

# Healthy brain aging and nutrition

Invecchiamento, nutrizione  
salute mentale

*Stefano Govoni*

*Dept. Drug Sciences, University of Pavia*



**DO WE BELIEVE THAT  
NUTRITION AND  
INTEGRATORS MAY PREVENT  
OR MODIFY THE NATURAL  
HISTORY OF A DISEASE?...**

**SIAMO CONVINTI CHE LA DIETA/GLI  
INTEGRATORI POSSANO AVERE UN RUOLO  
PREVENTIVO IN MEDICINA O  
INFLUENZARE/MODIFICARE IL DECORSO  
NATURALE DI UNA MALATTIA?**



# AN EXAMPLE



# DASH: DIETARY APPROACHES TO STOP HYPERTENSION

U.S. Department of Health & Human Services

National Institutes of Health

Contact Us Get Email Alerts Font Size



[Accessible Search Form](#)

[Advanced Search](#)

NHLBI Entire Site

SEARCH

- Public
- Health Professionals
- Networks
- Funding & Research
- Clinical Trials
- Training & Careers
- Researchers
- Educational Campaigns
- News & Resources
- About NHLBI

Home » Health Information for the Public » Health Topics » DASH Eating Plan » What Is...

## Explore DASH Eating Plan

WHAT IS...

BENEFITS

FOLLOWING DASH

HEALTHY LIFESTYLE

GETTING STARTED

LINKS

[E-MAIL](#) | [PRINT PAGE](#) | [PRINT ENTIRE TOPIC](#) | [SHARE](#) +

## What Is the DASH Eating Plan?

Dietary Approaches to Stop Hypertension (DASH) is a flexible and balanced eating plan. DASH was one of three eating plans that were compared in research studies sponsored by the National Heart, Lung, and Blood Institute (NHLBI).

The goal of this research was to study the effects of diet on [high blood pressure](#). The results showed that the DASH eating plan lowers blood pressure. The plan:

- Is low in saturated fat, cholesterol, and total fat
- Focuses on fruits, vegetables, and fat-free or low-fat dairy products
- Is rich in whole grains, fish, poultry, beans, seeds, and nuts
- Contains fewer sweets, added sugars and sugary beverages, and red meats than the typical American diet

The DASH eating plan also is lower in sodium (salt) than the typical American diet. The DASH research showed that an eating plan containing 2,300 milligrams (mg) of sodium per day lowered blood pressure. An eating plan containing only 1,500 mg of sodium per day even further lowered blood pressure.

### Clinical Trials

[Clinical trials](#) are research studies that explore whether a medical strategy, treatment, or device is safe and effective for humans.

### Related Topics

[High Blood Pressure](#)



**FACING NOW THE QUESTION  
WITH AN OPEN MIND, AND  
ACCEPTING THE CONCEPT  
THAT NUTRITIONAL  
INTERVENTIONS MAY BE  
EFFICACIOUS...**

**SE AFFRONTIAMO ORA IL PROBLEMA CON  
UNA MENTE PIÙ APERTA, ACCETTANDO  
L'IDEA CHE GLI INTERVENTI NUTRIZIONALI  
SIANO EFFICACI...**



# **SEVERAL OPEN QUESTIONS UNDERScore A LACK OF KNOWLEDGE**

**VI SONO NUMEROSE  
DOMANDE APERTE CHE  
RIFLETTONO UN VUOTO DI  
CONOSCENZA...**



**WHAT IS THE TIMELINE  
BETWEEN NUTRITION  
DEFECTS AND DISEASE AND  
WHAT IS THE TIME WINDOW  
USEFUL FOR NUTRITIONAL  
INTERVENTION?**

**QUALE È LA RELAZIONE TEMPORALE TRA  
MALATTIA E SCORRETTA ALIMENTAZIONE  
E QUALE È LA FINESTRA TEMPORALE  
UTILE PER L'INTERVENTO  
NUTRIZIONALE?**



# **THE EASIEST WAY: EXPLORING DEVELOPMENTAL AGES**

**LA VIA INTUITIVAMENTE PIÙ FACILE: LO  
STUDIO DELL'ETÀ DELLO SVILUPPO**





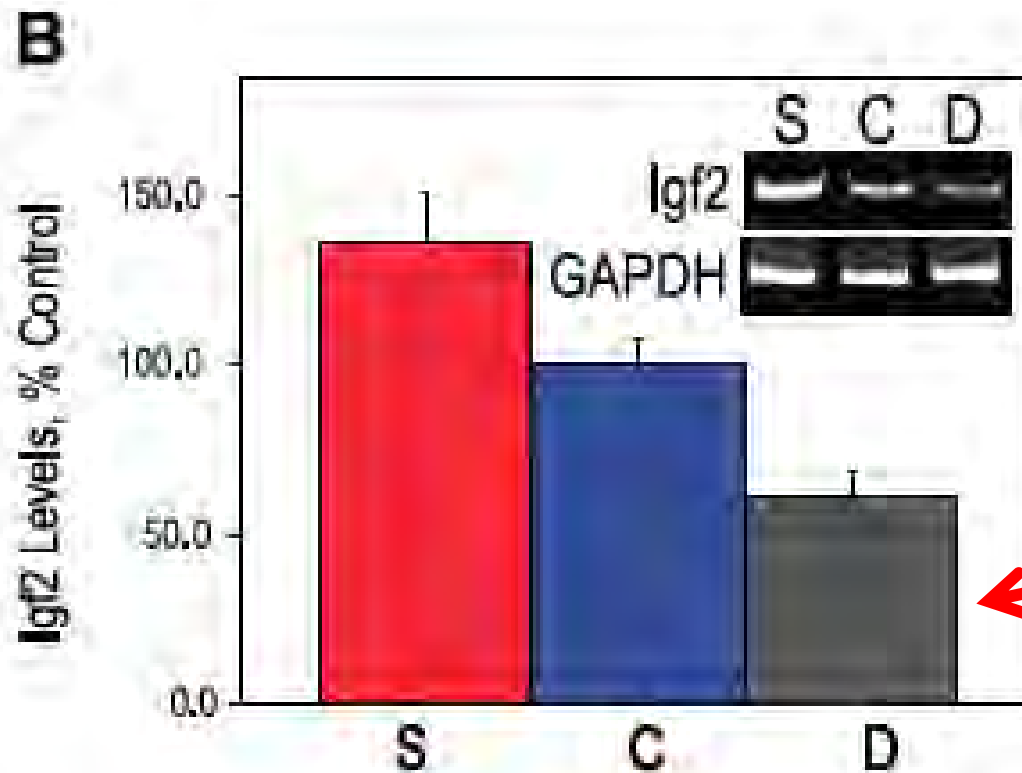
## Prenatal choline availability modulates hippocampal and cerebral cortical gene expression

Tiffany J. Mellott,\* Maximillian T. Follettie,<sup>†</sup> Veronica Diesl,<sup>†</sup> Andrew A. Hill,<sup>‡</sup> Ignacio Lopez-Coviella,<sup>\*,†</sup> and Jan Krzysztof Blusztajn<sup>\*,†,1</sup>

**The data show that prenatal choline modifies the expression of genes relevant to learning and memory processes during development.**

**I dati indicano che la supplementazione prenatale di colina influenza il pattern di espressione di geni che influenzano apprendimento e memoria durante lo sviluppo.**





**Brain concentrations of a growth factor mRNA (for Igf2) after birth, at the end of development, following 7 days of choline deficiency during embrional life**

**Concentrazioni cerebrali a fine sviluppo di mRNA per un fattore di crescita dopo carenza prenatale di colina.**

**NOW, CONSIDERING THE DIFFICULT  
"CORE BUSINESS", THE HEALTHY BRAIN  
AGING, THE INVESTIGATION OF THE  
TIME OF NUTRITIONAL INTERVENTION  
HAS BEEN STUDIED, ALTHOUGH NOT  
SYSTEMATICALLY.**

**ENTRANDO NELLO SPECIFICO DEL TEMA  
"INVECCHIAMENTO E MALATTIE  
NEURODEGENERATIVE" LO STUDIO DEI TEMPI  
DELL'INTERVENTO NUTRIZIONALE È STATO  
AFFRONTATO IN QUALCHE CONDIZIONE  
SPERIMENTALE, MA NON SISTEMATICAMENTE.**



# **EPIDEMIOLOGY AND LITERATURE DATA**

**CHE COSA DICONO L'EPIDEMIOLOGIA E  
LA LETTERATURA INTERNAZIONALE?**



# Nutrition and neurodegeneration: epidemiological evidence and challenges for future research

Sophie Gillette-Guyonnet,<sup>1,2,3</sup> Marion Secher<sup>1</sup> & Bruno Vellas<sup>1,2,3</sup>

*<sup>1</sup>Gerontopole, Toulouse University Hospital, Department of Internal Medicine and Geriatrics, Purpan University Hospital, Toulouse F-31059, <sup>2</sup>Inserm 1027, Toulouse F-31073 and <sup>3</sup>University of Toulouse III, Toulouse F-31073, France*

British Journal of Clinical Pharmacology © 2013



**Due to the lack of a cure and thanks to data showing favourable brain activity of various nutrients it is reasonable to investigate life style and nutritional interventions during normal and pathological brain aging.**

**In assenza di un trattamento curativo, è razionale e adeguatamente sicuro indagare l'intervento sullo stile di vita e sulle abitudini alimentari nell'invecchiamento cerebrale normale e patologico.**





**The traditional Randomized Controlled Clinical Trial design may not be suitable to study nutritional interventions**

**New population based studies and big data analysis may be more apt to approach such topics.**

**I tradizionali studi clinici randomizzati sono però poco adatti ad affrontare tale tipo di problema scientifico.**

**Occorreranno indagini di nuovo disegno e studi di popolazione, non facili da organizzare ed interpretare.**



**The key question what can  
be the biological mechanism  
of interaction between  
nutrients and brain activity?  
The brave new world of the  
“omics”**

**La domanda centrale: quale può  
essere il meccanismo d'interazione  
tra nutrienti e cervello?  
Il nuovo pianeta degli “omics”**





# **PROTEOMICS, METABOLOMICS, LIPIDOMICS, TRANSCRIPTOMICS, EPIGENETICS, NUTRIGENOMICS**

## **“OMICS” AS A NEW LEVEL OF COMPLEXITY IN BIOLOGICAL RESEARCH**

**PROTEOMICA, METABOLOMICA,,  
LIPIDOMICA,, TRASCRIPTOMICA,,  
EPIGENETICA, E NUTRIGENOMICA**

**GLI “...OMICS”, UN NUOVO LIVELLO DI  
COMPLESSITÀ DELLA RICERCA**



# **AN INTRODUCTION AND AN EXAMPLE LIMITED TO EPIGENETICS**

**UNA PREMESSA E UN ESEMPIO  
LIMITATI ALL'EPIGENETICA**

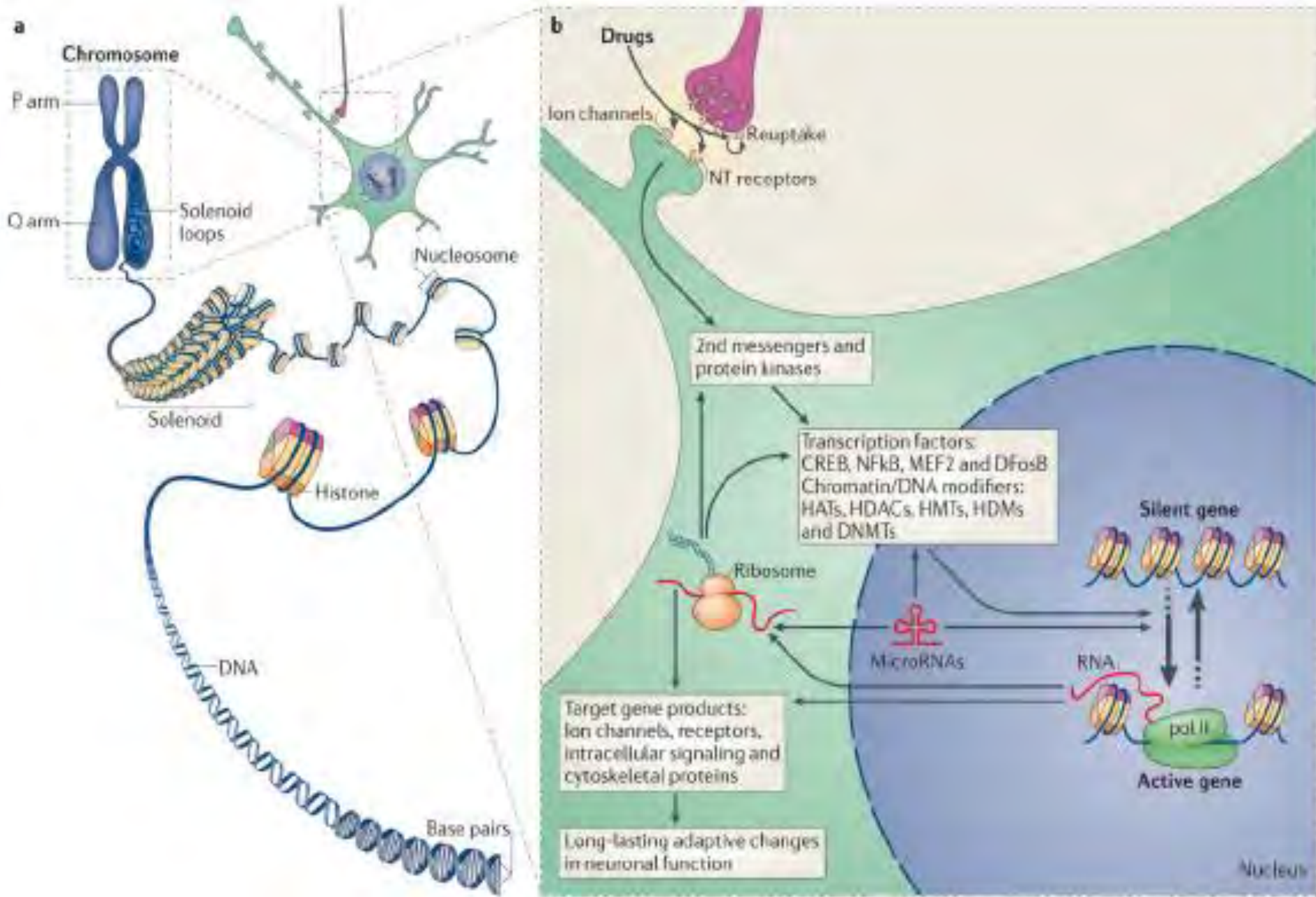




# **WINDING UNWINDING A RIBBON**

**AVVOLGERE E  
SVOLGERE UN  
NASTRO**









**NIH Public Access**

**Author Manuscript**

*J Mol Neurosci*. Author manuscript, available in PMC 2014 March 26.

Published in final edited form as:

*J Mol Neurosci*. 2014 February ; 52(2): 202–215. doi:10.1007/s12031-013-0122-5.

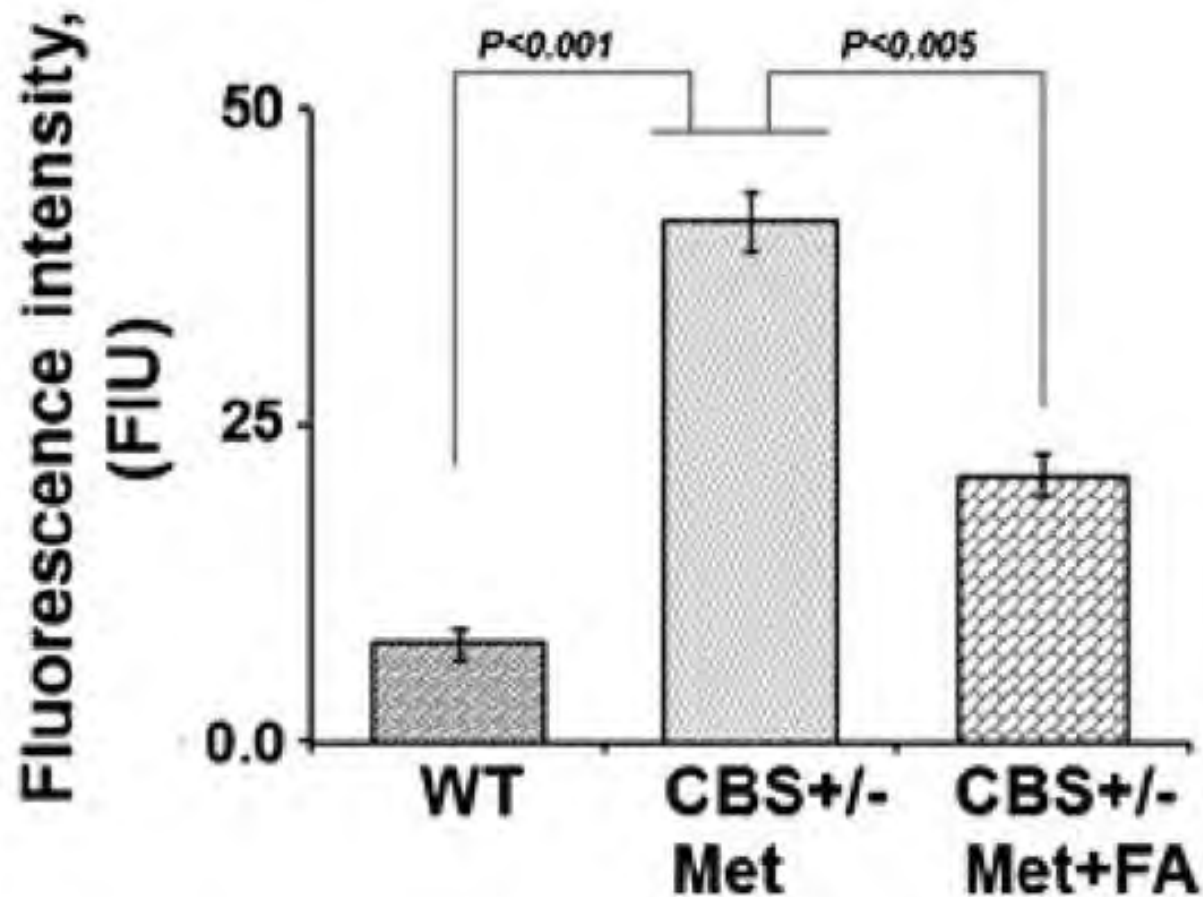
## **Nutri-epigenetics Ameliorates Blood–Brain Barrier Damage and Neurodegeneration in Hyperhomocysteinemia: Role of Folic Acid**

**Anuradha Kalani,**

Department of Physiology and Biophysics, School of Medicine, University of Louisville, 500 South Preston Street, Louisville, KY 40202, USA

**Pradip K. Kamat,**

Department of Physiology and Biophysics, School of Medicine, University of Louisville, 500 South Preston Street, Louisville, KY 40202, USA

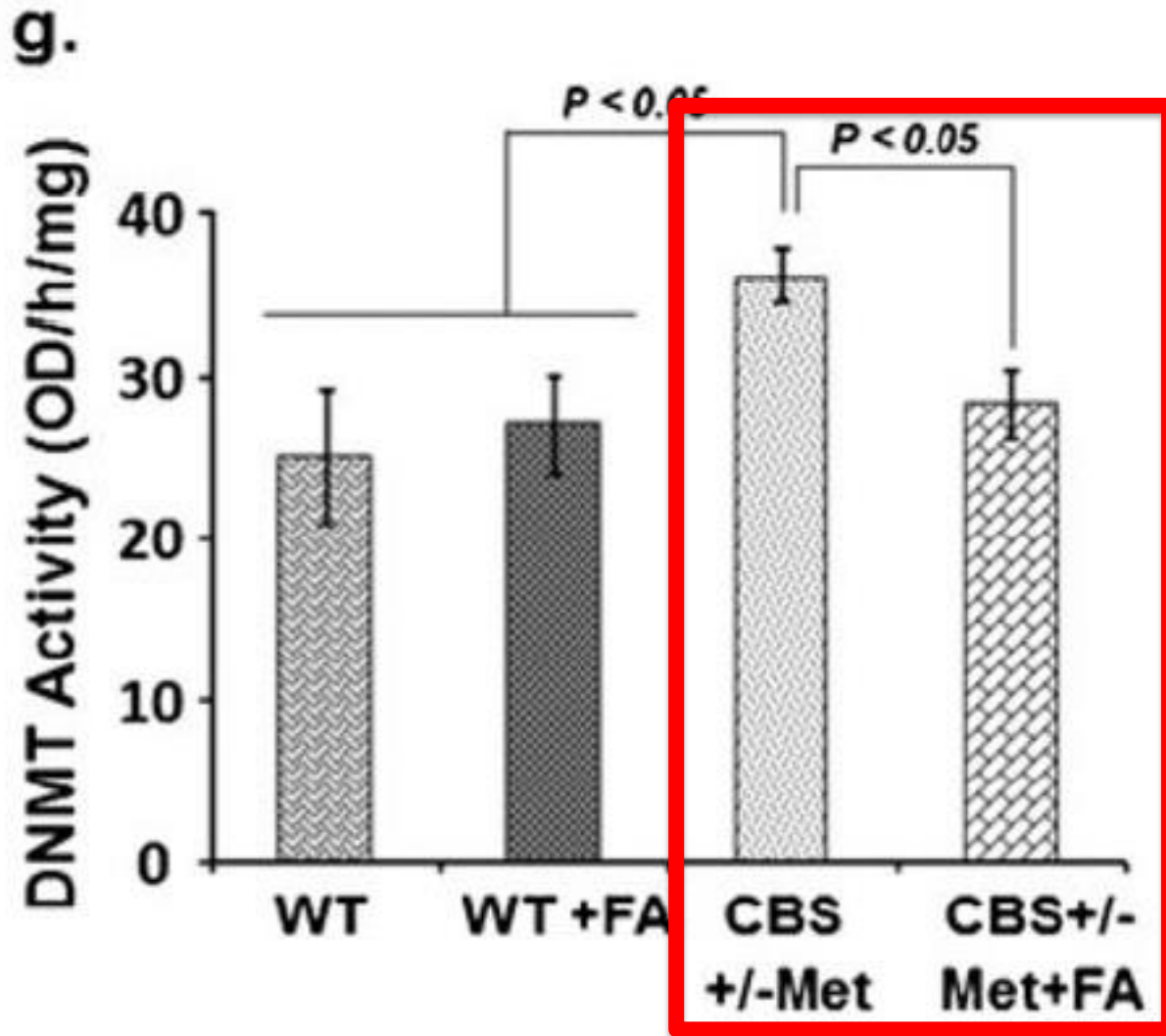


**Fig 8.**

Effect of folic acid on macromolecular leakage of pial venules. **a** Fluorescence images recorded after infusion of BSA-FITC in WT, CBS<sup>+/-</sup>+ Met, and CBS<sup>+/-</sup>+Met+FA mice. **b** Representative bar graph for BSA leakage assessed by the fluorescence intensity of fluorescein isothiocyanate-bovine serum albumin in the *rectangular area of interest* shown on images



# Effect of folic acid on DNA methyltransferase activity



# **AN EXAMPLE OF NUTRITIONAL INTERVENTION IN A MOUSE MODEL OF NEURODEGENERATION**

**UN ESEMPIO DI UN INTERVENTO  
NUTRIZIONALE COMPLESSO IN UN  
MODELLO MURINO DI  
NEURODEGENERAZIONE**





Contents lists available at [ScienceDirect](#)

## Neuropharmacology

journal homepage: [www.elsevier.com/locate/neuropharm](http://www.elsevier.com/locate/neuropharm)



# Neuroprotective and cognitive enhancing effects of a multi-targeted food intervention in an animal model of neurodegeneration and depression

Yuliya E. Borre<sup>a,b,\*</sup>, Theodora Panagaki<sup>a</sup>, Pim J. Koelink<sup>a</sup>, Mary. E. Morgan<sup>a</sup>,  
Hendrikus Hendriksen<sup>a,b</sup>, Johan Garssen<sup>a,c</sup>, Aletta D. Kraneveld<sup>a</sup>, Berend Olivier<sup>a,b</sup>,  
Ronald S. Oosting<sup>a,b</sup>

<sup>a</sup>Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Faculty of Science, Utrecht University, PO Box 80082, 3508 TB Utrecht, The Netherlands

<sup>b</sup>Rudolf Magnus Institute of Neuroscience, Utrecht University, PO Box 80082, 3508 TB Utrecht, The Netherlands

<sup>c</sup>Danone Research, Center for Specialized Nutrition, Wageningen, The Netherlands

Neuropharmacology 79 (2014) 738e749



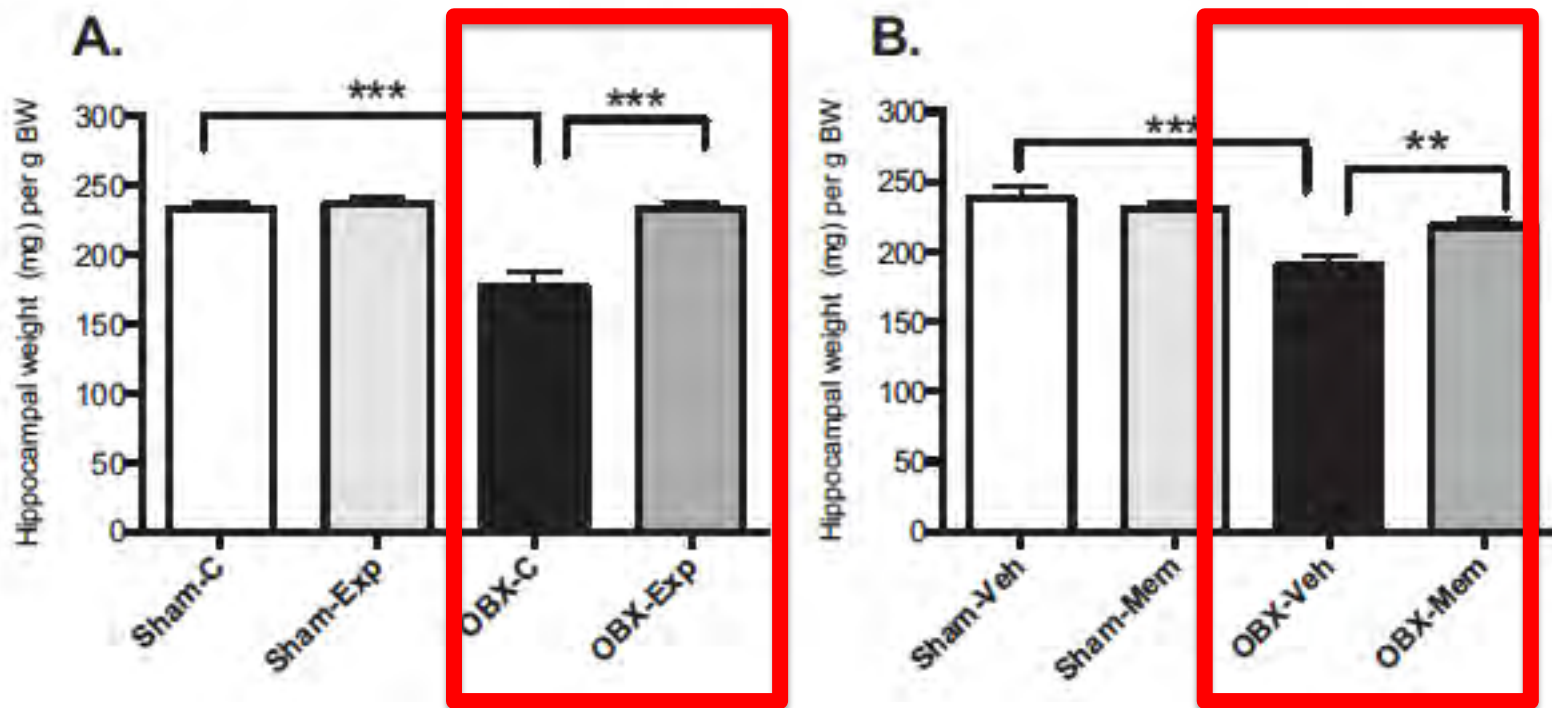
Experimental and control diet compositions. Rats were given 20 g of the diet per day. The delivered dose is on a mg/kg of food.

Active ingredient	Control (AIN-93) g/kg diet	Experimental diet
Zinc	0.03	1.63
Curcumin	0	0.25
Piperine	0	0.06
Melatonin	0	0.03
Choline	1.09	9.5
Uridine	0	15.48
Soy oil	7%	3% soya+4% tuna oil (25% DHA/6% EPA)

Neuropharmacology 79 (2014) 738e749



# EXPERIMENTAL DIET (A) AND MEMANTINE (B) ATTENUATED OBX-INDUCED HIPPOCAMPAL ATROPHY.



Neuropharmacology 79 (2014) 738e749



This proof of concept study shows that both a neuroprotective drug treatment and the nutritional intervention improved the brain atrophy and memory in lesioned mice.

I dati mostrano che sia l'intervento dietetico sia memantina hanno migliorato la memoria e l'atrofia cerebrale dei topi con atrofia dell'ippocampo



# **PRECLINICAL DATA OPENED THE PATHWAY TO CLINICAL STUDIES**

**I DATI PRECLINICI HANNO  
FORNITO IL RAZIONALE  
PER STUDI CLINICI**



# The Effect of Souvenaid on Functional Brain Network Organisation in Patients with Mild Alzheimer's Disease: A Randomised Controlled Study

Hanneke de Waal<sup>1\*</sup>, Cornelis J. Stam<sup>2</sup>, Marieke M. Lansbergen<sup>3</sup>, Rico L. Wieggers<sup>3</sup>,  
Patrick J. G. H. Kamphuis<sup>3</sup>, Philip Scheltens<sup>1</sup>, Fernando Maestú<sup>4</sup>, Elisabeth C. W. van Straaten<sup>2,3</sup>

<sup>1</sup> Alzheimer Center & Department of Neurology, Neuroscience Campus Amsterdam, VU University Medical Center, Amsterdam, The Netherlands, <sup>2</sup> Department of Clinical Neurophysiology, Neuroscience Campus Amsterdam, VU University Medical Center, Amsterdam, The Netherlands, <sup>3</sup> Nutricia Research, Utrecht, The Netherlands, <sup>4</sup> Laboratory of Cognitive and Computational Neuroscience, UCM-UPM Center for Biomedical Technology, Madrid, Spain

**Conclusions:** The current results suggest that Souvenaid preserves the organisation of brain networks in patients with mild AD within 24 weeks, hypothetically counteracting the progressive network disruption over time in AD. The results strengthen the hypothesis that Souvenaid affects synaptic integrity and function. Secondly, we conclude that advanced EEG analysis, using the mathematical framework of graph theory, is useful and feasible for assessing the effects of interventions.

**BEYOND THE  
"VOLEMOSE BENE"**

**SIAMO DUNQUE OLTRE  
IL "VOLEMOSE BENE",  
MA...**





# Epigenetics: Relevance and Implications for Public Health

Laura S. Rozek,<sup>1</sup> Dana C. Dolinoy,<sup>1</sup>  
Maureen A. Sartor,<sup>1,2</sup> and Gilbert S. Omenn<sup>1,2</sup>

<sup>1</sup>Department of Environmental Health Sciences, and <sup>2</sup>Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan 48109; email: gomenn@umich.edu, rozekl@umich.edu, ddolinoy@umich.edu, sartorma@umich.edu

Annu. Rev. Public. Health. 2014.35:105-122





***I'm aware that you all are afraid of the change. I do not know the future nor what will be the end of this story. I'm here to tell you how the story begins. I will show the people a world with no borders where everything is possible. Soon everything that you know will change.***

***"So che mi state ascoltando, avverto la vostra presenza, so che avete paura di cambiare. Io non conosco il futuro, non sono venuto qui a dirvi come andrà a finire; sono venuto a dirvi come comincerà. Adesso ... farò vedere a tutta questa gente quello che non volete che vedano, mostrerò loro un mondo senza frontiere e confini, un mondo in cui tutto è possibile .....***  
***Presto tutto quello che conoscete cambierà"***

**Morpheus in MATRIX**

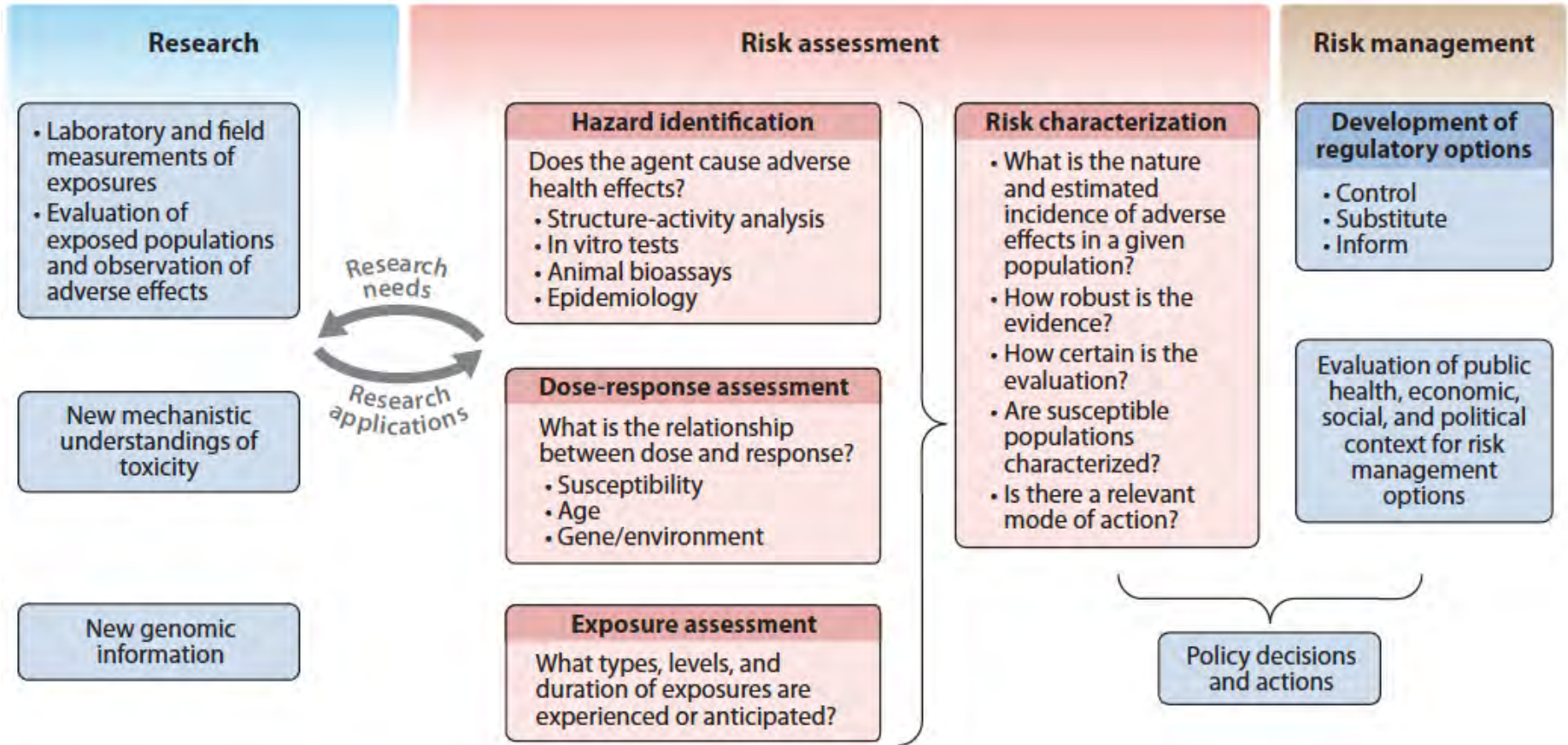




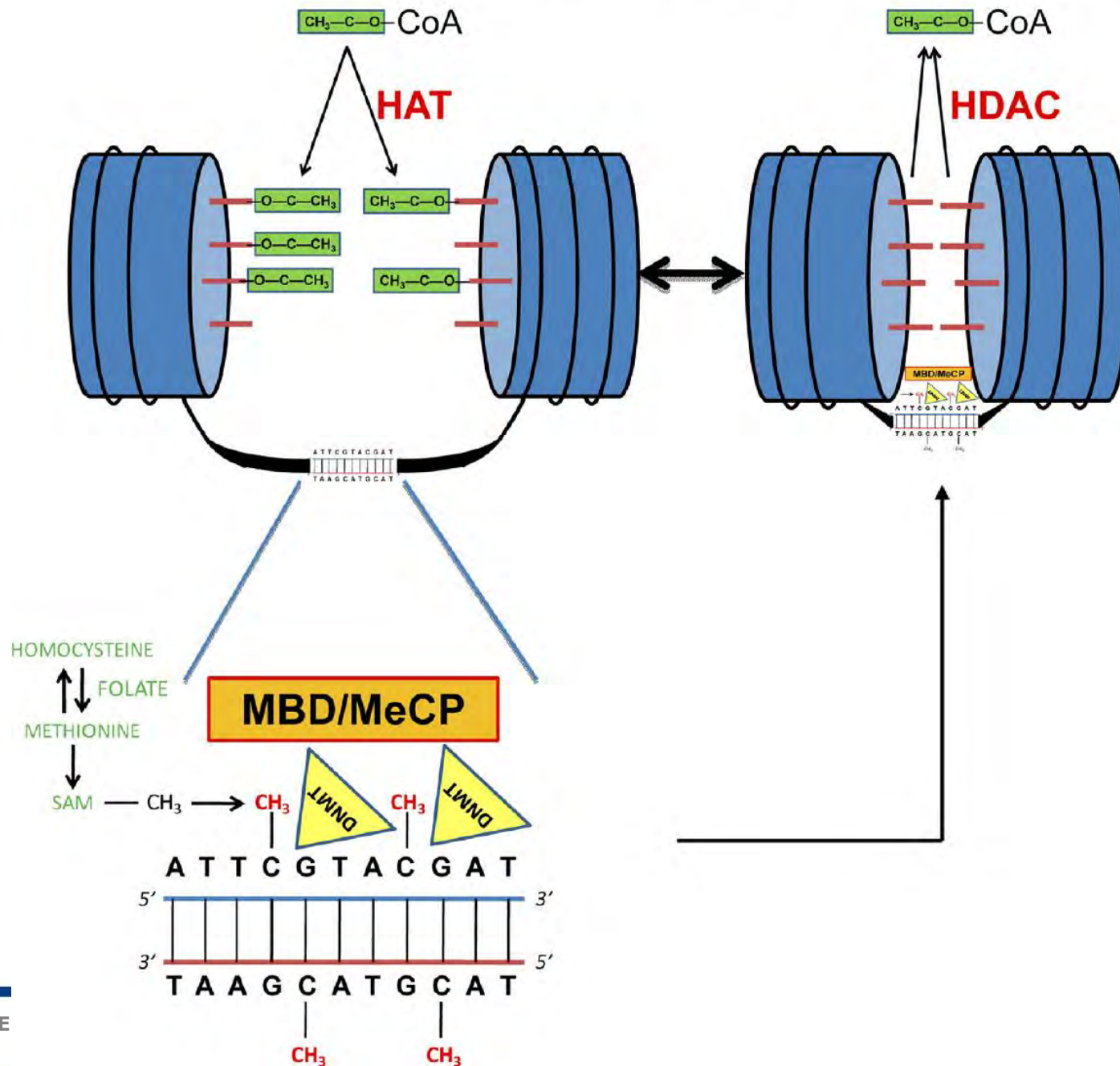
# **DIET, LIFE STYLE AND NUTRITIONAL INTERVENTIONS BASED ON INTEGRATORS**

**DIETA, STILE DI VITA E  
INTERVENTI NUTRIZIONALI  
BASATI SULL'USO DI  
INTEGRATORI**





**Figure 2**  
 Risk assessment/risk management framework. This framework shows, under the red highlighting, the four key steps of risk assessment: hazard identification, dose-response assessment, exposure assessment, and risk characterization. It shows an interactive, two-way process where research needs from the risk assessment process drive new research, and new research findings modify risk assessment outcomes. This figure is reprinted with permission from Faustman & Omenn (28).







We are not following a  
myth

Non siamo alla ricerca di  
un mito

