

# **Nutrizione e Fattori Protettivi**

**Dall'Epidemia delle Malattie Autoimmuni alla Pandemia COVID19:  
Cosa Possiamo Fare per Proteggerci e Prolungare la Vita Sana?**

[www.Fit4Pandemic.com](http://www.Fit4Pandemic.com)

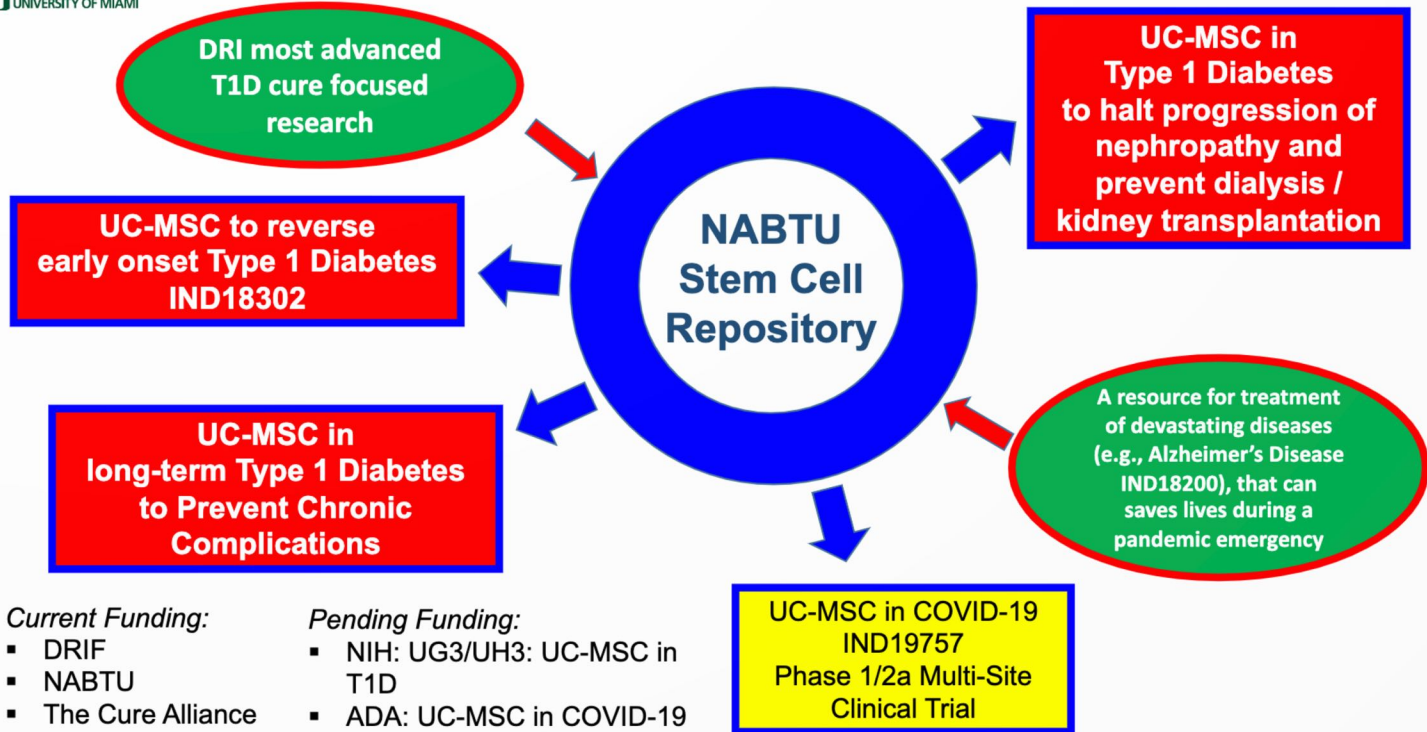
## **Camillo Ricordi, MD, FNAI**

Stacy Joy Goodman Professor and Director, Diabetes Research Institute  
and Cell Transplant Center, University of Miami  
Chairperson, NIH Clinical Islet Transplantation Consortium SC  
Fellow, National Academy of Inventors, USA  
Member, Supreme Council of Health, Italy

# Diabetes Research Institute Federation



# cGMP Advanced Cell and Biologic Product Manufacturing Facility





## Autoimmune Disease List

Home > Autoimmune Disease List

Our Mission

Our Team

Our Organization

### ▶ There are more than 100 Autoimmune Diseases ◀

There are many different types of autoimmune disease. These diseases can affect one, ten, one hundred.... a million ... or more people. Learn more about some of them right here or visit their site for more information.

Approximately 50 million Americans, 20 percent of the population or one in five people, suffer from autoimmune diseases. Women are more likely than men to be affected; some estimates say that 75 percent of those affected—some 30 million people—are women. Still, with these statistics, autoimmunity is rarely discussed as a women's health issue.



# Healthspan Potential

## Age 0 - 40

INFLAMMATORY DIET



1%

50%

100%

Healthy Lifespan Potential

ANTI-INFLAMMATORY DIET



# Healthspan Potential

## Age 40 - 70

INFLAMMATORY DIET

1%

50%

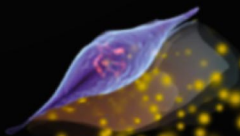
100%

Healthy Lifespan Potential

ANTI-INFLAMMATORY DIET



## UC - Mesenchymal Stem Cells for COVID-19



**Paracrine Effect**

**Resolution of Inflammation**

**Resolution of Cytokine Storm**

**Antimicrobial Activity**

**Lung Regeneration**

**Inhibition of Lung Fibrosis**

# Cosa Hanno in Comune

- Epidemia delle Malattie Autoimmuni (Diabete Tipo 1, Lupus, Psoriasi, Crohn's, e il centinaio di malattie autoimmuni che affliggono il 20% della popolazione)
- Accorciamento della Longevita' Sana (aumento malattie croniche legate all'invecchiamento)
- Suscettibilita' alle Forme Gravi di Infezioni Virali (COVID-19)

# The Perfect (Disease Predisposing) Storm



- Increased Omega-6
- Increased Refined Carbohydrates

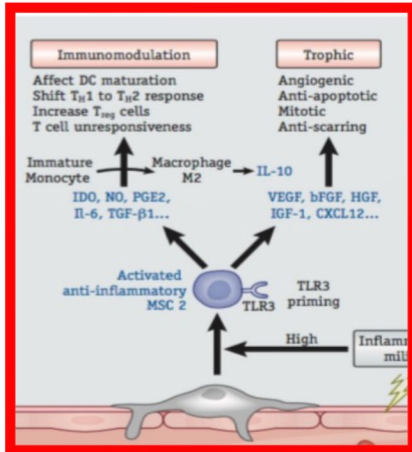


- Decreased Omega-3
- Decreased Polyphenols
- Decreased Vitamin D

# MSCs, Vitamin D, Omega 3

## Shared Anti-Inflammatory and Immunomodulation Pathways

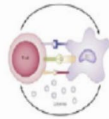
### MSCs



### Vitamin D

Immune system

≥ 40 ng/mL



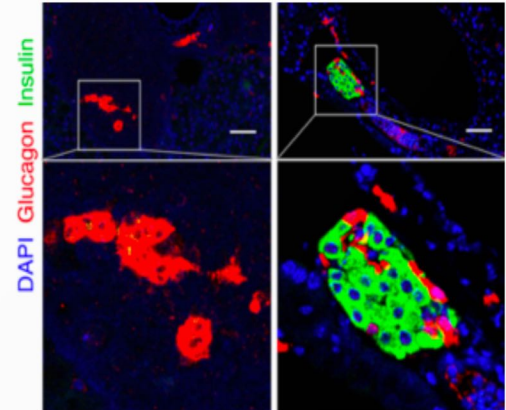
↑ macrophage differentiation and activation

↑ cathelicidin, β2-defensin

↓ Th<sub>1</sub>, Th<sub>17</sub> cells ↑ Treg cells

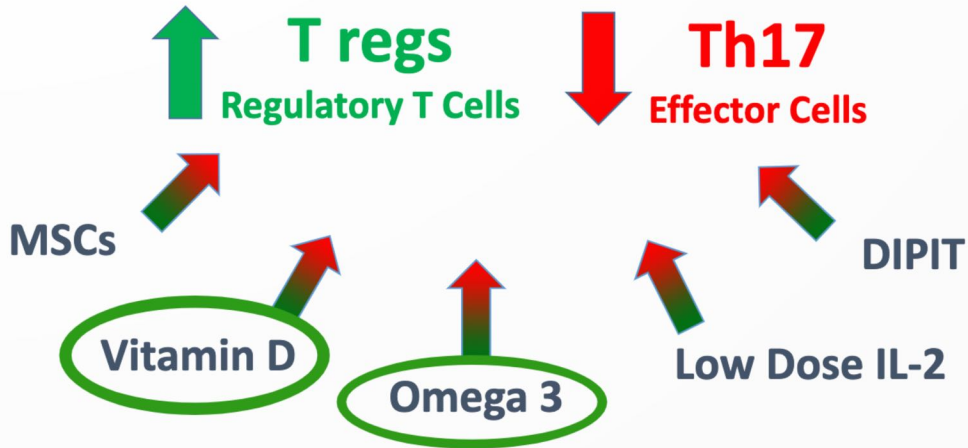
ward off: - type1 diabetes  
- hashimoto's thyroiditis  
- inflammatory bowel disease  
- multiple sclerosis

### Omega 3





# MODULATION OF INFLAMMATION AND HYPER-IMMUNE RESPONSES



## Assessing Omega 6 / Omega 3 ratio: AA/EPA Ratio as Healthspan Predictor

**Table 2**  $\omega$ 6 to  $\omega$ 3 ratios in various populations

Population	$\omega$ 6: $\omega$ 3	Reference
Palaeolithic	0.97*,†	Eaton <i>et al</i> <sup>37</sup>
Greece prior to 1960	1.00–2.00	Simopoulos <sup>14</sup>
Current USA	16.74	Eaton <i>et al</i> <sup>37</sup>
UK and Northern Europe	15.00	Sanders (2000) <sup>39</sup>
Japan	4.00	Sugano and Hirahana (2000) <sup>40</sup>
India rural	5–6.1	Pella <i>et al</i> (2003) <sup>41</sup>
India urban	38–50	Pella <i>et al</i> (2003) <sup>41</sup>

\*Data from Eaton *et al*.<sup>37</sup>

†Assuming an energy intake of 35:35 of animal:plant sources.

# Rapporto AA/EPA e Rischio di Mortalita'



## HHS Public Access

Author manuscript

*J Clin Lipidol.* Author manuscript; available in PMC 2018 January 12.

Published in final edited form as:

*J Clin Lipidol.* 2017 ; 11(1): 250–259.e5. doi:10.1016/j.jacl.2016.12.013.

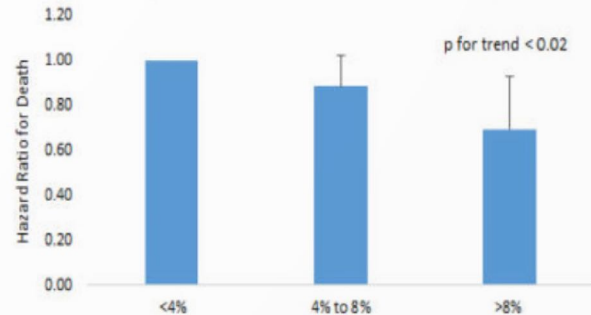
## Red Blood Cell Polyunsaturated Fatty Acids and Mortality in the Women's Health Initiative Memory Study<sup>1,2,3,4</sup>

William S. Harris, PhD<sup>a,b</sup>, Juhua Luo, PhD<sup>c</sup>, James V. Pottala, PhD<sup>a</sup>, Mark A. Espeland, PhD<sup>d</sup>, Karen L. Margolis, MD., MPH<sup>e</sup>, JoAnn E. Manson, MD, DrPH<sup>f</sup>, Lu Wang, MD, PhD<sup>f</sup>, Theodore M. Brasky, PhD<sup>g</sup>, and Jennifer G. Robinson, MD, MPH<sup>h</sup>

**Table 2** RBC fatty acids (percent of total) by mortality status at last contact (medians and interquartile ranges)

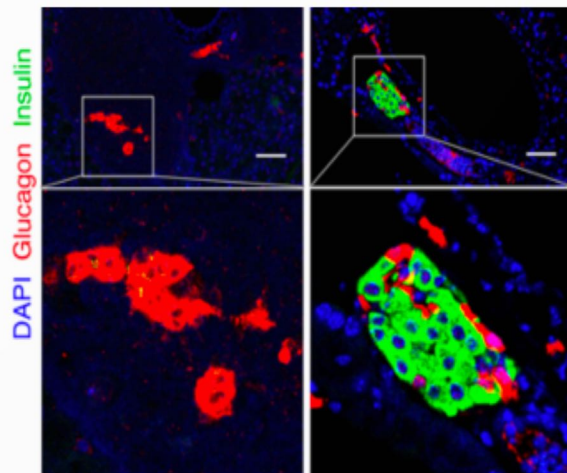
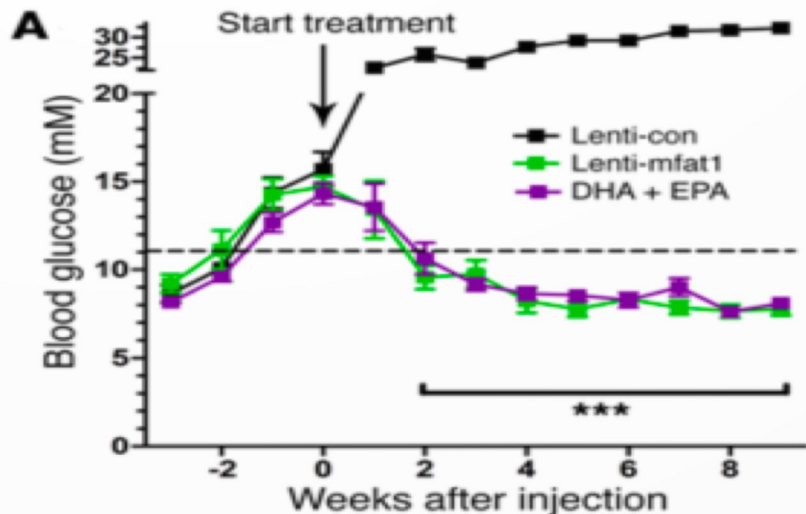
RBC PUFA metric	Alive (n = 4650)			Dead (n = 1851)			P value
	Median	25th	75th	Median	25th	75th	
Omega-3 index (EPA + DHA)	5.04	4.25	6.10	4.92	4.13	5.89	.0003
Eicosapentaenoic (EPA)	0.64	0.50	0.83	0.61	0.48	0.78	<.0001
Docosahexaenoic (DHA)	4.40	3.68	5.31	4.31	3.61	5.14	.0016
Linoleic	11.89	10.87	12.98	11.84	10.74	12.91	.15
PUFA factor score*	-6.75	-6.98	-6.49	-6.81	-7.03	-6.56	<.0001
Alpha-linolenic	0.16	0.13	0.20	0.16	0.13	0.19	.08
Docosapentaenoic n-3 (DPAn-3)	2.55	2.31	2.79	2.49	2.26	2.74	<.0001
Arachidonic acid (ARA)	17.06	15.94	18.08	17.03	15.93	18.12	.98
ARA/EPA ratio	27.04	20.34	34.05	28.55	21.82	35.52	<.0001
N-6/N-3 ratio	6.88	5.89	7.85	7.03	6.05	7.97	<.0001

## Omega-3 Index Predicts Total Mortality



Omega-3 Index (RBC EPA+DHA)

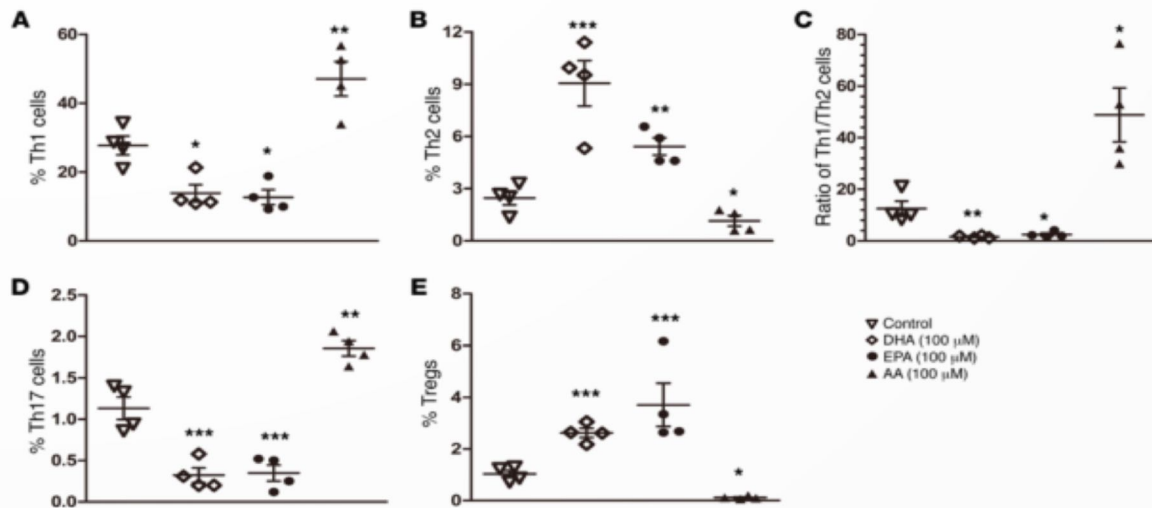
# $\omega$ -3 polyunsaturated fatty acids ameliorate type 1 diabetes and autoimmunity



# PBMC from Subjects with T1D

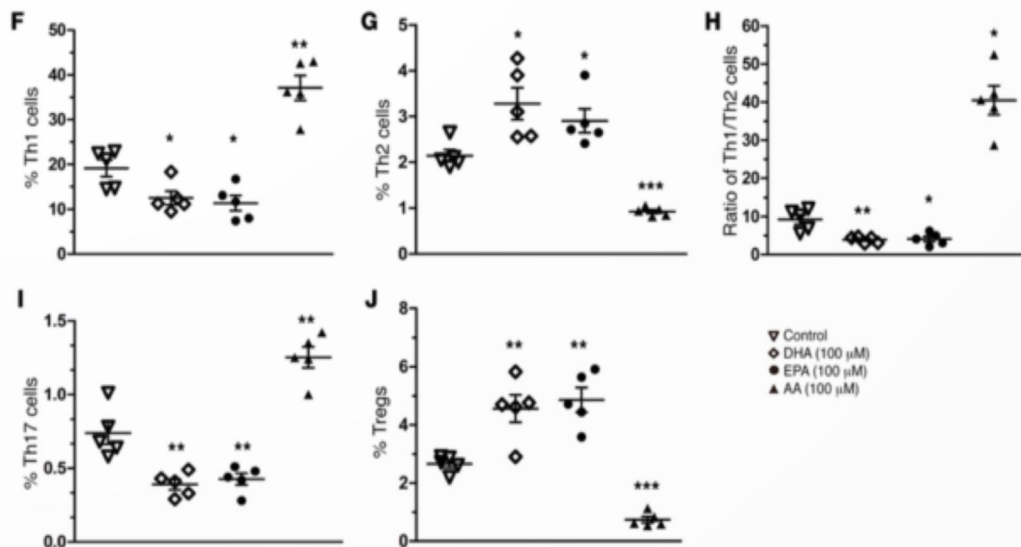
The Journal of Clinical Investigation

RESEARCH ARTICLE



**Figure 10.**  $\omega$ -3 and  $\omega$ -6 PUFAs readjust CD4<sup>+</sup> T cell differentiation in PBMCs from T1D patients and nondiabetic donors *in vitro*. Quantification of the percentage of intracellular staining of IFN- $\gamma$ <sup>+</sup>, IL-4<sup>+</sup>, IL-7<sup>+</sup>, and CD25<sup>+</sup>FoxP3<sup>+</sup> Th cells in PBMCs from 4 T1D patients (A–E) and 5 nondiabetic donors (F–J). Cells were cultured for 24 hours under PMA and ionomycin stimulation in the presence of DHA, EPA, and AA (100  $\mu$ M) added at the time of activation. Representative flow cytometric images are shown in Supplemental Figures 9 and 10. \* $P$  < 0.05, \*\* $P$  < 0.01, and \*\*\* $P$  < 0.0001 compared with the control group (Student's  $t$  test). Each point represents an individual patient or donor, and the data are representative of 3 independent experiments. All values represent the mean  $\pm$  SEM.

## PBMC from Non Diabetic Subjects



**Figure 10.**  $\omega$ -3 and  $\omega$ -6 PUFAs readjust CD4<sup>+</sup> T cell differentiation in PBMCs from T1D patients and nondiabetic donors *in vitro*. Quantification of the percentage of intracellular staining of IFN- $\gamma$ , IL-4, IL-7, and CD25<sup>+</sup>FoxP3<sup>+</sup> Th cells in PBMCs from 4 T1D patients (A-E) and 5 nondiabetic donors (F-J). Cells were cultured for 24 hours under PMA and ionomycin stimulation in the presence of DHA, EPA, and AA (100  $\mu$ M) added at the time of activation. Representative flow cytometric images are shown in Supplemental Figures 9 and 10. \* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.0001$  compared with the control group (Student's t test). Each point represents an individual patient or donor, and the data are representative of 3 independent experiments. All values represent the mean  $\pm$  SEM.





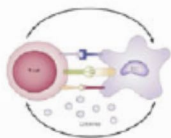
REVIEW

## Vitamin D: not just the bone. Evidence for beneficial pleiotropic extraskeletal effects

Massimiliano Caprio<sup>1,2</sup> · Marco Infante<sup>3</sup> · Matilde Calanchini<sup>3</sup> · Caterina Mammi<sup>1</sup> ·  
Andrea Fabbri<sup>3</sup>

Immune system

≥ 40 ng/mL



↑ macrophage differentiation  
and activation

↑ cathelicidin,  $\beta$ 2-defensin

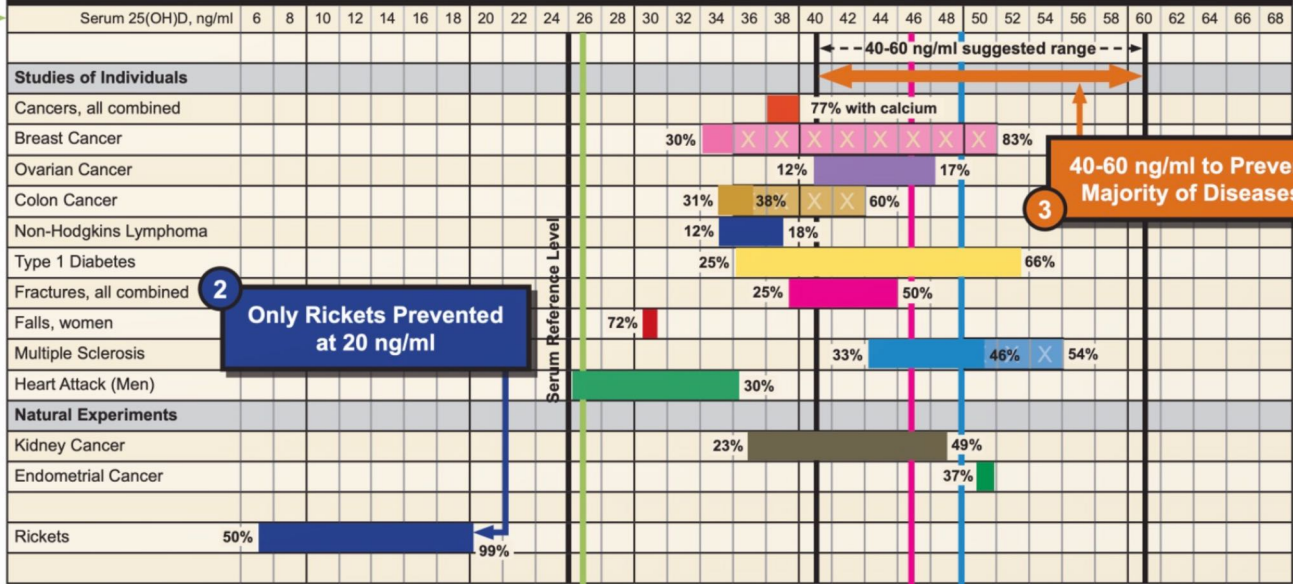
↓ Th<sub>1</sub>, Th<sub>17</sub> cells    ↑ Treg cells

ward off:

- type 1 diabetes
- hashimoto's thyroiditis
- inflammatory bowel disease
- multiple sclerosis

**Serum Level**

# Disease Incidence Prevention by Serum 25(OH)D Level



**2**  
Only Rickets Prevented at 20 ng/ml

**3**  
40-60 ng/ml to Prevent Majority of Diseases

US & Canadian Average

Tribal East Africans

Outdoor Workers in Late Summer

**Legend:**

All percentages reference a common baseline of 25 ng/ml as shown on the chart. %'s reflect the disease prevention % at the beginning and ending of available data. Example: Breast cancer incidence is reduced by 30% when the serum level is 34 ng/ml vs the baseline of 25 ng/ml. There is an 83% reduction in incidence when the serum level is 50 ng/ml vs the baseline of 25 ng/ml. The x's in the bars indicate 'reasonable extrapolations' from the data but are beyond existing data.

September 24, 2019



## DiabetesPro® SmartBrief

News for diabetes health professionals

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### DIABETES IN FOCUS

#### **Low vitamin D may increase diabetes-related mortality risk**

Vitamin D deficiency in adults may increase their risk of death from diabetes complications, compared with having a normal vitamin D level, but the risk varied by age, researchers reported at the European Association for the Study of Diabetes annual meeting. Higher vitamin D levels were associated with a reduced risk for all-cause mortality.

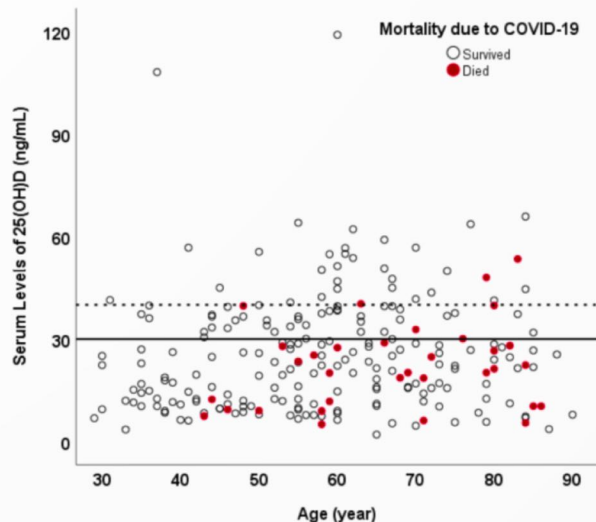
# The Lancet (pre-print 07/2020)

## Vitamin D Sufficiency Reduced Risk for Morbidity and Mortality in COVID-19 Patients

Z Maghbooli, M Ebrahimi, A Shirvani, M Nasiri Marzieh Pazoki, S Kafan, H Moradi Tabriz, A Hadadi, M Montazeri, M Ali Sahraian, and MF Holick

Boston University Medical Center Boston, MA USA

- After adjusting for confounding factors, there was a significant association between vitamin D sufficiency and reduction in clinical severity, inpatient mortality
- Only 9.7% of patients older than 40 years who were vitamin D sufficient succumbed to the infection compared to 20% who had a circulating level of 25(OH)D <30 ng/mL
- A significant reduction in serum CRP, and increased lymphocytes percentage were observed, suggesting that vitamin D may help modulate the immune response possibly by reducing the risk for cytokine storm in response to this viral infection
- Improving vitamin D status in the general population and in hospitalized could reduce the morbidity and mortality associated with COVID-19

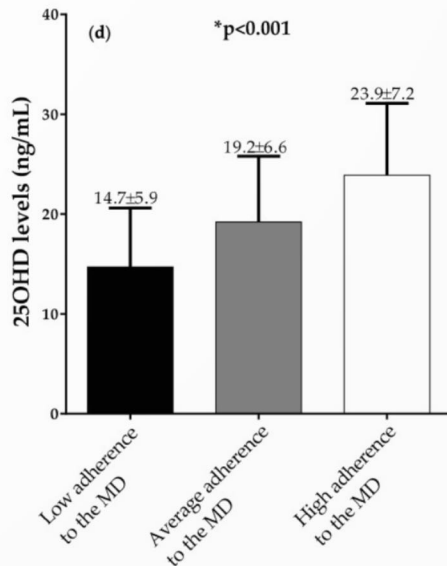


Article

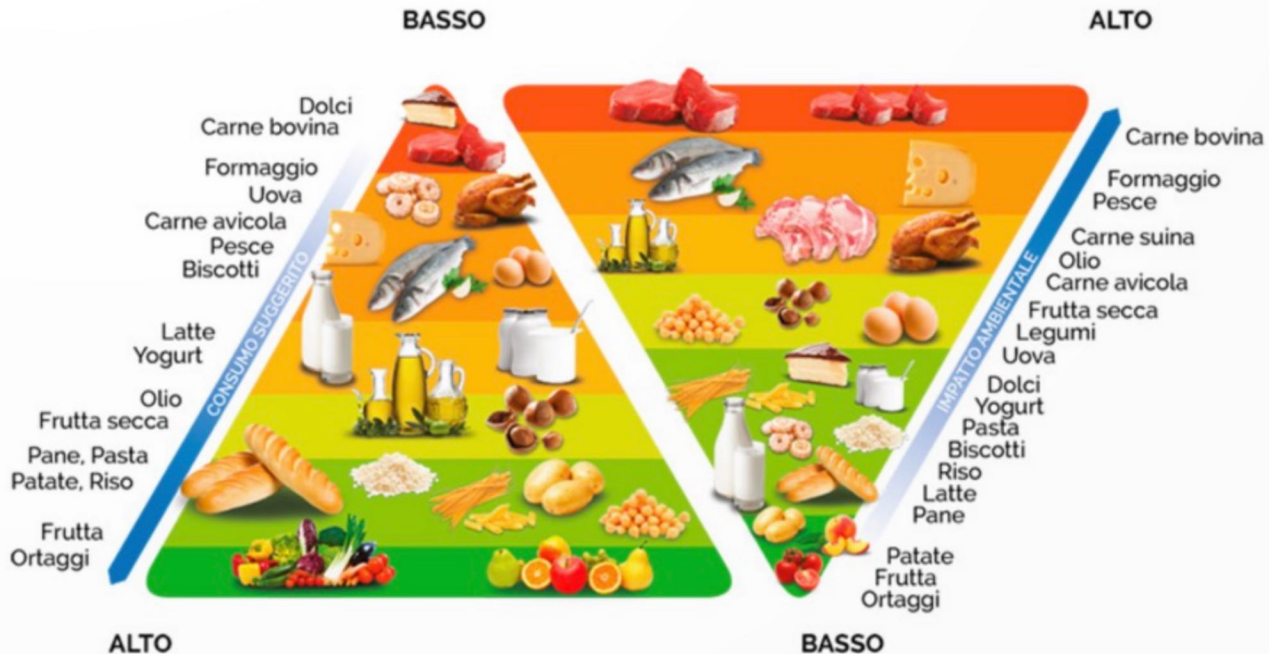
# Influence of the Mediterranean Diet on 25-Hydroxyvitamin D Levels in Adults

Luigi Barrea <sup>1,2,\*</sup>, Giovanna Muscogiuri <sup>1,2,†</sup>, Daniela Laudisio <sup>1,2</sup>, Gabriella Pugliese <sup>1,2</sup>, Giulia de Alteriis <sup>1</sup>, Annamaria Colao <sup>1,2,3</sup> and Silvia Savastano <sup>1,2</sup>

- <sup>1</sup> Dipartimento di Medicina Clinica e Chirurgia, Unit of Endocrinology, Federico II University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy; giovanna.muscogiuri@gmail.com (G.M.); dani.laudisio@libero.it (D.L.); robinia.pugliese@gmail.com (G.P.); dealteriisgiulia@gmail.com (G.d.A.); colao@unina.it (A.C.); sisavast@unina.it (S.S.)
- <sup>2</sup> Centro Italiano per la cura e il Benessere del Paziente con Obesità (C.I.B.O), Department of Clinical Medicine and Surgery, Endocrinology Unit, University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy
- <sup>3</sup> Cattedra Unesco “Educazione alla Salute e allo Sviluppo Sostenibile”, Federico II University Medical School of Naples, Via Sergio Pansini 5, 80131 Naples, Italy



# PIRAMIDE AMBIENTALE



# PIRAMIDE ALIMENTARE



# Il progetto SU-EATABLE LIFE

I nostri sistemi alimentari sono responsabili fino al 37% delle emissioni mondiali di gas ad effetto serra (GHG) e sono intensivi in termini di consumo di acqua.

Il progetto SU-EATABLE LIFE sostiene i cittadini europei nell'adozione di una dieta sana e sostenibile con l'obiettivo di ridurre le emissioni di GHG e il consumo idrico nell'UE, con sperimentazioni in mense aziendali e universitarie nel Regno Unito e in Italia. Le attività sono volte ad aumentare la consapevolezza degli utenti, incoraggiare le scelte sane e sostenibili, e migliorare l'offerta delle mense.

Fondazione Barilla, capofila dell'iniziativa, collabora con i partner greenApes, Wageningen University, e la Sustainable Restaurant Association. Tra le realtà coinvolte: Università di Parma, Ducati Motor Holding S.p.A., City, University London.

Gli obiettivi del Progetto :

- 5.000 persone impegnate per un risparmio di
- 5.300 tonnellate di CO<sub>2</sub> eq
- 2 milioni di metri cubi d'acqua



# 8 principi per una dieta sana e sostenibile



Mangia verdure, legumi, frutta fresca, frutta secca e cereali integrali



Non consumare troppa carne, soprattutto rossa, salumi e insaccati



Scegli ingredienti di stagione, varietà locali o della tradizione



Non esagerare con formaggi, burro e latte



Mangia cibo fresco e quanto più possibile preparato naturalmente



Non sprecare cibo: metti nel piatto solo ciò che ti serve



Bevi molta acqua, possibilmente del rubinetto, e non sprecarla



Riduci gli imballaggi e i materiali usa e getta, riusa, ricicla

[www.sueatablelife.eu](http://www.sueatablelife.eu)



**Barilla**  
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FOR FOOD  
& NUTRITION

Article

# Tripartite Combination of Candidate Pandemic Mitigation Agents: Vitamin D, Quercetin, and Estradiol Manifest Properties of Medicinal Agents for Targeted Mitigation of the COVID-19 Pandemic Defined by Genomics-Guided Tracing of SARS-CoV-2 Targets in Human Cells

Gennadi V. Glinsky

Institute of Engineering in Medicine, University of California, San Diego, 9500 Gilman Dr. MC 0435, La Jolla, CA 92093-0435, USA; gginskii@ucsd.edu; Tel.: +1-858-401-3470

Received: 25 April 2020; Accepted: 15 May 2020; Published: 21 May 2020



- The observations support recent studies describing numerous beneficial clinical effects of the vitamin D supplementations
- Many detrimental effects of the vitamin D insufficiency and deficiency, underscore the significant COVID-19 mitigation potential of vitamin D
- Two recent interventional RCT to evaluate the effect of vitamin D on the prevention and treatment of COVID-19 are ongoing (<https://www.clinicaltrials.gov/ct2/show/NCT04334005> and <https://clinicaltrials.gov/ct2/show/NCT04344041>).

- A computational screening of a chemical library of over 687 million compounds for binding at the recently solved crystal structure of the main protease of SARS-CoV-2 coronavirus identified two highly similar to Quercetin molecules, namely taxifolin and rhamnetin, among the top-scoring candidate inhibitors of the SARS-CoV-2 main protease (<https://doi.org/10.26434/chemrxiv.11923239.v2>)

Review

# Diet Supplementation, Probiotics, and Nutraceuticals in SARS-CoV-2 Infection: A Scoping Review

Fabio Infusino <sup>1</sup>, Massimiliano Marazzato <sup>2</sup>, Massimo Mancone <sup>1</sup>, Francesco Fedele <sup>1</sup>, Claudio Maria Mastroianni <sup>2</sup>, Paolo Severino <sup>1</sup>, Giancarlo Ceccarelli <sup>2</sup>, Letizia Santinelli <sup>2</sup>, Elena Cavarretta <sup>3,4</sup>, Antonino G. M. Marullo <sup>3</sup>, Fabio Miraldi <sup>1</sup>, Roberto Carnevale <sup>3,4</sup>, Cristina Nocella <sup>1</sup>, Giuseppe Biondi-Zoccai <sup>3,4</sup>, Cristiano Pagnini <sup>5</sup>, Sonia Schiavon <sup>3</sup>, Francesco Pugliese <sup>6</sup>, Giacomo Frati <sup>3,7</sup> and Gabriella d’Ettorre <sup>2,\*</sup>

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<sup>2</sup> Department of Public Health and Infectious Diseases, Sapienza, University of Rome, 00185 Rome, Italy; massimiliano.marazzato@uniroma1.it (M.M.); claudio.mastroianni@uniroma1.it (C.M.M.); giancarlo.ceccarelli@uniroma1.it (G.C.); letizia.santinelli@uniroma1.it (L.S.)

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<sup>4</sup> Mediterranea Cardiocentro, 80133 Naples, Italy

<sup>5</sup> Department of Gastroenterology and Digestive Endoscopy, Azienda Ospedaliera San Giovanni Addolorata, 00184 Rome, Italy; cpagnini@hsangiovanni.roma.it

<sup>6</sup> Department of General Surgery and Surgical Specialities “Paride Stefanini”, Sapienza, University of Rome, 00185 Rome, Italy; francesco.pugliese@uniroma1.it

<sup>7</sup> IRCCS NeuroMed, 86077 Pozzilli (IS), Italy

\* Correspondence: gabriella.dettorre@uniroma1.it; Tel.: +39-06-4997-9046; Fax: +39-06-4997-9047

- The possible role of non-pharmacological substances such as supplements, probiotics, and nutraceuticals in reducing the risk of Sars-CoV-2 infection or mitigating the symptoms of COVID-19 was assessed
- These substances are generally easily available, and have negligible side effects if administered at the already used and tested dosages
- Large scientific evidence supports the benefits that some bacterial and molecular products may exert on the immune response to respiratory viruses
- These could also have a regulatory role in systemic inflammation or endothelial damage, which are two crucial aspects of COVID-19
- Rigorous clinical trials should be conducted to confirm the putative benefits of diet supplementation, probiotics, and nutraceuticals in the current pandemic.

# Fit4Pandemic (The Batman Project)

([www.fit4Pandemic.com](http://www.fit4Pandemic.com))

- Bats have evolved to modulate their immune and inflammatory responses to avoid complications of viral infections
- Can lifestyle, diet and supplements help us prevent severe complications of viral infections, triggered by hyper-inflammatory and hyper-immune responses?
- Pro-inflammatory diets and insufficient of protective factors can predispose us to hyper-inflammatory and hyper-immune reactions that result an increased susceptibility to triggering events of autoimmunity. Similarly, these factors can increase the risk of life-threatening complications of viral infections, such as those associated with severe cases of COVID-19
- While we are working to treat autoimmune diseases such as Type 1 Diabetes and severe cases of COVID-19 with anti-inflammatory and immuno-modulating stem cell infusions, we are launching an international collaboration (The Batman Project), to study how bioactive dietary components and supplements could complement healthy diets to modulate inflammation, immunity, and other variables associated with disease progression



<b>SOSTANZE PROTETTIVE</b>	<b>CONSUMO GIORNALIERO (selezionare un prodotto a scelta)</b>	<b>CALORIE</b>
40 mg di <b>RESVERATROLO</b>	10-12 L di vino rosso	6.000 – 7.800
	27 L di vino bianco	17.550
	33 – 60 Kg di Uva Nera	21.650 – 39.000
	22 kg di arachidi	124.740
	13 kg di cacao	2.964
60 mg di <b>PTEROSTILBENE</b>	10 kg di mirtilli	5.700
	16 kg di ribes neri	10.080
200 mg di <b>POLIDATINA</b>	200 g di radice di SOPHORA JAPONICA	Difficile da trovare e poco digeribile
80 mg di <b>ACIDO ELLAGICO</b>	2 L di succo fresco di MELAGRANA	1.080
30 mg di <b>ONOCIOLO</b>	100 g di corteccia di Magnolia	Difficile da trovare e poco digeribile
5 g di <b>OMEGA 3</b> (EPA+DHA)	6 kg di aragoste	8.580
	2 kg di tonno	2.588
	600 g di salmone	1.236
2 g di <b>Vitamina C</b>	4.5 kg arance	2.025
	1.5 kg peperoncino rosso fresco	600
7.000 UI di <b>Vitamina D</b>	159 uova	11.448



SOSTANZE PROTETTIVE	CONSUMO GIORNALIERO (selezionare un prodotto a scelta)	CALORIE
40 mg di <b>RESVERATROLO</b>	10-12 L di vino rosso 27 L di vino bianco 33 – 60 Kg di Uva Nera 22 kg di arachidi 13 kg di cacao	6.000 – 7.800 17.550 21.650 – 39.000 124.740 2.964
60 mg di <b>PTEROSTILBENE</b>	10 kg di mirtilli 16 kg di ribes neri	5.700 10.080
200 mg di <b>POLIDATINA</b>	200 g di radice di SOPHORA JAPONICA	Difficile da trovare e poco digeribile
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30 mg di <b>ONOCIOLO</b>	100 g di corteccia di Magnolia	Difficile da trovare e poco digeribile
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2 g di <b>Vitamina C</b>	4.5 kg arance 1.5 kg peperoncino rosso fresco	2.025 600
7.000 UI di <b>Vitamina D</b>	159 uova	11.448

**SIRT500+**



### **PTEROSTILBENE**

Present in blueberries, grapes and bark of the Indian Kino tree. It has demonstrated antiviral properties. Thanks to its ability to bind the protein S of SARS-CoV-2, it could inhibit its attack on the cell by reducing its virulence ([https://chemrxiv.org/articles/Targeting SARS-CoV-2 Spike Protein of COVID-19 with Naturally Occurring Phytochemicals An in Silco Study for Drug Development/12094203/1?file=22237578](https://chemrxiv.org/articles/Targeting_SARS-CoV-2_Spike_Protein_of_COVID-19_with_Naturally_Occurring_Phytochemicals_An_in_Silico_Study_for_Drug_Development/12094203/1?file=22237578)). It also has protective effects against age-related diseases, including Alzheimer's disease, cellular stress and inflammation



### **POLIDATINA**

Extracted from the POLYGONUM CUSPIDATUM. It has antioxidant, anti-inflammatory, antiviral, anti-aging and anti-platelet aggregation activity. It also has the ability to modulate pathways affecting SARS-CoV-2 infection ([https://chemrxiv.org/articles/Establishment and Validation of a Drug-Target Microarray for SARS-CoV-2/12362618](https://chemrxiv.org/articles/Establishment_and_Validation_of_a_Drug-Target_Microarray_for_SARS-CoV-2/12362618)).



### **ONOCHIOLO**

Derived from Magnolia. It has demonstrated anti-inflammatory, antioxidant and antiviral properties. Onochiolo can inhibit the replication of the SARS virus and could potentially have also an anti-viral role against SARS-CoV-2 (<https://europepmc.org/article/med/17663539>).



**BARRY SEARS, Ph.D.**



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# AKNOWLEDGEMENTS

## Batman Project



**Prof. David Della Morte**  
**Dott.ssa Francesca**  
**Pacifici**  
**Dott.ssa Valentina**  
**Rovella**



**Prof. Enrico Garaci**



**Prof.ssa Anna Teresa**  
**Palamara**  
**Prof.ssa Lucia Nencioni**  
**Dott.ssa Marta De Angelis**



**Prof.ssa Paola Stefanelli**

- **SIRT500 SAGL**
- **Lugano, Svizzera**

# AKNOWLEDGEMENTS UC-MSC for COVID19



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