DON	Glifosa	Conc. Cadmi	Conc. Piomb	Giudizio
Formato	del Campion	(ppb)	(mg/kg)	(mg/kg)	(mg/kg)	GranoSalus
Spaghetti	*Barilla*	161	0.102	0.032	<0.01	Negativo
"	*Voiello*	180	0.050	0.036	<0.01	Negativo
"	*De Cecco*	80	0.052	0.042	<0.01	Negativo
"	*Divella*	381	0.110	0.044	<0.01	Negativo
"	*Garofalo*	199	0.062	0.021	<0.01	Negativo
"	*La Molisana*	253	0.033	0.035	<0.01	Negativo
"	*Coop*	128	0.013	0.027	<0.01	Negativo
"	*Granoro 100*	99	0.039	0.018	<0.01	Negativo

Fonte: *Laboratorio Europeo Accrditato*; Elab. GranoSalus

Fonte: *Laboratorio Certificato Accredia*
Test GranoSalus del 26.02.17

Baked Snapper

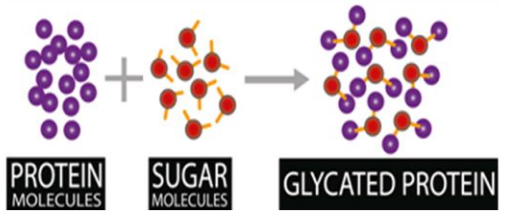
LOW AGE: 827 kU / serve

Fish and Chips

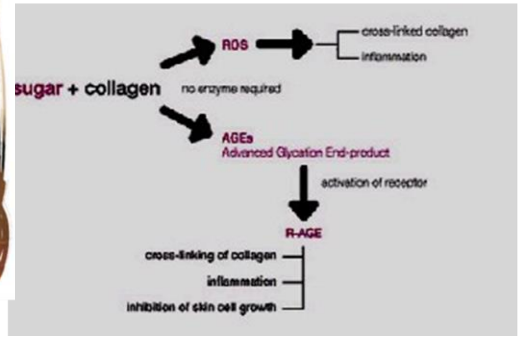
High AGE: 7897 kU / serve

UN PROCESSO DEGENERATIVO

Normalmente la glicazione inizia intorno ai 35 anni e progressivamente diventa importante dopo i 50



Fasi progressive della glicazione



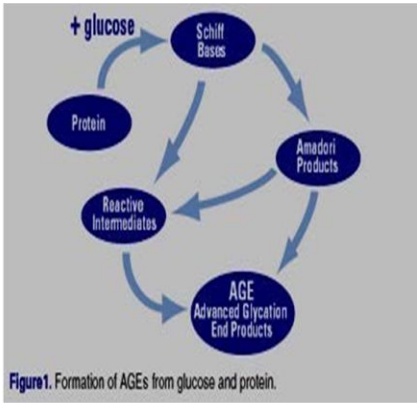


Figure1. Formation of AGEs from glucose and protein.

L'accumulo di AGE è un fattore significativo nei processi degenerativi, soprattutto in caso di insufficienza renale, cecità, malattie cardiovascolari e complicanze del diabete mellito.
Gli AGE sono implicati anche nei disturbi neurologici come il morbo di Alzheimer: i pazienti in fase precoce di demenza e con diabete hanno un rischio significativamente più alto di sviluppo di rigidità muscolare/ipertonia rispetto a quelli con demenza, ma senza diabete

5.963 kU per 100 g di carne → 2.700 kU per 100 g

Clorprofam
Erbicida
antigermogliante

Effect of temperature

160 °C
27 ppb

170 °C
70 ppb

180 °C
326 ppb

Acrylamide levels in potato chips fried for 4 minutes increased with frying oil temperature.

Regolamento UE 2017/2158 che istituisce misure di attenuazione e livelli di riferimento per la riduzione della presenza di acrilammide negli alimenti

Chronic intake of potato chips in humans increases the production of reactive oxygen radicals by leukocytes and increases plasma C-reactive protein: a pilot study[1–3]

Marek Naruszewicz, Danuta Zapolska-Downar, Anita Kośmider, Grażyna Nowicka, Małgorzata Kozłowska-Wojciechowska, Anna S Vikström, and Margareta Törnqvist

Disegno:

160g patatine fritte = 257mg di Acrilammide

Ogni giorno per 4 settimane (28 giorni)

14 volontari sani

Età media 35
Donne: 8
Fumatori: 6 (20 sigarette/giorno)

Parametri significativamente aumentati

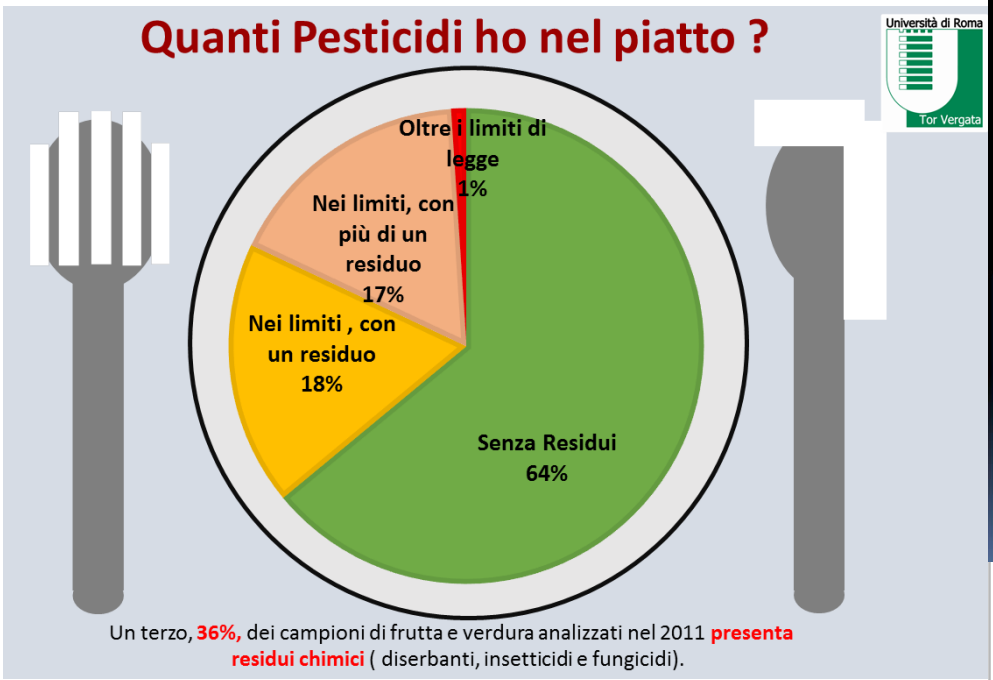
LDLox
hs IL-6
Hs CRP

C-glutamiltransferasi

Produzione di ROS
- Monociti
- Linfociti
- Granulociti

Espressione di CD14 nei Macrofagi (LPS?)

Naruszewicz M.et al., 2009.
Chronic intake of potato chips in humans increases the production of reactive oxygen radicals by leukocytes and increases plasma C-reactive protein: a pilot study1–3.
American Journal of Clinical Nutrition, 89(6), pp.1951–1951.



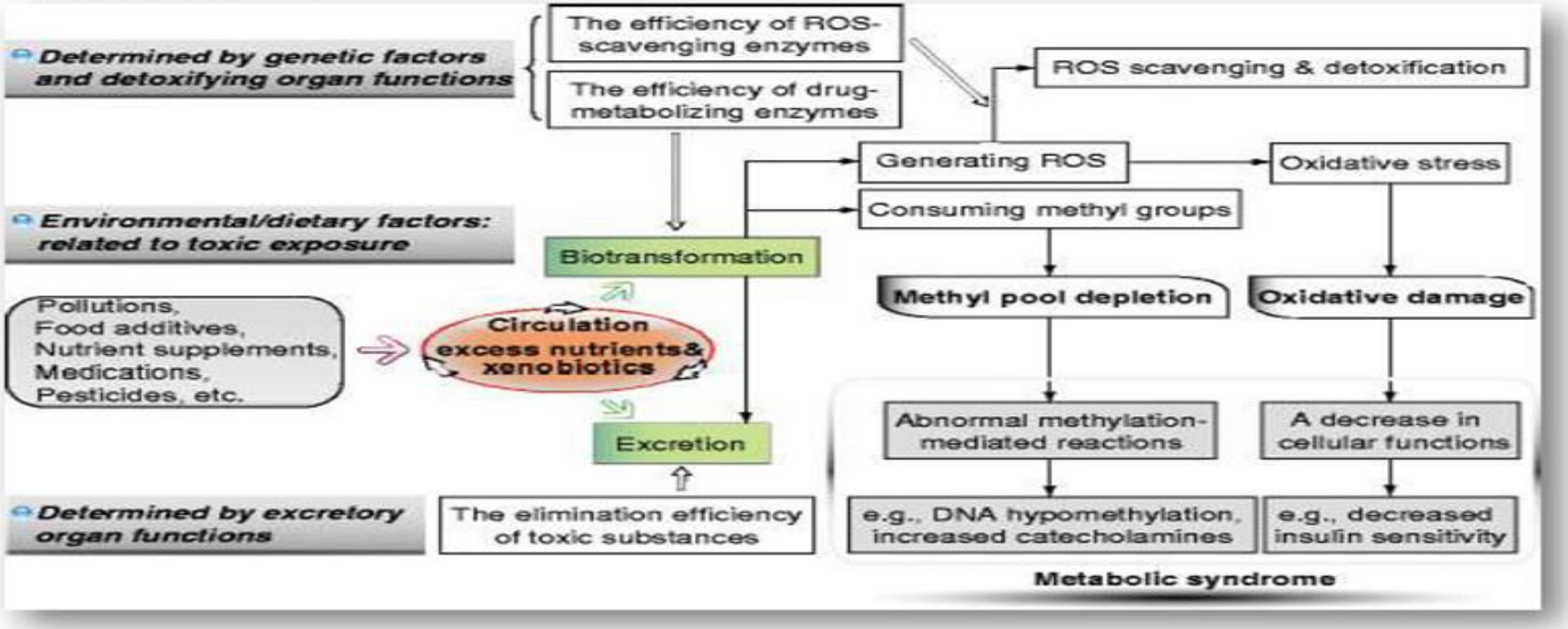
Miscele chimiche

L'EFSA ha avviato un'iniziativa pioneristica chiamata **MixTox,** per sviluppare metodi di valutazione del rischio da esposizione combinata a più sostanze chimiche. Facciamo appello ai portatori di interesse del mondo scientifico e della società civile d'Europa, e non solo, perché contribuiscano a configurare questo lavoro prima del suo inizio.

Possible link among environmental/dietary factors, genetic factors, oxidative stress, and aberrant methylation profile in MetS.

Increased xenobiotic and synthetic-nutrient exposure may be the primary cause of Metabolic Syndrome

ROS, reactive oxygen species.



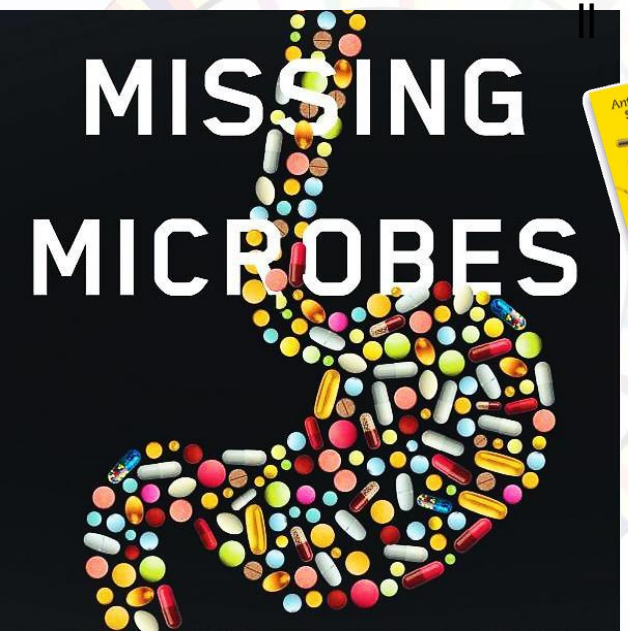
- Zhou SS, Zhou YM, Li D, Lun YZ. Dietary methyl-consuming compounds and metabolic syndrome. Hypertens Res. 2011;34:1239-1245. doi: 10.1038/hr.2011.133.
- Shi-Sheng Zhou, Da Li, Yi-Ming Zhou, and Ji-Min Cao. **The skin function: a factor of anti-metabolic syndrome.** Diabetol Metab Syndr. 2012; 4: 15

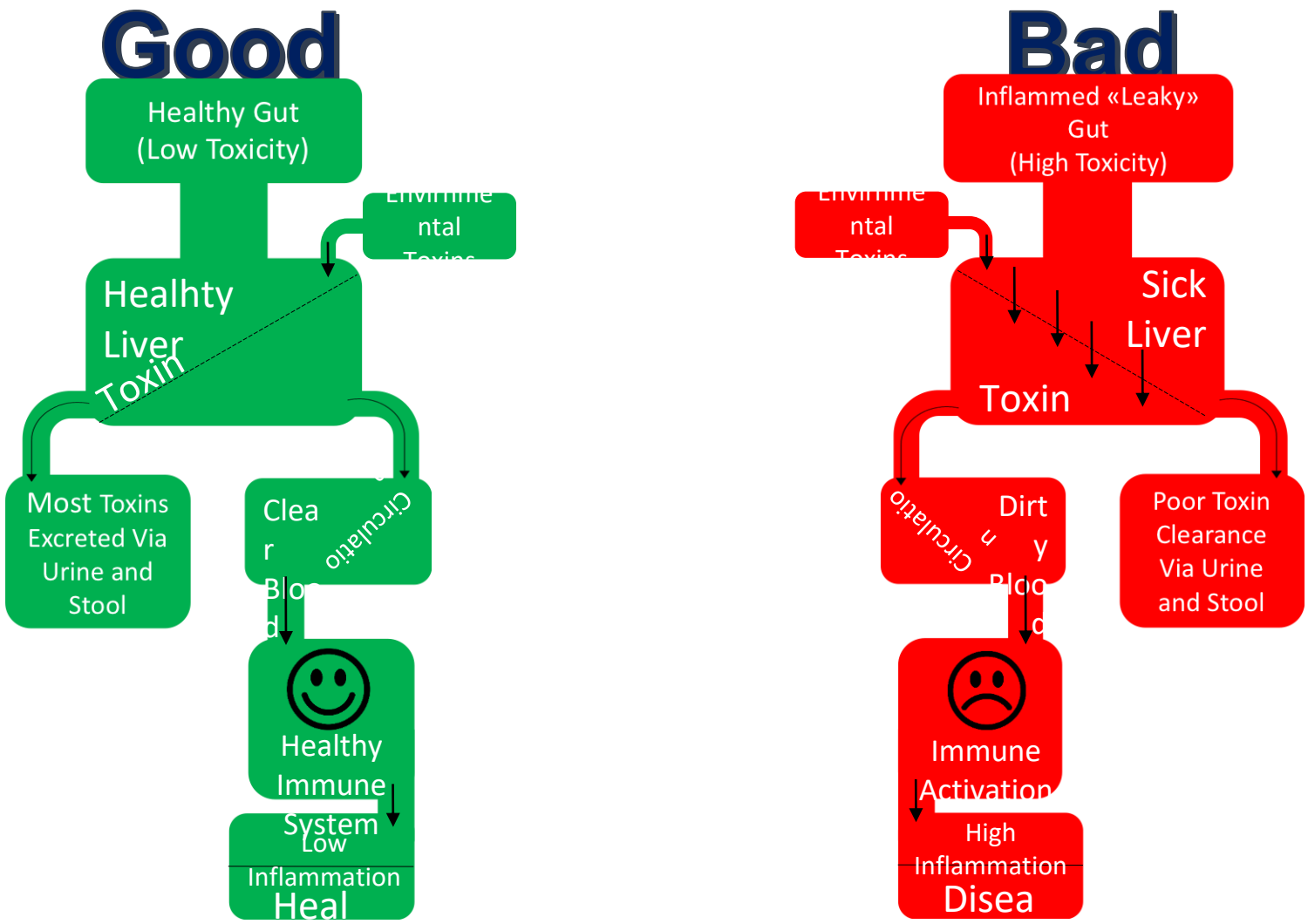
Microbiota

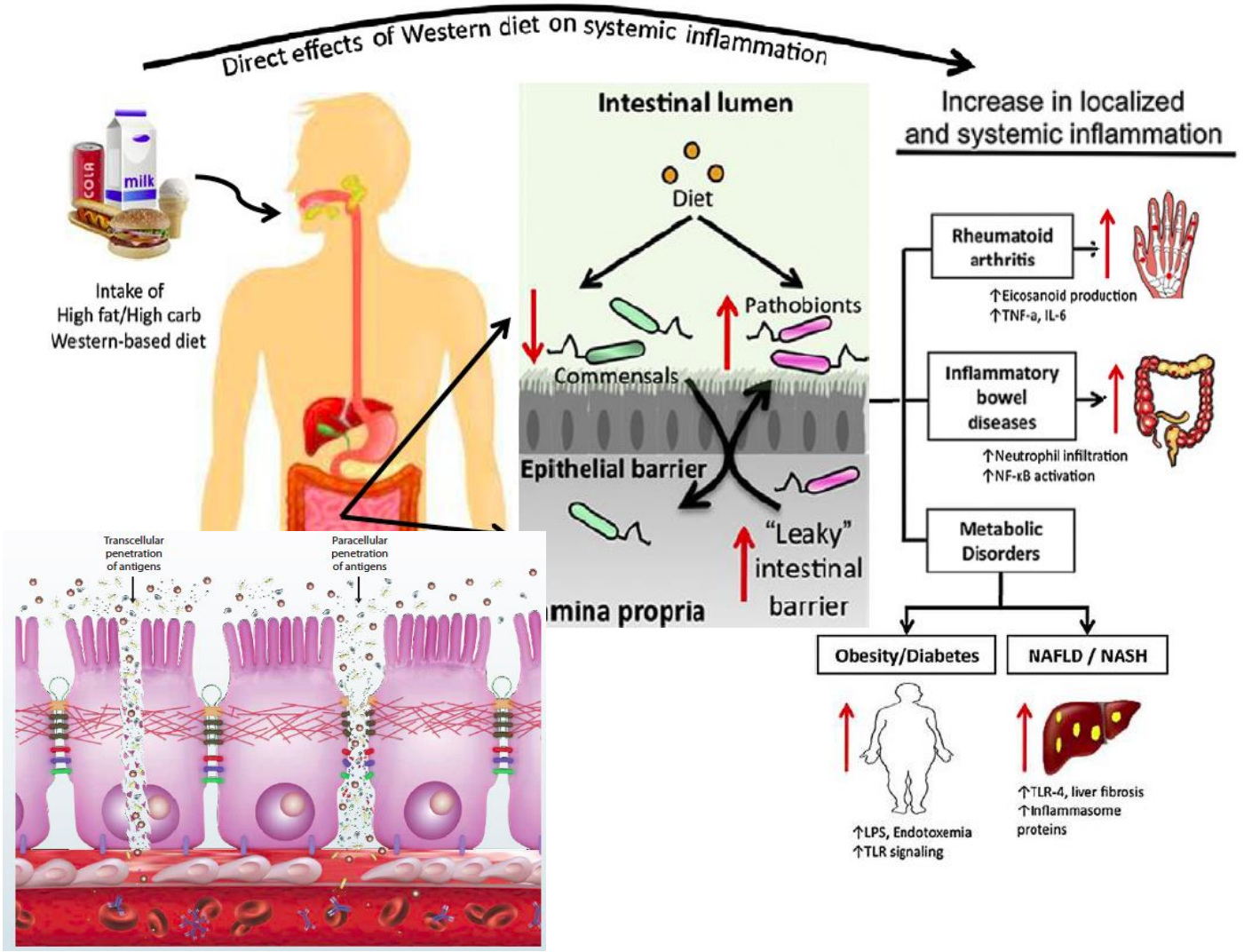
- The microorganisms that live in an established environment

Microbiome

- The full complement of microbes, their genes, and genomes in a particular environment




Good
Healthy Gut
(Low Toxicity)
Healhty
Liver
Toxin
Most Toxins
Excreted Via
Urine and
Stool
Healthy
Immune
System
Low
Inflammation
Bad
Inflammed «Leaky»
Gut
(High Toxicity)
Sick
Liver
Toxin
Poor Toxin
Clearance
Via Urine
and Stool
Immune
Activation
High
Inflammation


Direct effects of Western diet on systemic inflammation
Intake of
High fat/High carb
Western-based diet
Intestinal lumen
Diet
Pathobionts
Commensals
Epithelial barrier
"Leaky"
intestinal
barrier
mina propria
Increase in localized
and systemic inflammation
Rheumatoid
arthritis
↑Eicosanoid production
↑TNF-a, IL-6
Inflammatory
bowel
diseases
↑Neutrophil infiltration
↑NF-κB activation
Metabolic
Disorders
Obesity/Diabetes
NAFLD / NASH
↑LPS, Endotoxemia
↑TLR signaling
↑TLR-4, liver fibrosis
↑Inflammasome
proteins
Transcellular
penetration
of antigens
Paracellular
penetration
of antigens

Singh *et al. J Transl Med (2017) 15:73*
DOI 10.1186/s12967-017-1175-y

Influence of diet on the gut microbiome and implications for human health

Journal of Translational Medicine

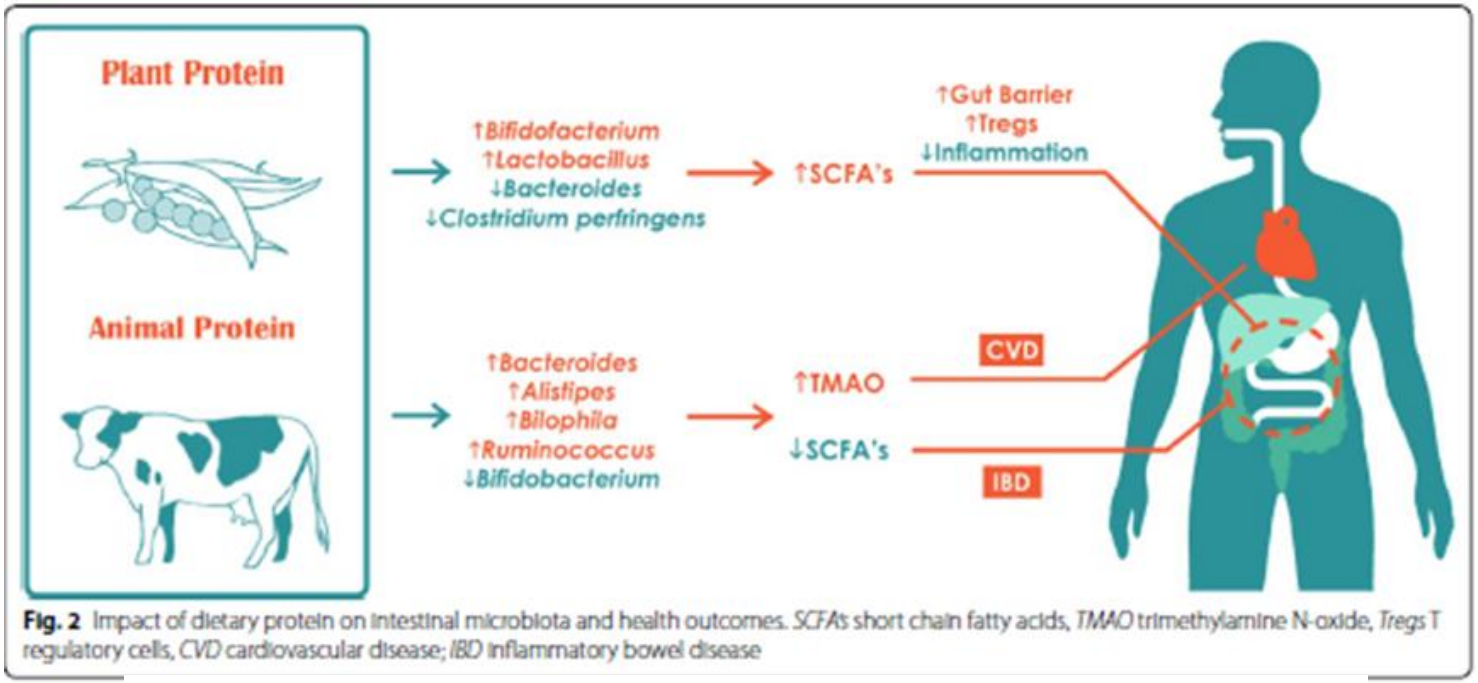


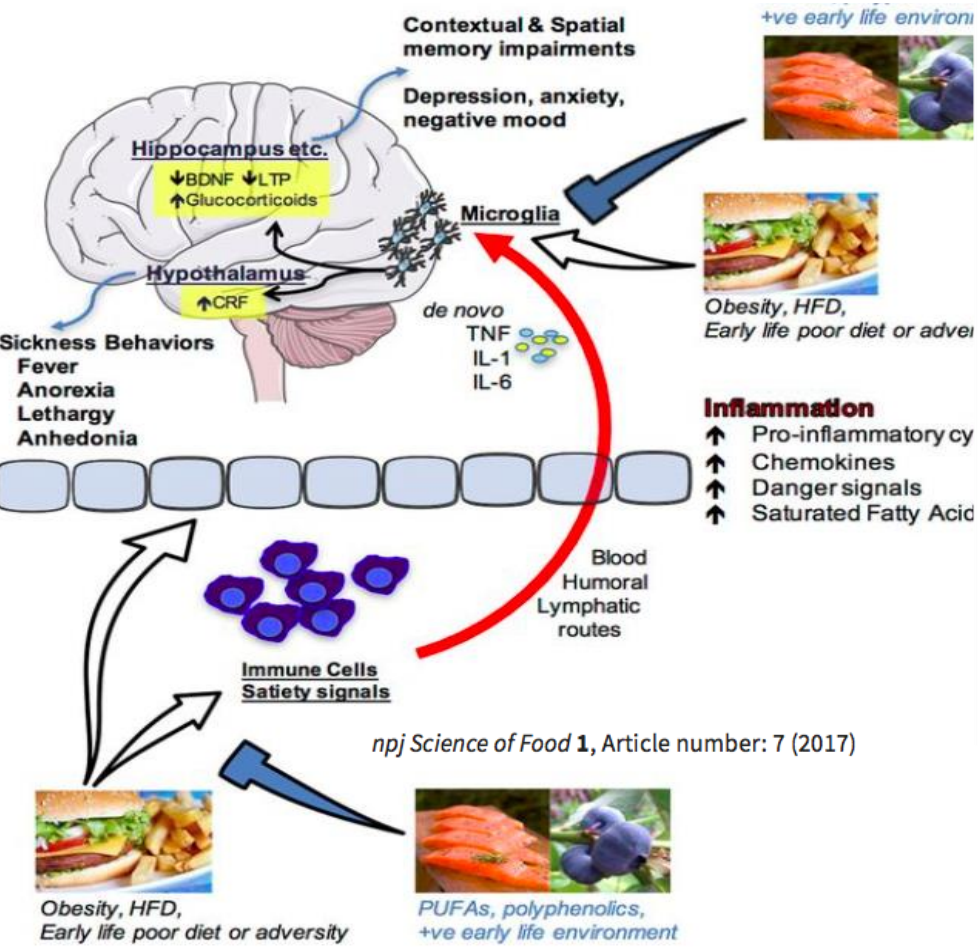
Fig. 2 Impact of dietary protein on intestinal microbiota and health outcomes. *SCFAs* short chain fatty acids, *TMAO* trimethylamine N-oxide, *Tregs* T regulatory cells, *CVD* cardiovascular disease; *IBD* inflammatory bowel disease

Table 2 Effects of protein on gut microbiota

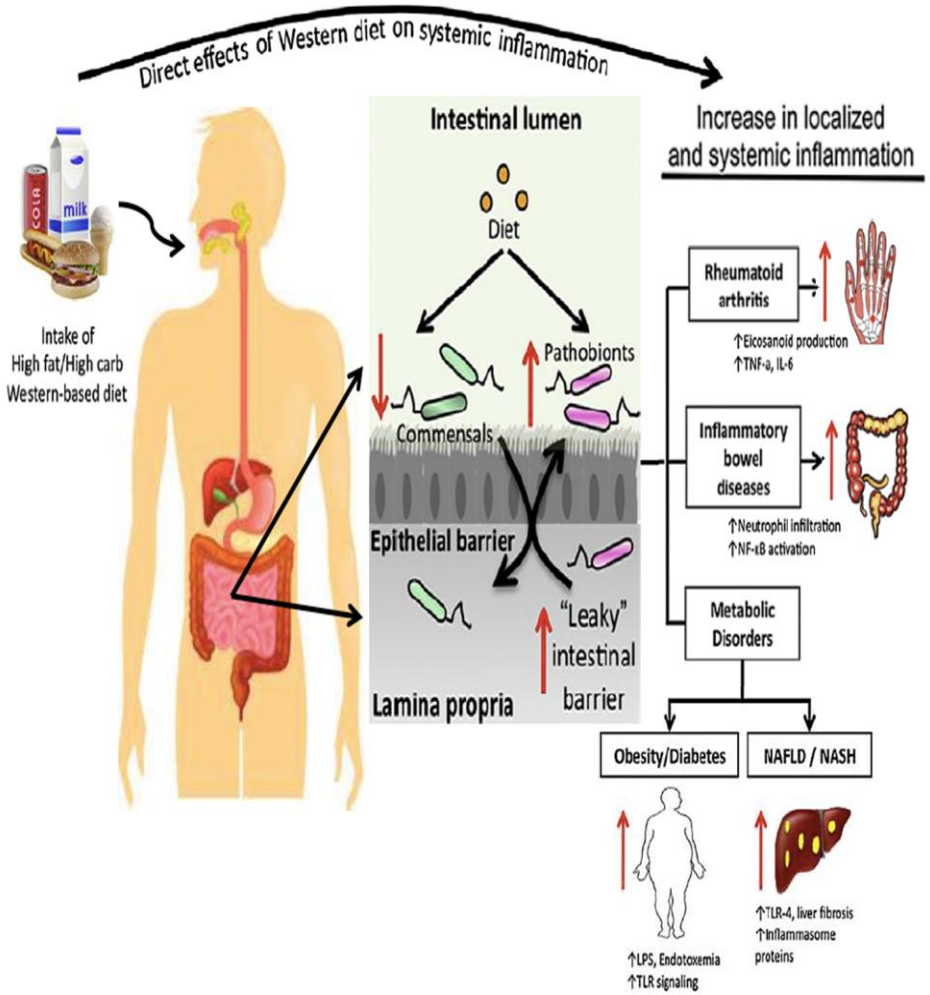
	Microbial diversity	*Bifidobacteria*	*Lactobacilli*	*Bacteroides*	*Alistipes*	*Bilophila*	*Clostridia*	*Roseburia*	*Eubacterium Rectale*	References
Animal protein	↑	↑↓		↑↓	↑	↑	↑	↓	↑↓	[13, 29–35, 38–40]
Whey protein extract	↑	↑	↑	↓			↓			[32, 33]
Pea protein extract	↑	↑	↑							[31]

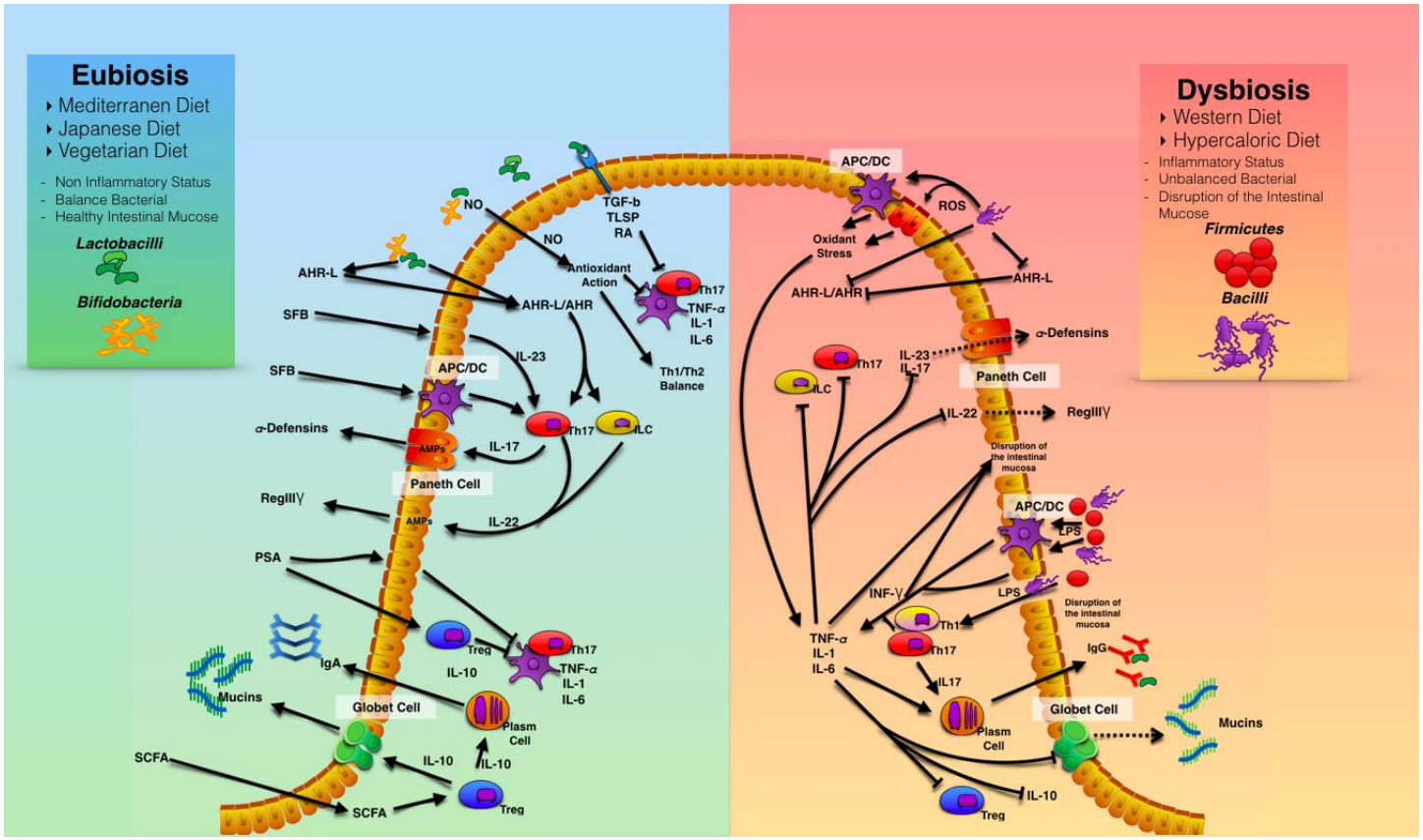
Arrow thickness corresponds to relative number of studies supporting the relationship

Food for thought: how nutrition impacts cognition and emotion



npj Science of Food **1**, Article number: 7 (2017)





J Transl Med. 2018 Mar 20;16(1):75. doi: 10.1186/s12967-018-1448-0.

The influence of diet on anti-cancer immune responsiveness.

Soldati L[1], Di Renzo L[2], Jirillo E[3], Ascierto PA[4], Marincola FM[5], De Lorenzo A[2].

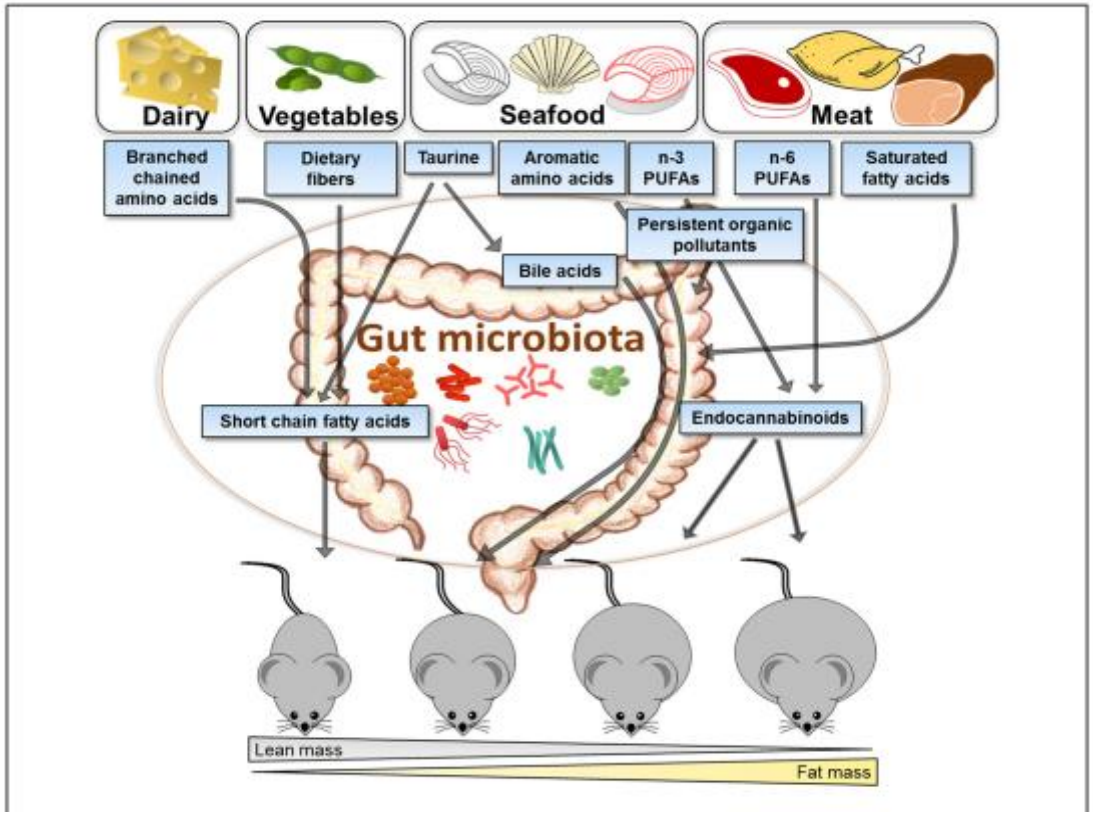
frontiers in Physiology

Links between Dietary Protein Sources, the Gut Microbiota, and Obesity

REVIEW
published: 19 December 2017
doi: 10.3389/fphys.2017.01047

Lise Madsen[1, 2, 3]*, *Lene S. Myrmel*[1], *Even Fjære*[1], *Bjørn Liaset*[1] and *Karsten Kristiansen*[2, 3]

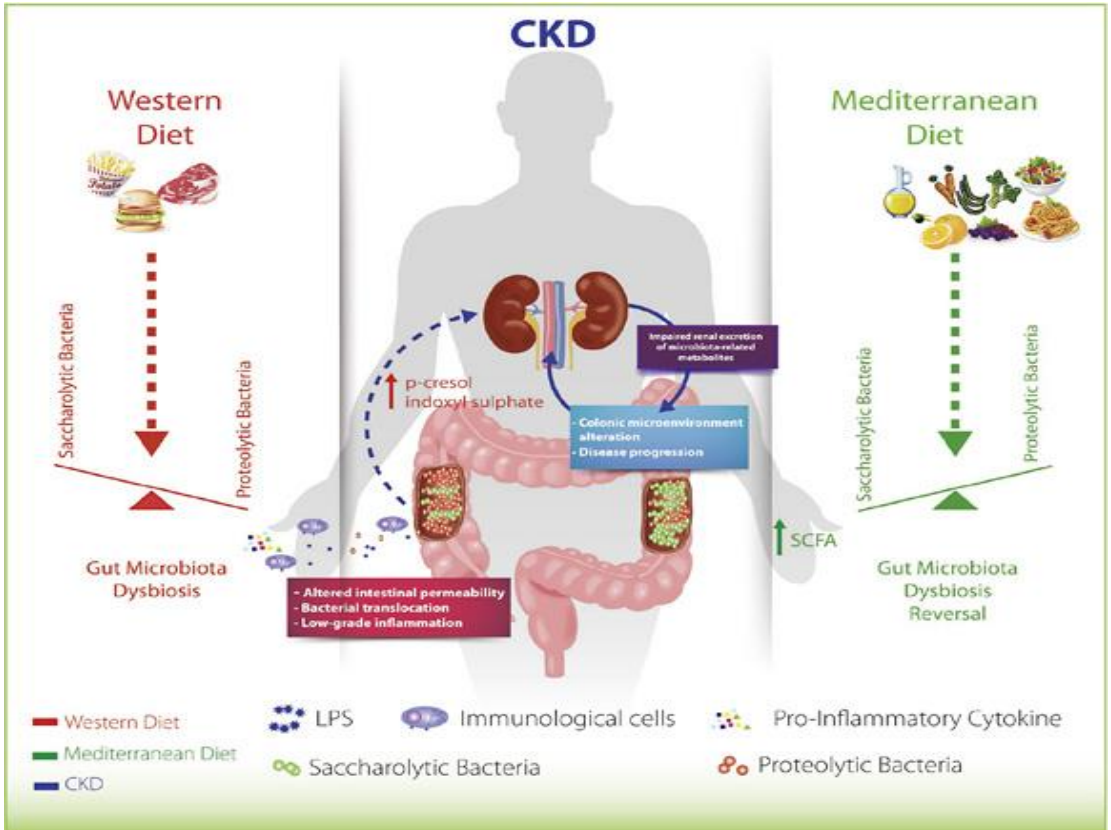
[1] National Institute of Nutrition and Seafood Research, Bergen, Norway, [2] Laboratory of Genomics and Molecular Biomedicine, Department of Biology, University of Copenhagen, Copenhagen, Denmark, [3] BGI-Shenzhen, Shenzhen, China



What Would You Like to Eat, Mr CKD Microbiota?

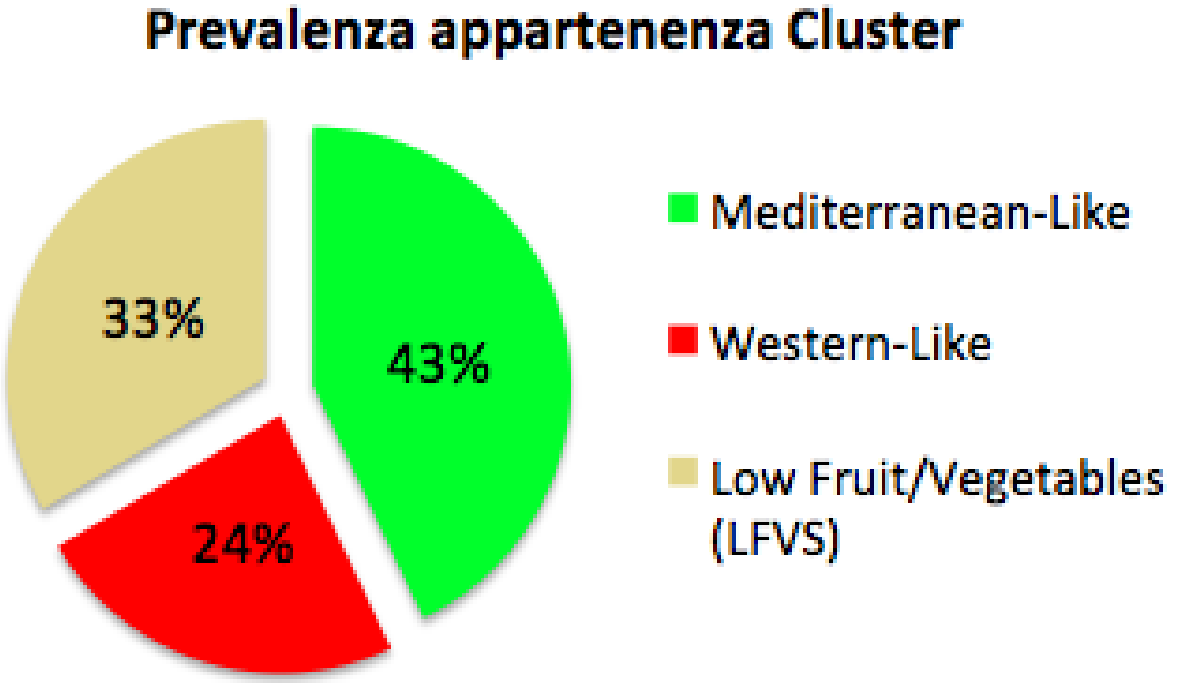
A Mediterranean Diet, please!

Montemurno E. Kidney Blood Press Res 2014;39:114-123



Clustering eating habits: frequent consumption of different dietary patterns among the Italian general population in the association with obesity, physical activity, sociocultural characteristics and psychological factors.

Eat Weight Disord; DOI 10.1007/s40519-015-0225-9 Denoth F, Scalese M, Siciliano V, Di Renzo L, De Lorenzo A, Molinaro S.



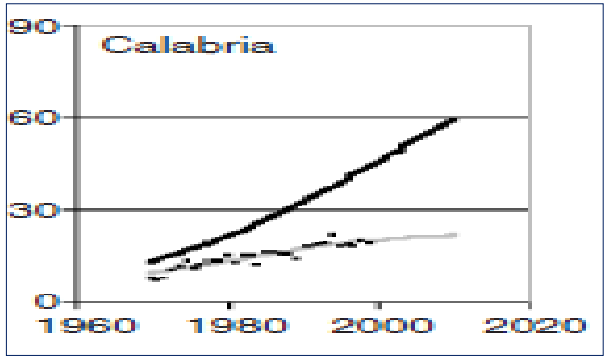
5278 subjects

Tumori, 93: 352-359, 2007

REGIONAL ESTIMATES OF COLORECTAL CANCER BURDEN IN ITALY

Enrico Grande[1], Riccardo Inghelmann[1], Silvia Francisci[1], Ardulno Verdecchia[1], Andrea Michell[2], Paolo Balli[2], Riccardo Capocaccia[1], and Roberta De Angelis[1]

Men



Women

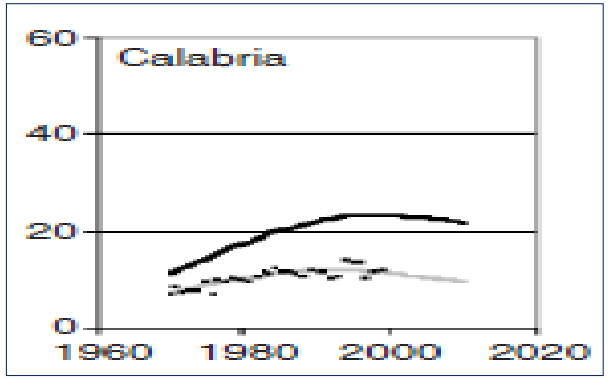


Table 2 - Estimated colorectal cancer mortality in Italy and in Italian regions for the year 2005 by gender. Number of cases, crude and European age-standardized (age-std) rates per 100,000 person years. Age 0-84 years

Macro-area and regions	Men			Women		
	no. of cases	crude rates	age-std rates	no. of cases	crude rates	age-std rates
North	4496	37	23	3214	26	12
Piemonte	766	38	23	530	25	12
Valle d'Aosta	22	38	23	15	25	12
Lombardia	1497	35	24	1116	25	13
Liguria	355	49	25	243	31	12
Trentino Alto Adige	160	35	24	112	24	12
Veneto	756	35	24	534	24	12
Friuli Venezia Giulia	191	35	24	137	24	12
Emilia Romagna	748	41	23	527	27	12
Center	1967	38	23	1431	26	13
Toscana	647	40	22	478	28	13
Umbria	176	45	24	126	31	14
Marche	294	43	24	197	28	14
Lazio	851	34	23	631	24	13
South	2859	28	21	2169	21	13
Abruzzo	246	41	25	136	22	11
Molise	63	41	25	35	22	11
Campania	708	25	22	562	19	13
Puglia	498	25	19	413	20	12
Basilicata	110	37	25	75	25	14
Calabria	288	29	21	179	17	10
Sicilia	685	28	20	577	22	14
Sardegna	260	33	25	192	23	14
Italy*	9360	34	23	6792	24	13

*National estimate was obtained by applying a specific model and not as the sum of regional estimates.

Nutrients **2015**, *7*, 7863-7888; doi:10.3390/nu7095367

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nutrients
ISSN 2072-6643
www.mdpi.com/journal/nutrients

Review

Mediterranean Diet and Cardiovascular Disease: A Critical Evaluation of *A Priori* Dietary Indexes

Annunziata D'Alessandro [1,*] and Giovanni De Pergola [2]

The MAI, computed in random samples of men surveyed for their eating habits and belonging to 16 cohorts of the *Seven Countries Study*, was inversely associated with the 25-year death rates from CHD ($r = -0.72$; $p = 0.001$) [32]. The HR for 1 unit of natural log of MAI (approximately corresponding to 2.7 units of MAI) was associated with a CHD mortality decrease of 26% (multivariate adjusted RR: 0.74; 95% CI: 0.55, 0.99) in 20 years of follow-ups and of 21% (multivariate adjusted RR: 0.79; 95% CI: 0.64, 0.97) in 40 years of follow-ups in two Italian rural cohorts of the *Seven Countries Study*, Crevalcore and Montegiorgio. The statistical analysis was multivariate adjusted for the covariates [33].

The increase of 2.7 index MAI units is associated with a decreased mortality from cardiovascular diseases:

26% in 20 yrs and 21 % in 40 yrs

European Review for Medical and Pharmacological Sciences 2007; 11: 185-192

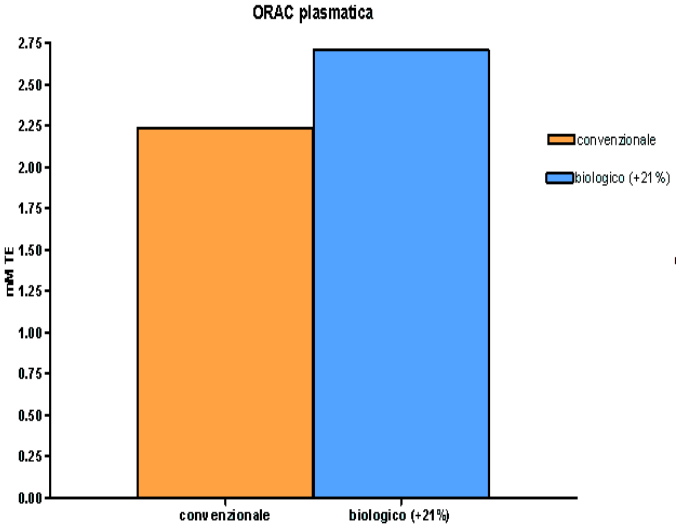
Is antioxidant plasma status in humans a consequence of the antioxidant food content influence?

L. DI RENZO[1,2], D. DI PIERRO[3], M. BIGIONI[1], V. SODI[1], F. GALVANO[4], R. CIANCI[1,5], L. LA FAUCI[4], A. DE LORENZO[1]

[1]Department of Neuroscience, Division of Human Nutrition, University of Tor Vergata, Rome (Italy)
[2]I.N.Di.M., National Istitute for Mediterranean Diet and Nutrigenomic, Reggio Calabria (Italy)

Table I. Antioxidant capacity in conventional and organic produts.

	Conventional		Organic		
	Median	Range	Median	Range	_%
Garlic	2572,5	70	3816,5	52	48**
Orange	900	50	1606	56	79**
Banana	205,9	16	339	38,6	65**
Carrot	116,4	27,2	166,8	58,4	43**
Beans	50,4	21,2	207,6	31,2	312**
Strawberry	846,7	37,2	921,2	41,6	9**
Lettuce	756,3	99,8	608,5	80,8	-20**
Limon	1505	54	1603	48	7**
Apple	454	81,9	610,5	47	34**
Potato	298,8	4,4	423,6	50,8	42**
Tomato Souce	205,2	19,8	213,8	58,8	4
Pear	246,4	132,2	185,3	58,4	-25**
Peas	88,2	41,8	164,8	65	87**
Tomato	280,8	72,6	475,2	98,4	69**
Celery	265,7	119,8	414,9	40,4	56**
Wine	3132	280,2	4725	164	51**
Courgettes	774	148,8	894	60,6	15**
Milk	195,8	78,4	216,6	38,6	11*



Current Pharmaceutical Design, 2010, *16*, 000-000

The effects of Italian Mediterranean Organic Diet (IMOD) on Health Status

A. De Lorenzo[1,2,*], A. Noce[3], M. Bigioni[1], V. Calabrese[4], D.G. Della Rocca[1], N. Di Daniele[5], C. Tozzo[3] and Laura Di Renzo[1,2]

[1]Department of Neuroscience, Division of Human Nutrition, University of Tor Vergata, Rome, Italy; [2]I.N.Di.M., National Institute for Mediterranean Diet and Nutrigenomic, Reggio Calabria, Italy;[3]Nephrology and Dialysis Service, University Hospital "Tor Vergata", Rome, Italy; [4]Biochemistry & Molecular Biology Section, Department of Chemistry, Faculty of Medicine, University of Catania, Catania, Italy; [5]Department of Internal Medicine, University Hospital Tor Vergata, Rome, Italy

Table 4. Laboratory Parameters in Healthy Subjects and in CKD Patients at T1 and T2

	Healthy Subjects					CKD Patients				
	T1		T2			T1		T2		
	Mean	SD	Mean	SD	*P**	Mean	SD	Mean	SD	*P**
Homocysteine(μM/L)	23.06	± 5.17	12.71	± 6.15	0.0106	22.12	± 5.17	17.81	± 5.29	0.0026
Azotemia (mg/dl)	33.20	± 11.33	30.66	± 8.51	NS	83.21	± 47.49	80.76	± 50.92	NS•
Creatinine (mg/dl)	0.88	± 0.29	0.95	± 0.18	NS	1.75	± 0.61	1.67	± 0.27	NS
Total Cholesterol (mg/dl)	167.02	± 60.55	189.66	± 36.21	NS	181.57	± 14.84	165.57	± 27.71	0.0369
HDL cholesterol (mg/dl)	33.04	± 12.30	39	± 6.86	NS	30.92	± 7.41	32.07	± 6.76	NS

	Healthy Subjects					CKD Patients				
	T1		T2			T1		T2		
	Mean	SD	Mean	SD	*P**	Mean	SD	Mean	SD	*P**
Triglycerides (mg/dl)	98.44	± 47.56	113.44	± 26.70	NS	168.71	± 54.33	156.85	± 37.88	NS
Calcium (mg/dl)	9.64	± 0.16	9.43	± 0.37	NS	9.93	± 0.57	9.33	0.44	<0.0001
Phosphorus (mg/dl)	4.64	± 0.15	3.01	± 0.13	<0,0001	4.10	± 0.88	3.54	± 0.26	0.0382
Sodium (mEq/L)	140.97	± 0.86	139.51	± 1.11	0,0141	140.85	± 1.09	140.57	± 0.85	NS
Potassium (mEq/L)	4.34	± 0.15	4.31	± 0.39	NS	4.90	± 0.34	4.67	±0.65	NS
Glucose (mg/dl)	98.91	± 24.28	92.66	± 22.02	NS	86.78	± 6.71	90.23	±8.55	NS
Vitamin B_{12} (pg/ml)	217.33	± 20.10	259.11	± 22.65	0.0019	574.92	± 247.49	516.42	±195.42	NS
Microalbuminuria (mg/L)	-	-	-	-	-	93.55	± 121.9	71.7	±100.48	0.00286
hs-CRP (mg/dl)	0.44	±0.64	0.05	±0.01	0.001	5.63	±4.82	4.51	±4.94	<0.001

PLOS | ONE

RESEARCH ARTICLE

N-3 Polyunsaturated Fatty Acids (PUFAs) Reverse the Impact of Early-Life Stress on the Gut Microbiota

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Competing Interests: The authors have the following interests. The APC has conducted research funded by Pfizer, GlaxoSmithKline, Proctor and Gamble, Mead Johnson, Suntory and Cremo. TGD

Abstract

Background

Early life stress is a risk factor for many psychiatric disorders ranging from depression to anxiety. Stress, especially during early life, can induce dysbiosis in the gut microbiota, the key modulators of the bidirectional signalling pathways in the gut-brain axis that underline several neurodevelopmental and psychiatric disorders. Despite their critical role in the development and function of the central nervous system, the effect of n-3 polyunsaturated fatty acids (n-3 PUFAs) on the regulation of gut-microbiota in early-life stress has not been explored.

Methods and Results

Here, we show that long-term supplementation of eicosapentaenoic acid (EPA)/docosahexaenoic acid (DHA) (80% EPA, 20% DHA) n-3 PUFAs mixture could restore the disturbed gut-microbiota composition of maternally separated (MS) female rats. Sprague-Dawley female rats were subjected to an early-life stress, maternal separation procedure from postnatal days 2 to 12. Non-separated (NS) and MS rats were administered saline, EPA/DHA 0.4 g/kg/day or EPA/DHA 1 g/kg/day, respectively. Analysis of the gut microbiota in adult rats revealed that EPA/DHA changes composition in the MS, and to a lesser extent the NS rats, and was associated with attenuation of the corticosterone response to acute stress.

Conclusions

In conclusion, EPA/DHA intervention alters the gut microbiota composition of both neurodevelopmentally normal and early-life stressed animals. This study offers insights into the interaction between n-3 PUFAs and gut microbes, which may play an important role in advancing our understanding of disorders of mood and cognitive functioning, such as anxiety and depression.

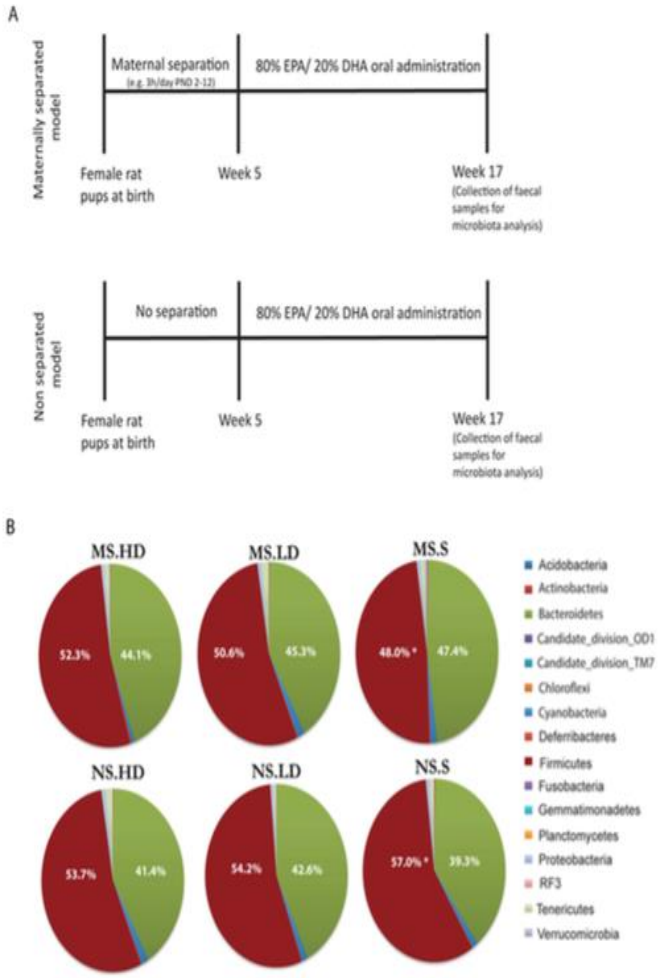

Fig 1. Schematic representation of the time course of the maternal separation procedure and EPA/DHA treatment. (B) Global average microbial composition of faecal 17 weeks old rats samples (n = 10 per group) at phylum-level. * Indicate bacterial group significantly different between MS and NS groups.

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Effects of almond and pistachio consumption on gut
in a randomised cross-over human feeding study

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(Submitted 3 July 2013 – Final revision received 16 January 2014 – Accepted 20 January 2014 – First pu

Abstract

The modification of microbiota composition to a 'beneficial' one is a promising approach for im
Natural fibres and phytochemicals that reach the proximal colon, such as those present in var
tenance of healthy and diverse microbiota. The effects of increased consumption of specific nu
phytonutrients, on human gut microbiota composition have not been investigated to date. The
mine the effects of almond and pistachio consumption on human gut microbiota compositi
samples collected from volunteers in two separate randomised, controlled, cross-over feedi
study and *n* 16 for the pistachio feeding study) with 0, 1·5 or 3 servings/d of the respective
was analysed using a 16S rRNA-based approach for bacteria and an internal transcribed spac
The 16S rRNA sequence analysis of 528 028 sequence reads, retained after removing low-quali
operational taxonomic units that appeared to be affected by nut consumption. The effect of
composition was much stronger than that of almond consumption and included an increas
butyrate-producing bacteria. Although the numbers of bifidobacteria were not affected by the
sumption appeared to decrease the number of lactic acid bacteria ($P<0·05$). Increasing the con
to be an effective means of modifying gut microbiota composition.

Key words: **Commensal microbiota: Flora: Nutrition: Diet**

Food and Nutrition Sciences, 2014, 5, 79-88
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http://dx.doi.org/10.4236/fns.2014.51011

Scientific Research

Nutrient Analysis Critical Control Point (NACCP): Hazelnut as a Prototype of Nutrigenomic Study

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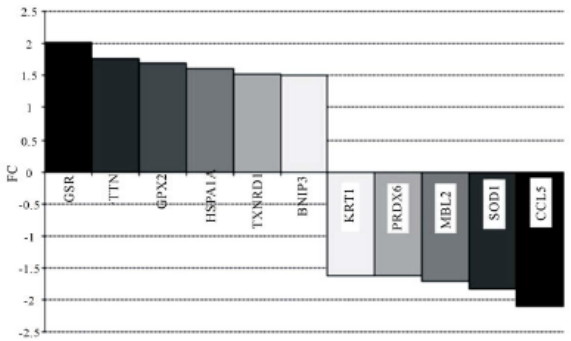

Figure 3. Different significant level of genes expression after 40 g/die hazelnut's supplementation. The up-regulated genes were: *BNIP3* (*BCL2/adenovirus E1B 19 kDa interacting protein 3*; NM_004052), *GPX2* (*glutathione peroxidase 2*; NM_002083), *GSR* (*glutathione reductase*; NM_000637), *HSPA1A* (*Heat shock 70 kDa protein 1A*; NM_005345) TTN (*titin*; NM_003319) and TXNRD1 (*thioredoxin reductase 1*; NM_003330). The down-regulated genes were: *CCL5* (*chemokine (C-C motif) ligand 5*; NM_002985) KRT1 (*keratin*; NM_006121), MBL2 (*mannose-binding lectin (protein C) 2 soluble*; NM_000242), *PRDX6* (*peroxiredoxine 6*; NM_004905), *SOD1* (*superxide dismutase 1, soluble*; NM_000454). The significant values are expressed as $p \leq 0.05$.

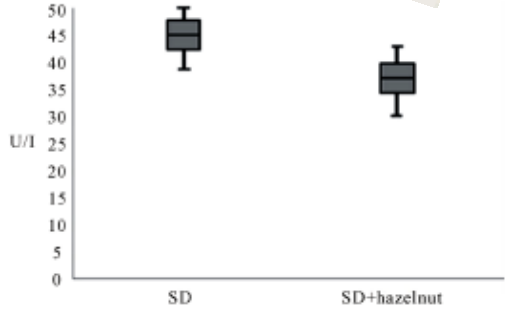

Figure 4. Effect of 40 g/die of hazelnuts on LDL-ox. The values of oxidized LDL show a significant decrease ($p \leq 0.005$) with the combination of hazelnuts. The value found with the standard meal in association with hazelnuts was 36.99 ± 5.45 U/l (min 28.58 - max 47.75), meanwhile the consumption of the meal without hazelnuts showed an average value of 40.38 ± 6.02 (min 33.95 - min 50.58).

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ELSEVIER

REVIEWS: CURRENT TOPICS

The role of virgin olive oil components in the modulation of endothelial function

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Received 30 September 2005; received in revised form 27 October 2005; accepted 1 November 2005

Differential anti-inflammatory effects of phenolic compounds from extra virgin olive oil identified in human whole blood cultures

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ORIGINAL CONTRIBUTION

Effect of virgin olive oil and thyme phenolic compounds on blood lipid profile: implications of human gut microbiota

Sandra Martín-Peláez[1,2] · Juana Ines Mosele[3] · Neus Pizarro[4,5] · Marta Farràs[1,2,5] · Rafael de la Torre[2,4,6] · Isaac Subirana[7,8] · Francisco José Pérez-Cano[9] · Olga Castañer[1,2] · Rosa Solà[10] · Sara Fernandez-Castillejo[10] · Saray Heredia[1] · Magí Farré[4,6] · María José Motilva[3] · Montserrat Fitó[1,2]

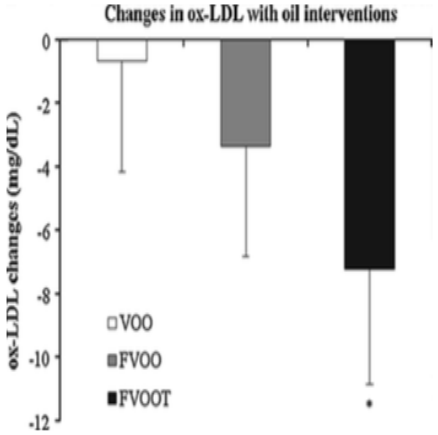

Fig. 1 Changes in serum oxidized LDL (after–before interventions values) with olive oil interventions. Values are given as means of mg/dL and SE *bars* $n = 12$ subjects. *$P < 0.05$, for the differences within the same olive oil intervention

Table 2 Bacterial enumerations determined by FISH-flow cytometry in faecal samples collected before (B) and after (A) each olive oil intervention

Probe		VOO	FVOO	FVOOT	P^a		
					VOO–FVOO	VOO–FVOOT	FVOO–FVOOT
Ato291	B	8.80 ± 0.09	8.86 ± 0.11	8.72 ± 0.10			
	A	8.78 ± 0.09	8.64 ± 0.09	8.72 ± 0.09	0.319	0.947	0.293
Bac303	B	8.68 ± 0.38	8.87 ± 0.42	8.64 ± 0.40			
	A	8.75 ± 0.39	8.73 ± 0.39	8.73 ± 0.40	0.423	0.917	0.373
Bif164	B	8.33 ± 0.25	8.29 ± 0.27	8.14 ± 0.26			
	A	8.10 ± 0.25	8.11 ± 0.26	8.32 ± 0.26	0.818	0.044	0.073
Fprau645	B	8.90 ± 0.06	9.03 ± 0.07	8.96 ± 0.06			
	A	8.90 ± 0.06	8.92 ± 0.06	8.93 ± 0.06	0.420	0.831	0.558
Lab158	B	8.30 ± 0.20	8.43 ± 0.22	8.24 ± 0.21			
	A	8.44 ± 0.20	8.32 ± 0.21	8.27 ± 0.21	0.145	0.512	0.427
Prop853	B	8.81 ± 0.08	8.99 ± 0.10	8.81 ± 0.09			
	A	8.98 ± 0.08	8.79 ± 0.08	8.80 ± 0.08	0.066	0.338	0.364
Rrec584	B	8.74 ± 0.08	8.81 ± 0.10	8.63 ± 0.09			
	A	8.76 ± 0.09	8.61 ± 0.09	8.79 ± 0.09	0.303	0.461	0.085

Values are given as adjusted means of log10 bacteria/g dry faeces ± SE; $n = 12$ subjects

VOO, 80 mg/kg of phenolic compounds (PC) from olive oil; FVOO, 500 mg/kg of PC from olive oil; FVOOT, 250 mg/kg of PC from olive oil and 250 mg/kg from thyme

[a] *P* values for inter-dietary intervention comparisons

Review Article

Wine consumption and intestinal redox homeostasis

Fiorella Biasi [a], Monica Deiana [b], Tina Guina [a], Paola Gamba [a], Gabriella Leonarduzzi [a], Giuseppe Poli [a,*]

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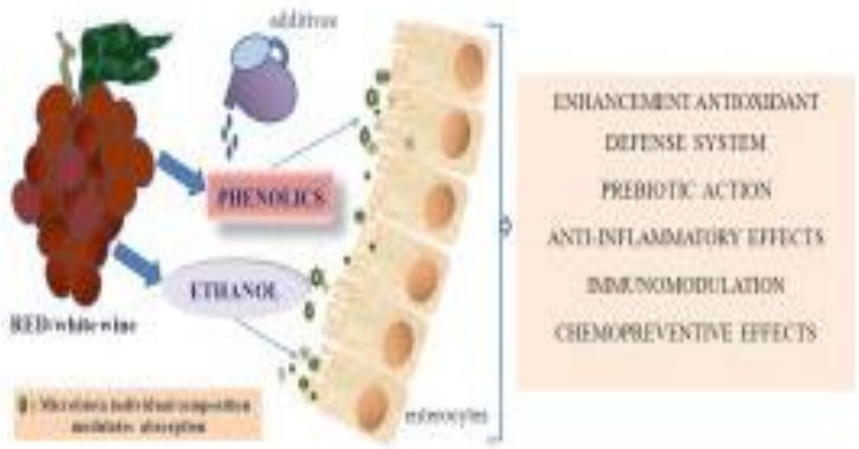
ABSTRACT

Regular consumption of moderate doses of wine is an integral part of the Mediterranean diet, which has long been considered to provide remarkable health benefits. Wine's beneficial effect has been attributed principally to its non-alcoholic portion, which has antioxidant properties, and contains a wide variety of phenolics, generally called polyphenols. Wine phenolics may prevent or delay the progression of intestinal diseases characterized by oxidative stress and inflammation, especially because they reach higher concentrations in the gut than in other tissues. They act as both free radical scavengers and modulators of specific inflammation-related genes involved in cellular redox signaling. In addition, the importance of wine polyphenols has recently been stressed for their ability to act as prebiotics and antimicrobial agents.

Wine components have been proposed as an alternative natural approach to prevent or treat inflammatory bowel diseases. The difficulty remains to distinguish whether these positive properties are due only to polyphenols in wine or also to the alcohol intake, since many studies have reported ethanol to possess various beneficial effects. Our knowledge of the use of wine components in managing human intestinal inflammatory diseases is still quite limited, and further clinical studies may afford more solid evidence of their beneficial effects.



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Research Article

Changes in LDL Oxidative Status and Oxidative and Inflammatory Gene Expression after Red Wine Intake in Healthy People: A Randomized Trial

Laura Di Renzo,[1] Luigi Tonino Marsella,[2] Alberto Carraro,[1] Roberto Valente,[1] Paola Gualtieri,[1] Santo Gratteri,[3] Diego Tomasi,[4] Federica Gaiotti,[4] and Antonino De Lorenzo[1,5]

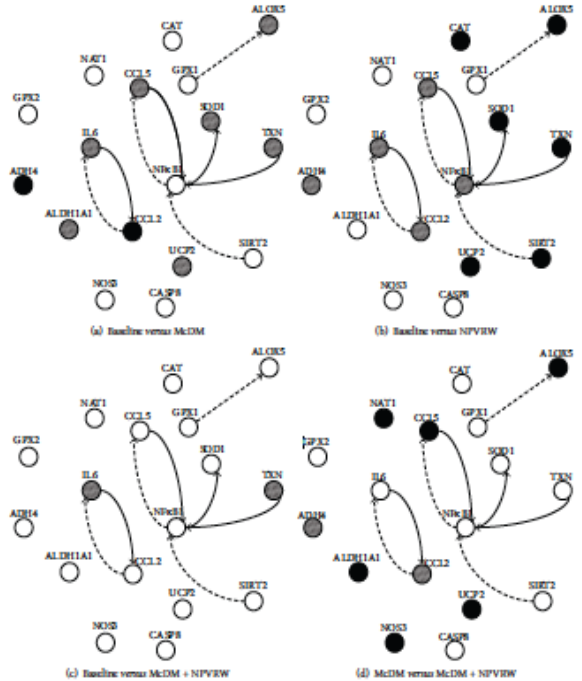

FIGURE 7: Nutrigenomic networking. Network showing upregulation (solid arrows) and downregulation (dashed arrows) of genes involved in inflammation, oxidative stress, and drug metabolism, in comparison with (a) baseline versus McD, (b) baseline versus NPVRW, (c) baseline versus McD + NPVRW, and (d) McD versus McD + NPVRW. Filled circle indicates upregulation in response to treatment; dashed circle indicates downregulation in response to treatment; empty circle indicates not significant genes. *Oxidative stress genes*: *CAT*, Catalase (NM_1752); *GPX1*, Glutathione Peroxidase 1 (NM_581); *GPX2*, Glutathione Peroxidase 1 (gastrointestinal) (NM_2083); *UCP2*, Uncoupling Protein 2 (Mitochondrial Proton Carrier) (NM_3355); *SOD 1*, Superoxide Dismutase 1 Soluble (NM_454); *NOX4*, Nadph. Oxidase 4 (NM_16931); *ALB*, Albumin (NM_477); *CCL5*, Copper Chaperone for Superoxide Dismutase (NM_2985). *Inflammasome genes*: *CASP8*, Caspase 1 Apoptosis Related Cysteine Peptidase (NM_1228); *NFKB1*, Nuclear Factor of Kappa Light Polypeptides Gene Enhancer in B-Cells 1 (NM_3998); *CCL2*, Chemokine (C-C motif) Ligand 2 (NM_2982); *PYCARD*, Pyd and Card Domain Containing (NM_13258); *RPLP0*, Ribosomal Protein Large P0 (NM_1002); NLRP12, Nrl Family Pyrin Domain Containing 12 (NM_33297); IL 6, Interleukin 6 (Interferon Beta 2) (NM_600). *Human Drug Metabolism genes*: *NAT1*, N-Acetyltransferase 1 (Arylamine N-Acetyltransferase) (NM_662); *NOS3*, Nitric Oxide Synthase 3 (Endothelial Cell) (NM_603); *APOE*, Apolipoprotein E (NM_41); *ADH4*, Alcohol Dehydrogenase 4-Class 2 Pi Polypeptide (NM_670); *ALOX15*, Arachidonate 15-Lipoxygenase (NM_1140); *ALOX5*, Arachidonate 5-Lipoxygenase (NM_698); *HSD17 B2*, Hydroxysteroid (17 Beta) Dehydrogenase 2 (NM_2153); *ALDH1A1*, Aldehyde Dehydrogenase 1 Family Member A1 (NM_689); *MT2A*, Metallothionein 2a (NM_5953).

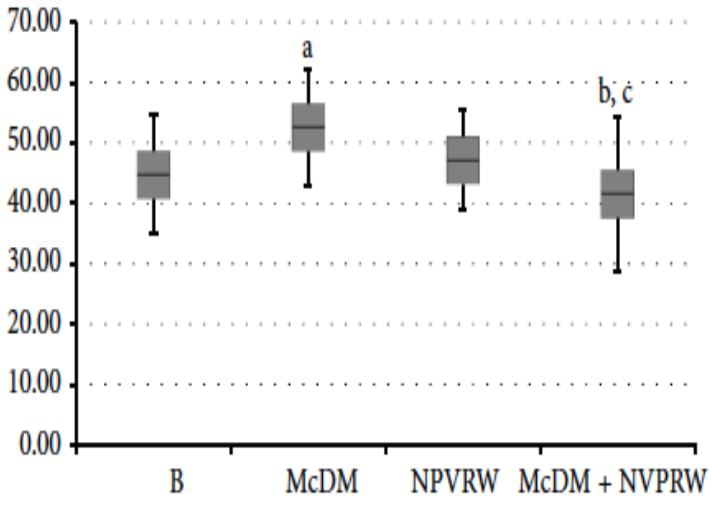

FIGURE 2: Comparative values of ox-LDL level for each treatment intervention. The significant values are expressed as (a) baseline *versus* McDonald's meal ($P \leq 0.05$); (b) McDonald's meal *versus* McDonald's meal + not pruned vineyard red wine ($P \leq 0.05$); (c) baseline *versus* not pruned vineyard red wine ($P > 0.05$); baseline *versus* McDonald's meal + not pruned vineyard red wine ($P > 0.05$).

J Proteome Res. 2009 Dec;8(12):5568-79. doi: 10.1021/pr900607v.

Metabolic effects of dark chocolate consumption on energy, gut microbiota, and stress-related metabolism in free-living subjects.

Martin FP[1], Rezzi S, Peré-Trepat E, Kamlage B, Collino S, Leibold E, Kastler J, Rein D, Fay LB, Kochhar S.

Author information

Abstract

Dietary preferences influence basal human metabolism and gut microbiome activity that in turn may have long-term health consequences. The present study reports the metabolic responses of free living subjects to a daily consumption of 40 g of dark chocolate for up to 14 days. A clinical trial was performed on a population of 30 human subjects, who were classified in low and high anxiety traits using validated psychological questionnaires. Biological fluids (urine and blood plasma) were collected during 3 test days at the beginning, midtime and at the end of a 2 week study. NMR and MS-based metabonomics were employed to study global changes in metabolism due to the chocolate consumption. Human subjects with higher anxiety trait showed a distinct metabolic profile indicative of a different energy homeostasis (lactate, citrate, succinate, trans-aconitate, urea, proline), hormonal metabolism (adrenaline, DOPA, 3-methoxy-tyrosine) and gut microbial activity (methylamines, p-cresol sulfate, hippurate). Dark chocolate reduced the urinary excretion of the stress hormone cortisol and catecholamines and partially normalized stress-related differences in energy metabolism (glycine, citrate, trans-aconitate, proline, beta-alanine) and gut microbial activities (hippurate and p-cresol sulfate). The study provides strong evidence that a daily consumption of 40 g of dark chocolate during a period of 2 weeks is sufficient to modify the metabolism of free living and healthy human subjects, as per variation of both host and gut microbial metabolism.

European Review for Medical and Pharmacological Sciences 2013; 17: 2257-2266

Effects of dark chocolate in a population of Normal Weight Obese women: a pilot study

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Table III. Biochemical parameters before (T0) and after (T1) DC consumption[§].

Parameters	T0 mean ± SD	T1 mean ± SD
Total Cholesterol (mmol/L)	5.02 ± 0.98	4.87 ± 0.97
HDL Cholesterol (mmol/L)	1.44 ± 0.28	1.57 ± 0.27*
LDL Cholesterol (mmol/L)	3.01 ± 0.94	2.89 ± 0.86
Fibrinogen (µmol/L)	7.16 ± 0.74	7.86 ± 1.03
hs-CRP (mg/L)	0.97 ± 0.66	1.51 ± 1.63
ESR (mm/h)	11.28 ± 6.21	10.43 ± 8.08
AST (U/L)	30.86 ± 32.87	17.71 ± 3.54
ALT (U/L)	18.71 ± 15.70	16.14 ± 7.82
BUN (mmol/L)	12.7 ± 3.60	11.7 ± 2.30
Creatinine (µmol/L)	64 ± 3.60	65 ± 7,00
Fasting glucose (mg/dL)	85.28 ± 21.18	84.28 ± 22.62
Fasting insulin (mg/dL)	6.25 ± 2.21	8.33 ± 2.77
HOMA-IR	1.38 ± 0.66	1.72 ± 0.77
IL-1α (pg/mL)	2.74 ± 0.68	2.70 ± 0.83
IL-1β (pg/mL)	1.17 ± 0.55	0.83 ± 0.35
IL-6 (pg/mL)	1.81 ± 2.35	1.22 ± 1.75
TNF-α (pg/mL)	0.16 ± 0.10	0.13 ± 0.13
IL-1Ra (pg/mL)	80.94 ± 19.79	54.14 ±13.12**

[§]All values are arithmetic ± SD. *$p \leq 0.05$; **$p \leq 0.01$ (paired *t*-test). T0, baseline; T1, after 7-d DC consumption; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; BUN, Blood Urea Nitrogen; ESR, Erythrocyte Sedimentation Rate; hs-CRP, high sensitivity C-Reactive Protein; HOMA-IR Homeostasis Model Assessment of Insulin Resistance.

Di Renzo *et al. Journal of Translational Medicine* _####################_
DOI 10.1186/s12967-015-0484-2

JOURNAL OF TRANSLATIONAL MEDICINE

METHODOLOGY Open Access

Food safety and nutritional quality for the prevention of non communicable diseases: the Nutrient, hazard Analysis and Critical Control

Journal of Translational Medicine 2015, **13**:128 doi:10.1186/s12967-015-0484-2

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Abstract (provisional)

Background The important role of food and nutrition in public health is being increasingly recognized as crucial for its potential impact on health-related quality of life and the economy, both at the societal and individual levels. The prevalence of non-communicable diseases calls for a reformulation of our view of food. The Hazard Analysis and Critical Control Point (HACCP) system, first implemented in the EU with the Directive 43/93/CEE, later replaced by Regulation CE 178/2002 and Regulation CE 852/2004, is the internationally agreed approach for food safety control. Our aim is to develop a new procedure for the assessment of the Nutrient, hazard Analysis and Critical Control Point (NACCP) process, for total quality management (TMQ), and optimize nutritional levels. Methods NACCP was based on four general principles: i) guarantee of health maintenance; ii) evaluate and assure the nutritional quality of food and TMQ; iii) give correct information to the consumers; iv) ensure an ethical profit. There are three stages for the application of the NACCP process: 1) application of NACCP for quality principles; 2) application of NACCP for health principals; 3) implementation of the NACCP process. The actions are: 1) identification of nutritional markers, which must remain intact throughout the food supply chain; 2) identification of critical control points which must monitored in order to minimize the likelihood of a reduction in quality; 3) establishment of critical limits to maintain adequate levels of nutrient; 4) establishment, and implementation of effective monitoring procedures of critical control points; 5) establishment of corrective actions; 6) identification of metabolic biomarkers; 7) evaluation of the effects of food intake, through the application of specific clinical trials; 8) establishment of procedures for consumer information; 9) implementation of the Health claim Regulation EU 1924/2006; 10)starting a training program. Results and discussion We calculate the risk assessment as follows: Risk (R) = probability (P) x damage (D). The NACCP process considers the entire food supply chain "from farm to consumer"; in each point of the chain it is necessary implement a tight monitoring in order to guarantee optimal nutritional quality.

Review Article

The influence of Mediterranean, carbohydrate and high protein diets on gut microbiota composition in the treatment of obesity and associated inflammatory state

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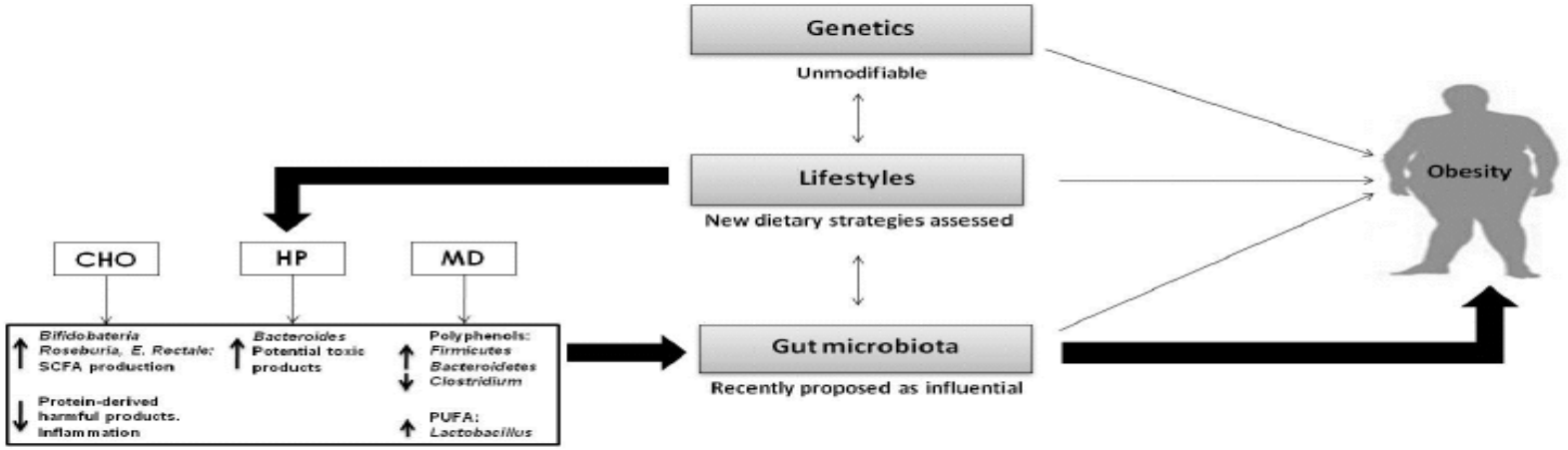

Figure 1. Interplay between genetics, lifestyles and microbiota in the obesity development. Role of specific dietary components on bacterial composition. CHO: carbohydrates; HP: high protein; MD: mediterranean diet; SCFA: short chain fatty acids; PUFA: polyunsaturated fatty acids.

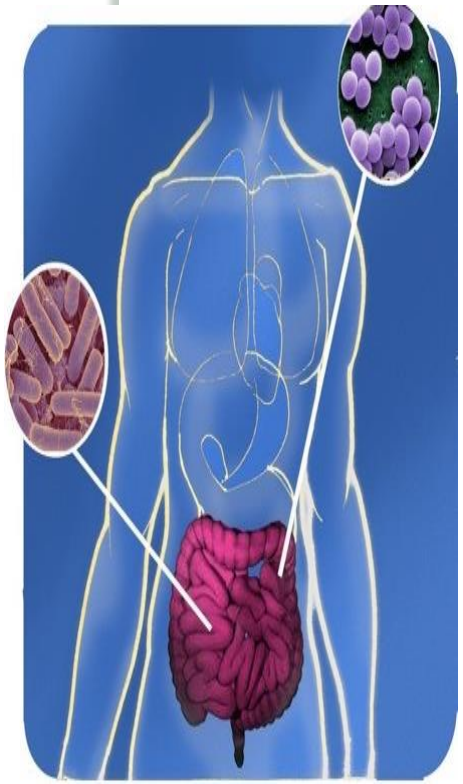

Table 1. Shifts in gut microbiota derived from different dietary strategies of dietary modifications.

Dietary strategy	Basis/Mechanism	Affected species	Observed effects	References
Carbohydrate ↓	Related with beneficial effects because of the association with SCFA production and phenolic compounds, known to have anti-inflammatory effects.	*Bifidobacteria* ↓ *Clostridium* ↓ *Bacteroidetes* ↓	Decrease SCFA: Butyrate production. Decrease fiber-derived phenolic acids.	33, 34, 35, 36
Protein ↑	Proteolitic fermentation produces beneficial compounds, but putrefaction is considered detrimental for the host's health.	*Bacteroidetes* ↑ *Lactobacillus* ↑ *Bifidobacterium* ↑	Amelioration of obesity, inflammation and metabolic complications.	11, 31, 35
Mediterranean ↑	Widely accepted as a healthy dietary pattern, with many specific components (polyphenols, PUFA).	Polyphenols: *Prevotella* ↑ *Enterococcus* ↑ *Bifidobacteria* ↑ *Lactobacillus* ↑ *Bacteroides* ↑ *Clostridium* ↓ PUFA: *Lactobacillus* ↑	Improvement of obesity, lipid profile and inflammation. An adults' microbiome is not particularly enriched in genes involved in fatty acid metabolism.	6, 8, 52, 53, 54

SCFA: short chain fatty acids; PUFA: polyunsaturated fatty acids.

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Journal of Translational Medicine

REVIEW Open Access

Why primary obesity is a disease?

Antonino De Lorenzo[1], Santo Gratteri[2], Paola Gualtieri[1*], Andrea Cammarano[1], Pierfrancesco Bertucci[3] and Laura Di Renzo[1]

Abstract

Obesity must be considered a real pathology. In the world wide, obesity represent one of the major public health issue associated with increased morbidity and mortality. Overweight or obesity, in fact, significantly increases the risk of contracting diseases, such as: arterial hypertension, dyslipidemia, type 2 diabetes mellitus, coronary heart disease, cerebral vasculopathy, gallbladder lithiasis, arthropathy, ovarian polycytosis, sleep apnea syndrome, and some neoplasms. Despite numerous informative campaigns, unfortunately, the fight against obesity does not seem to work: in the last years, the prevalence continued to increase. The progressive and rapid increase in the incidence of obesity, which has characterized most of the economically advanced countries in the last decade, has been the main stimulus for the research of the mechanisms underlying this pathology and the related disorders. The aims of this review is to provide a revision of the literature in order to define obesity as diseases, secondly to highlight the limits and the inaccuracy of common tools used for the diagnosis of obesity, and as a third thing to strengthen the concept of the complexity of obesity as a disease among political health care providers. Obesity may be viewed as a multifactorial pathology and chronic low-grade inflammatory disease. In fact, people affected by obesity have greater risk of developing comorbility and morbility, respect to healthy. Hence, the absolute therapeutic benefit is directly proportional to the basic risk. So, internationally interest on early diagnosis of obesity is growing to avoid under- and overdiagnosis consequences. Therefore, the consequences are an aggravation of the disease and an increase in obesity related pathology like diabetes, cardiovascular disease, and cancer. The most widely used parameter for diagnosis, body mass index (BMI) is not suitable for assessing the body fat. In fact, several studies demonstrate that BMI alone cannot define obesity, which consists not so much in weight gain as in excess fat mass. The use of suitable tools for the assessment of fat mass percentage combined with clinical and genetic analysis allowed to identify different phenotypes of obesity, which explain the various paradoxes of obesity. It is essential to adopt all possible strategies to be able to combat obesity, ameliorate the suffering of patients, and reduce the social and treatment costs of obesity.

Keywords: Obesity, Pathology, Phenotype, Obesity paradox

World Journal of Gastroenterology

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TOPIC HIGHLIGHT

2016 Laparoscopic Surgery: Global view

New obesity classification criteria as a tool for bariatric surgery indication

Antonino De Lorenzo, Laura Soldati, Francesca Sarlo, Menotti Calvani, Nicola Di Lorenzo, Laura Di Renzo

	MUO	MHO	MONW	NWO	NWL
BMI (kg/m^2)	27.9 ± 4.6[147]	32.3 - 33.3[191]	22.5 ± 2.0[168]	22.6 ± 1.9[147]	19.2 ± 1.5[147]
Waist (cm)	85.8 ± 10.2[147]	101.9 - 105.3[191]	77.5 ± 0.3[174]	72.3 ± 4.9[147]	65.1 ± 3.9[147]
Fat mass (%)	42.9 ± 7.3[147]	38.3 ± 18.5[171]	31.8 ± 5.9[168]	34.9 ± 5.0[147]	23.3 ± 2.2[147]
Glucose (mmol/L)	5.4 ± 0.11[147]	4.90 - 5.05[191]	4.4 ± 0.4[168]	5.1 ± 0.16[147]	5.20 ± 0.18[147]
Total cholesterol (mmol/L)	5.65 ± 0.63[147]	4.80 - 5.16[191]	5.3 ± 0.9[168]	4.87 ± 0.67[147]	4.60 ± 0.45[147]
High-density lipoprotein (mmol/L)	1.82 ± 0.51[147]	1.39 - 1.49[191]	1.7 ± 0.5[168]	1.76 ± 0.32[147]	1.79 ± 0.17[147]
Low-density lipoprotein (mmol/L)	3.00 ± 0.91[147]	2.89 - 3.18[191]	3.1 ± 0.9[168]	2.69 ± 0.63[147]	2.77 ± 0.90[147]
Triglycerides (mmol/L)	1.26 ± 0.19[147]	1.03 - 1.24[191]	2.4 ± 0.7[168]	0.97 ± 0.16[147]	0.75 ± 0.12[147]
Insuline (pmol/L)	63.2 ± 7.6[147]	61.8 - 66.6[191]	60 ± 20[168]	44.4 ± 12.5[147]	45.8 ± 9.7[147]
hs-CRP (mg/L)	-	0.8 - 2.7[195]	0.6 - 2.2[195]	-	0.5 - 1.6[195]

	NWL	NWO	MONW	MHO	MUO
BMI (kg/m^2)	22.4 - 22.7[191]	24.1 ± 0.7[156]	22.87 ± 0.07[174]	32.3 - 33.3[191]	31.59 ± 0.74[203]
Waist (cm)	83.8 - 85.2[191]	89.4 ± 1.6[156]	82.5 ± 0.3[174]	108.3 - 112.1[191]	108 ± 7[172]
Fat mass (%)	19.4 ± 0.2[174]	26.4 ± 1.3[156]	22.3 ± 0.2[174]	31.1 ± 3.4[181]	26.44 ± 0.53[203]
Glucose (mmol/L)	5.1 - 5.2[191]	2.53 ± 0.19[156]	5.38 ± 0.02[174]	5.1 - 5.3[191]	5.44 ± 0.10[203]
Total cholesterol (mmol/L)	4.8 - 5.0[191]	5.09 ± 0.72[156]	5.08 ± 0.04[174]	4.8 - 5.2[191]	5.11 ± 0.99[203]
High-density lipoprotein (mmol/L)	1.3 - 1.4[191]	1.23 ± 0.24[156]	1.18 ± 0.01[174]	1.2 - 1.3[191]	1.23 ± 0.36[203]
Low-density lipoprotein (mmol/L)	4.8 - 5.0[191]	3.09 ± 0.62[156]	2.73 ± 0.04[174]	4.8 - 5.2[191]	3.20 ± 0.94[203]
Triglycerides (mmol/L)	1.1 - 1.3[191]	3.84 ± 1.77[156]	2.47 - 2.64[174]	1.2 - 1.4[191]	1.86 ± 0.19[203]
Insuline (pmol/L)	44.5 - 48.1[191]	42.3 ± 19.4[156]	52.8 - 55.8[174]	63.1 - 73.2[191]	16.37 ± 1.76[203]
hs-CRP (mg/L)	0.5 - 1.6[195]	-	0.6 - 2.2[195]	0.8 - 2.7[195]	-

Figures 2 Characteristic of the four obese phenotypes. A: Women; B: Men. NWO: Normal weight obese; MONW: metabolically obese normal weight; MHO: metabolically healthy obese; MUO: metabolically unhealthy obese; BMI: body mass index; hsP: High-sensitive C-reactive protein. Data are expressed as average ± SD (a ± b), or as minimum-maximum (a - b), according to the references.

Metabolically Obese Normal Weight (MONW)

Metabolically Healthy

High Visceral Fat
Low BMI
High Fat mass
Low Lean Body Mass
Low Insulin Sensitivity
High Liver Fat
High Triglycerides

Low Visceral Fat
Low BMI
Low Fat mass
High Lean Body Mass
High Insulin Sensitivity
Low Liver Fat
Low Triglycerides

Metabolically Healthy Obese (MHO)

"At Risk" Obese

Low Visceral Fat
High BMI
High Fat mass
High Insulin Sensitivity
High HDL
Low Triglycerides

High Visceral Fat
High BMI
High Fat mass
Low Insulin Sensitivity
Low HDL
High Triglycerides

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Normal weight obese (NWO) women: An evaluation of a candidate new syndrome

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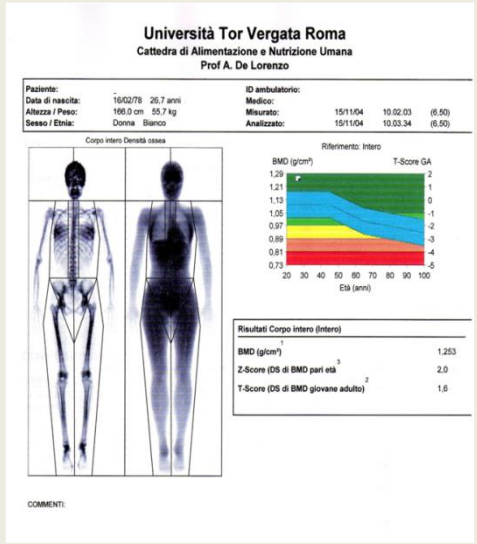
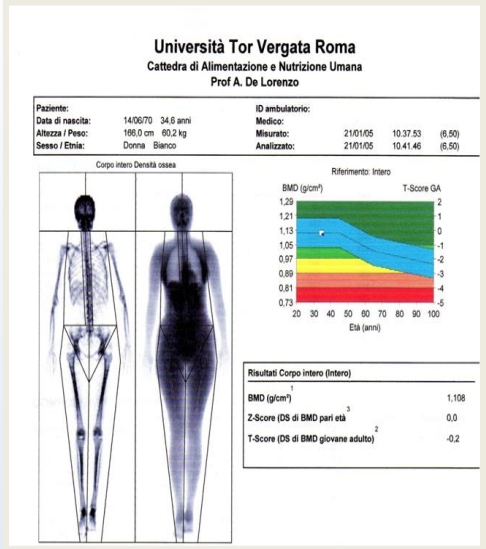
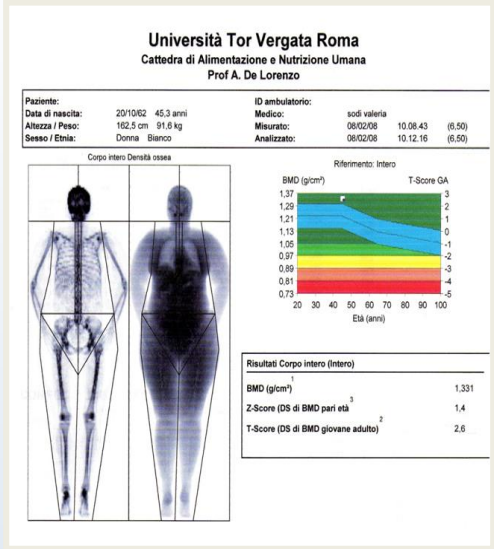
Normal weight



NWO



Preobese-obese



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Normal weight obese (NWO) women: An evaluation of a candidate new syndrome

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Control	Normal Weight Obese (NWO)	PreObese-Obese
		
BMI 18÷25 kg/m²	BMI 18÷25 kg/m²	BMI > 25 kg/m²
FM < 30%	FM > 30%	FM > 30%
LEANLEGL = 6.97±0.90 kg	LEANLEGL = 6.08±0.54 kg	LEANLEGL = 6.48±0.88
RMR = 1389.20±132.49 kcal/day	RMR = 1225.14±342.55kcal/day	RMR=1442.05 ±319.01 kcal/day
CVD Risk Indexes:	CVD Risk Indexes:	CVD Risk Indexes:
TC/HDL chol = 2.56 ±0.54	TC/HDL chol = 3.46±1.25	TC/HDL chol = 3.64±0.83
LDL/HDL chol = 1.29 ±0.37	LDL/HDL chol = 2.14 ±1.19	LDL/HDL chol = 2.22 ±0.68
TG/HDL chol = 0.78 ±0.33	TG/HDL chol = 0.72 ±0.61	TG/HDL chol = 1.00 ±0.41

European Heart Journal Advance Access published November 20, 2009

European Heart Journal
doi:10.1093/eurheartj/ehp487

CLINICAL RESEARCH

Normal weight obesity: a risk factor for cardiometabolic dysregulation and cardiovascular mortality

Abel Romero-Corral[1], Virend K. Somers[1], Justo Sierra-Johnson[2], Yoel Korenfeld[1], Simona Boarin[3], Josef Korinek[1], Michael D. Jensen[1], Gianfranco Parati[3], and Francisco Lopez-Jimenez[1]*

Aims We hypothesized that subjects with a normal body mass index (BMI), but high body fat (BF) content [normal weight obesity (NWO)], have a higher prevalence of cardiometabolic dysregulation and are at higher risk for cardiovascular (CV) mortality.

Methods and results We analysed 6171 subjects >20 years of age from the Third National Health and Nutrition Examination Survey (NHANES III) and the NHANES III mortality study, whose BMI was within the normal range (18.5–24.9 kg/m^2), and who underwent a complete evaluation that included body composition assessment, blood measurements, and assessment of CV risk factors. Survival information was available for >99% of the subjects after a median follow-up of 8.8 years. We divided our sample using sex-specific tertiles of BF%. The highest tertile of BF (>23.1% in men and >33.3% in women) was labelled as NWO. When compared with the low BF group, the prevalence of metabolic syndrome in subjects with NWO was four-fold higher (16.6 vs. 4.8%, $P < 0.0001$). Subjects with NWO also had higher prevalence of dyslipidaemia, hypertension (men), and CV disease (women). After adjustment, women with NWO showed a significant 2.2-fold increased risk for CV mortality (HR = 2.2; 95% CI, 1.03–4.67) in comparison to the low BF group.

Conclusion Normal weight obesity, defined as the combination of normal BMI and high BF content, is associated with a high prevalence of cardiometabolic dysregulation, metabolic syndrome, and CV risk factors. In women, NWO is independently associated with increased risk for CV mortality.

Conclusions: NWO is associated with a high prevalence of cardiometabolic dysregulation, metabolic syndrome and CV risk factors. In women, NWO is independently linked to increased risk for CV mortality.

Eat Weight Disord
DOI 10.1007/s40519-015-0215-y

ORIGINAL ARTICLE

Association of body composition and eating behavior in the normal weight obese syndrome

Laura Di Renzo[1] · Elaine Tyndall[1] · Paola Gualtieri[1] · Chiara Carboni[1] · Roberto Valente[1] · Alessia Sabrina Ciani[1] · Maria Giovanna Tonini[1] · Antonino De Lorenzo[1,2]

Table 2 Comparison of normal weight lean, normal weight obese and pre-obese/obese groups of women

Subscale EDI-2	NWL (n = 18) Mean ± SD (min–max)	NWO (n = 38) Mean ± SD (min–max)	PreOB/OB (n = 23) Mean ± SD (min–max)	p
DT	2.89 ± 4.63 (0.00–20.00)	6.16 ± 6.58 (0.00–21.00)	**8.38 ± 7.61**[a,b] (0.00–18.00)	0.003
B	1.00 ± 2.45 (0.00–10.00)	0.92 ± 1.60 (0.00–7.00)	**3.42 ± 4.02**[c,d] (0.00–16.00)	<0.001
BD	5.28 ± 6.09 (0.00–23.00)	9.95 ± 7.66 (0.00–27.00)	**13.92 ± 7.05**[e,f] (0.00–24.00)	<0.001
I	1.39 ± 2.20 (0.00–6.00)	3.26 ± 4.40 (0.00–18.00)	**5.46 ± 5.99**[g] (0.00–20.00)	<0.001
P	3.83 ± 3.54 (0.00–14.00)	4.79 ± 3.15 (0.00–12.00)	3.46 ± 3.96 (0.00–16.00)	0.977
ID	2.22 ± 2.49 (0.00–9.00)	3.47 ± 3.49 (0.00–16.00)	3.96 ± 3.65 (0.00–11.00)	0.138
IA	3.28 ± 3.86 (0.00–11.00)	4.63 ± 5.95 (0.00–25.00)	**6.08 ± 6.38**[h,i] (0.00–24.00)	0.009
MF	7.78 ± 5.15 (1.00–21.00)	5.55 ± 3.46 (0.00–14.00)	5.83 ± 4.59 (1.00–20.00)	0.599
A	3.56 ± 2.57 (0.00–9.00)	3.34 ± 1.92 (0.00–7.00)	**5.13 ± 2.89**[l,m] (1.00–12.00)	<0.001
IR	1.50 ± 2.20 (0.00–8.00)	3.50 ± 4.29 (0.00–16.00)	2.83 ± 3.67 (0.00–14.00)	0.508
SI	2.28 ± 2.02 (0.00–7.00)	4.21 ± 3.25 (0.00–15.00)	4.29 ± 3.91 (0.00–14.00)	0.414

Values of $p < 0.05$ are considered significant

Bold values indicate statistically significant results

NWL normal weight lean, *NWO* normal weight obese, *PreOB/OB* Pre-obese/obese, *EDI-2* eating disorder inventory-2, *DT* drive for thinness, *B* bulimia, *BD* body dissatisfaction, *I* ineffectiveness, *P* perfectionism, *ID* interpersonal distrust, *IA* interoceptive awareness, *MF* maturity fears, *A* asceticism, *IR* impulse regulation, *SI* social insecurity, *SD* standard deviation

[a,c,e,g,h] NWL vs PreOB/OB $p < 0.05$

[b,d,f,i] NWO vs PreOB/OB $p < 0.05$

[l] NWL vs PreOB/OB $p = 0.006$

[m] NWO vs PreOB/OB $p < 0.001$

Normal-weight obese syndrome: early inflammation?[1–3]

Antonino De Lorenzo, Vera Del Gobbo, Maria Grazia Premrov, Mario Bigioni, Fabio Galvano, and Laura Di Renzo

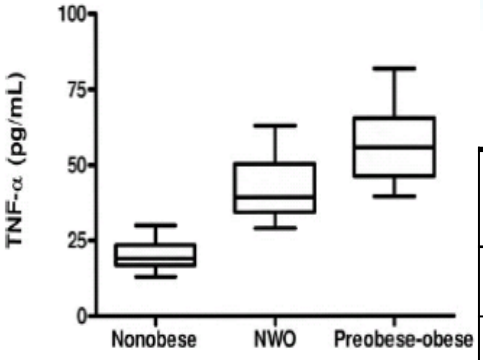


FIGURE 1. Plasma tumor necrosis factor α (TNF-α) concentrations in nonobese (n = 20), normal-weight obese (NWO; n = 20), and preobese-obese (n = 20) women. The plasma concentration was measured in duplicate by using the multiplex sandwich enzyme-linked immunosorbent assay (SearchLight Human Inflammatory Cytokine Array; Endogen, Perbio, IL). The lower limit of detection for the assay was 1.6 pg/mL. Differences between groups were assessed by using Tukey's test. Nonobese compared with NWO: $P < 0.001$; nonobese compared with preobese-obese: $P < 0.001$; NWO compared with preobese-obese: NS.

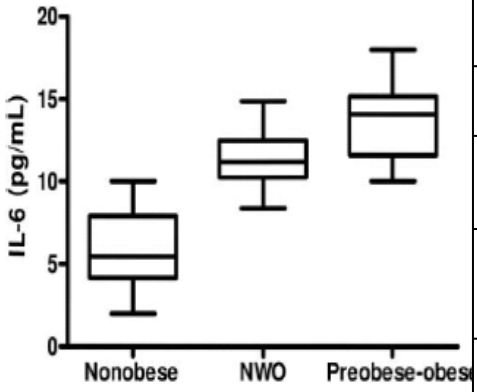


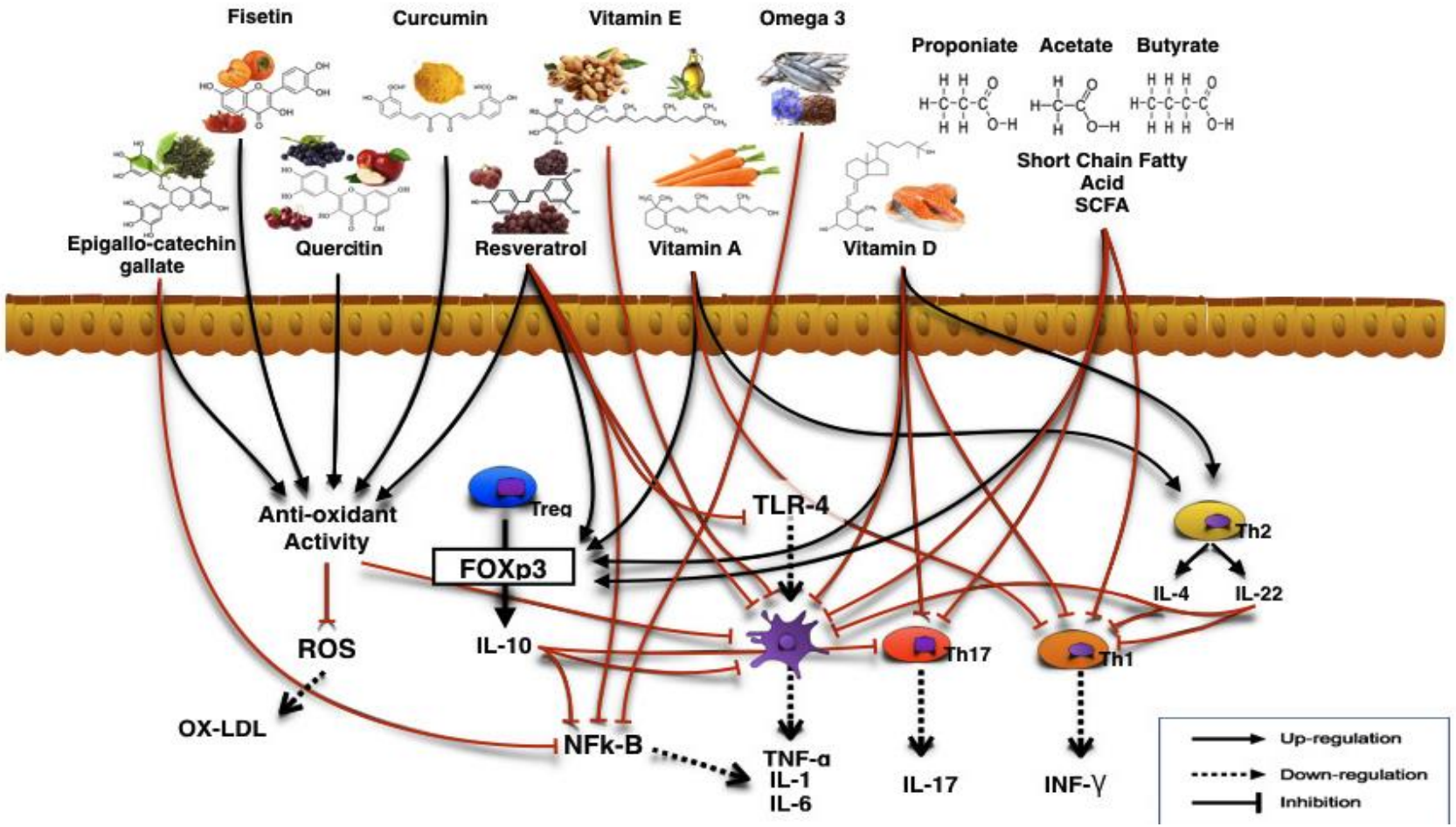
FIGURE 2. Plasma interleukin 6 (IL-6) concentrations in nonobese (n = 20), normal-weight obese (NWO; n = 20), and preobese-obese (n = 20) women. The plasma concentration was measured in duplicate by using the multiplex sandwich enzyme-linked immunosorbent assay (SearchLight Human Inflammatory Cytokine Array; Endogen, Perbio, IL). The lower limit of detection for the assay was 0.2 pg/mL. Differences between groups were assessed by using Tukey's test. Nonobese compared with NWO: $P < 0.001$; nonobese compared with preobese-obese: $P < 0.001$; NWO compared with preobese-obese: NS.

Cytokine	Control	NWO	Preobese-Obese
IL-1 α	14.8 ± 1.8[a]	26.9 ± 4.5[b]	29.8 ± 5.3[b]
IL-1 β	5.0 ± 2.6[a]	15.0 ± 3.1[b]	19.0 ± 4.1[b]
IL-2	12.3 ± 1.5[a]	14.7 ± 3.6[a]	16.6 ± 3.9[a]
IL-6	5.950 ± 2.28[a]	11.42 ±1.77 [b]	13.68 ± 2.29[b]
IL-8	0.9 ± 0.2[a]	2.39 ± 0.62[b]	2.0 ± 0.7[b]
IL-10	3.4 ± 0.8[a]	3.83 ± 1.3[a]	4.7 ± 1.9[a]
IL-12p70	14.2 ± 2.2[a]	19.1 ± 3.7[a]	32.96 ± 4.6[b]
TNF α	20.10 ± 4.95[a]	42.77 ± 10.54[b]	56.37 ± 11.77[b]
INF- γ	17.7 ± 4.8[a]	25.3 ± 5.3[a]	39.93 ± 6.1[b]

Am J Clin Nutr 2007;85:40–5. Printed in USA.

"The influence of diet on anti-cancer immune responsiveness"

Soldati L., Di Renzo L., Jirillo E., Ascierto P.A., Marincola F.M., De Lorenzo A. JTM 2017



Forkhead box P3(FOXP3); Helper T cell (Th);Interferon-γ (INF-γ);Interleukin (IL); Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) ;Oxidized Low-Density Lipoprotein (OX-LDL); Reactive oxygen species (ROS); Regulatory T cell (Treg) Toll like receptor (TLR); Tumor necrosis factor α (TNF-α).

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo[a], Duccio Cavalieri[a], Monica Di Paola[b], Matteo Ramazzotti[c], Jean Baptiste Poullet[d], Sebastien Massart[d], Silvia Collini[b], Giuseppe Pieraccini[e], and Paolo Lionetti[b,1]

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PNAS

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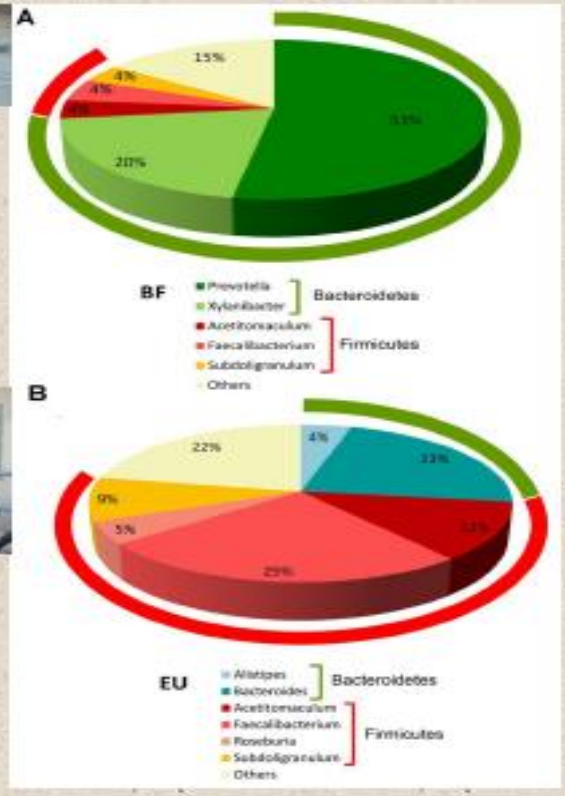
In This Issue

The effect of diet on human gut microbial composition

The trillions of microbes that inhabit the human gut are considered an essential "organ" that helps to digest food, protect against pathogens, and limit inflammation, but researchers do not yet fully understand how environment and diet affect the gut's microbial ecology. Carlotta De Filippo et al. (pp. 14691–14696) used rDNA sequencing and biochemical analysis to compare the fecal microbiota of 15 children, aged 1 to 6 years, from a rural African village with a similar population of children from Florence, Italy. The researchers found that the African children had a lower proportion of microbes associated with obesity in adults, and greater abundance of fatty acids known to protect against inflammation. The African children's diet, which may resemble human diets shortly after the birth of agriculture, consisted mainly of cereals, legumes, and vegetables, whereas the Italian children ate higher quantities of meat, fat, and sugar. Only children who were still breast-feeding harbored bacterial compositions that resembled children from the other geographical group, indicating that diet may supersede factors such as ethnicity, sanitation, geography, or climate, according to the authors. They suggest that diets common to industrialized nations may reduce microbial richness, potentially contributing to a rise in allergic and inflammatory diseases in the last half-century. — J.M.

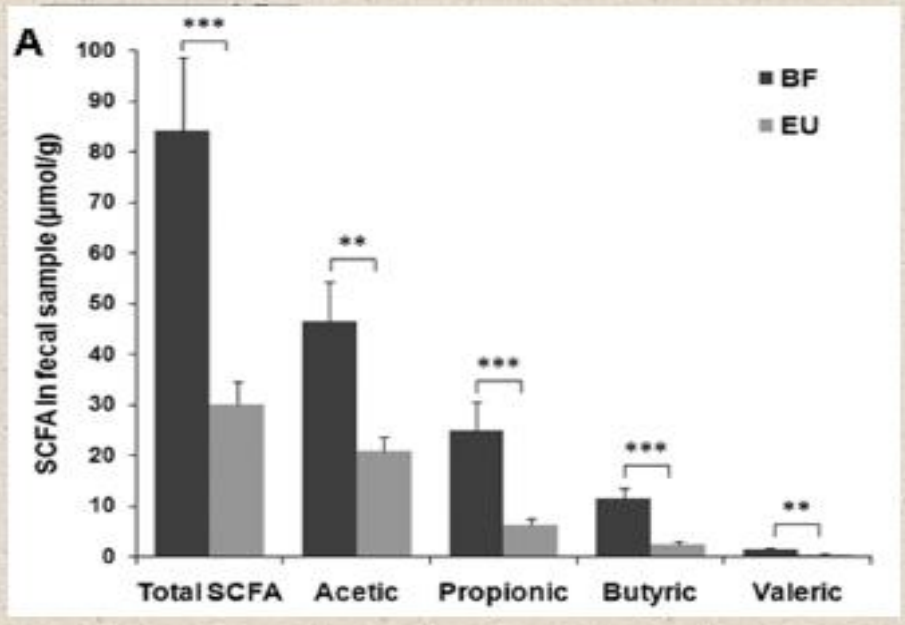
Millet and sorghum grain and flour.

Top 10 Most Cited



Xylanibacter ia una dieta ricca in fibre e polisaccaridi di piante

Porta a un aumento di acidi grassi a catena corta che prevengono l'insorgenza di malattie



De Filippo et al. Proc Natl Acad Sci USA. 2010, 107:14691-6.

REVIEW 10.1111/1469-0691.12172

Gut bacterial microbiota and obesity

M. Million[1], J.-C. Lagier[1], D. Yahav[2] and M. Paul[2]

1) *Unité de Recherche sur les Maladies Infectieuses et Tropicales Emergentes, Faculté de Médecine, CNRS UMR 7278, IRD 198, Aix-Marseille Université, Marseille, France and 2) Unit of Infectious Diseases, Rabin Medical Centre, Beilinson Hospital and Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel*

Abstract

Although probiotics and antibiotics have been used for decades as growth promoters in animals, attention has only recently been drawn to the association between the gut microbiota composition, its manipulation, and obesity. Studies in mice have associated the phylum *Firmicutes* with obesity and the phylum *Bacteroidetes* with weight loss. Proposed mechanisms linking the microbiota to fat content and weight include differential effects of bacteria on the efficiency of energy extraction from the diet, and changes in host metabolism of absorbed calories. The independent effect of the microbiota on fat accumulation has been demonstrated in mice, where transplantation of microbiota from obese mice or mice fed western diets to lean or germ-free mice produced fat accumulation among recipients. The microbiota can be manipulated by prebiotics, probiotics, and antibiotics. Probiotics affect the microbiota directly by modulating its bacterial content, and indirectly through bacteriocins produced by the probiotic bacteria. Interestingly, certain probiotics are associated with weight gain both in animals and in humans. The effects are dependent on the probiotic strain, the host, and specific host characteristics, such as age and baseline nutritional status. Attention has recently been drawn to the association between antibiotic use and weight gain in children and adults. We herein review the studies describing the associations between the microbiota composition, its manipulation, and obesity.

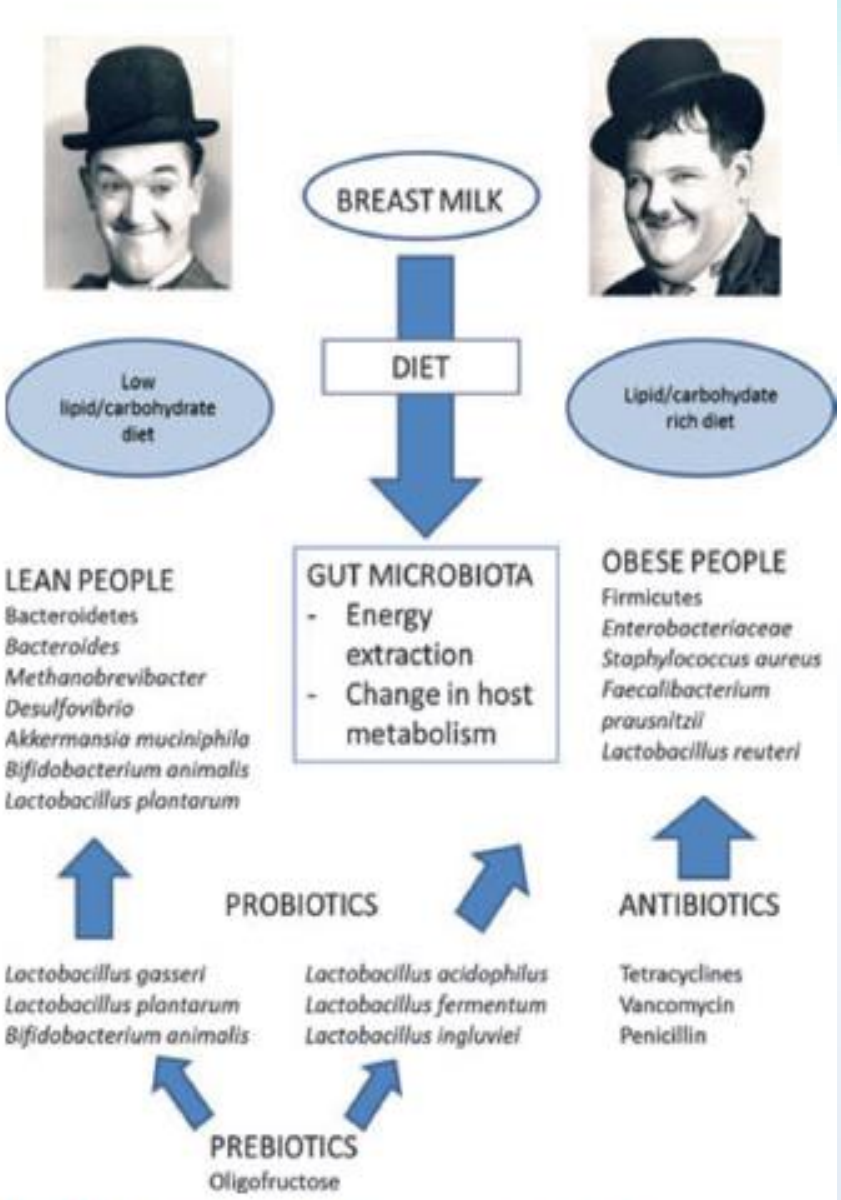


FIG. 1. Factors affecting gut microbiota and obesity.

PHYSIOLOGY

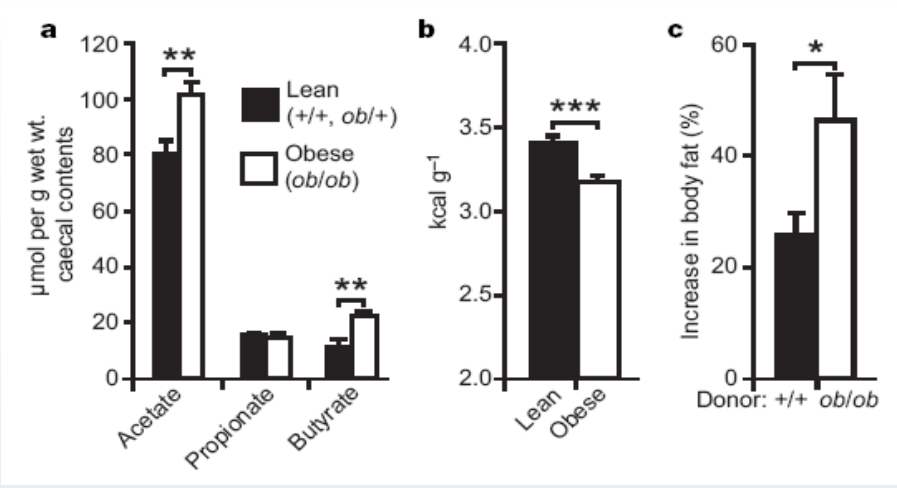
Obesity and gut flora

Matej Bajzer and Randy J. Seeley

Figure 1 | Home for an abundant microbiological flora. The human gut and (inset) a scanning electron micrograph of part of the small intestine, with some bacterial inhabitants picked out in green.

An obesity-associated gut microbiome with increased capacity for energy harvest

Peter J. Turnbaugh[1], Ruth E. Ley[1], Michael A. Mahowald[1], Vincent Magrini[2], Elaine R. Mardis[1,2] & Jeffrey I. Gordon[1]



Biochemical analysis and microbiota transplantation experiments confirm that the ob/ob microbiome has an increased capacity for dietary energy harvest.

Journal of Psychiatric Research 63 (2015) 1–9

Contents lists available at ScienceDirect

Journal of Psychiatric Research

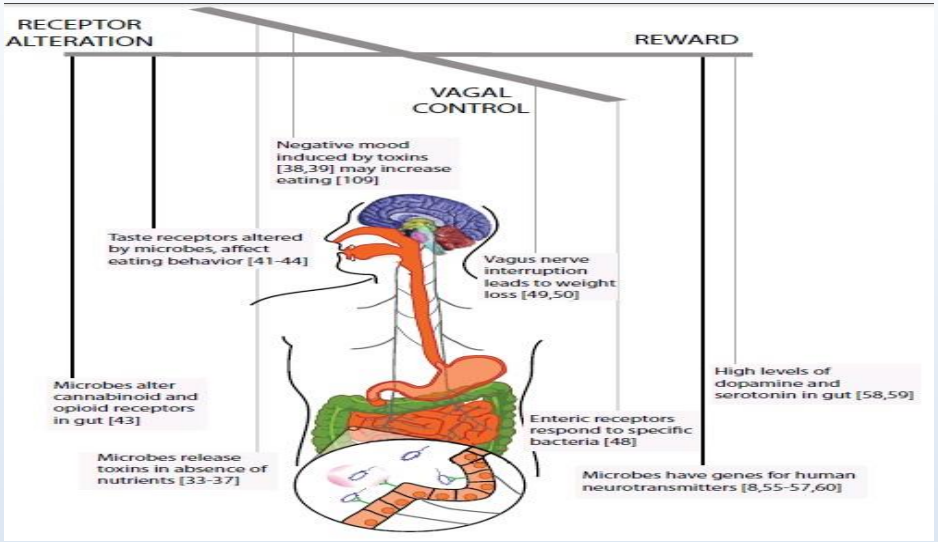
journal homepage: www.elsevier.com/locate/psychires

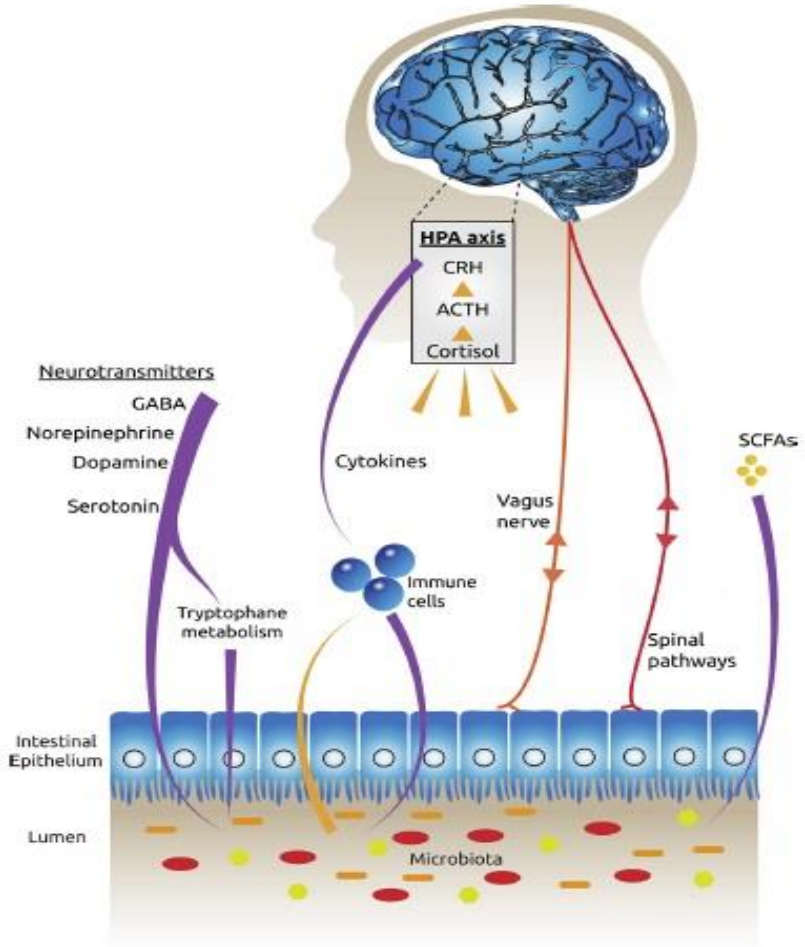
Review

Collective unconscious: How gut microbes shape human behavior

Timothy G. Dinan [a, b, *], Roman M. Stilling [a, d], Catherine Stanton [a, b, c], John F. Cryan [a, d]

The multiple bidirectional routes of communication between the brain and the gut microbiota. These routes include the vagus nerve, the hypothalamic-pituitary-adrenal axis (HPA), cytokines produced by the immune system, tryptophan metabolism and production of short chain fatty acids.





Behavioural Brain Research 356 (2019) 390–399

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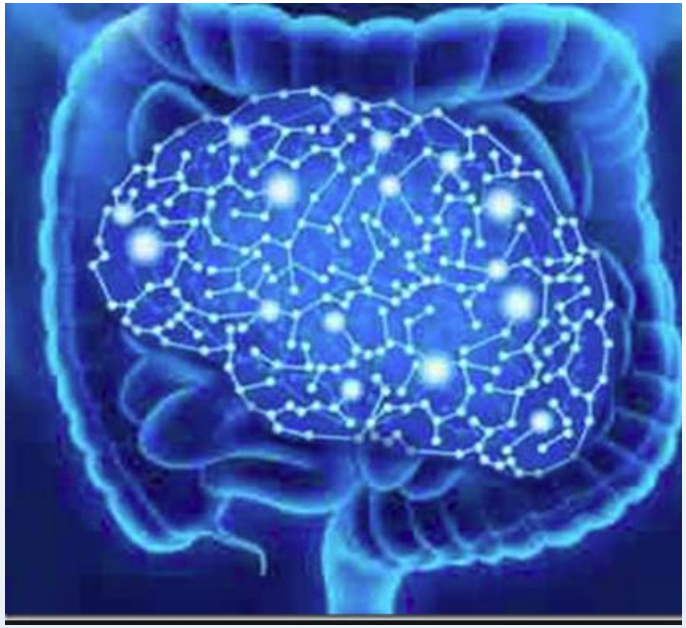
Behavioural Brain Research

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

Research report

Probiotics modify body weight together with anxiety states via pro-inflammatory factors in HFD-treated Syrian golden hamster

Ennio Avolio[a,b,*], Gilda Fazzari[a], Merylin Zizza[a], Antonino De Lorenzo[b], Laura Di Renzo[b], Raffaella Alò[a], Rosa Maria Facciolo[a], Marcello Canonaco[a]



3g/die:

- *Streptococcus thermophilus* (CNCM strain number I-1630) 1.5×10^{10} UFC
- *Lactobacillus bulgaricus* (CNCM strain numbers I-1632 and I-1519) 1.5×10^{10} UFC
- *Lactococcus lactis subsp lactis* (CNCM strain number I-1631) 1.5×10^{10} UFC *B*
- *lactis* (CNCM I-2494/DN-173 010) 1.2×10^{9} UFC *Lactobacillus acidophilus* 1.5×10^{10} UFC
- *Streptococcus thermophilus* 1.5×10^{10} UFC
- *Lactobacillus Plantarum* 1.5×10^{10} UFC
- *Bifidobacterium lactis* (CNCM I-2494) 1.5×10^{10} UFC *Lactobacillus Reuteri* (DSM 17938) $1.5 \times 1\ 1^{010}$ UFC

(Biocult strong, HOMEOSYN , Roma, Italia).

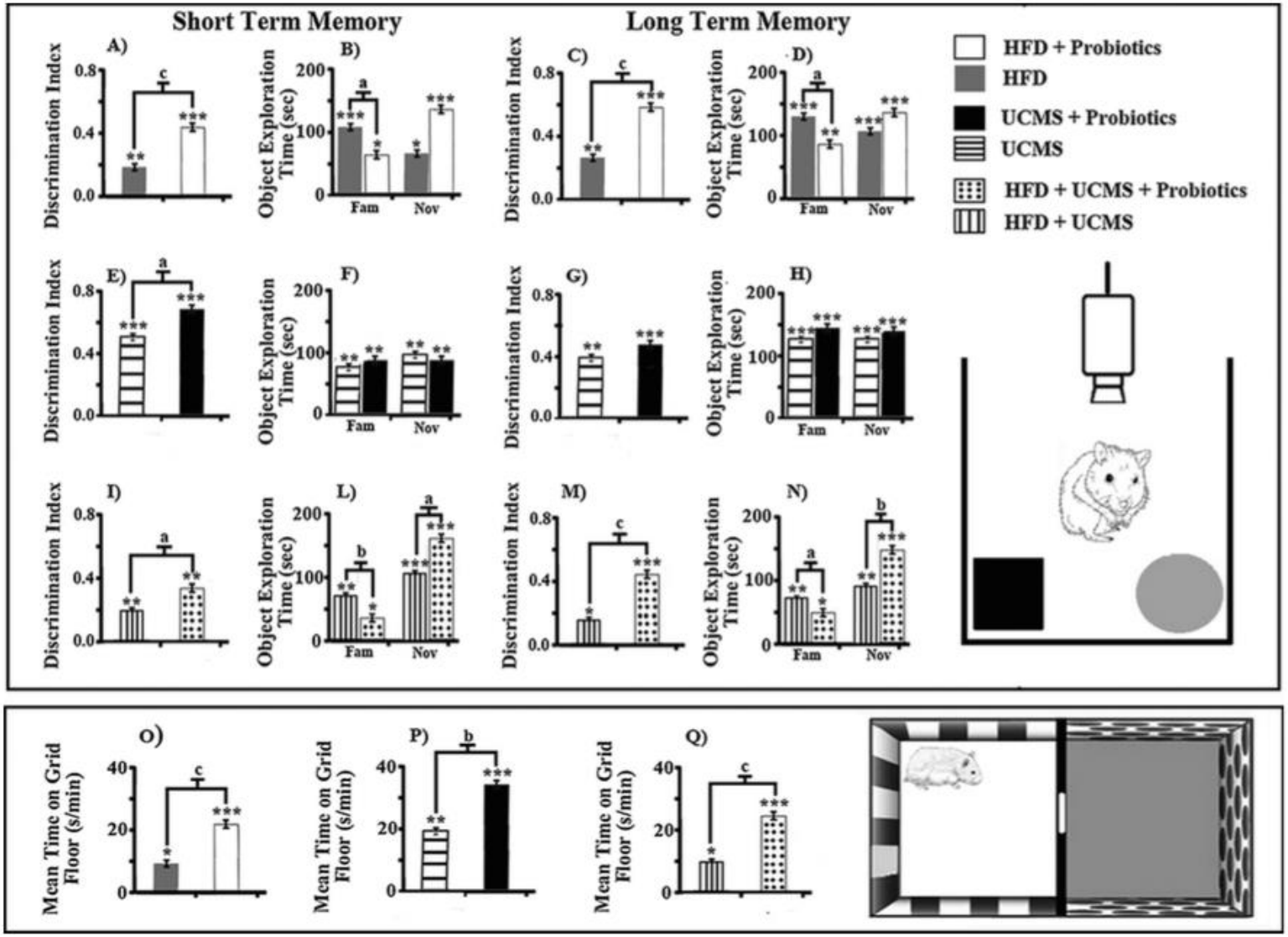


Fig. 2. Effects of probiotics on memory performances of hamsters.

Effects of treatments n = 6/treatment groups) on memory performances were evaluated in animals that received HFD + probiotics, HFD, UCMS + probiotics, UCMS, UCMS + HFD + probiotics, UCMS + HFD with respect to unstressed control (*) during Novel Object (A–N) plus Conditioned Place Preference Tests (O–Q). Animals treated with probiotics received a single daily dose directly dissolved in water (3 g/200 ml to each hamster per day). Each bar represents % mean ± S.E.M. of discrimination index (A, C, E, G, I, M) and object exploration time (B, D, F, H, L, N; short and long term memory) along with mean time on grid floor box (O, P, Q). Behavioral changes were determined by ANOVA plus a *post hoc* Newman–Keuls test when $p < 0.05$, $^{*,a}p < 0.05$, $^{**,b}p < 0.01$ and $^{***,c}p < 0.001$.

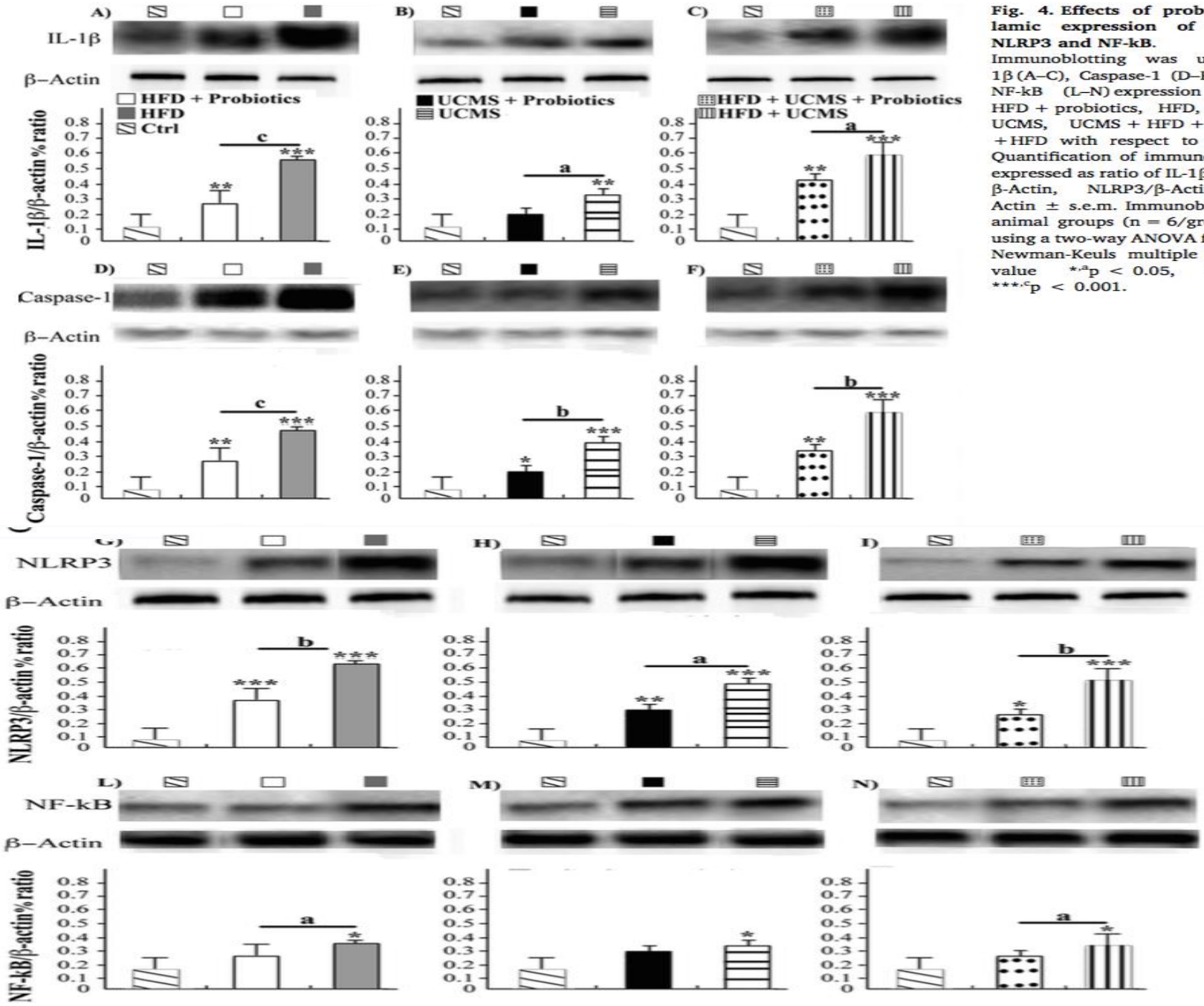


Fig. 4. Effects of probiotics on hypothalamic expression of IL-1β, Caspase-1, NLRP3 and NF-kB.

Immunoblotting was used to detect IL-1β (A–C), Caspase-1 (D–F), NLRP3 (G–I) and NF-kB (L–N) expression in the HTH of HFD + probiotics, HFD, UCMS + probiotics, UCMS, UCMS + HFD + probiotics, UCMSd + HFD with respect to unstressed controls. Quantification of immunoblotting results was expressed as ratio of IL-1β/β-Actin, Caspase-1/β-Actin, NLRP3/β-Actin and NF-kB/β-Actin ± s.e.m. Immunoblotting differences in animal groups (n = 6/group) were evaluated using a two-way ANOVA followed by a *post hoc* Newman-Keuls multiple range test when *p*-value $^{*,a}p < 0.05$, $^{**,b}p < 0.01$ and $^{***,c}p < 0.001$.

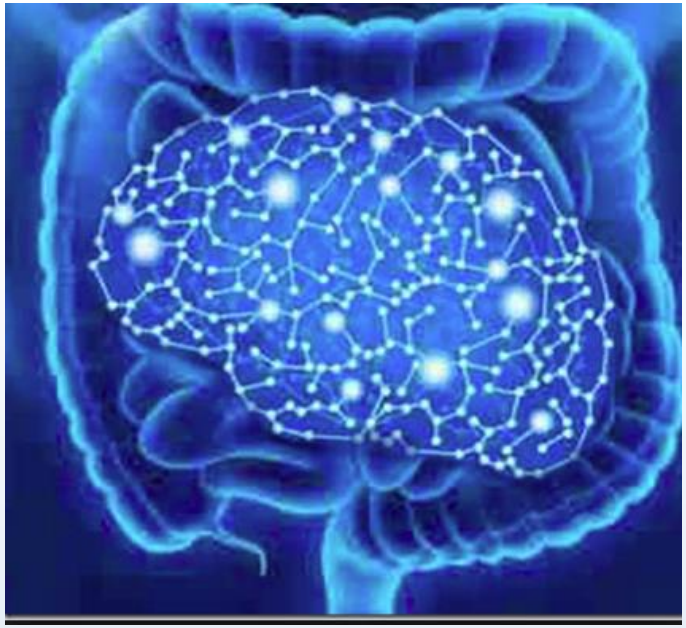
De Lorenzo *et al. J Transl Med* (2017) 15:135
DOI 10.1186/s12967-017-1236-2

Journal of Translational Medicine

RESEARCH Open Access

Can psychobiotics intake modulate psychological profile and body composition of women affected by normal weight obese syndrome and obesity? A double blind randomized clinical trial

Antonino De Lorenzo[1,8*], Micaela Costacurta[2], Giuseppe Merra[3], Paola Gualtieri[4], Giorgia Cioccoloni[4], Massimiliano Marchetti[5,6], Dimitrios Varvaras[7], Raffaella Docimo[2] and Laura Di Renzo[1]



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•*Lactococcus lactis subsp lactis* (CNCM strain number I-1631) 1.5 × 10^{10} UFC *B*

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(Biocult strong, HOMEOSYN , Roma, Italia).

Università di Roma Tor Vergata

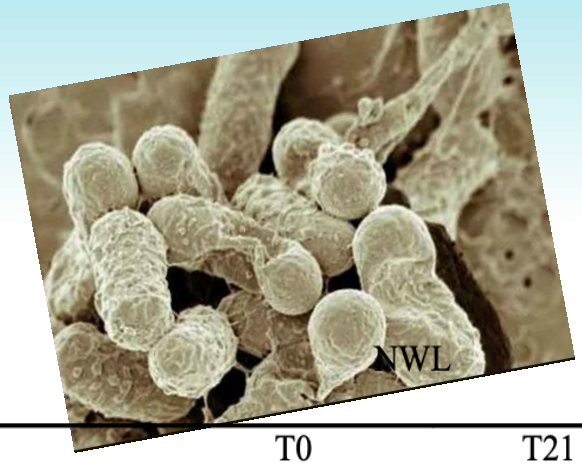
Table 1 Comparison of body composition parameters of normal weight lean, normal weight obese and pre-obese/obese groups between baseline and after 3 weeks POS treatment

	NWL		NWO		PreobOB	
	Baseline	POS	Baseline	POS	Baseline	POS
Age (years)	30.18 ± 2.04 (28.00–33.00)		40.00 ± 12.56 (27.00–56.00)		33.57 ± 10.57 (24.00–50.00)	
Height (cm)	164.64 ± 4.03 (160.00–170.00)		162.90 ± 6.60 (154.00–168.00)		158.33 ± 1.86 (155.60–160.00)	
Weight (kg)	55.55 ± 4.65[¤,°] (50.50–62.50)	54.84 ± 5.63[ϰ,ϑ] (49.20–63.00)	63.50 ± 3.97[¥] (59.00–68.30)	63.10 ± 3.27 (59.00–66.60)	69.47 ± 6.07 (63.80–78.00)	63.35 ± 0.16[b] (63.20–63.50)
BMI (kg/m^2)	20.47 ± 1.04[¤,°] (19.48–22.41)	20.49 ± 1.40[ϰ,ϑ] (18.98–22.59)	23.94 ± 0.93[¥] (22.74–24.88)	23.80 ± 0.84[a,ϭ] (22.92–24.88)	27.68 ± 1.92 (25.56–30.47)	25.78 ± 0.48[b] (25.32–26.23)
Waist (cm)	67.41 ± 4.22 (64.50–75.00)°	67.98 ± 4.60[ϰ,ϑ] (63.80–75.00)	74.25 ± 5.08 (69.50–79.00)	75.33 ± 4.70 (70.00–81.00)	80.17 ± 8.02 (73.00–91.00)	73.75 ± 2.35[b] (71.50–76.00)
Hip (cm)	94.09 ± 4.57 [¤,°] (87.00–97.00)	93.23 ± 4.35 [ϰ,ϑ] (87.50–97.00)	103.25 ± 5.61[¥] (98.00–108.50)	101.00 ± 3.72[ϭ] (98.00–106.00)	107.73 ± 0.54 (107.00–108.20)	106.75 ± 0.78[b] (106.00–107.50)
Resistance (Ohm)	595.89 ± 85.36 (501.00–735.00)	598.33 ± 69.50 [ϑ] (497.00–690.00)	576.67 ± 55.46 (526.00–650.00)	567.00 ± 53.60[a] (513.00–636.00)	565.13 ± 35.34 (526.00–611.00)	523.00 ± 24.02[b] (500.00–[illegible])
TBFat (%)	26.55 ± 2.83[¤,°] (24.10–29.00)	–	35.25 ± 1.44[¥] (33.90–36.60)	–	43.80 ± 0.00 (43.80–43.80)	–
TBFat (kg)	15.15 ± 0.01[¤,°] (15.14–15.16)	–	21.73 ± 1.73[¥] (20.11–23.34)	–	34.10 ± 0.00 (34.10–34.10)	–
TBLean (kg)	40.17 ± 5.98 (34.99–45.35)	–	37.61 ± 0.57 (37.08–38.14)	–	41.26 ± 0.00 (41.26–41.26)	–
FM (kg)	11.35 ± 2.86[¤,°] (8.10–15.10)	11.80 ± 3.12[c,ϰ,ϑ] (8.10–16.00)	18.00 ± 1.64 (15.90–19.70)	17.27 ± 1.80[a] (15.80–19.70)	18.65 ± 0.99 (17.70–19.60)	16.95 ± 0.99[b] (16.00–17.90)
FM (%)	20.30 ± 4.06[¤,°] (16.10–26.40)	21.05 ± 4.43[c,ϰ,ϑ] (16.50–27.80)	28.37 ± 2.09 (26.90–31.20)	27.57 ± 2.58[a] (25.00–30.90)	29.10 ± 1.36 (27.80–30.40)	26.70 ± 1.46[b] (25.30–28.10)
FFM (kg)	44.23 ± 3.57 (42.20–50.00)	43.75 ± 4.06 (41.10–50.30)	45.50 ± 3.25 (43.10–49.90)	45.83 ± 3.32[a] (43.20–50.30)	45.50 ± 0.63 (44.90–46.10)	46.40 ± 0.84[b] (45.60–47.20)
FFM (%)	79.70 ± 4.06[¤,°] (73.60–83.90)	78.95 ± 4.43[c,ϰ,ϑ] (72.20–83.50)	71.63 ± 2.09 (68.80–73.10)	72.43 ± 2.58[a] (69.10–75.00)	70.90 ± 1.36 (69.60–72.20)	73.30 ± 1.46[b] (71.90–74.70)

Results are expressed in mean value ± standard deviation, and minimum and maximum for each parameter. Values of $p < 0.05$ are considered significant

BMI body mass index, *ECW* extracellular water, *FM* fat mass, *FFM* fat free mass, *ICW* intracellular water, *NWL* normal weight lean, *NWO* normal weight obese, *PA* phase angle, *PreOB/OB* preobese–obese, *TB* total body, *TBW* total body water

[a] NWO T0 vs T1 $p < 0.05$; [b] PreOB/OB T0 vs T1 $p < 0.05$ [c] NWL T0 vs T1. For Anova-test at baseline $p < 0.05$; [¤] NWL vs NWO $p < 0.05$; [¥] NWO vs PreOB/OB $p < 0.05$; [°] NWL vs PreOB/OB $p < 0.05$. Anova-test after POS $p < 0.05$; [ϰ] NWL vs NWO $p < 0.05$; [ϭ] NWO vs PreOB/OB $p < 0.05$; [ϑ] NWL vs PreOB/OB $p < 0.05$



	NWL		NWO		PreOB/OB	
	T0	T21	T0	T21	T0	T21
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)
EDI-2_B	1.00±2.45 (0.00 - 10.00)	0.39±1.24 (0.00 - 5.00)	0.91±1.64 (0.00 - 7.00)	0.53±1.16 [a] (0.00 - 5.00)	3.64±4.12 (0.00 - 16.00)	2.50±2.89 [b] (0.00 - 10.00)
EDI-2_BD	5.28±6.09 (0.00 - 23.00)	4.94±6.01 (0.00 - 23.00)	9.29±7.81 (0.00 - 27.00)	7.50±7.18 [a] (0.00 - 25.00)	14.09±6.35 (2.00 - 24.00)	11.91±5.76 [b] (0.00 - 20.00)
EDI-2_I	1.39±2.20 (0.00 - 6.00)	1.22±1.90 (0.00 - 5.00)	3.26±4.29 (0.00 - 17.00)	1.62±2.85 [a] (0.00 - 10.00)	5.82±4.92 (1.00 - 19.00)	3.68±4.51 [b] (0.00 - 16.00)

Hindawi
Mediators of Inflammation
Volume 2017, Article ID 5650627, 10 pages
https://doi.org/10.1155/2017/5650627

Clinical Study

Evidences of a New Psychobiotic Formulation on Body Composition and Anxiety

Carmela Colica,[1] Ennio Avolio,[2] Patrizio Bollero,[3] Renata Costa de Miranda,[4,5] Simona Ferraro,[6] Paola Sinibaldi Salimei,[7] Antonino De Lorenzo,[7] and Laura Di Renzo[7]

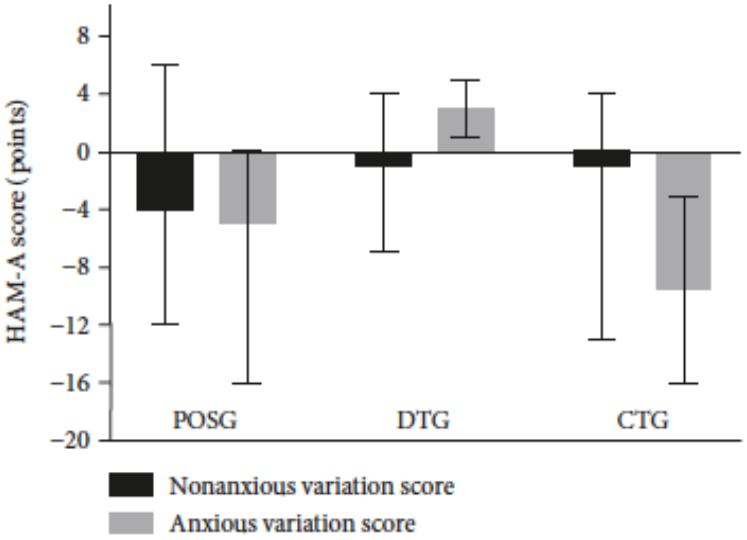


FIGURE 2: Hamilton anxiety rating scale (HAM-A) score variation before and after treatments in anxious and nonanxious subjects. Nonanxious subjects (negative test) if total score < 18 and anxious subjects (positive test) if total score ≥ 18. Variation score is shown as median, minimum, and maximum. 609 statistical significance attributed to results with $p < 0.05$ by Kruskal Wallis test. Anxious variation score among groups: $p = 0.10$ and nonanxious variation score among groups: $p = 0.67$. POSG: psychobiotics oral suspension group; DTG: dietary treatment group; CTG: combined treatment group.

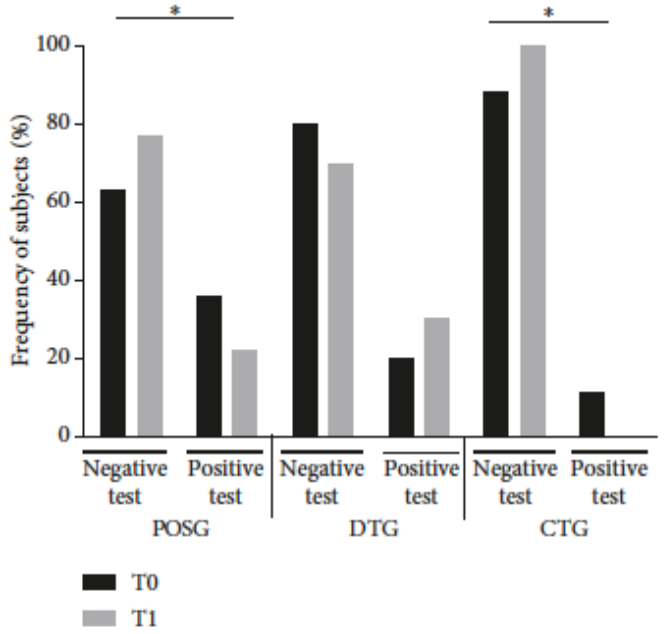


FIGURE 3: Frequency change of anxious subjects in POSG, DTG, and CTG after treatment. Frequency of anxiety was evaluated before and after treatment in POSG, DTG, and CTG. Negative test (nonanxious 619 subjects) if total score < 18 and positive test (anxious subjects) if total score ≥ 18. Statistical significance attributed to results with $^*p < 0.05$ between T0 and T1 by McNemar test. POSG: $p = 0.03^*$; DTG: $p = 0.10$; CTG: $p = 0.01^*$. POSG: psychobiotics oral suspension group; DTG: dietary treatment group; CTG: combined treatment group.

α-Melanocyte-stimulating hormone (α-MSH)

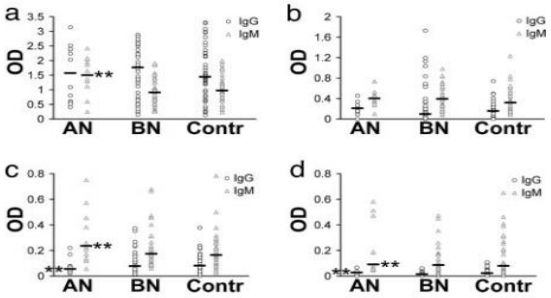


Fig. 4. Levels (OD, optic density in ELISA) of IgM and IgG autoAbs against α-MSH (*a*), ACTH (*b*), OT (*c*), and VP (*d*) in AN and BN patients and controls. Bars show median values (Kruskal–Wallis, **, $P < 0.001$ vs. controls).

Autoantibodies against neuropeptides are associated with psychological traits in eating disorders

PNAS October 11, 2005 vol. 102 no. 41 14867 NE

OPEN

Citation: Transl Psychiatry (2014) 4, e458; doi:10.1038/tp.2014.98

www.nature.com/tp

ORIGINAL ARTICLE

Bacterial ClpB heat-shock protein, an antigen-mimetic of the anorexigenic peptide α-MSH, at the origin of eating disorders

N Tennoune[1,2], P Chan[2,3], J Breton[1,2], R Legrand[1,2], YN Chabane[2,4], K Akkermann[5], A Järv[6], W Ouelaa[1,2], K Takagi[1,2], I Ghouzali[1,2], M Francois[1,2], N Lucas[1,2], C Bole-Feysot[1,2], M Pestel-Caron[2,7,8], J-C do Rego[2,9], D Vaudry[2,9], J Harro[5], E Dé[2,4], P Déchelotte[1,2,8] and SD Fetissov[1,2]

The molecular mechanisms at the origin of eating disorders (EDs), including anorexia nervosa (AN), bulimia and binge-eating disorder (BED), are currently unknown. Previous data indicated that immunoglobulins (Ig) or autoantibodies (auto-Abs) reactive with α-melanocyte-stimulating hormone (α-MSH) are involved in regulation of feeding and emotion; however, the origin of such auto-Abs is unknown. Here, using proteomics, we identified ClpB heat-shock disaggregation chaperone protein of commensal gut bacteria *Escherichia coli* as a conformational antigen mimetic of α-MSH. We show that ClpB-immunized mice produce anti-ClpB IgG crossreactive with α-MSH, influencing food intake, body weight, anxiety and melanocortin receptor 4 signaling. Furthermore, chronic intragastric delivery of *E. coli* in mice decreased food intake and stimulated formation of ClpB- and α-MSH-reactive antibodies, while ClpB-deficient *E. coli* did not affect food intake or antibody levels. Finally, we show that plasma levels of anti-ClpB IgG crossreactive with α-MSH are increased in patients with AN, bulimia and BED, and that the ED Inventory-2 scores in ED patients correlate with anti-ClpB IgG and IgM, which is similar to our previous findings for α-MSH auto-Abs. In conclusion, this work shows that the bacterial ClpB protein, which is present in several commensal and pathogenic microorganisms, can be responsible for the production of auto-Abs crossreactive with α-MSH, associated with altered feeding and emotion in humans with ED. Our data suggest that ClpB-expressing gut microorganisms might be involved in the etiology of EDs.

Translational Psychiatry (2014) 4, e458; doi:10.1038/tp.2014.98; published online 7 October 2014

INTRODUCTION

Anorexia nervosa (AN), bulimia nervosa (BN) and binge-eating disorder (BED) are the main forms of eating disorders (EDs) with a combined prevalence of up to 5% of women and 2% of men.[1] Although significant advances in understanding the neurobiological changes of ED have been achieved,[2,3] the molecular mechanisms triggering the onset and maintenance of ED still remain unknown, and the specific genetic influence is uncertain.[4] Accordingly, the unknown pathophysiology of ED explains the absence of specific pharmacological treatment.[5]

One novel line of clinical and experimental research, further developed in the present study, suggests that biological mechanisms of ED may involve immunoglobulins (Ig) or autoantibodies (auto-Abs) reactive with peptide hormones regulating appetite and emotion. In fact, after the initial identification of serum IgG from AN and BN patients binding to α-melanocyte-stimulating hormone (α-MSH) in hypothalamic neurons,[7] the relevance of α-MSH-reactive auto-Abs to ED was shown by significant correlations of their plasma levels and the ED Inventory-2 (EDI-2) scores in AN and BN patients.[8] Moreover, it was shown that production of α-MSH auto-Abs in rats is physiologically regulated and can be influenced by stress, food restriction and intestinal inflammation, that is, factors that often preceded ED.[9,10] Furthermore, it was shown that changes in levels, Ig class and affinity properties of α-MSH auto-Abs differentially influenced α-MSH-mediated feeding and anxiety.[9,10] α-MSH is a 13 amino-acid (a.a.) peptide[11] critically involved in regulation of energy balance by decreasing food intake and increasing energy expenditure via activation of the melanocortin receptor type 4 (MC4R),[12] both centrally and peripherally.[13,14] α-MSH also regulates mood and emotion, for example, increasing anxiety.[15,16] Determining the origin of α-MSH-reactive auto-Abs may, hence, shed new light on the ED etiology.

A molecular mimicry concept has been developed to explain the origin of auto-Abs crossreacting with microbial pathogens and host proteins, and that may cause some infection-triggered autoimmune diseases.[17] By applying this concept to the origin of auto-Abs crossreactive with α-MSH, we previously studied by an *in silico* approach, the sequence homology, of at least five consecutive amino acids, between appetite-regulating peptide hormones and proteins from bacteria, viruses, fungi and archea.[18,19] To our surprise, such homology was present in several bacterial species of the gut microbiota, for example, between α-MSH and both commensal and pathogenic *Escherichia coli* bacteria.[19] This indicates that some gut bacteria may be constitutively involved in production of host Ig modulating the biological activity of peptide hormones, and, hence, may be physiologically and/or pathophysiologically involved in regulation of appetite and emotion.[20] In support of this link, studies in germ-free mice showed stimulatory effects of gut microbiota on plasma levels of all classes of Ig.[21] The presence of amino-acid sequence

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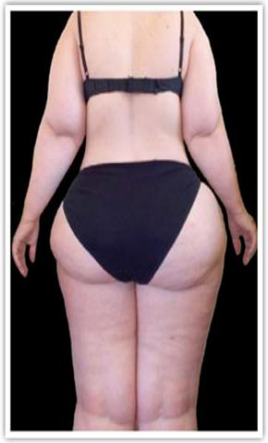
Eat Weight Disord. 2019 May 6. doi: 10.1007/s40519-019-00703-x. [Epub ahead of print]

The effect of lipedema on health-related quality of life and psychological status: a narrative review of the literature.

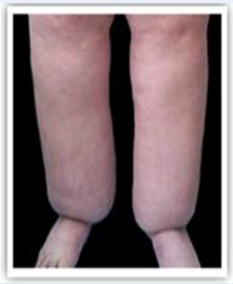
Alwardat N[1,2], Di Renzo L[3], Alwardat M[4,5], Romano L[6], De Santis GL[6], Gualtieri P[3], Carrano E[6], Nocerino P[3], De Lorenzo A[3].

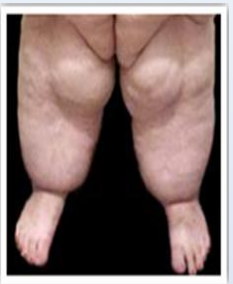
- It is a chronic, progressive and potentially disabling disease that affects almost exclusively the female sex.
- The exact prevalence is not known, but some research on the German population estimates it from 0.06% to 10%.



CLINICAL CHARACTERISTICS

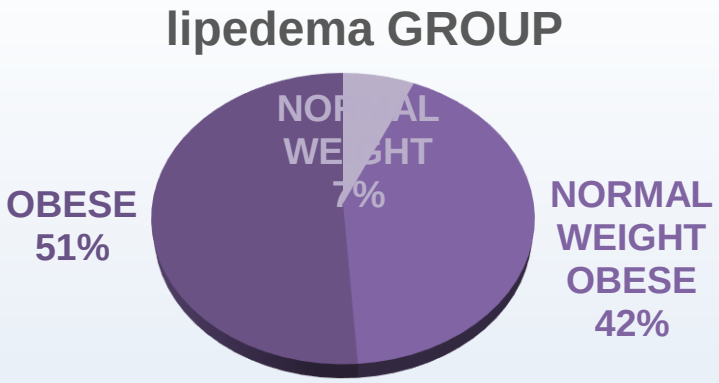
- ➢ Subcutaneous accumulation of bilateral and symmetrical adipose tissue at the extremities, mainly at the lower extremities
- ➢ Onset and progression during periods of hormonal changes (puberty, pregnancy and menopause)
- ➢ Alteration of sensitivity and pain, haematomas, ecchymosis and edema
- ➢ Feeling of systemic fatigue and loss of muscle strength
- ➢ Resistance of fat deposits to diet and exercise
- ➢ Deterioration of the psychological state

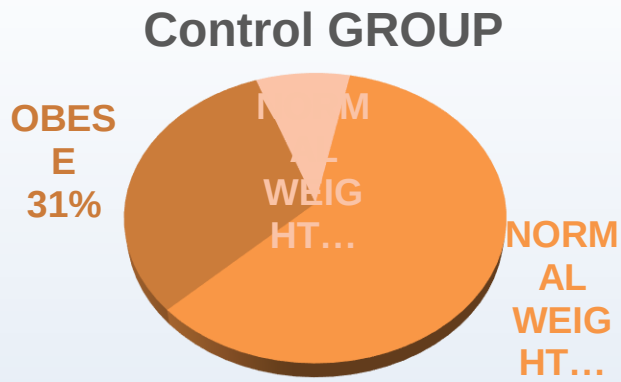




Sezione di Nutrizione cliniac e Nutrigenomica
CASE-CONTROL STUDY

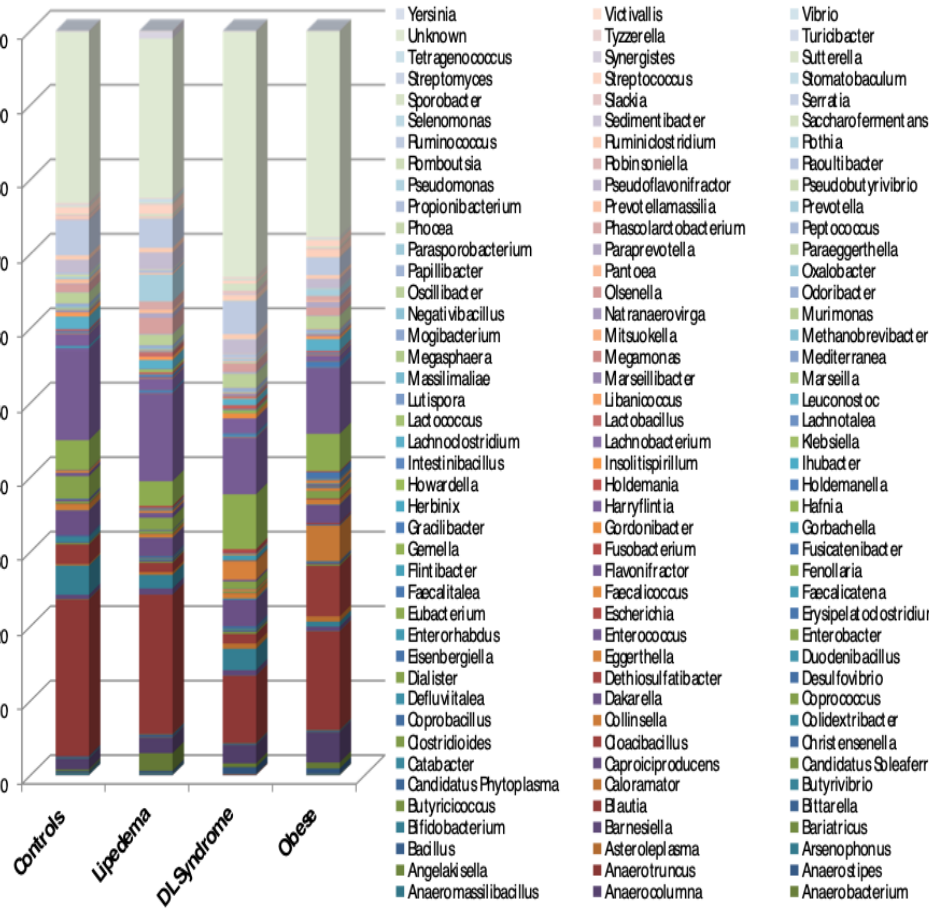
- In Italy, 200 women were diagnosed with lipedema. To date, we have visited 45 women and, in the continuation of the project, it is estimated to evaluate the triple
- The control group was recruited on a voluntary basis at the Clinical Nutrition and Nutrigenomics Section of the Department of Biomedicine and Prevention of the Faculty of Medicine of Tor Vergata and includes 50 women who are not diagnosed with lipedema





- The control group is heterogeneous but, being made up of 90% obese in each group. This study could also provide useful indicators for differential diagnosis with obesity

Genus



	GENUS			
OTUs	Lipedema	Control	FDR	P-value
Acetanaerobacterium	0,018%	0,000%	2,45903E-09	9,58062E-11
Acidaminobacter	0,017%	0,000%	7,46436E-05	1,06634E-05
Aeromonas	0,012%	0,000%	3,93725E-09	2,30099E-10
Akkermansia	2,375%	0,208%	0,017907412	0,004713701
Alloprevotella	0,033%	0,019%	0,008823656	0,002062673
Angelakisella	0,038%	0,000%	1,20907E-13	7,85112E-16
Arsenophonus	0,011%	0,000%	7,11626E-06	7,39351E-07
Candidatus Soleaferrea	0,013%	0,000%	2,71788E-08	1,94134E-09
Catenibacterium	0,055%	0,000%	0,008608071	0,00195638
Clostridioides	0,015%	0,000%	5,95673E-08	4,64161E-09
Denitrobacterium	0,030%	0,000%	0,0007728	0,000127404
Enterobacter	0,039%	0,000%	1,03507E-05	1,20982E-06
Enterococcus	0,027%	0,000%	3,53536E-09	1,83655E-10
Enterorhabdus	0,024%	0,000%	0,0007728	0,000126882
Ercella	0,056%	0,016%	0,014526191	0,003678711
Escherichia	0,247%	0,026%	0,0007728	0,000130473
Fastidiosipila	0,027%	0,000%	0,002199852	0,000428543
Fenollaria	0,014%	0,000%	5,23657E-12	1,02011E-13
Fournierella	0,010%	0,000%	2,70825E-09	1,23102E-10
Fusobacterium	0,031%	0,000%	0,010973823	0,002636568
Harryflintia	0,035%	0,000%	1,43527E-06	1,39799E-07
Hespellia	0,011%	0,000%	1,06712E-08	6,92938E-10
Howardella	0,026%	0,000%	0,043992714	0,013997682
Klebsiella	0,382%	0,000%	1,69057E-07	1,42711E-08
Mailhella	0,019%	0,000%	0,02093515	0,005845529
	0,052%	0,148%	0,000960147	0,000174572
Oxalobacter	0,012%	0,000%	0,013363216	0,003297417
Pantoea	0,020%	0,000%	1,19715E-05	1,477E-06
Paraprevotella	0,642%	0,085%	0,030287141	0,008850139
Phascolarctobacterium	1,103%	0,055%	0,000943192	0,000165365
Porphyromonas	0,016%	0,000%	3,3791E-11	1,09711E-12
Prevotella	3,571%	0,267%	4,28031E-05	5,55884E-06
Prevotellamassilia	0,228%	0,000%	7,07484E-05	9,6475E-06
Propionibacterium	0,332%	0,015%	0,005397952	0,001086601
Provencibacterium	0,012%	0,000%	0,02093515	0,005715935
Saccharofermentans	0,040%	0,000%	8,63619E-12	2,24317E-13
Selenomonas	0,013%	0,000%	4,63688E-12	6,02193E-14
Serratia	0,027%	0,000%	0,001186263	0,000223387
Staphylococcus	0,027%	0,000%	0,036844369	0,01124471
Tetragenococcus	0,394%	0,000%	7,38873E-06	8,15639E-07
Veillonella	0,955%	0,092%	0,000311171	4,64735E-05
Yersinia	0,023%	0,000%	0,005843866	0,001273547
Alkalibacter	0,010%	0,110%	0,042362476	0,013203889
Bittarella	0,000%	0,017%	1,04E-06	9,49E-08
Butyrivibrio	0,150%	0,748%	0,03465343	0,010351025
Flintibacter	0,050%	0,247%	0,005843866	0,001223807
Massilimaliae	0,000%	0,014%	0,005843866	0,001290204
Pseudobutyrivibrio	0,073%	0,329%	0,017907412	0,004767558
Turicibacter	0,030%	0,100%	0,023453814	0,00670109

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TOPIC HIGHLIGHT

WJG 20th Anniversary Special Issues (17): Intestinal microbiota

Gut microbiota and metabolic syndrome

Davide Festi, Ramona Schiumerini, Leonardo Henry Eusebi, Giovanni Marasco, Martina Taddia, Antonio Colecchia

Manipulation of gut microbiota through the administration of prebiotics or probiotics could reduce intestinal low grade inflammation and improve gut barrier integrity, thus, ameliorating metabolic balance and promoting weight loss.

Table 3 Studies conducted on humans showing effects of probiotics on metabolic disorders

Studied subjects	Probiotics	Duration of treatment	Effects	Ref.
Overweight humans	*Lactobacillus gasseri* SBT2055	12 wk	↓body weight, visceral and subcutaneous fat area, BMI, waist and hip circumference ↑serum adiponectin	[116]
Subjects with increased abdominal adiposity	*Lactobacillus gasseri* SBT2055	12 wk	↓body weight, visceral fat area, BMI, waist and hip circumference, body fat mass	[117]
Women affected by postmenopausal metabolic syndrome	*Lactobacillus plantarum*	90 d	↓serum glucose and homocysteine levels	[118]

BMI: Body mass index.

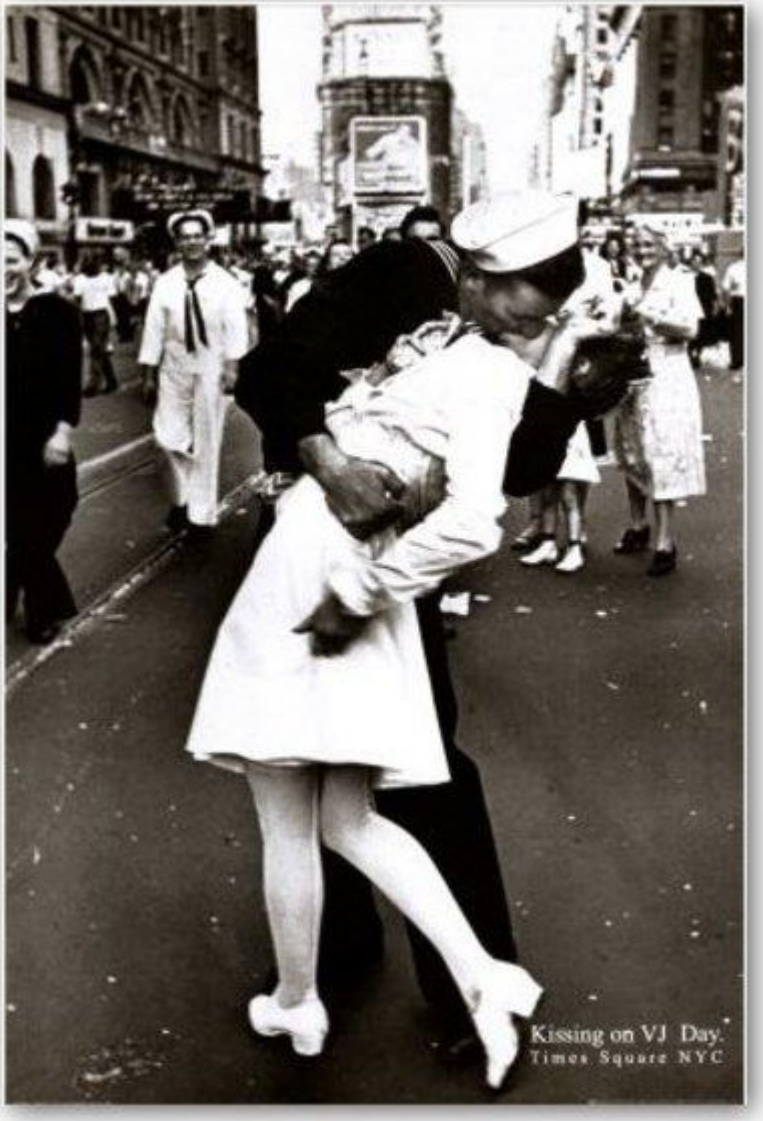
Table 5 Studies conducted on humans showing effects of prebiotics on metabolic disorders

Studied subject	Prebiotic	Duration of treatment	Effects	Ref.
Healthy men and women	OFS	2 wk	↓Food and energy intake, hunger ↑satiety	[132]
Healthy humans	GOS	12 wk	Significant ↑ *Bifidobacterium*	[133]
Obese women	Inulin-type fructans	3 mo	↑*Bifidobacterium* and *Faecalibacterium prausnitzii* ↓Circulating LPS, *Bacteroides*, *Propionibacterium*	[134]
Obese-dyslipidemic women	Yacon syrup (containing OFS)	120 d	↓Body weight, BMI, waist circumference, serum LDL cholesterol levels	[135]
Overweight and obese adults	OFS	12 wk	↓Body weight, ghrelin, calories intake, serum glucose, insulin ↑peptide YY	[136]

OFS: Oligofructose; GOS; Galactooligosaccharides; LPS: Lipopolysaccharides; BMI: Body mass index; LDL: Low-density lipoprotein.

Correction of immune dysfunctions with natural substances

Category name	Active compound	Effect or Molecular target	Ref
Prebiotics (Fruit and vegetables)	Vitamins A, B1, B2, B6, B3, B12, D, E (Tocopherols: α, β, γ, δ –tocopherol family (α T, β T, γ T, δ T) and α, β, γ, δ -tocotrienol (α TE, β TE, γ TE, δ TE)); MUFA, PUFA (ω-9, ω-6); iron and zinc; phytosterols; inuline; fiber.	↓Bcl-2, ↑BAX, ↓NF-kB, ↓Cyclin D1, ↓MMP-9, ↓iNOS, ↑Caspase, ↑GPX1, ↓IRAK1, ↓IL-1, ↓CAT, ↓CCL5, ↓DUOX2, ↑SOD1, ↓COX2, ↓TNF-α, ↓IL1, ↓IL6, ↓IL8	17,18,45, 152-165
Probiotics	*Bacteroides, Clostridium, Faecalibacterium, Eubacterium, Peptidococcus, Peptidostreptococcus and Bifidobacterium*	Restoration of innate and adaptative immunity; correction of the altered intestinal microbiota; T cell differentiation toward regulatory T (Treg) cells and Th2 phenotypes; anti-inflammatory activity; stimulation of the GALT, MLNs, ILFs, TLRs, expression of α- and β-defensins, cathericidin LL-37, lectins, and other antimicrobial proteins.	20,88,92, 102-111, 120-136
Postbiotics	Short chain fatty acids, p40 molecule, becteriocin, Lactocepin secreted by *L. paracasei, Lactobacillus plantarum,* S-layer protein A and polysaccharide A produced by *Bacteroides fragilis*	Improved epithelial barrier function, inactive IP-10, Increased production of mucins by the goblet cells, Decreased inflammatory process, Down-regulation of pro-inflammatory cytokine production by intestinal epithelial cells	127,128, 137
Poliphenols	Resveratrol, pterostilbene, and piceatannol	↓Survivin, ↓cyclin D1, ↓cyclin E, ↑p53, ↓Bcl-2, ↑BAX, ↑Caspase, ↓Bcl-XL, ↓CIAP, ↓Egr-1, ↓PKC, ↓PKD, ↓IL-6, ↓VEGF, ↓IL-1, ↓IL-8, ↓CYP1A1, ↓5-LOX, ↑HO-1, ↑Nrf2, ↓COX2, ↑SIRT2, ↓CCL5, ↓TNF-α ↓IL-1β, ↓NF-kB, ↑IL10, ↓IL-1β, ↓IL-1β, ↑IL10	174-184, 187-192, 199-205
	Hydroxytirosol	↓CCL5, ↓UCP2, ↓ Bcl-2, ↓DUOX2, ↓IRAK1, CAT, ↓NF-kB, ↑ SOD1	166, 167



GRAZIE PER L'ATTENZIONE