ngb | genetics

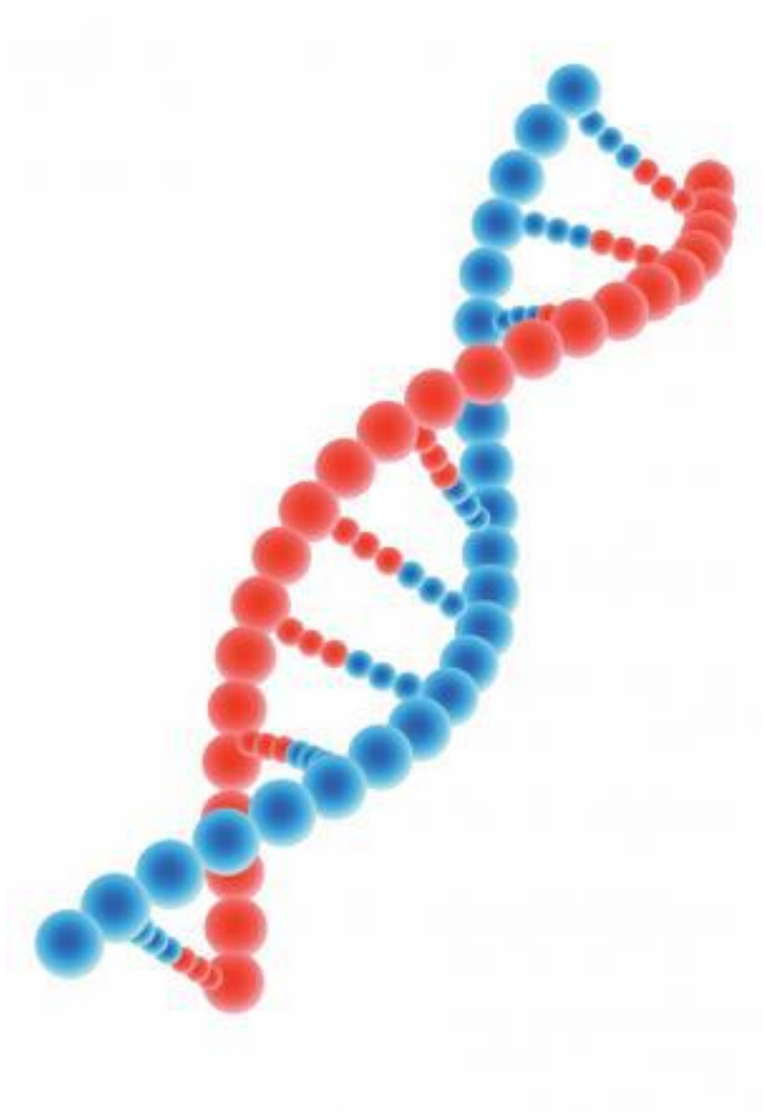
Genetica e Nutrizione

Conferenza dal Titolo: Genetica e Malattie Rare in Oftalmologia
Sede dell'incontro presso:
VOLABO in Via Scipione dal Ferro n. 4
Domenica 2 luglio 2017

Prof. Enzo Spisni – Università di Bologna
Dott. Vittorio Lucchini -NGB Genetics Srl - Spin off Università di Ferrara

LO SVILUPPO DI UN INDIVIDUO E' DATO DALL'INTERAZIONE DI DUE COMPONENTI:

LA COMPONENTE GENETICA + **LA COMPONENTE AMBIENTALE**



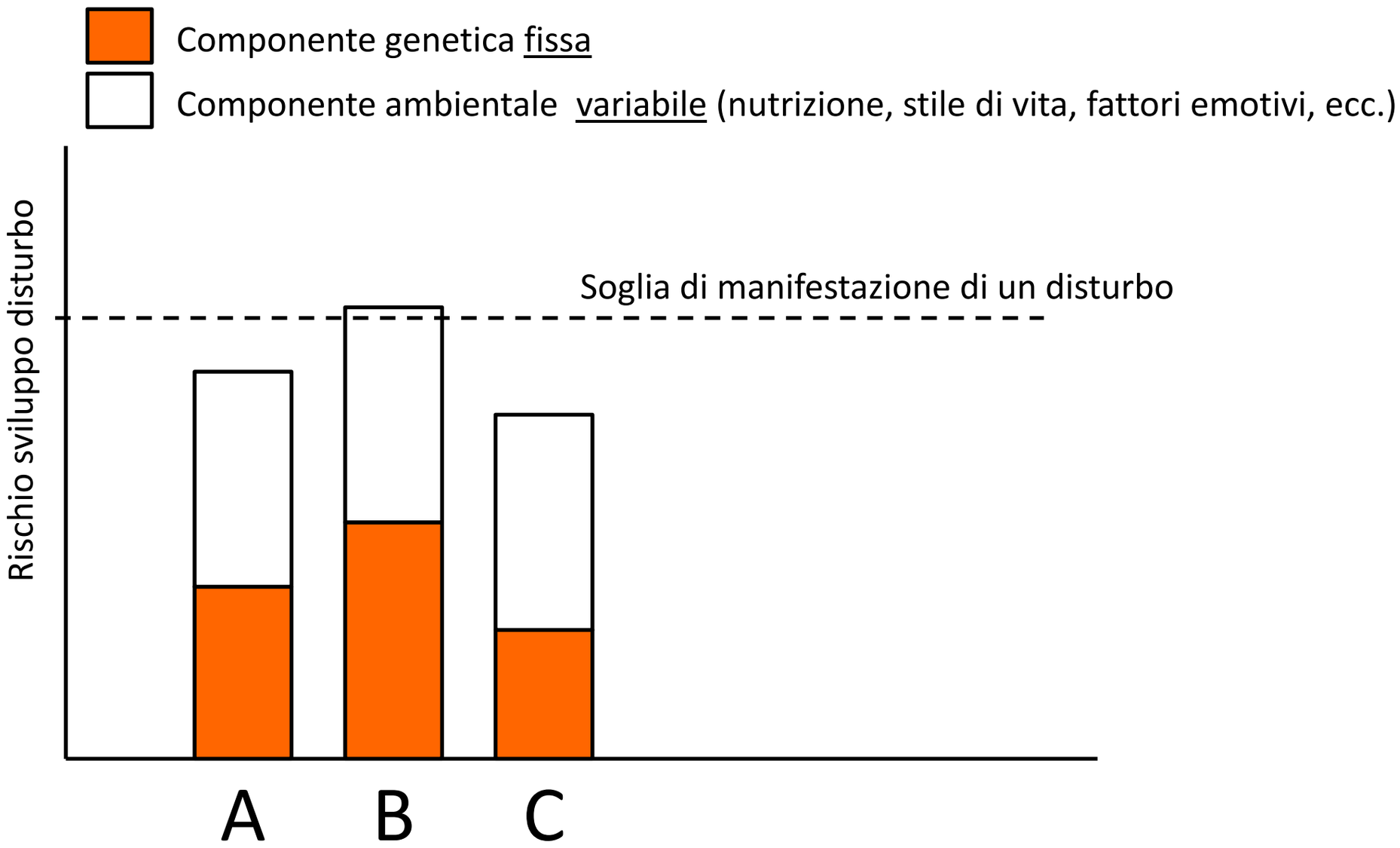
LA COMPONENTE GENETICA E' FISSA

LA COMPONENTE AMBIENTALE E' MODIFICABILE

TRA I FATTORI AMBIENTALI
PIU' IMPORTANTI VI SONO:

ALIMENTAZIONE E STILE DI VITA

Concetto di soglia di manifestazione



Conoscendo la componente genetica (fissa) si può lavorare con maggior specificità su alcuni aspetti della componente ambientale (nutrizione e stile di vita) per abbassare il livello sotto la soglia di manifestazione del disturbo.

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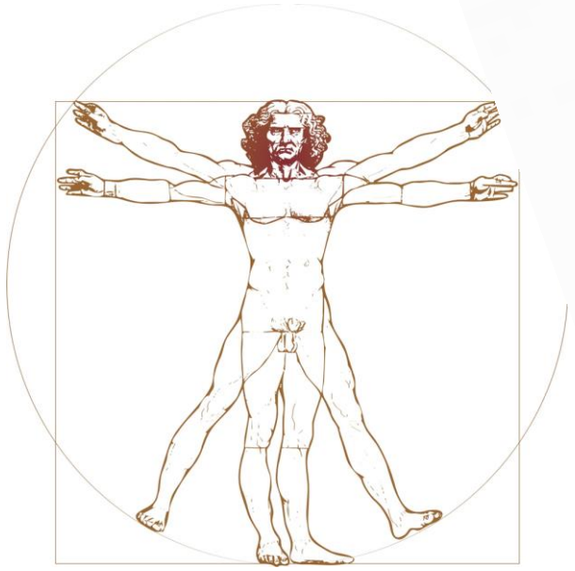
Perchè la Genetica è importante nell'alimentazione?

Nutrigenomica

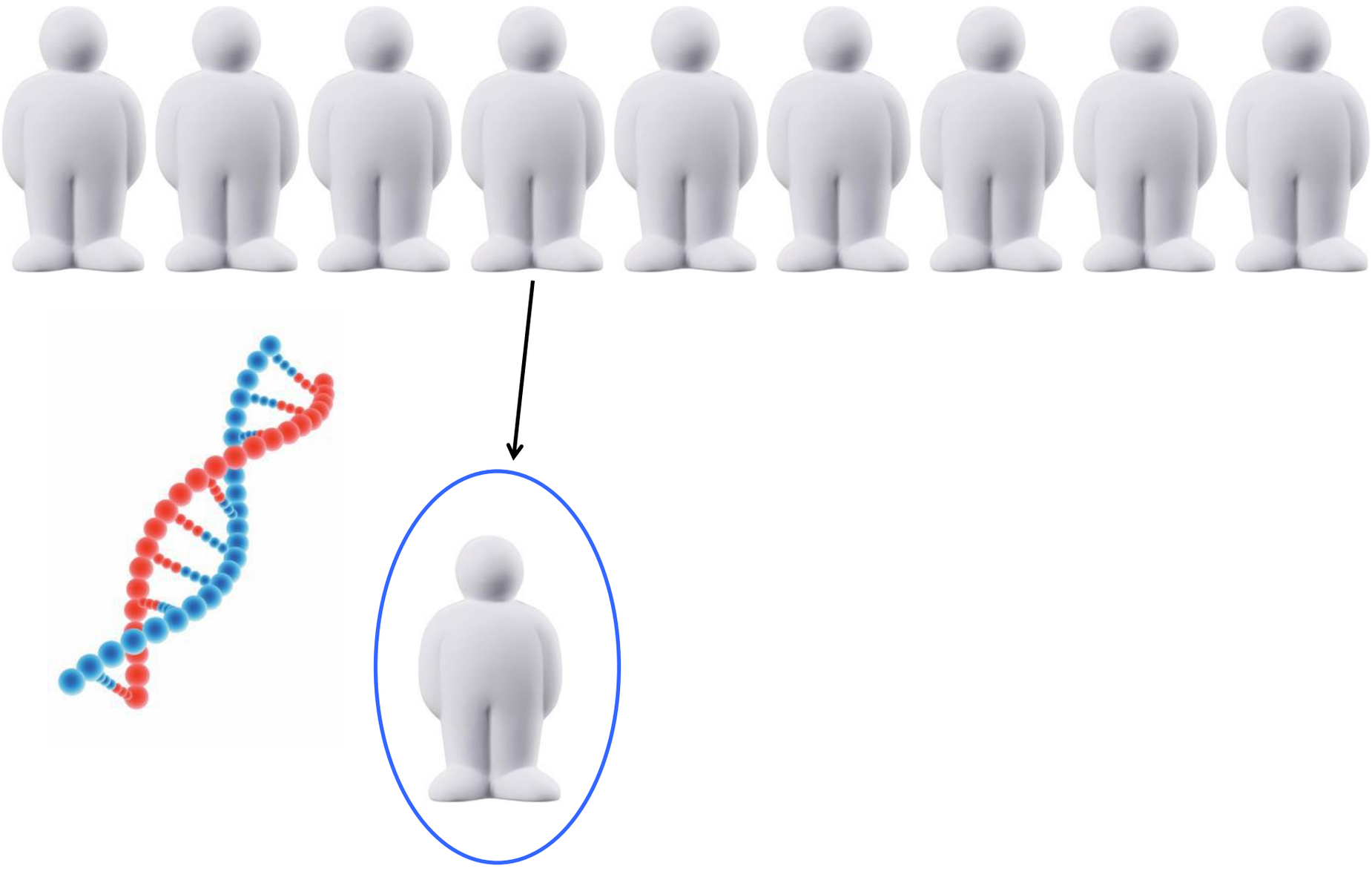


Nutrigenetica

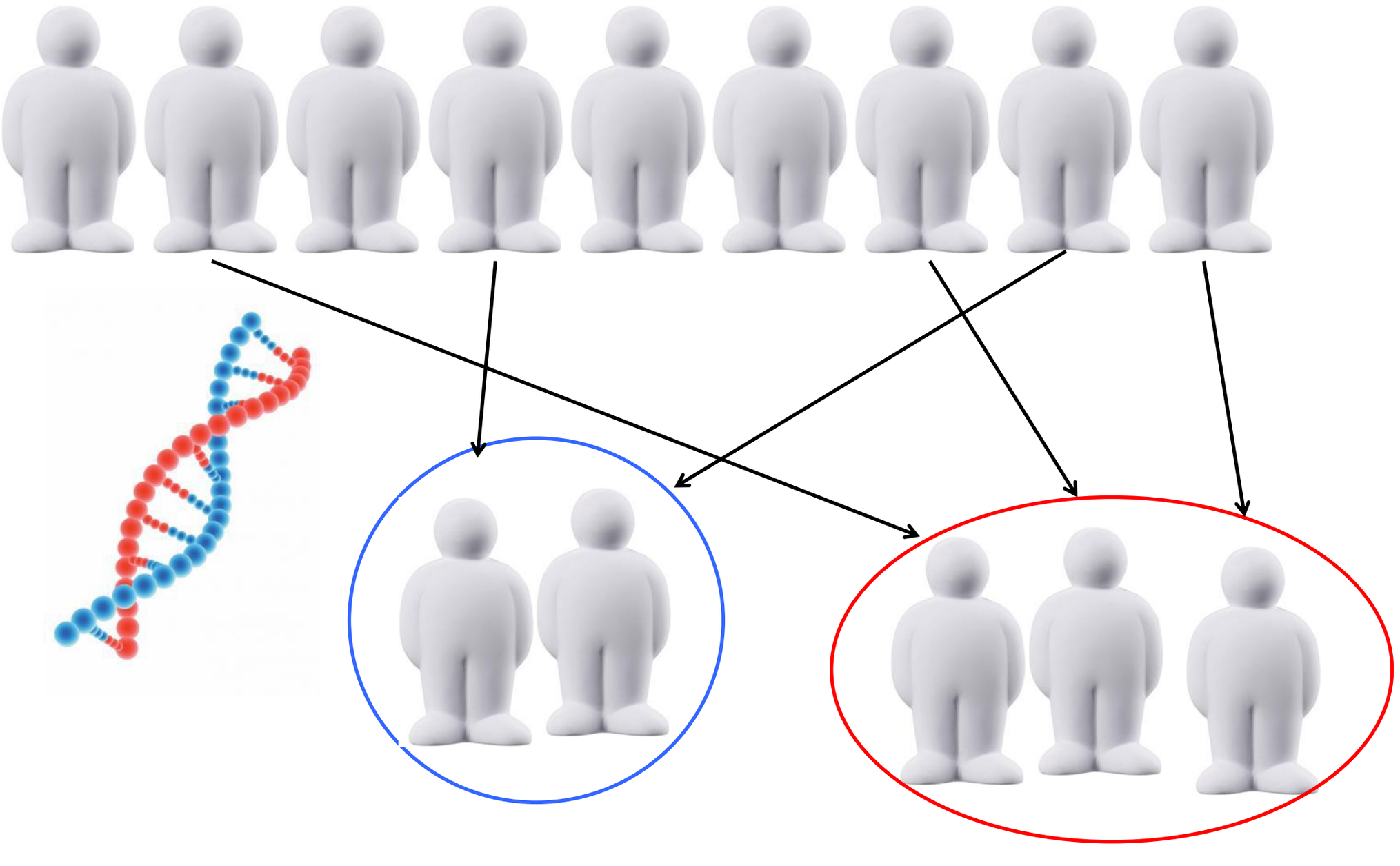
Perchè Cibo e DNA interagiscono profondamente influenzando il metabolismo dell'uomo

LE INDICAZIONI NUTRIZIONALI SONO INDICAZIONI MEDIE PER LA POPOLAZIONE

OGGI E’ POSSIBILE AVERE INFORMAZIONI A LIVELLO DELL’INDIVIDUO



..O PER GRUPPI PIU' OMOGENEI DI INDIVIDUI



I progressi della ricerca genetica sono molto rapidi

Retinite Pigmentosa

OXFORD

Human Molecular Genetics, 2017, Vol. 0, No. 0 1–10

doi: 10.1093/hmg/ddx185
Advance Access Publication Date: 16 May 2017
Invited Review

INVITED REVIEW

Toward an elucidation of the molecular genetics of inherited retinal degenerations

G. Jane Farrar[1,*], Matthew Carrigan[1], Adrian Dockery[1], Sophia Millington-Ward[1], Arpad Palfi[1], Naomi Chadderton[1], Marian Humphries[1], Anna Sophia Kiang[1], Paul F. Kenna[2] and Pete Humphries[1,*]

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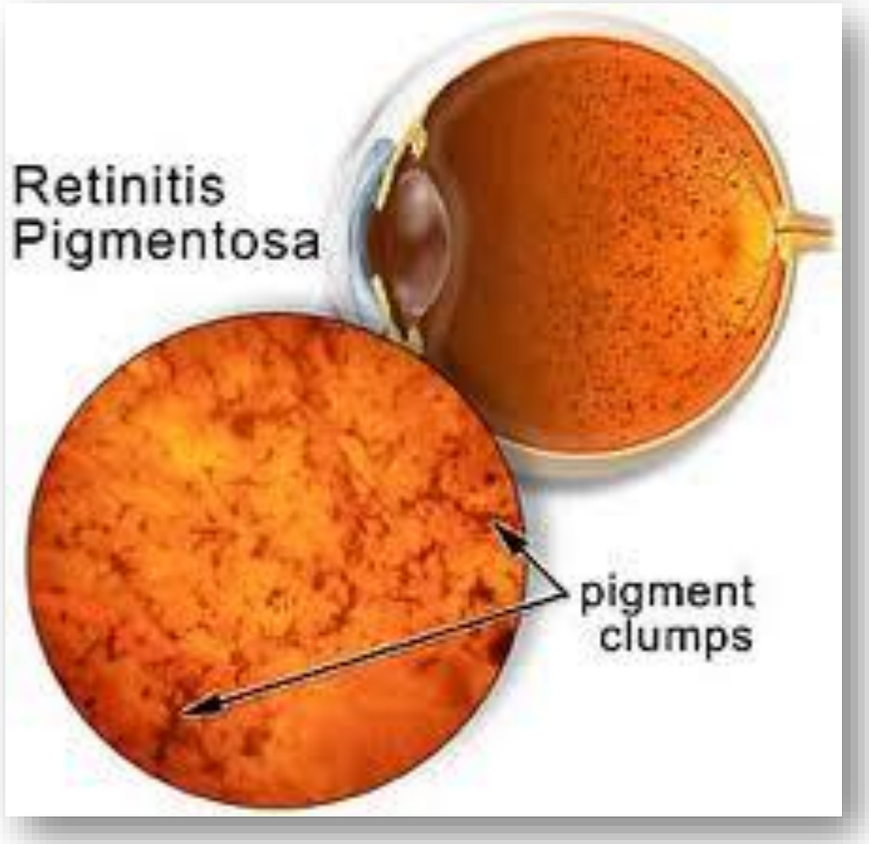
Abstract

While individually classed as rare diseases, hereditary retinal degenerations (IRDs) are the major cause of registered visual handicap in the developed world. Given their hereditary nature, some degree of intergenic heterogeneity was expected, with genes segregating in autosomal dominant, recessive, X-linked recessive, and more rarely in digenic or mitochondrial modes. Today, it is recognized that IRDs, as a group, represent one of the most genetically diverse of hereditary conditions - at least 260 genes having been implicated, with 70 genes identified in the most common IRD, retinitis pigmentosa (RP). However, targeted sequencing studies of exons from known IRD genes have resulted in the identification of candidate mutations in only approximately 60% of IRD cases. Given recent advances in the development of gene-based medicines, characterization of IRD patient cohorts for known IRD genes and elucidation of the molecular pathologies of disease in those remaining unresolved cases has become an endeavor of the highest priority. Here, we provide an outline of progress in this area.



La ricerca fa progressi nella comprensione delle basi genetiche...

...ma anche delle interazioni tra alimentazione e patologia.

RESEARCH ARTICLE Open Access

Dietary profile of patients with Stargardt's disease and Retinitis Pigmentosa: is there a role for a nutritional approach?

Francesco Sofi[1,2,3], Andrea Sodi[4*], Fabrizio Franco[4], Vittoria Murro[4], Dania Biagini[2], Alba Miele[4], Giacomo Abbruzzese[4], Dario Pasquale Mucciolo[1], Gianni Virgili[1,3], Ugo Menchini[4], Alessandro Casini[1,2] and Stanislao Rizzo[4]

Abstract

Background: Stargardt's disease (STGD) and Retinitis Pigmentosa (RP) are inherited retinal degenerations that may be affected, in opposite way, by diet.

Methods: Dietary profile was assessed in 24 patients with STGD and in 56 patients with RP. We documented in only 6 out of 24 (25 %) STGD patients a daily intake of vitamin A within the recommended range while 14/24 (58.3 %) reported a high daily intake and 4/24 (16.7 %) showed a low daily intake. With regard to RP, 4/56 (7.1 %) reported to be within the recommended range, 37/56 (66.1 %) reported high daily intake and 15/56 (26.8 %) showed low daily intake of vitamin A.

Results: Interestingly, STGD patients with low vitamin A intake (<600 μg RAE/day) showed significantly better visual acuity with respect to those introducing higher intake of vitamin A.

Conclusion: The present study suggests insuitable nutrient intakes among patients with STGD and RP, especially for daily intake of vitamin A. The results may be used to provide tailored nutritional interventions in these patients.

Keywords: Stargardt's disease, Retinitis Pigmentosa, Vitamin A, Diet

Background

Vitamin A plays a crucial role in the biochemistry of visual signal cascade and the maintenance of an optimal vitamin A status has been considered relevant for a normal retinal physiology [1, 2].

Stargardt's Disease (STGD) and Retinitis Pigmentosa (RP) are genetic-based relevant ocular diseases that may be affected, in opposite way, by vitamin A intake and other nutrients [3–5].

In an animal model of STGD vitamin A supplementation has been shown to accelerate the accumulation of toxic by-products, being prevented by a reduction of its serum levels with possible implications for the treatment [6]. Moreover, in such patients a supplementation with lutein, a retinal carotenoid, increases macula pigment density but it seems not to be associated with changes in central vision over a 6 months-follow up period [7]. Conversely, RP patients seems to get beneficial effects from a supplementation with vitamin A, since it has been associated with an improved preservation of cone electroretinogram amplitudes and has been proposed as a treatment to slow the progression of the disease [8]. Moreover, for RP patients assuming vitamin A therapy addition of the polyunsaturated fatty acid docosahexaenoic acid has been showed to slow the course of the disease over the first two years of supplementation [9–11]. Similarly, an increased dietary intake of lutein, a retinal carotenoid, seems to slow visual function loss in RP adult patients assuming vitamin A [12]. In the light of all these clinical observations, nutritional indications

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Ad esempio esiste una relazione tra vit. A e patologie oculari...

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Omega-3 Intake and Visual Acuity in Patients with Retinitis Pigmentosa on Vitamin A

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[1]Berman-Gund Laboratory for the Study of Retinal Degenerations, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, MA and [2]Department of Nutrition, Harvard School of Public Health, Boston, MA

Abstract

Objective—We evaluated whether a diet high in long chain omega-3 fatty acids can slow the rate of visual acuity loss among patients with retinitis pigmentosa on vitamin A palmitate.

Methods—We calculated dietary intake from questionnaires completed annually by 357 adult patients who were all receiving vitamin A 15,000 IU/day for 4–6 years. Rates of visual acuity decline were compared between those with high (≥ 0.20 g/day) versus low (<0.20 g/day) omega-3 intake. Analyses took age into account.

Results—Mean rates of decline of acuity were slower among those with high omega-3 intake; ETDRS distance acuity: high =0.59 letter/year, low=1.00 letter/year, p=0.001; Snellen retinal acuity: high = 1.5%/year; low = 2.8%/year, p=0.030.

Conclusions—We conclude that mean annual rates of decline in distance and retinal visual acuities in adults with retinitis pigmentosa taking vitamin A 15,000 IU/day are slower over 4–6 years among those consuming a diet rich in omega-3 fatty acids. To our knowledge this is the first report that nutritional intake can modify the rate of decline of visual acuity in retinitis pigmentosa.

L’assunzione di omega 3 riduce il decorso della patologia.

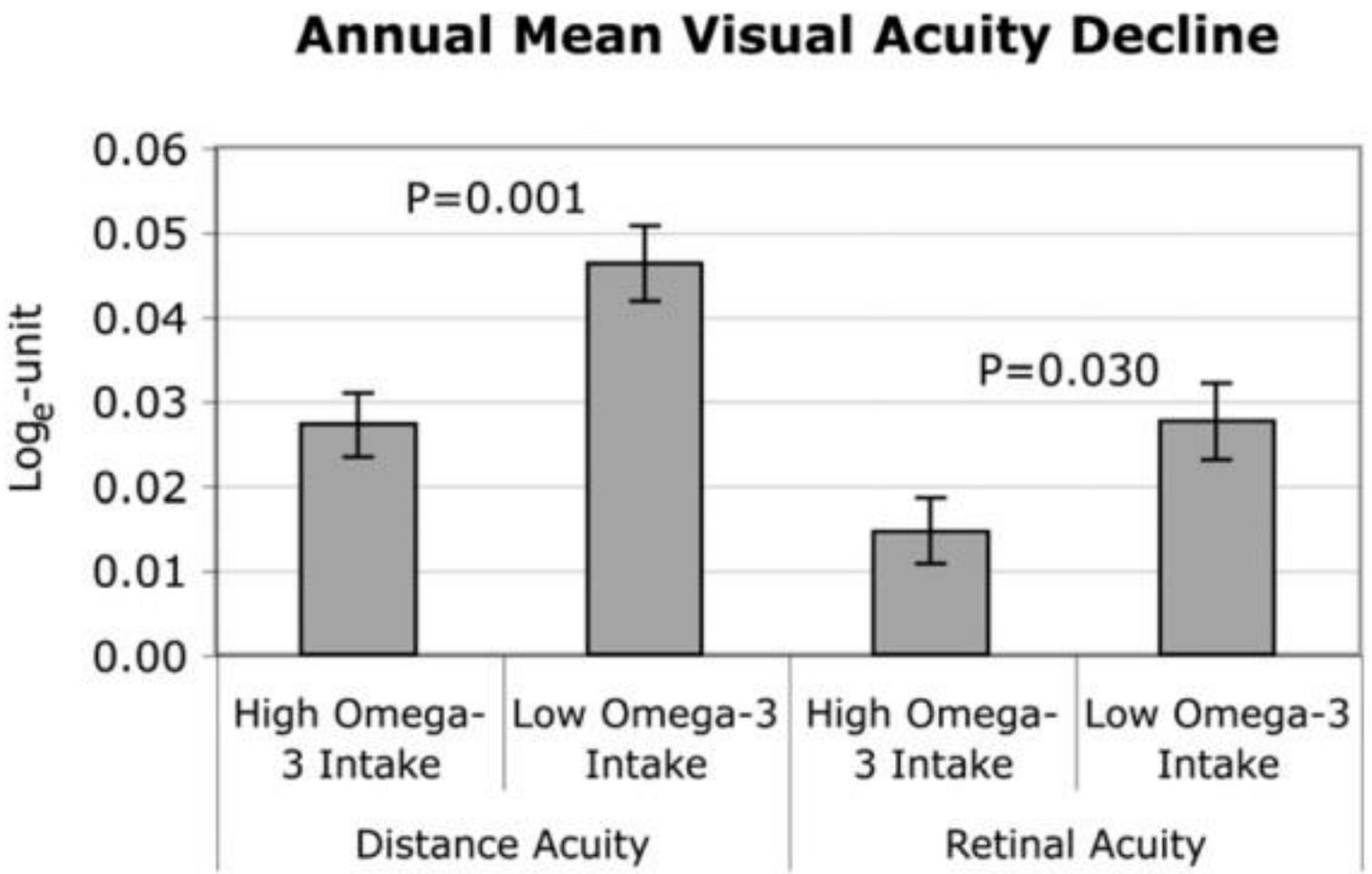
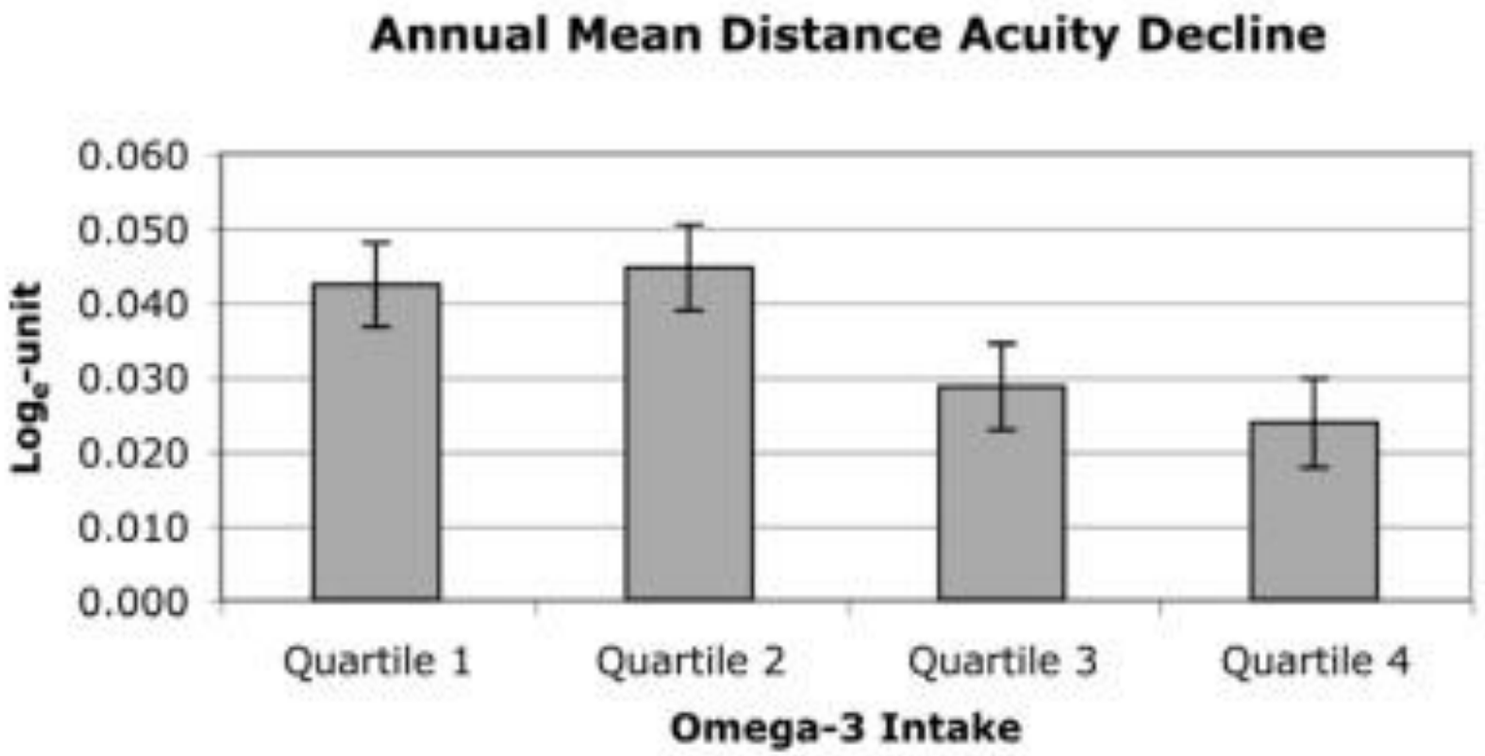
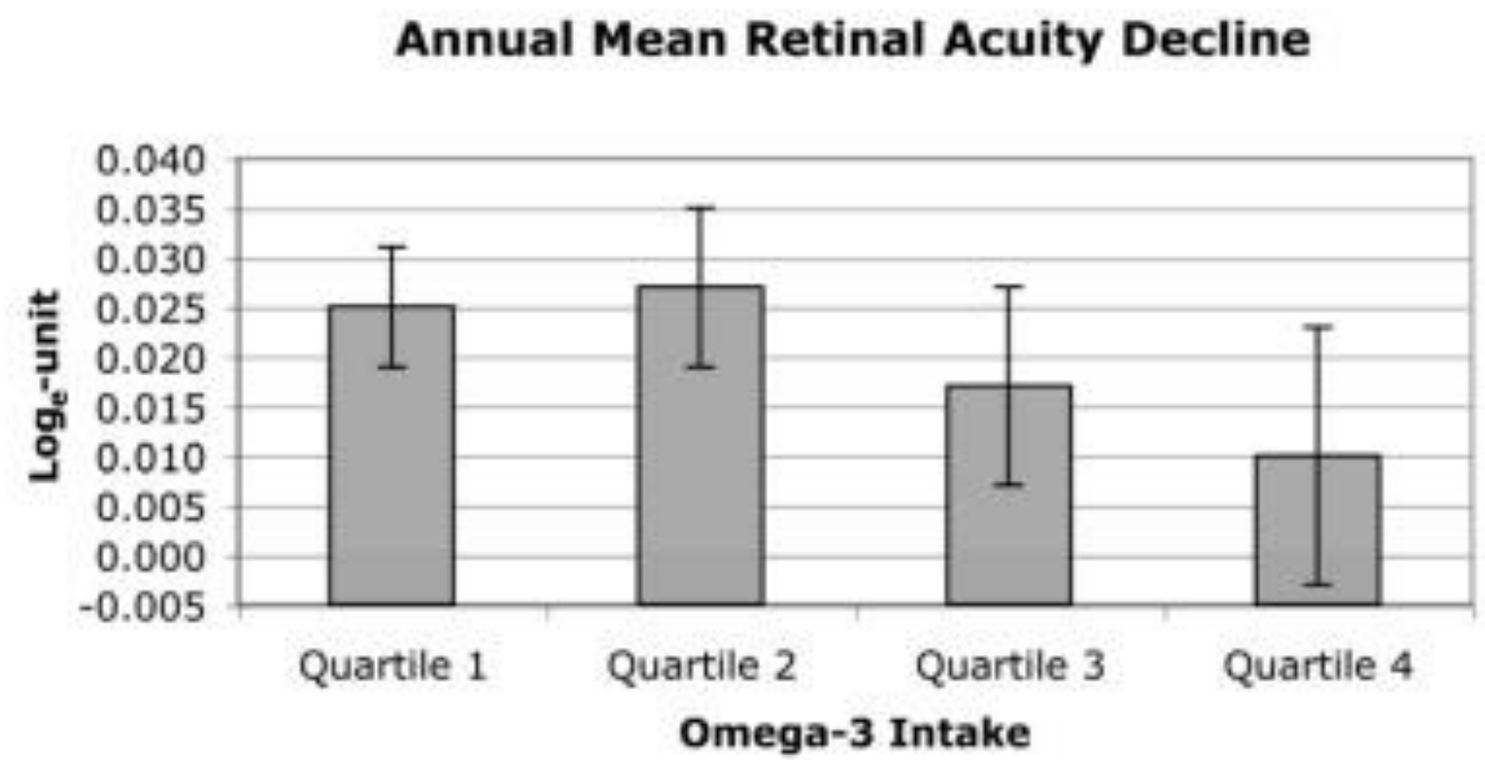


Figure 1.
Mean log rates of decline of distance and retinal visual acuity for patients with high dietary omega-3 intake versus low dietary omega-3 intake. Data represent means and standard errors.


Annual Mean Distance Acuity Decline
0.060
0.050
0.040
0.030
0.020
0.010
0.000
Log$_e$-unit
Quartile 1
Quartile 2
Quartile 3
Quartile 4
Omega-3 Intake


Annual Mean Retinal Acuity Decline
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
Log$_e$-unit
Quartile 1
Quartile 2
Quartile 3
Quartile 4
Omega-3 Intake

Esiste una relazione tra genetica e nutrienti.

nutrients

MDPI

Review

Genetic Variations Associated with Vitamin A Status and Vitamin A Bioavailability

Patrick Borel and Charles Desmarchelier

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Abstract: Blood concentration of vitamin A (VA), which is present as different molecules, i.e., mainly retinol and provitamin A carotenoids, plus retinyl esters in the postprandial period after a VA-containing meal, is affected by numerous factors: dietary VA intake, VA absorption efficiency, efficiency of provitamin A carotenoid conversion to VA, VA tissue uptake, etc. Most of these factors are in turn modulated by genetic variations in genes encoding proteins involved in VA metabolism. Genome-wide association studies (GWAS) and candidate gene association studies have identified single nucleotide polymorphisms (SNPs) associated with blood concentrations of retinol and β-carotene, as well as with β-carotene bioavailability. These genetic variations likely explain, at least in part, interindividual variability in VA status and in VA bioavailability. However, much work remains to be done to identify all of the SNPs involved in VA status and bioavailability and to assess the possible involvement of other kinds of genetic variations, e.g., copy number variants and insertions/deletions, in these phenotypes. Yet, the potential usefulness of this area of research is exciting regarding the proposition of more personalized dietary recommendations in VA, particularly in populations at risk of VA deficiency.

La biodisponibilità della vitamina A e la sua concentrazione ematica è influenzata da specifiche varianti genetiche.

Mol. Nutr. Food Res. 2016, 60, 381–389 DOI 10.1002/mnfr.201500594

RESEARCH ARTICLE

Gene-diet interaction of a common FADS1 variant with marine polyunsaturated fatty acids for fatty acid composition in plasma and erythrocytes among men

Markus J. Takkunen[1], Vanessa D. de Mello[1], Ursula S. Schwab[1,2], Johanna Kuusisto[3], Maija Vaittinen[1], Jyrki J. Ågren[4], Markku Laakso[3], Jussi Pihlajamäki[1,2] and Matti I. J. Uusitupa[1,5]

[1] Institute of Public Health and Clinical Nutrition, Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland
[2] Clinical Nutrition and Obesity Center, Kuopio University Hospital, Kuopio, Finland
[3] Department of Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland
[4] Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland
[5] Research Unit, Kuopio University Hospital, Kuopio, Finland

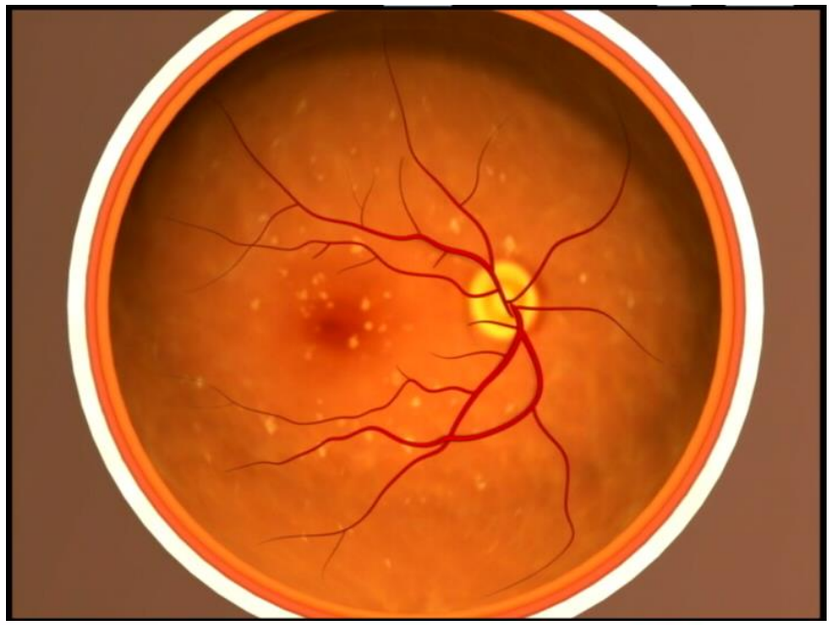
Received: July 27, 2015
Revised: September 13, 2015
Accepted: September 29, 2015

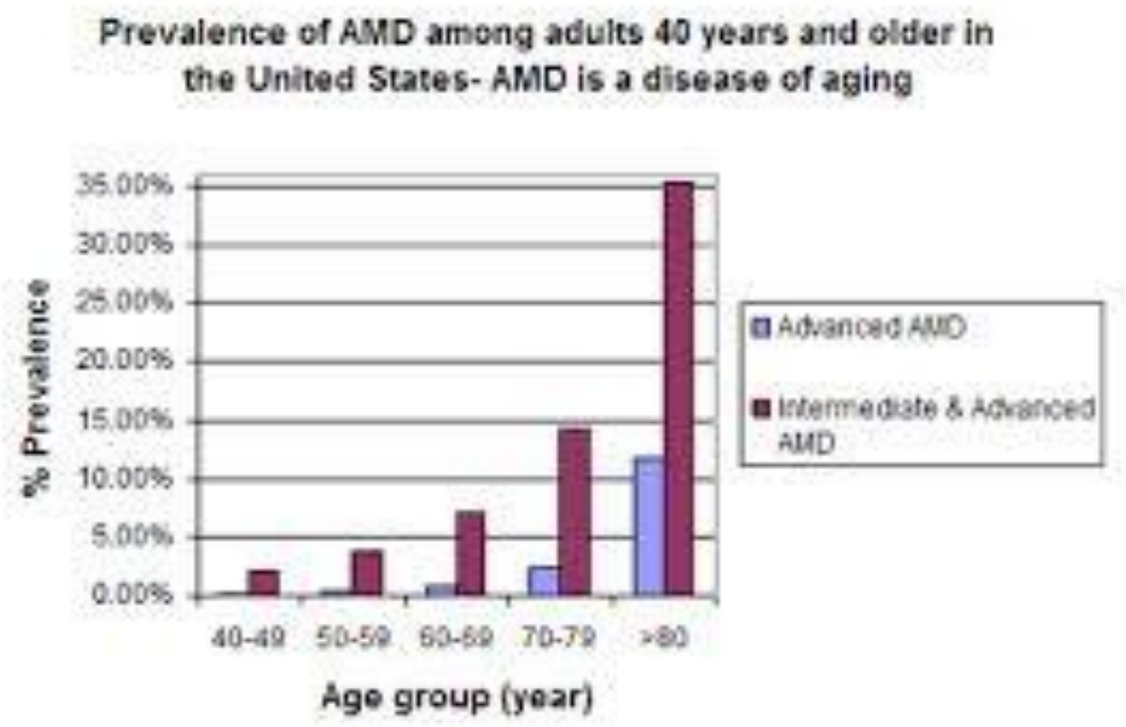
Scope: Limited information exists on how the relationship between dietary intake of fat and fatty acids in erythrocytes and plasma is modulated by polymorphisms in the *FADS* gene cluster. We examined gene-diet interaction of total marine PUFA intake with a known gene encoding Δ-5 desaturase enzyme *(FADS1)* variant (rs174550) for fatty acids in erythrocyte membranes and plasma phospholipids (PL), cholesteryl esters (CE), and triglycerides (TG).

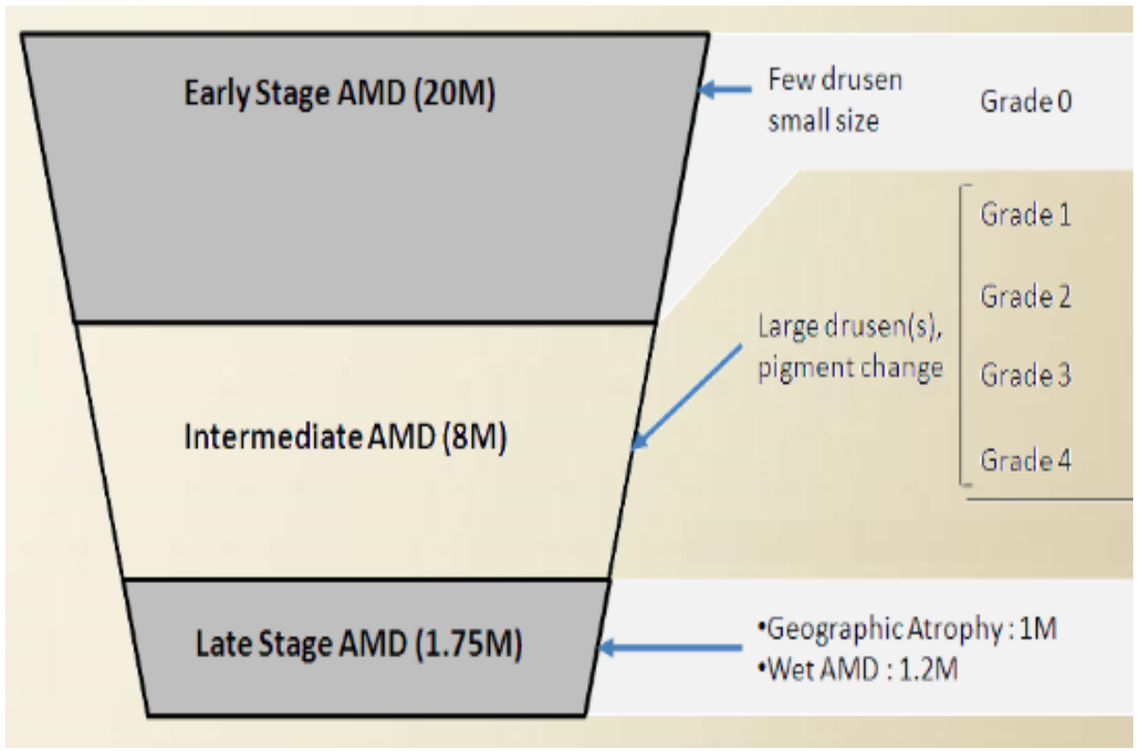
Methods and results: In this cross-sectional study, fatty acid compositions were measured using GC, and total intake of polyunsaturated fat from fish and fish oil was estimated using a food frequency questionnaire in a subsample ($n = 962$) of the Metabolic Syndrome in Men Study. We found nominally significant gene-diet interactions for eicosapentaenoic acid (EPA, 20:5*n*-3) in erythrocytes ($p_{interaction} = 0.032$) and for EPA in plasma PL ($p_{interaction} = 0.062$), CE ($p_{interaction} = 0.035$), and TG ($p_{interaction} = 0.035$), as well as for docosapentaenoic acid (22:5*n*-3) in PL ($p_{interaction} = 0.007$). After excluding omega-3 supplement users, we found a significant gene-diet interaction for EPA in erythrocytes ($p_{interaction} < 0.003$). In a separate cohort of the Kuopio Obesity Surgery Study, the same locus was strongly associated with hepatic mRNA expression of *FADS1* ($p = 1.5 \times 10^{-10}$).

Varianti genetiche specifiche possono modificare gli effetti dell'assunzione di omega 3 sul profilo lipidico plasmatico

Degenerazione Maculare Senile (AMD)







Degenerazione Maculare Senile (AMD)

AREDS 2
Age-Related Eye Disease Study 2
Funded by the National Institutes of Health

NIH National Eye Institute
Research Today...Vision Tomorrow

Gli studi AREDS e AREDS2 hanno mostrato una efficacia nel trattamento della AMD mediante supplementazione con :

- Luteina
- Zeaxantina
- Vitamina C
- Vitamina E
- Zinco

Ophthalmology

CFH and *ARMS2* Genetic Polymorphisms Predict Response to Antioxidants and Zinc in Patients with Age-related Macular Degeneration

Carl C. Awh, MD, Anne-Mar

Experimental Eye Research 115 (2013) 172–177

Contents lists available at ScienceDirect

Experimental Eye Research

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

Candidate gene study of macular response to supplemental lutein and zeaxanthin☆

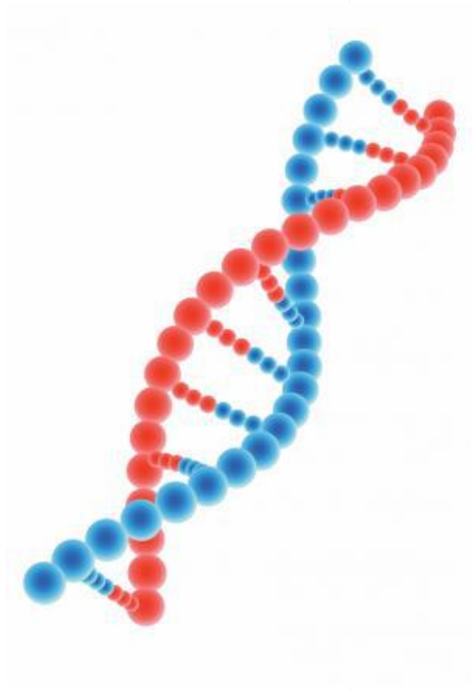
Ekaterina Yonova-Doing[a], Pirro G. Hysi[a], Cristina Venturini[b,a], Katie M. Williams[a], Abhishek Nag[a], Stephen Beatty[c], S.H. Melissa Liew[d], Clare E. Gilbert[e], Christopher J. Hammond[a,*]

L'efficacia del trattamento nutrizionale dipende anche dalle proprie caratteristiche genetiche

The Journal of Nutrition
JN THE JOURNAL OF NUTRITION
Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

CD36 and SR-BI Are Involved in Cellular Uptake of Provitamin A Carotenoids by Caco-2 and HEK Cells, and Some of Their Genetic Variants Are Associated with Plasma Concentrations of These Micronutrients in Humans[1–3]

Patrick Borel,[4-6]* Georg Lietz,[7] Aurélie Goncalves,[4-6] Fabien Szabo de Edelenyi,[4-6] Sophie Lecompte,[8] Peter Curtis,[7,9] Louisa Goumidi,[8] Muriel J. Caslake,[10] Elizabeth A. Miles,[11] Christopher Packard,[10] Philip C. Calder,[11] John C. Mathers,[7] Anne M. Minihane,[9] Franck Tourniaire,[4-7] Emmanuelle Kesse-Guyot,[12] Pilar Galan,[12] Serge Hercberg,[12] Christina Breidenassel,[13] Marcela González Gross,[14] Myriam Moussa,[4-6] Aline Meirhaeghe,[8] and Emmanuelle Reboul[4-6]



CFH Y402H rs1061170

ARMS2 rs10490924

BMCO1 rs6564851

SCARB1 rs11057841

CD36 rs1527479

RISK FACTORS

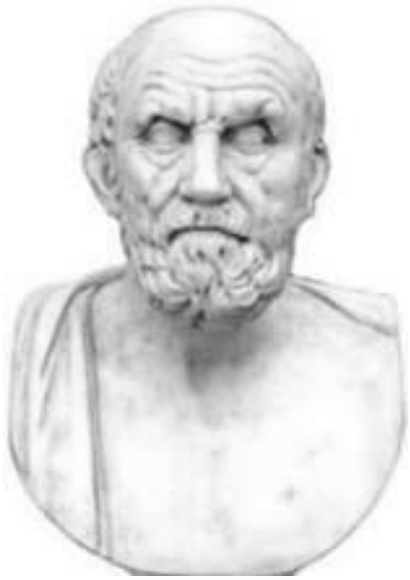
NUTRITIONAL INDICATION

ESISTE UNA RELAZIONE TRA:

- **GENETICA**
- **NUTRIZIONE**
- **EFFICACIA DELLA TERAPIA**

NON ESISTONO CONSIGLI BUONI PER TUTTI…

…MA CIASCUNO DOVREBBE RICEVERE QUELLI PIU’ ADATTI A LUI



Fa che il cibo sia la tua medicina
e che la medicina sia il tuo cibo
(Ippocrate)

GRAZIE