FLAVIOLA

Targeted delivery of dietary flavanols for optimal human cell function:
Effects on cardiovascular health

Marc W. Merx
on behalf of the
FLAVIOLA consortium

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Unwholesome diets and lack of physical activity are the leading causes of avoidable illness and premature death in Europe, and the rising prevalence of obesity across Europe is a major concern regarding public health.

► Epidemiological and medical anthropological investigations suggest that plant-based diets rich in flavanols exert cardiovascular health benefits.

VITIS VINIFERA (grape wine)

THEOBROMA CACAO (cocoa)

CAMELLIA SINENSIS (tea)

FLAVIOLA

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WP 1/2
- metabonomics
- targeted delivery
- intra- & inter-variability

WP 3/4
- (sub-)cellular mechanisms
- organ function
- organism vitality

FLAVIOLA

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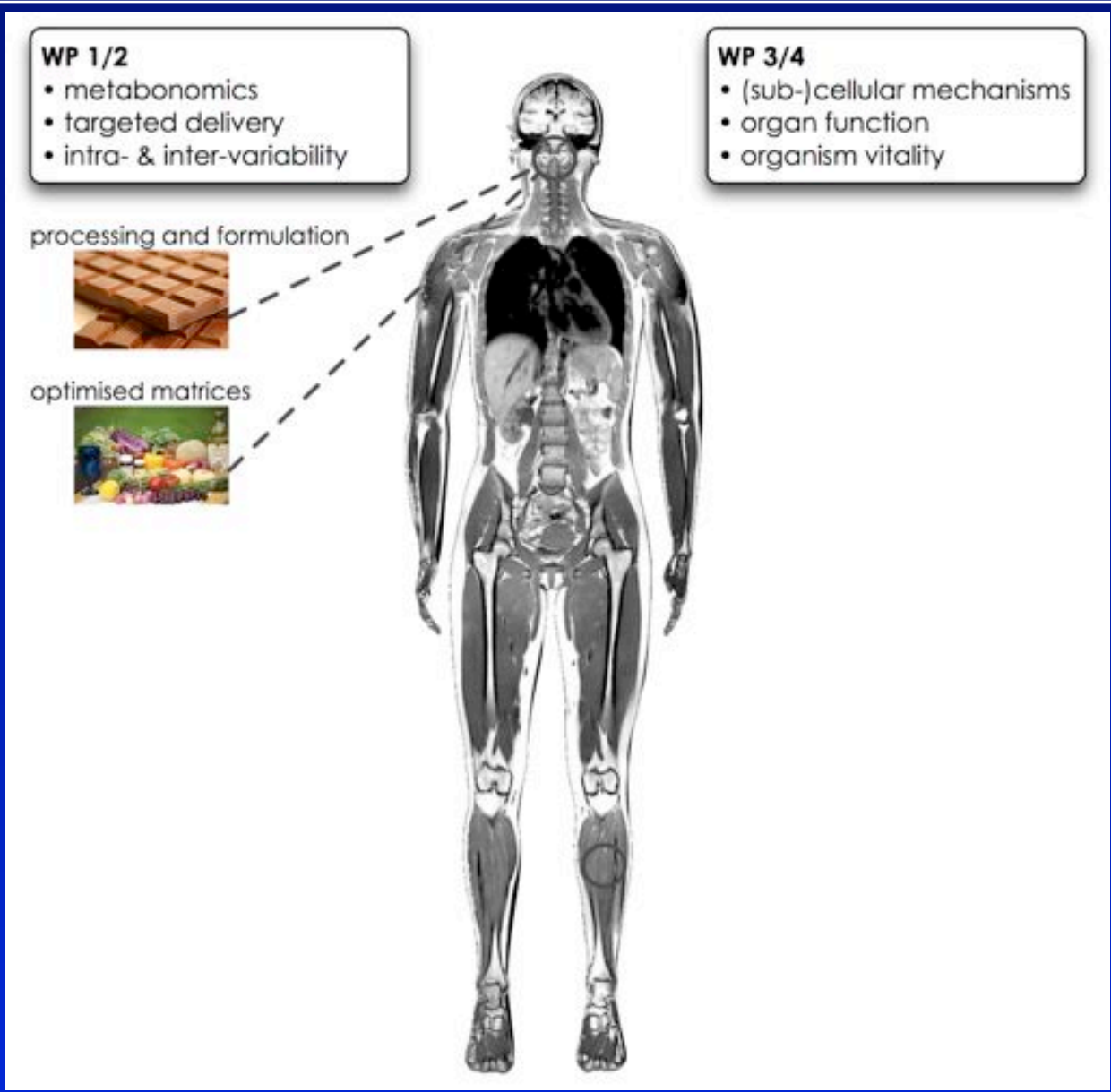

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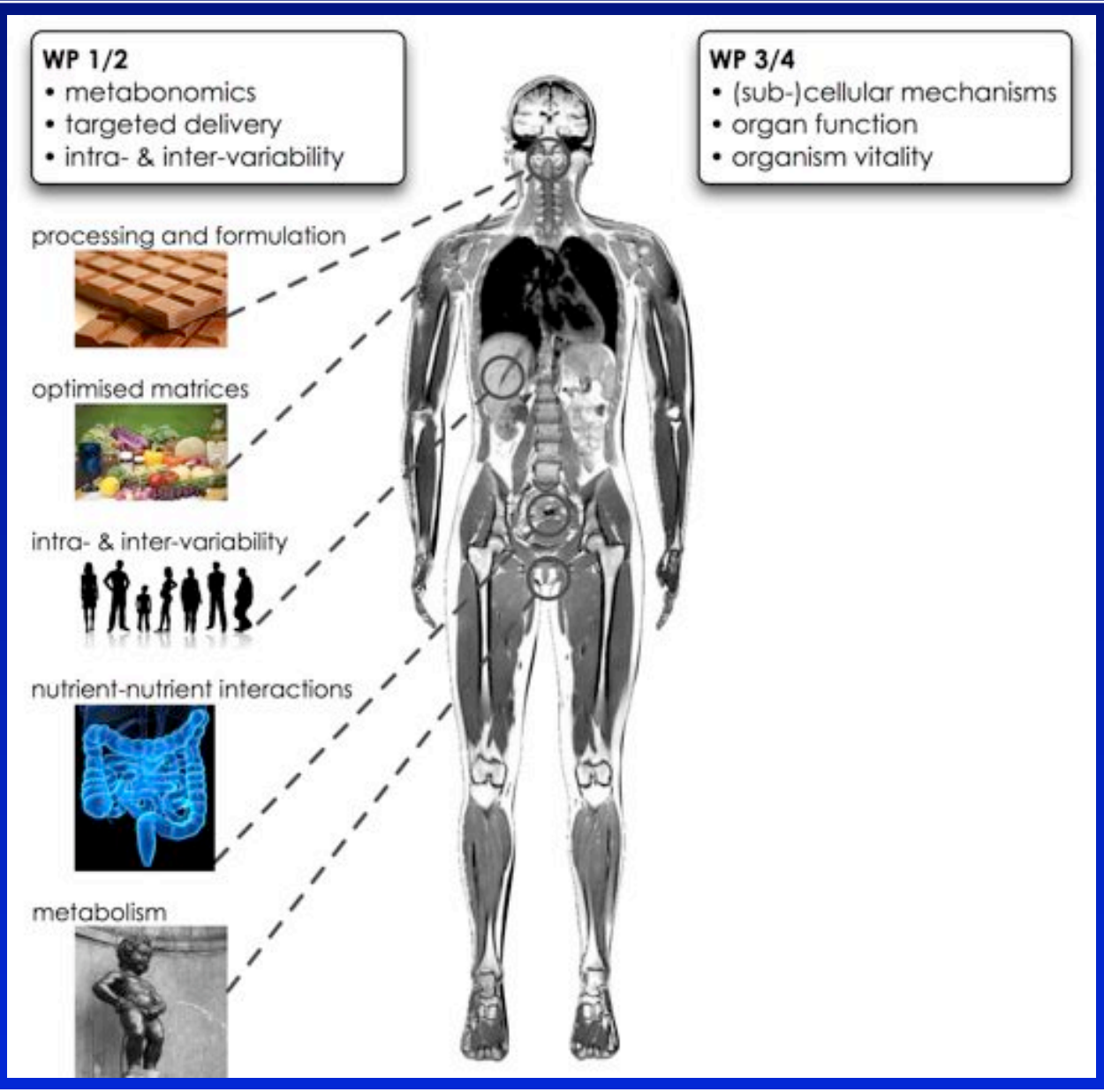

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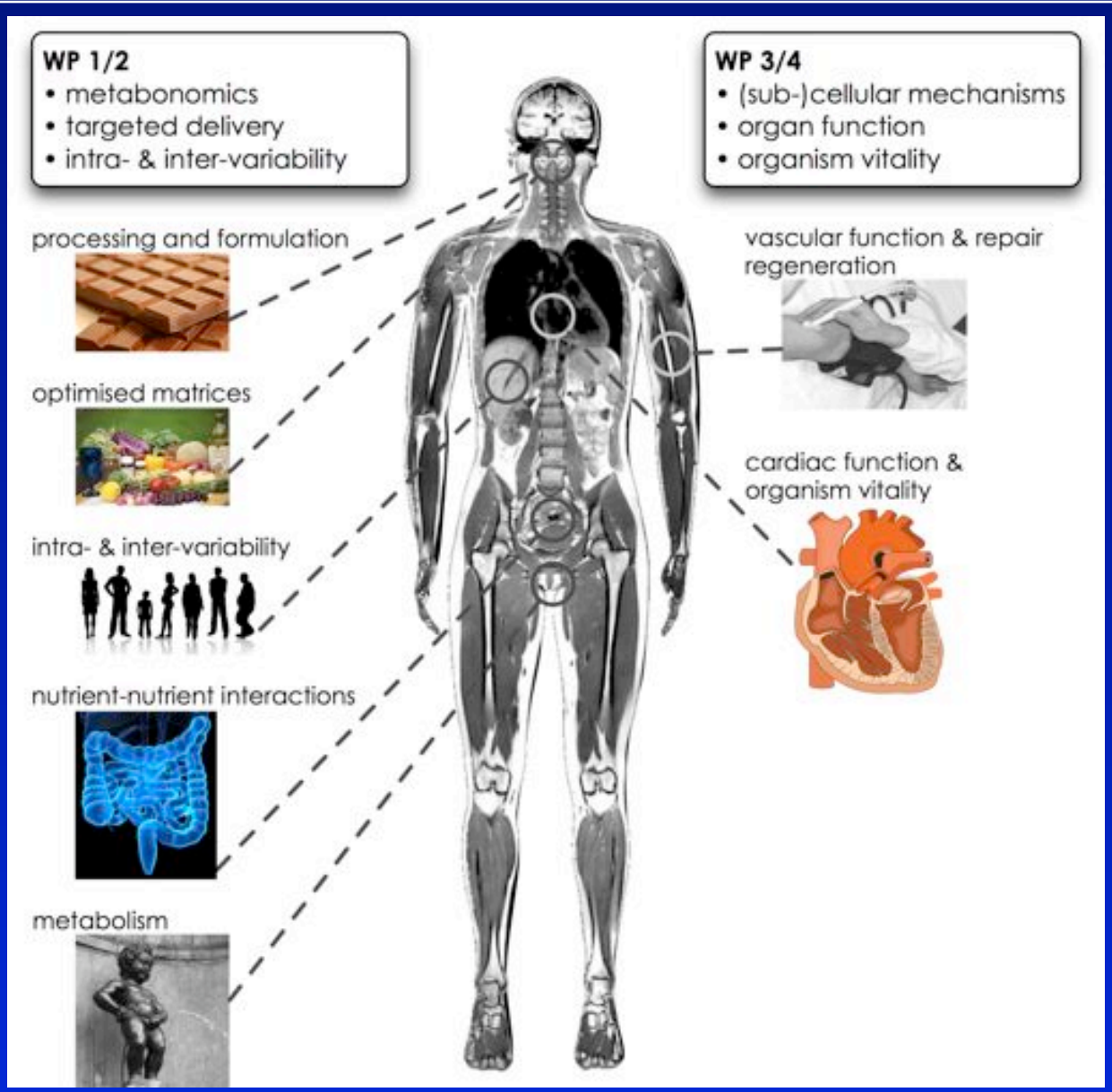

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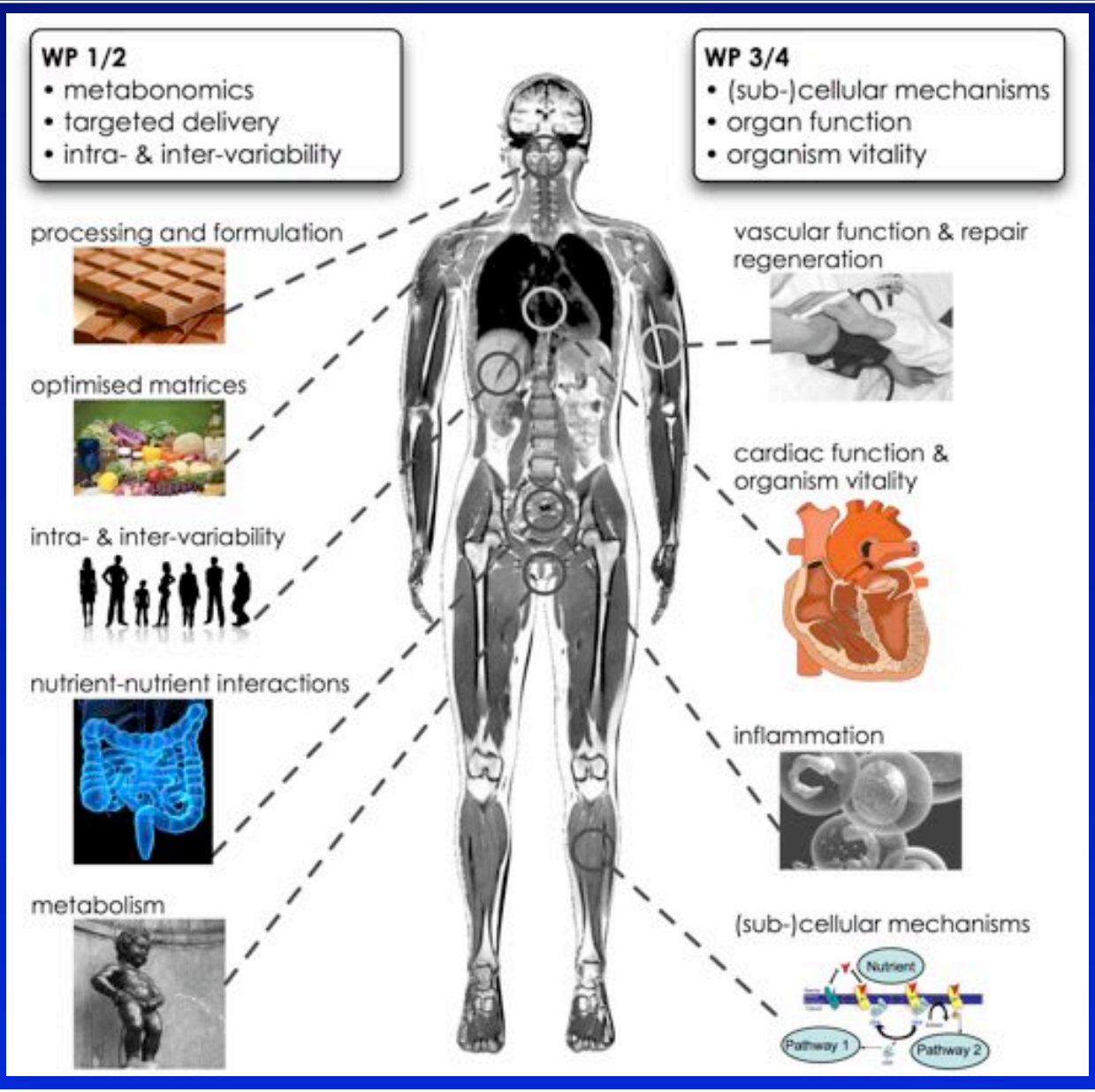

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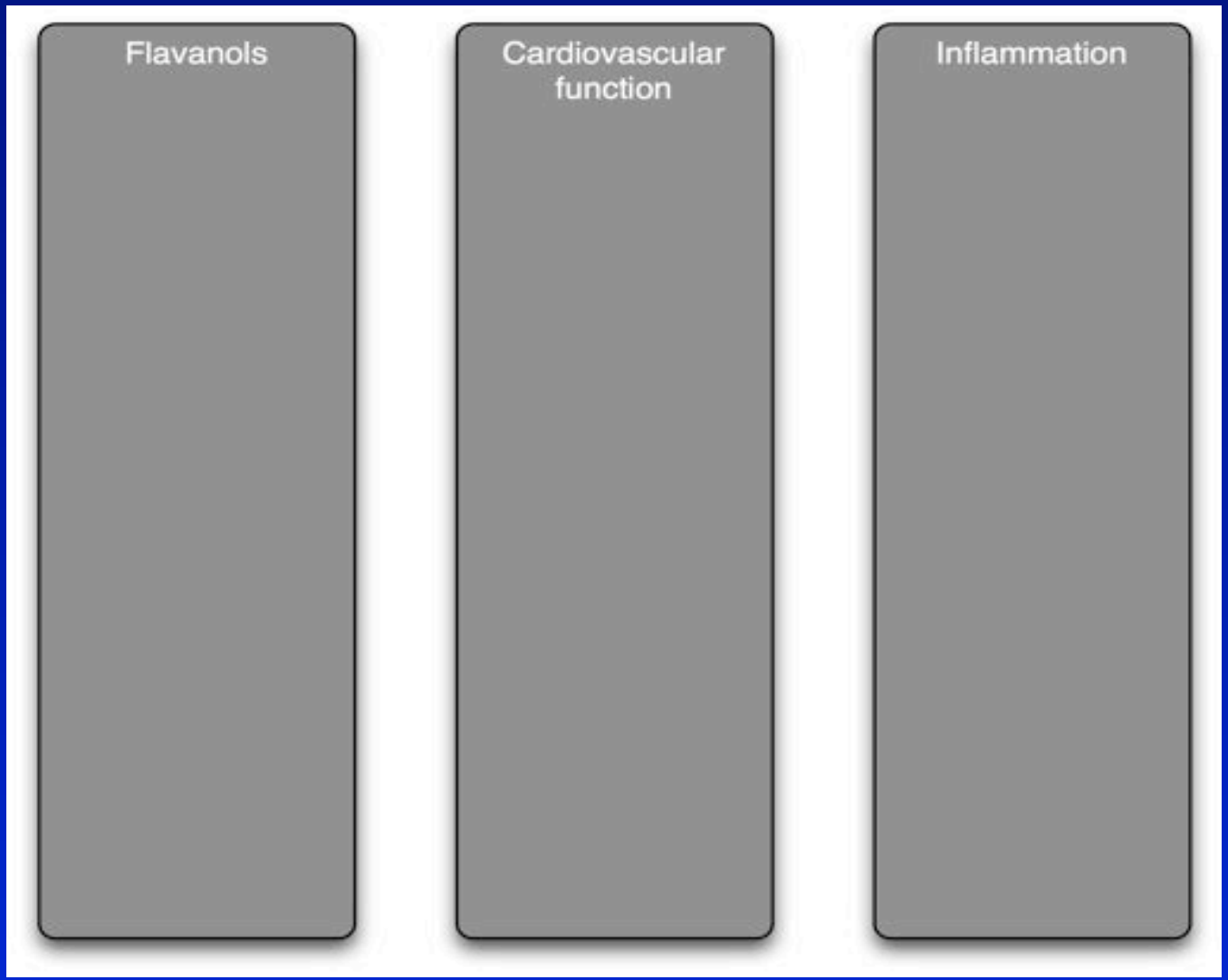

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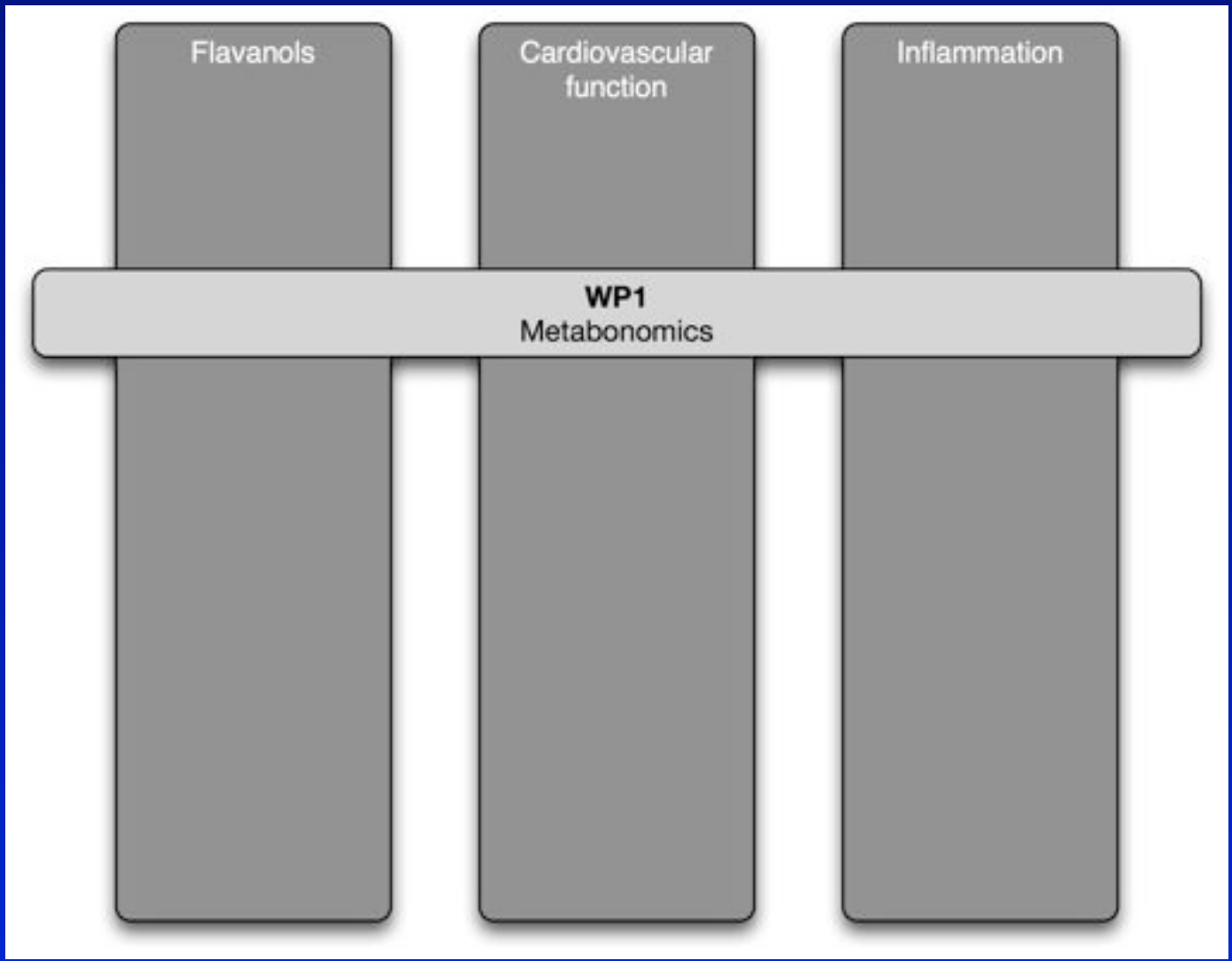

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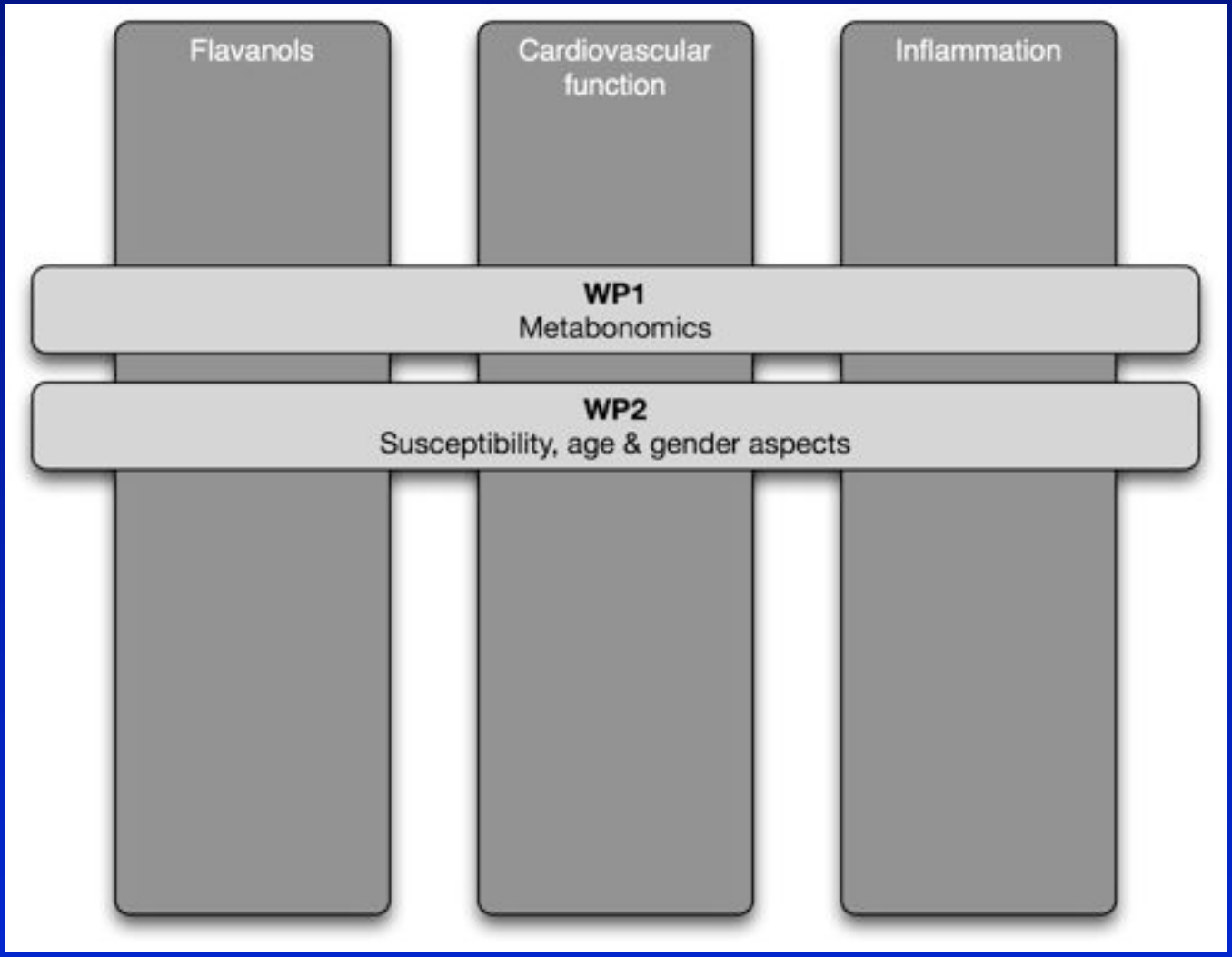

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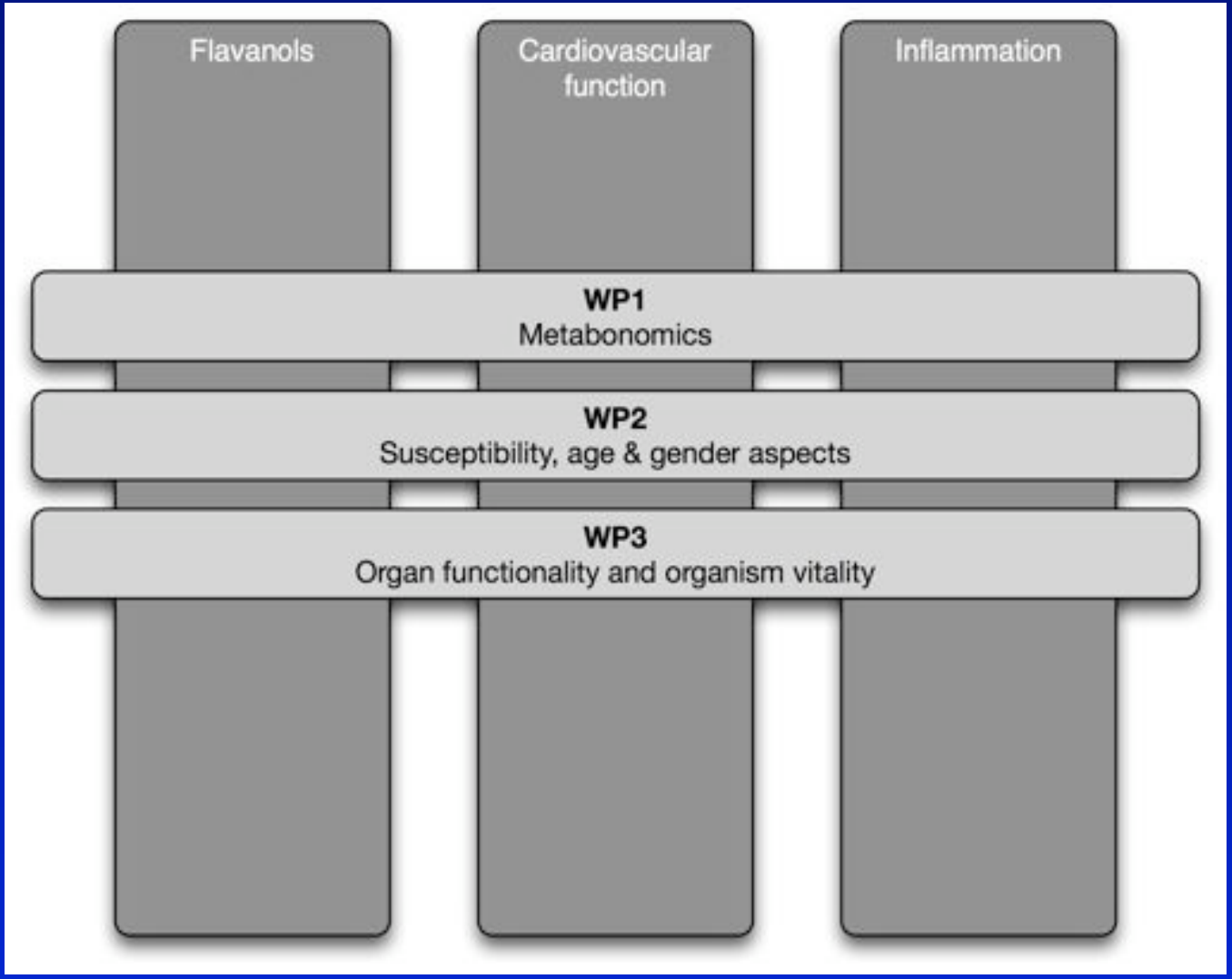

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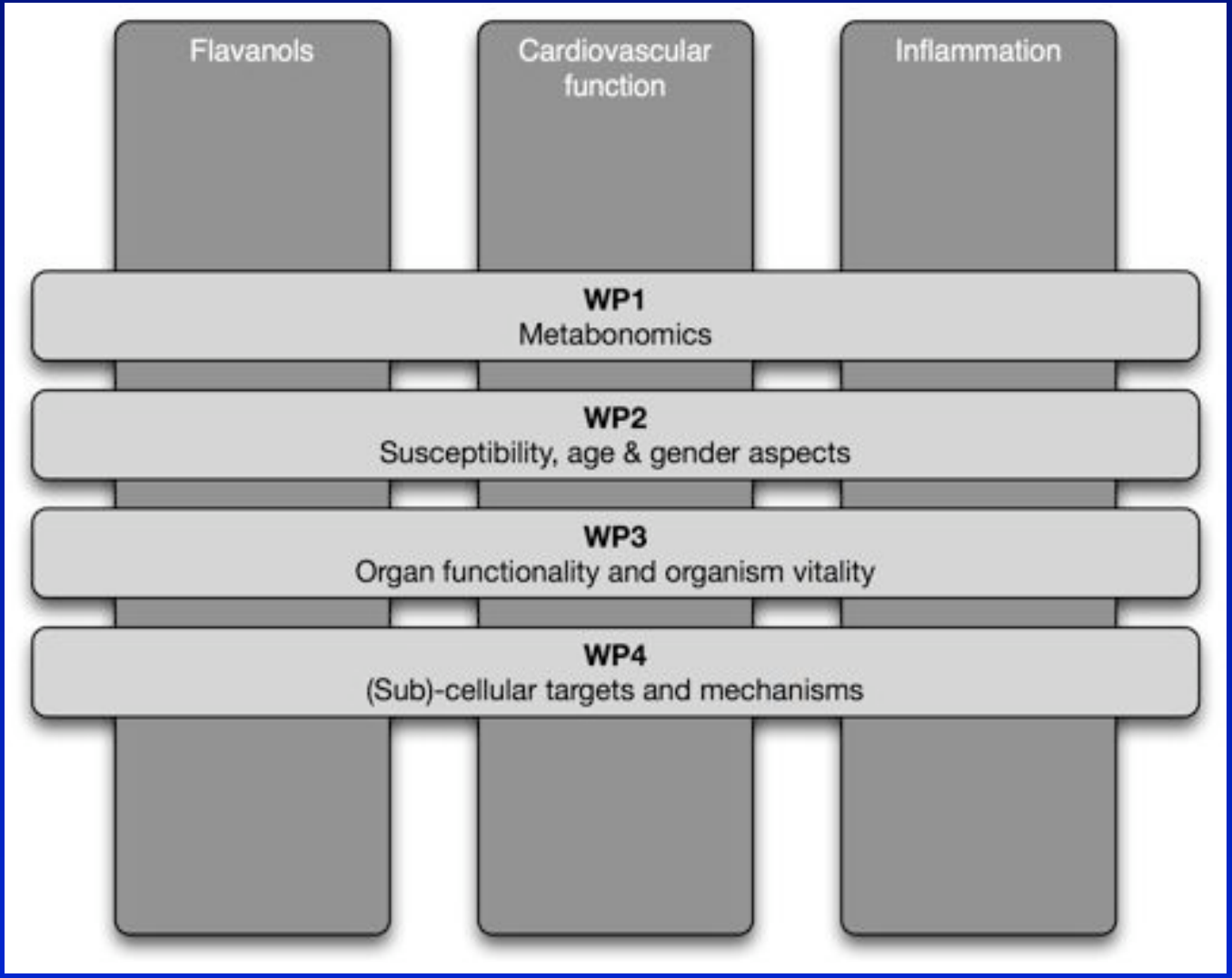

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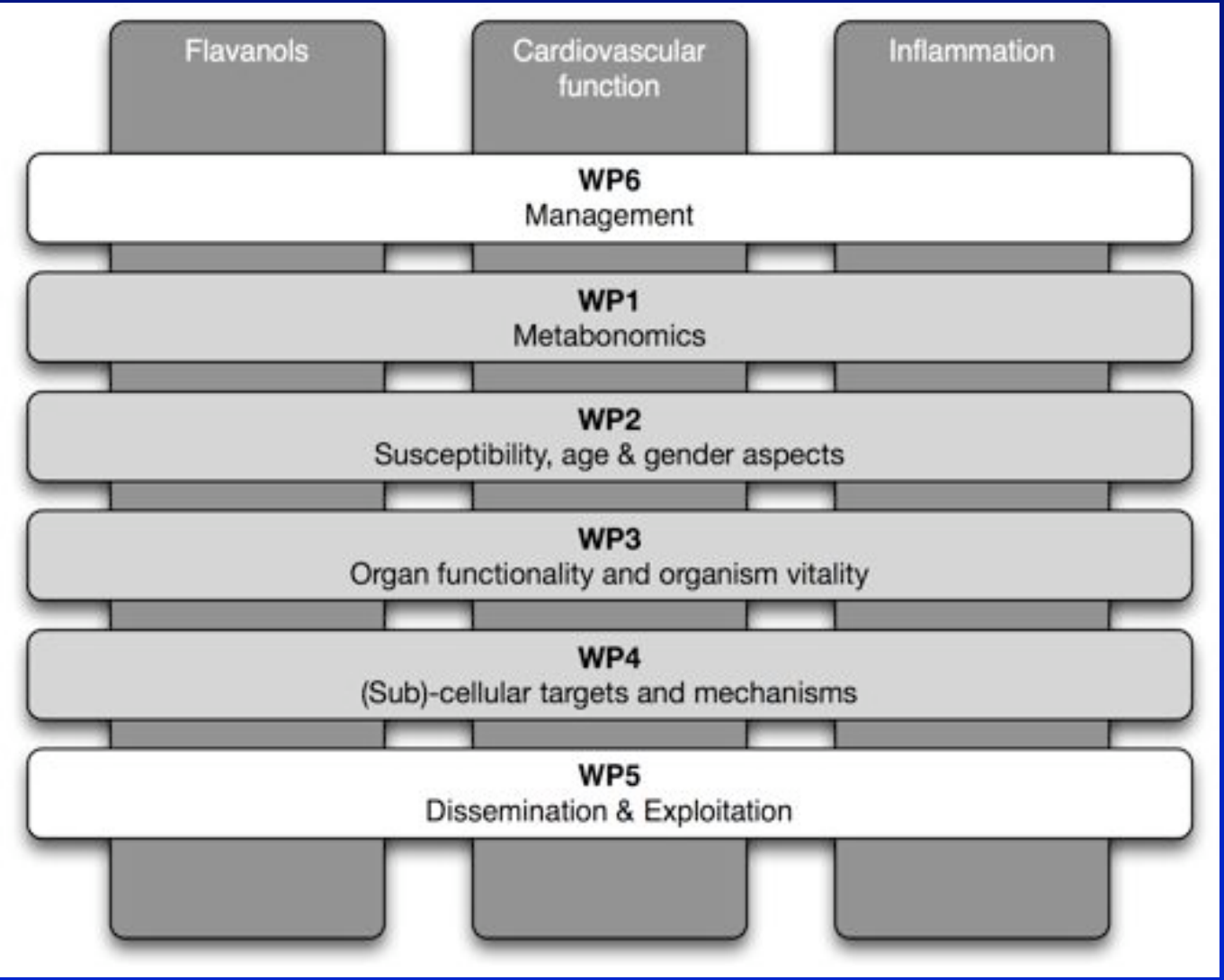

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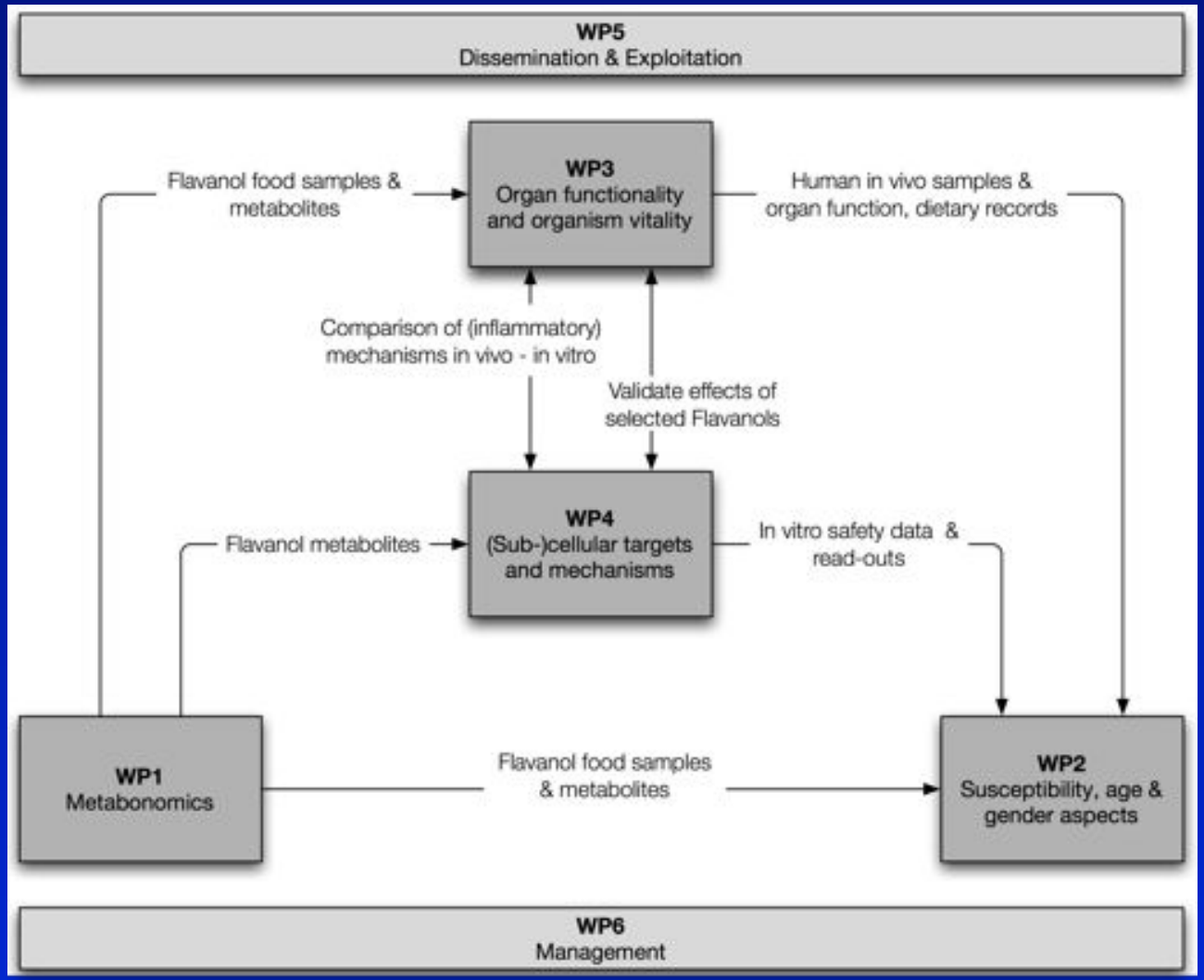


flaviola
Ghent - BE
UNIVERSITEIT GENT
Reading - UK
University of Reading
Stockholm - S
Karolinska Institutet
Düsseldorf - D
HEINRICH HEINE UNIVERSITÄT DÜSSELDORF
Brussels - BE
MARS incorporated
Clermont-Ferrand - F
INRA
UM
Maastricht - NL
SCIPROM
Scientific Project Management
St-Sulpice - CH

SCIPROM

- **Founded** in 2005, **7** team members
- **Supporting researchers in large collaborative projects:** Project office - Communication & dissemination (web site, brochures etc) - Project monitoring & reporting - Contractual, legal and financial management - Organisation of meetings & workshops
- **9 FP6** projects, **6 FP7** projects - different funding instruments and thematic priorities

SCIPROM
Scientific Project Management

Always there for you!

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Rue du Centre 70
1025 St-Sulpice
Switzerland

veronique.gobry@sciprom.ch
kirsten.leufgen@sciprom.ch
www.sciprom.ch

SCIPROM
Scientific Project Management

UNIVERSITEIT GENT

FACULTEIT WETENSCHAPPEN

Inflammation, NFkB signalling

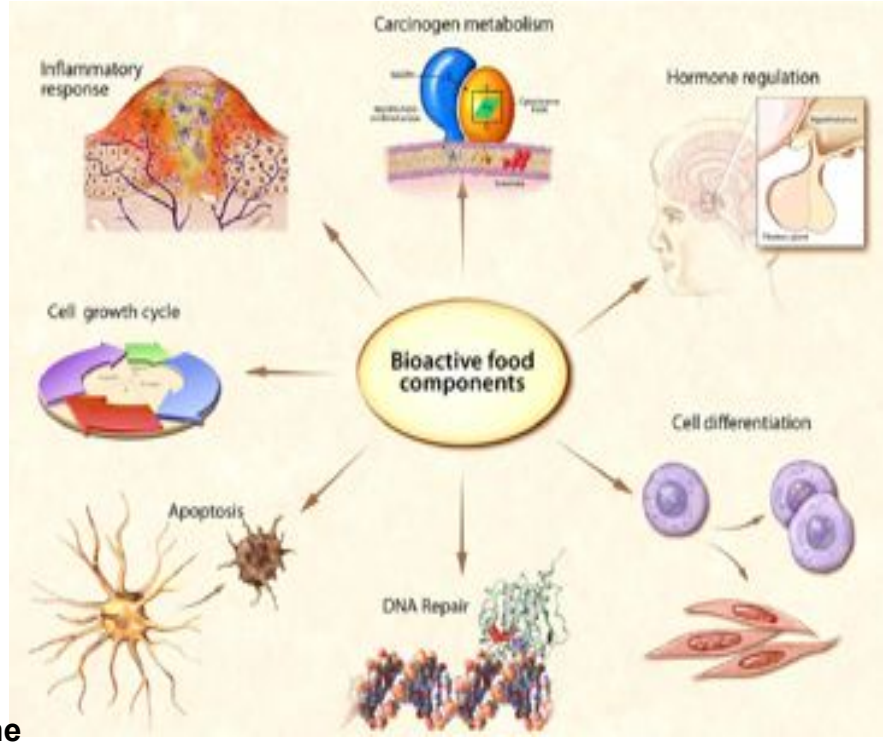
Hormone Signalling

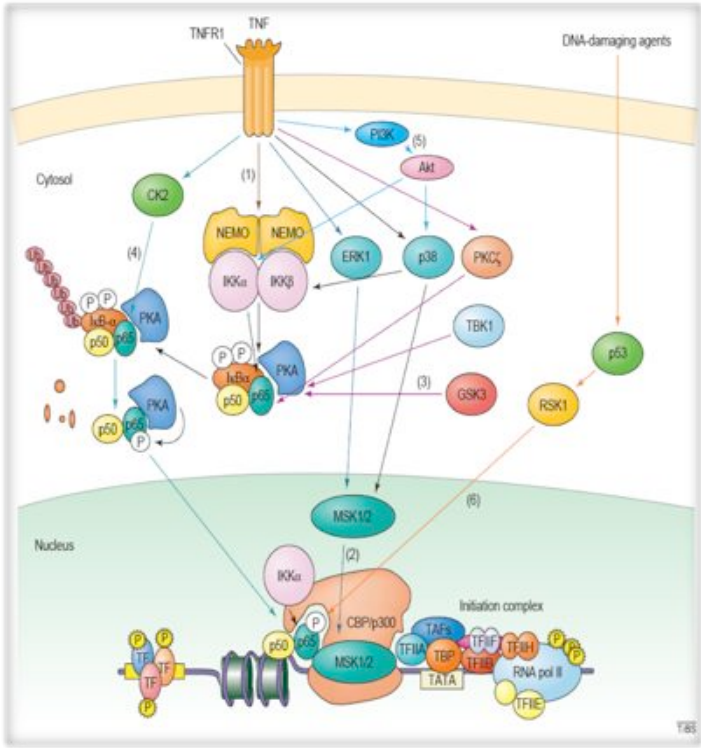
GPCR Signalling

LEGEST *Research* Laboratory of Eukaryotic Gene Expression & Signal Transduction

Prof. Dr. Guy Haegeman

Prof. Dr. Wim Vanden Berghe





UNIVERSITEIT GENT

FACULTEIT WETENSCHAPPEN

Inflammation, NFkB signalling

Hormone Signalling

GPCR Signalling

LEGEST *Applied Science* Laboratory of Eukaryotic Gene Expression & Signal Transduction

DIRECT ACCESS TO TOP-EXPERTS FOR INNOVATION

Ghent University wants to anticipate the new trends and developments in the food industry. The **Food2Know** *Center of Excellence* was created to make it possible to take an integrated and multidisciplinary approach to these innovation-driven research issues. This interfaculty Knowledge Center for Food Science, Nutrition and Health groups 30 research groups, spread out over the five life science faculties (Bioscience Engineering, Pharmaceutical Sciences, Veterinary Sciences, Sciences, and Medicine & Health Sciences).

ProDigest
Gastrointestinal Expertise

DISCOVERe

BioActor

BIOMARKED

Welcome at C-EviDeNT

evident

CENTER FOR EVIDENCE-BASED DEVELOPMENT OF NATURAL THERAPEUTICS

C-EviDeNT stands for:

Center for Evidence-based Development of Natural Therapeutics

200 Years
1810 – 2010

Karolinska Institutet

Research at Karolinska Institutet

22 departments

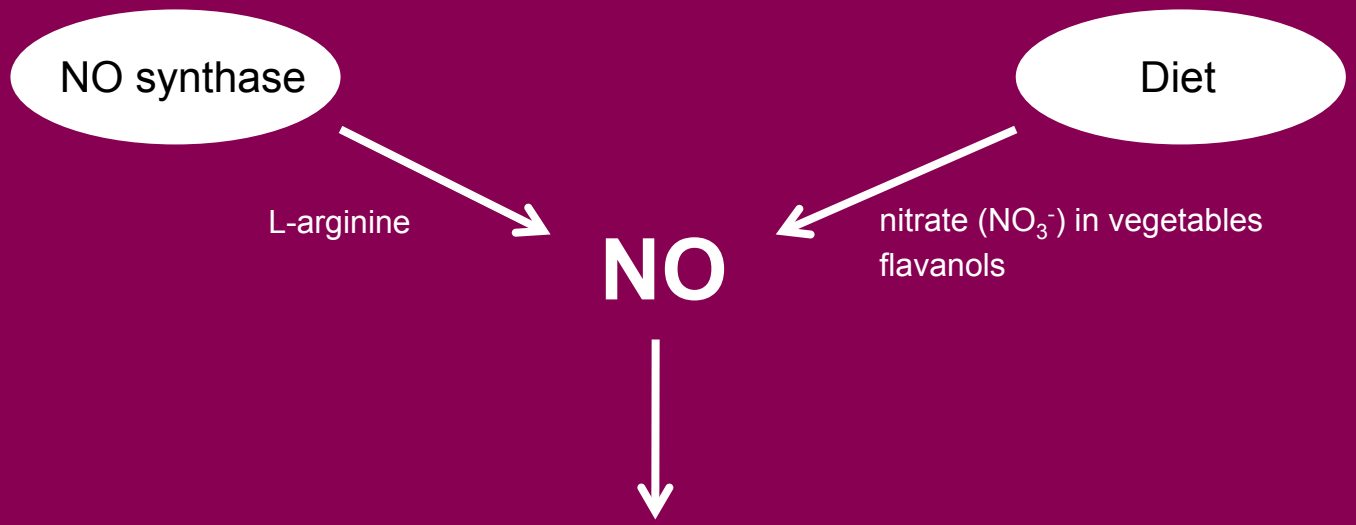
600 research groups

1,500 researchers/teachers including 316 professors

2,100 doctoral students

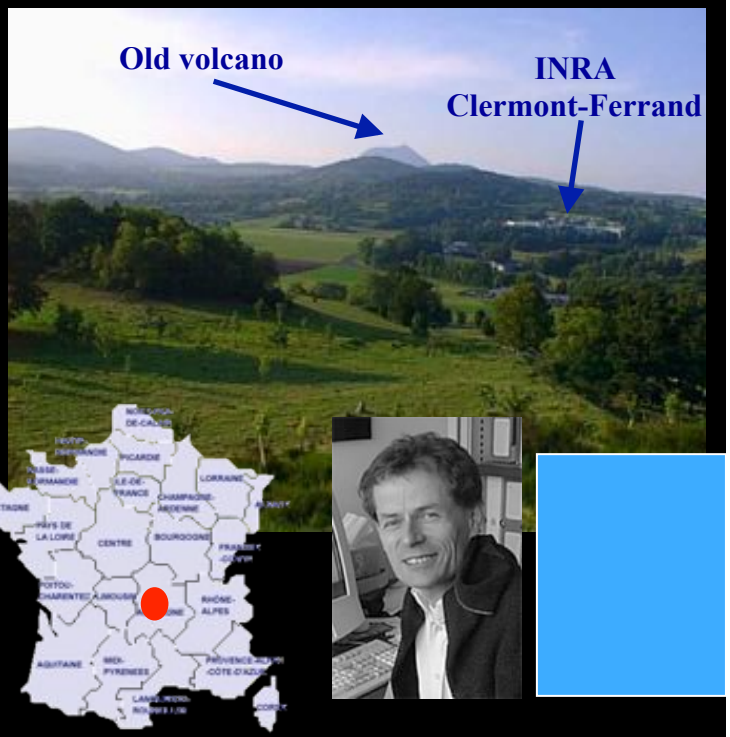
Annual research budget 350 M Euro

Principle Investigators Flaviola:
Jon Lundberg MD, PhD and Eddie Weitzberg MD, PhD
Department of Physiology and Pharmacology


NO synthase
Diet
L-arginine
NO
nitrate (NO_3^-) in vegetables
flavanols
Vasodilation
Reduced blood pressure
Cardioprotection
etc

INRA / Human Nutrition Unit

INRA : the largest European Institute for Research in Agriculture, Food and Environment (about 9000 permanent, scientific and administrative staff).



UNH : The Human Nutrition Unit gathers 150 persons in 8 teams, including a permanent staff of over 50 scientists

Research domain

Elucidation of key mechanisms involved in the prevention of ageing-associated diseases by nutrients and foods.

Micronutrients, Metabolism and Health : Research Group implicated in Flaviola project

Research areas in relation with FLAVIOLA project :

- Dietary polyphenols and cardiovascular function: protective effects and molecular mechanisms

- Metabolic effects of changes in the methyl donor supply on cardiovascular & cerebral tissues

FLAVIOLA - INRA contribution

In WP3

Identification of the key targets associated to the anti-inflammatory activity and methylation capacity of flavanols in myocardium using proteome approach :

Studied through :

- proteomic analysis of mice myocardium in myocardial ischemia models
- proteomic analysis of mice myocardium in "high-grade inflammation" (septic cardiomyopathy) model

Characterization of the impact of dietary flavanols on vascular function in patients with "low-grade" inflammation

Studied through :

- HPLC assays of homocysteine, S-adenosylmethionine/S-adenosylhomocysteine, ADMA in plasma

In WP4

Characterization of the impact of flavanol metabolites on endothelial cell function in relation with cardiovascular diseases :

Studied through:

- screening of isolated circulating metabolites through their impact on adhesion and transendothelial migration of monocytes
- identification of most active metabolites
- effect of metabolites on gene expression (mRNA and miRNA) to decipher implicated molecular mechanisms
- identification of transcription factors and signalling molecules possibly modulated
- functional validation of identified molecular targets

Maastricht University Leading in Learning!

Department of Pharmacology and Toxicology

nutrim

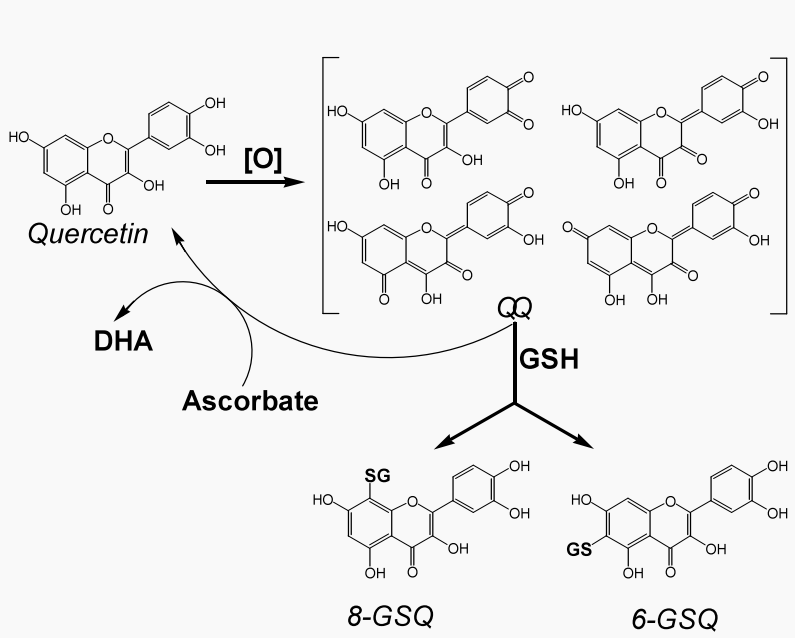
The research programs of the Department are part of the program of the Nutrition Research Institute Maastricht (NUTRIM) and the Cardiovascular Research Institute Maastricht (CARIM)

CARIM

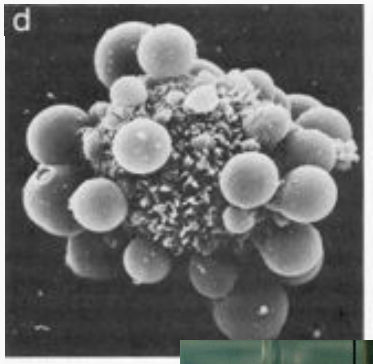
Research theme:
Effect of antioxidant drugs and antioxidant food components on disease

Prof. dr. Aalt Bast, Dr. Guido R.M.M. Haenen, Dr. Antje R. Weseler

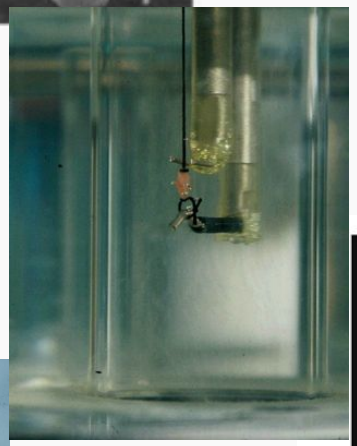
Antioxidants: from molecule to man



Chemistry

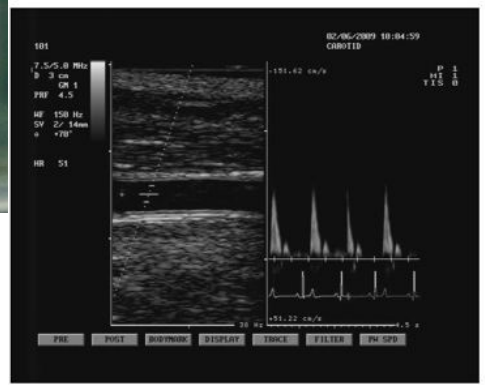


Cells



Isolated organs

In vivo animals e.g. telemetry



humans

Maastricht University Leading in Learning!

Molecular Nutrition Group

School of Chemistry, Food and Pharmacy

University of Reading

University of Reading

Dr. Jeremy P E Spencer

Dr. Ana Rodriguez-Mateos

Analytical Platform for Flavanol Analysis

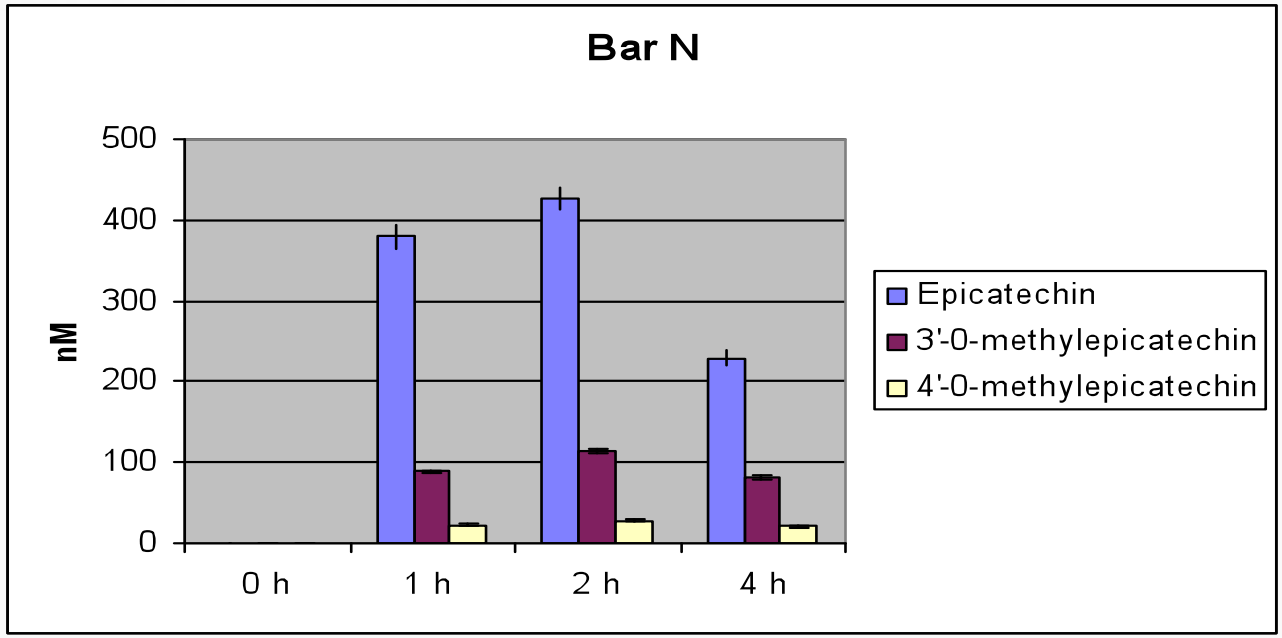
University of Reading

- Identification and quantification of flavanols and related metabolites in plasma and urine.

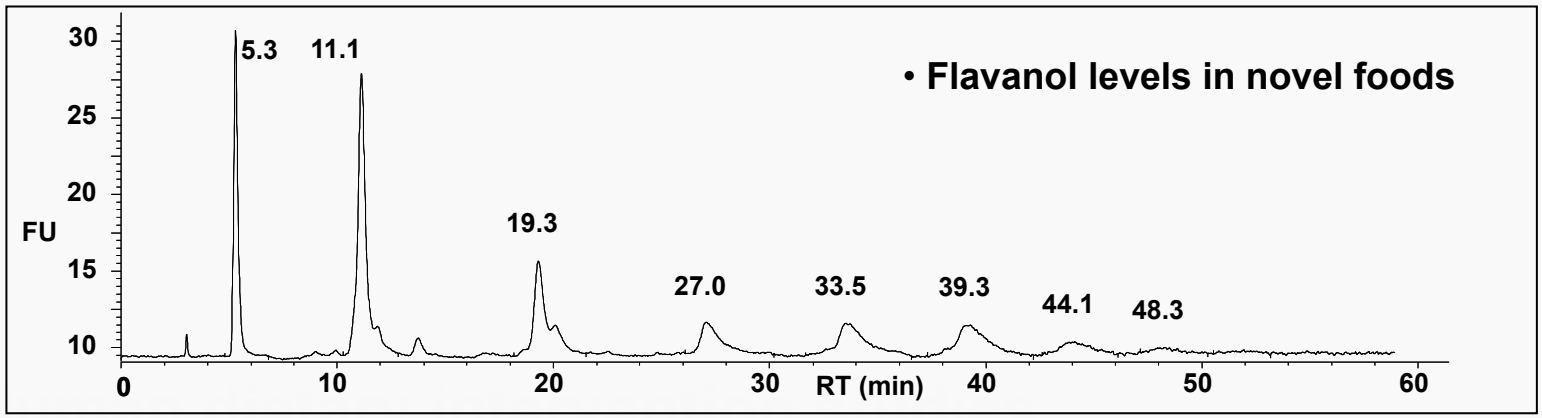
- Flavanol profile in new high-flavanol foods

• **Plasma flavanol levels following intervention**

University of Reading

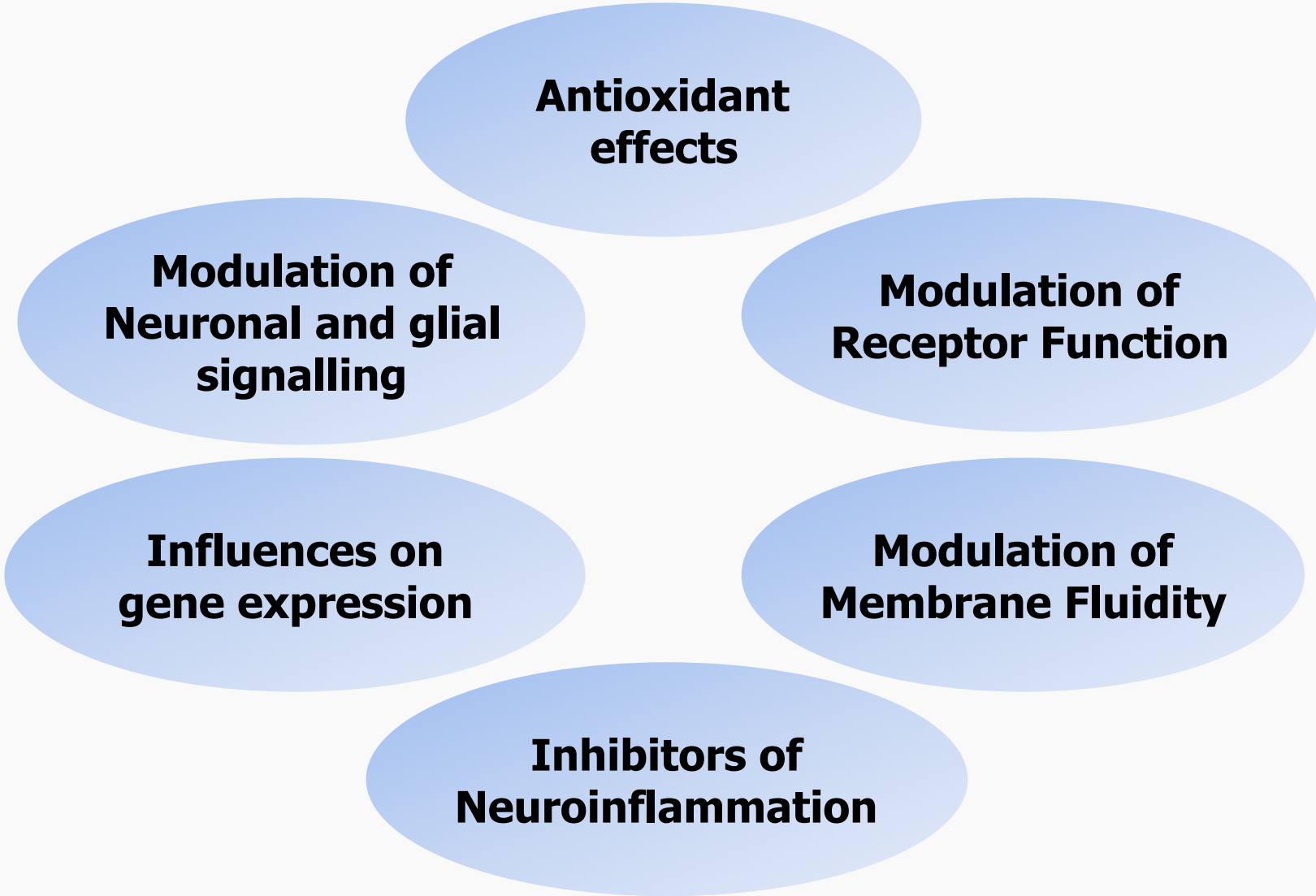


• **Flavanol levels in novel foods**



Mechanistic work related to flavonoids and human health

University of Reading



MARS
incorporated

Introduction and General Overview

- The MARS company was founded by Frank C. Mars and his wife Ethel in Tacoma, Washington, USA in 1911. Today headquartered in McLean, Virginia, MARS, Incorporated is a globally operating manufacturer still entirely owned by the Mars family.

- MARS, Inc. employs approximately 70000 people working at more than 300 sites in 75 countries world-wide. MARS, Inc. is the world's largest chocolate manufacturer, pet care provider [pet food and veterinary medicines/services], and branded rice product producer. In addition, we produce a wide variety of other food products.

- Most people will know MARS by our brands, including MARS, Snickers, M&Ms, Bounty, Wrigley's, Uncle Ben's, Dolmio as examples for confectionary and food products, and pet care-related brands such as Pedigree, Whiskas, Sheba, Chappie, as well as Banfield Pet Hospitals.

Science at MARS:

MARS incorporated

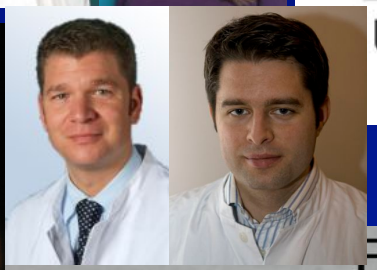
Our corporate research programs span from cocoa flavanols and health & nutrition to food technology research, as well as efforts in the areas of material sciences and the optimization of energy utilization. MARS is involved in the elucidating the genome of Theobroma Cacao as well as of the dog. In addition, we conduct research in sustainable agriculture, agro-forestry as well as marine- and ecosystems biology.

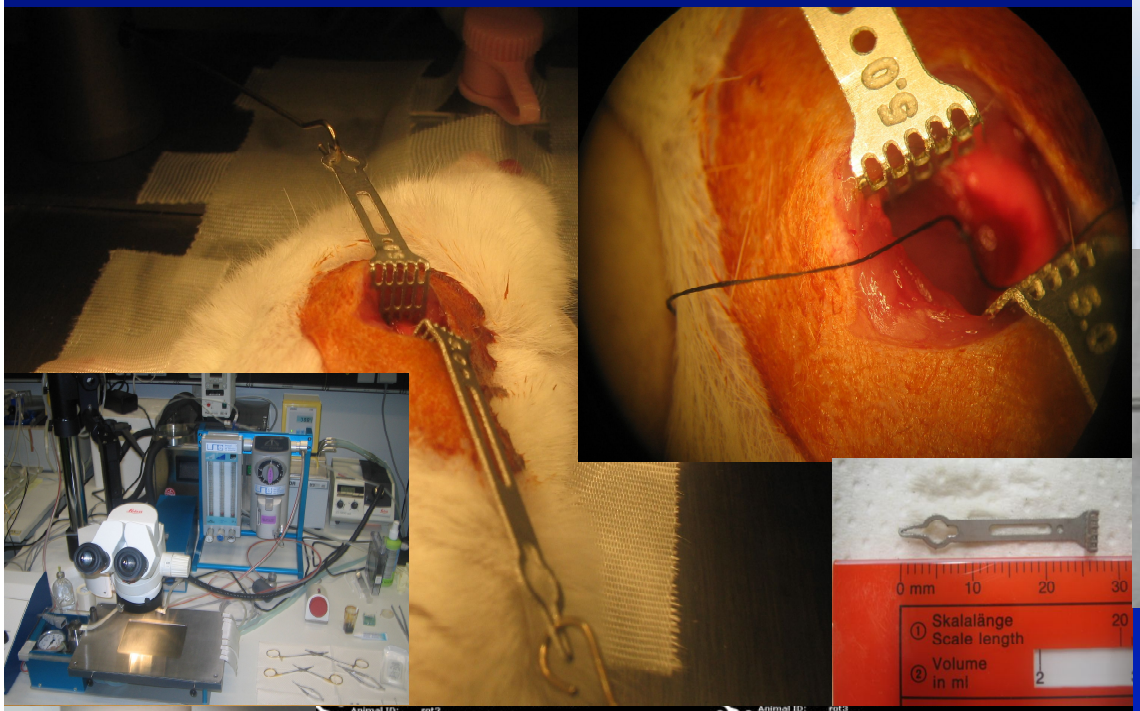
The Cocoa Genome Project: The USDA-ARS, MARS, Inc., and IBM decided to apply their combined scientific resources to sequence and analyze the cocoa genome. The project aims at creating healthier, stronger cocoa crops with pest- and disease resistance, and increased water and nutrient use efficiency. MARS will make its research results freely available through the Public Intellectual Property Resource for Agriculture (PIPRA).

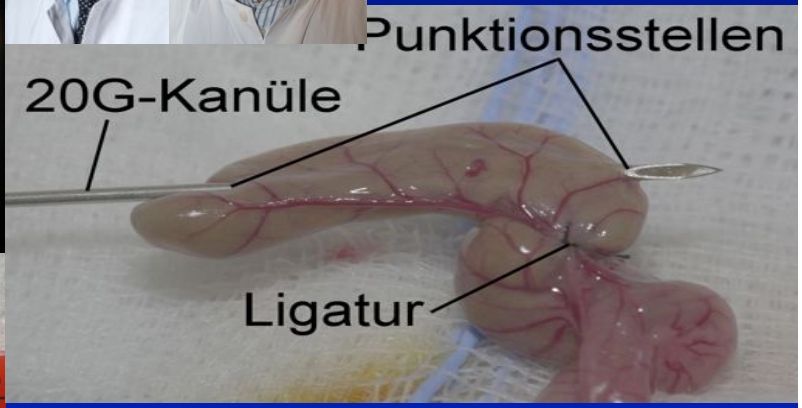
The Cocoa Flavanol Research Program: Initiated in the 1980s, and undertaken in collaboration with an international group of scientists from academia, industry, & government, the MARS Flavanol Research Program results in novel insights into the areas of flavanol analytics and chemistry, the biomedical properties of flavanols, and flavanol-preserving food processing technologies (represented in over 130 scientific papers & approximately 50 patents).

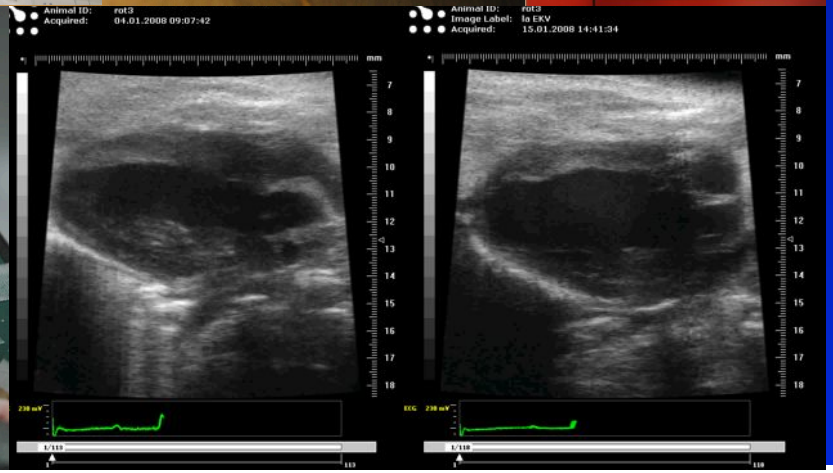
HEINRICH HEINE UNIVERSITÄT DÜSSELDORF

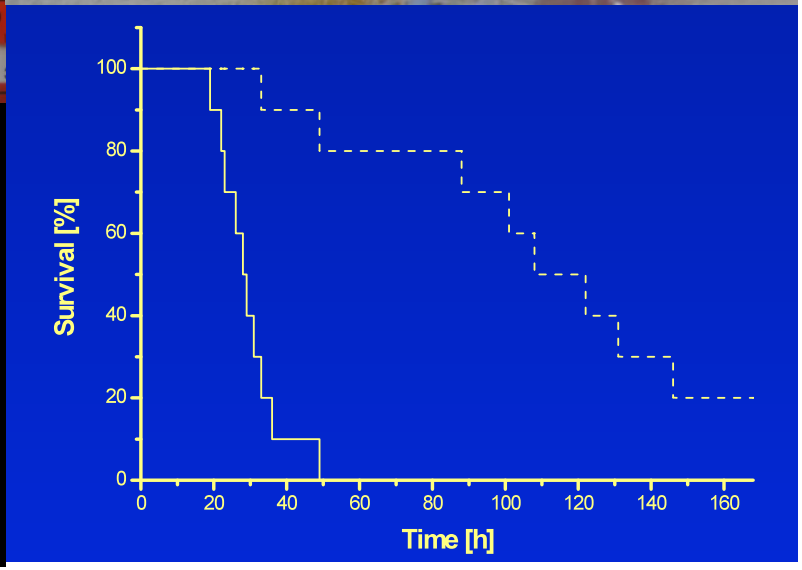
Universitätsklinikum Düsseldorf











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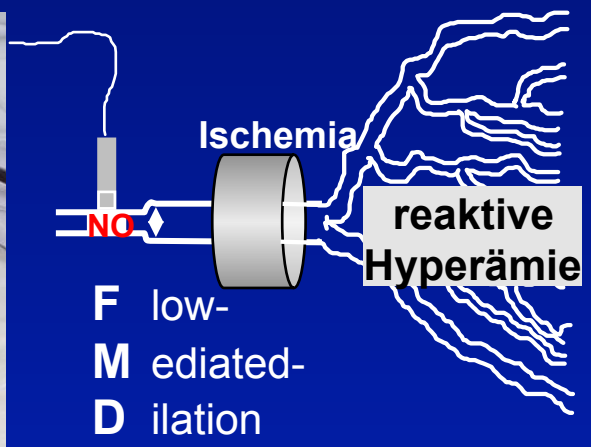

F low-
M ediated-
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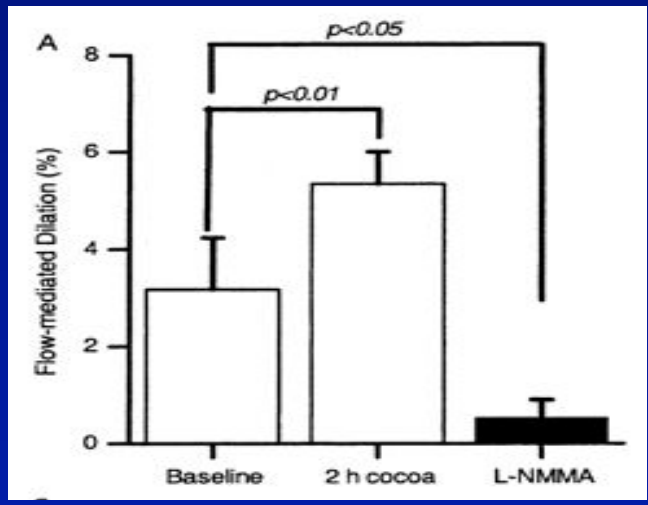
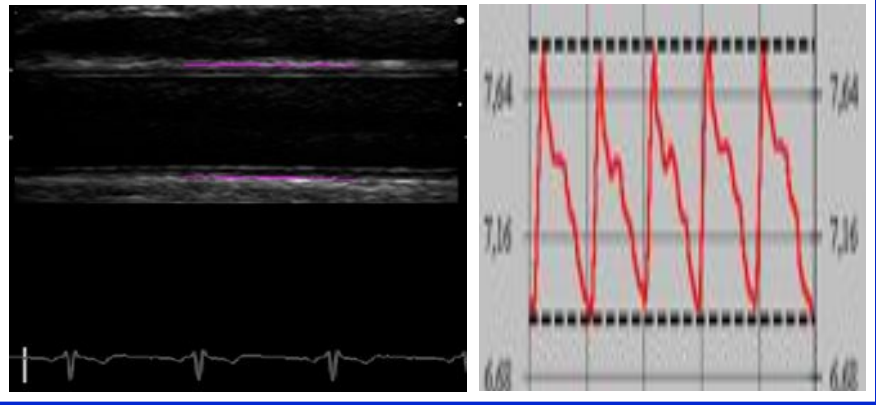


Endothelial Function – Flow Mediated Dilation



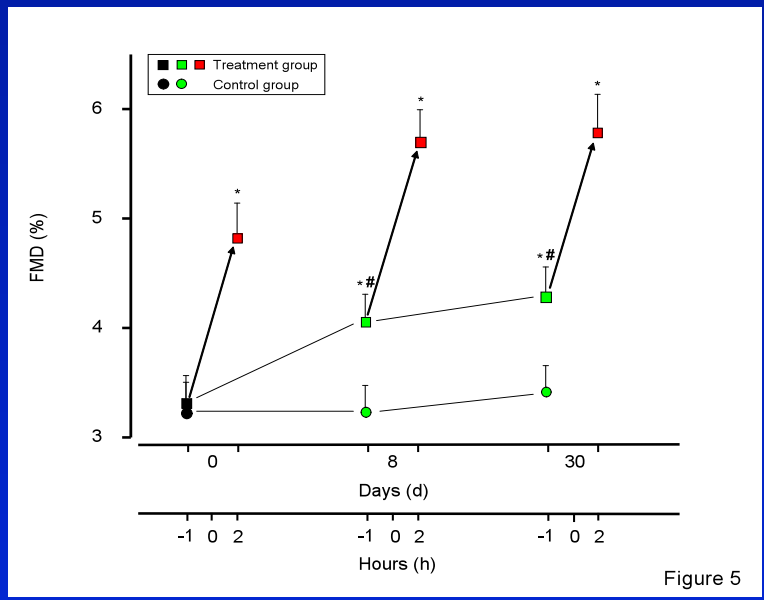


Figure 5


Thank you for your attention!
HEINRICH HEINE
UNIVERSITÄT
DÜSSELDORF
Malte Kelm & Marc W. Merx
Medizinische Klinik B
Klinik für Kardiologie, Pneumologie, Angiologie
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