# **The Gut Brain Axis**

### ILSI Europe's research from gut to brain

**Tobias Recker** 

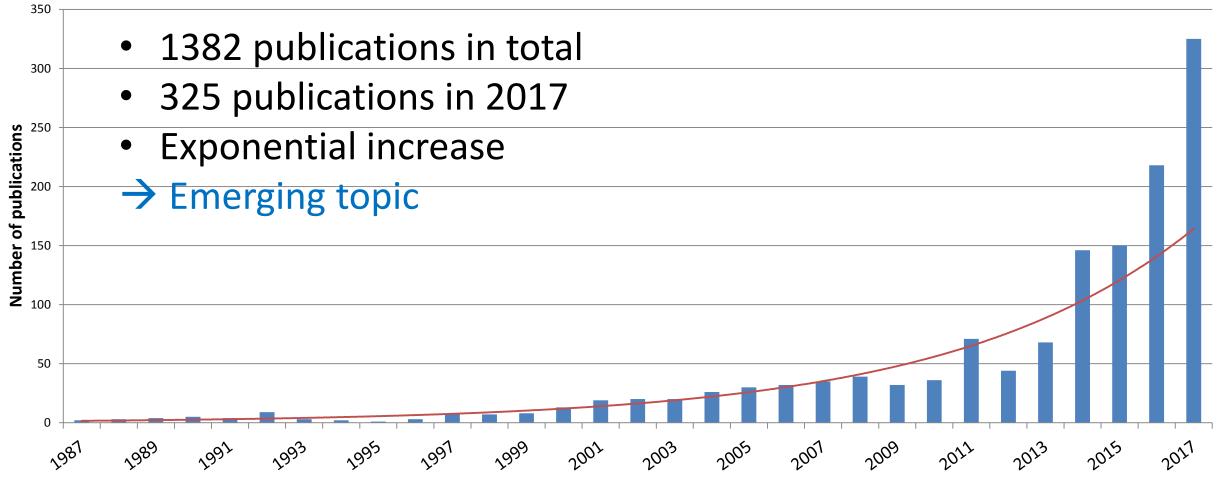


### 23 January, Southampton, Bermuda



International Life Sciences Institute

# Number of publications in pubmed on *gut brain axis* over the past 30 years



## **Current ILSI Europe Scientific Portfolio**

#### FOOD SAFETY

#### Microbiological Food Safety New Approaches for

- Control Options for Viruses in Food Processing
- Industrial Microbiological Risk Assessment -Completed
- Process Validation Protocols
  Next-Generation EU Project EFFORT

#### Contaminants

- Reactions & Potential Mitigation of Mycotoxins During Food Processing
- (Bio-)Markers of Exposure to Process-Related Contaminants
- Mineral Oil Risk Assessment

#### Low Dose Effect

- Cancer Potency Database
- Carcinogen Dose-Response Database for TTC
- Uncertainty in TTC

#### Food Alleray

- Food Safety ToxCast Data on Food
- Chemicals Micronutrient-Food Matrix
- Interactions
- Sequencing Application of Adverse
- Outcome Pathways Authenticity of Food
- Erasmus+ Programme SUIT4FOOD

#### Packaging

- 6th International Symposium on Food

- Packaging Applications PET and PS for Food

#### Verifying VITAL® 2.0 Reference Doses: Suitability of Analytical Methods Severity versus Dose with

- Respect to Allergic Reactions

### Joint Food Safety and

Alternatives to Animal Testing

#### NUTRITION, DEVELOPMENT & HEALTHY AGEING

Healthy Ageing Glycaemia & Inflammation Early Life Nutrition Nutrition for the Ageing Reduction of Post-Prandial Early Growth Velocity – Glycaemia Completed Brain Contrational Di Plant-Based Ingredients & Nutrition and Early Bacterial Colonisation Cognitive Performance Inflammageing Metabolic Syndrome Determinants of Immune Effect of Food Component Competence Interactions on Brain Studies Functions Fost-Francial Glycaemic Response in Children Nutrient Status of Energy Balance Population Groups Carbohydrate-Based Dietary Fibres & Satiety Adaptation to Changes in Recommendations for Satiety Dietary Guidelines Role of Sweet Taste Health Effects of Saturated on Nutrition & Food Fats Holistic Approaches to Preference Develop Alternative Strategies Nutrition Guidelines for NWO Project Satiation Diabetes

#### GUT MICROBIOTA & HEALTH

 Structure-Function Relationship for Prebiotic Compounds

#### **Probiotics**

- Probiotics: Interplay with the Intestinal

#### Oral & Gut Microbiota

- Oral & Systemic Health Resilience • Exploring the Role of Major Gut
- Microbiota Clusters Completed Microbiome Human Study Research
- Guidance
- Short Chain Fatty Acid Production for Health

#### **BIOMARKERS & FUNCTIONAL EFFECT MEASUREMENTS**

#### Biochemical and Immunological Markers of Nutrition

- Marker Validation Initiative Part III Completed
- Glycaemic Exposure Markers in the Non-Diabetic Population
- Efficacy Markers of Diabetes Risk
- Quality of Life Measures
- EU Project PATHWAY-27

### Packaging

#### In Vitro Bioassays for Food Contact Materials Safety

- Adhesives for Food
- Packaging Applications

#### **EXPOSURE & INTAKE ASSESSMENT**

#### Food Intake Assessment Methodology Uncertainties in Food Intake Assessments.

- Evaluation of New Methods for Dietary Intake Assessment
- Preferred Approaches for Quantifying the Impact of Modifying Nutrient Intakes
- Additive Occurence & Loyalty

#### Food Intake Data

- Adequacy of Dietary Fibre Intake
- Adequacies of Omega 3 & Omega 6 PUFA Intakes
- Dietary Supplements, Nutrient-Dense Food & Food Fortification & the Elderly
- Iodine Intake in Europe

#### **NUTRITION SECURITY & SOCIETAL ASPECTS**

#### Nutrition Security & Societal Aspects

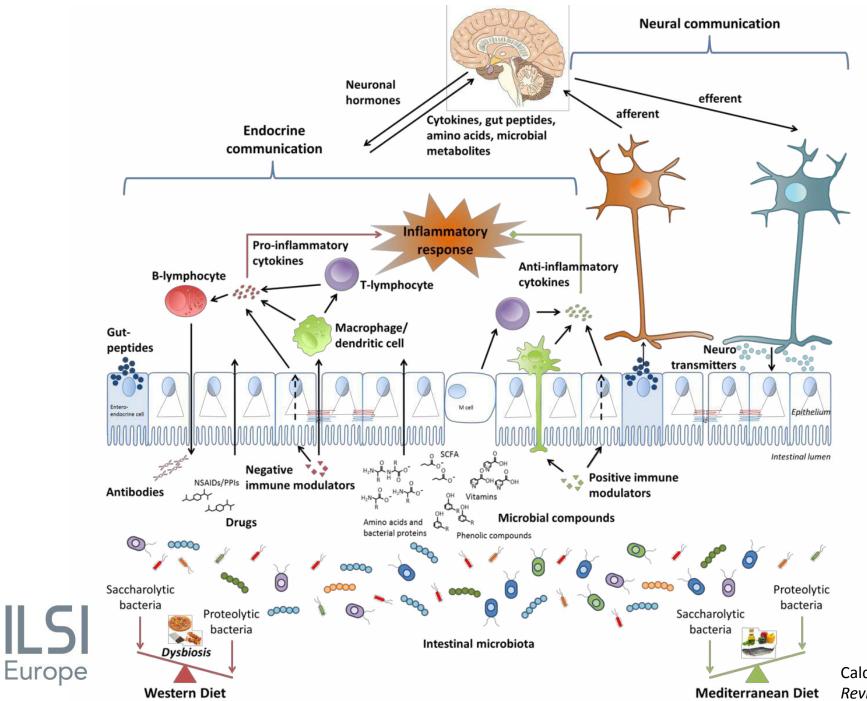
- Nudging Towards Healthier Food Choices
- EU Project SUSFANS
- EU Project FIT4FOOD2030



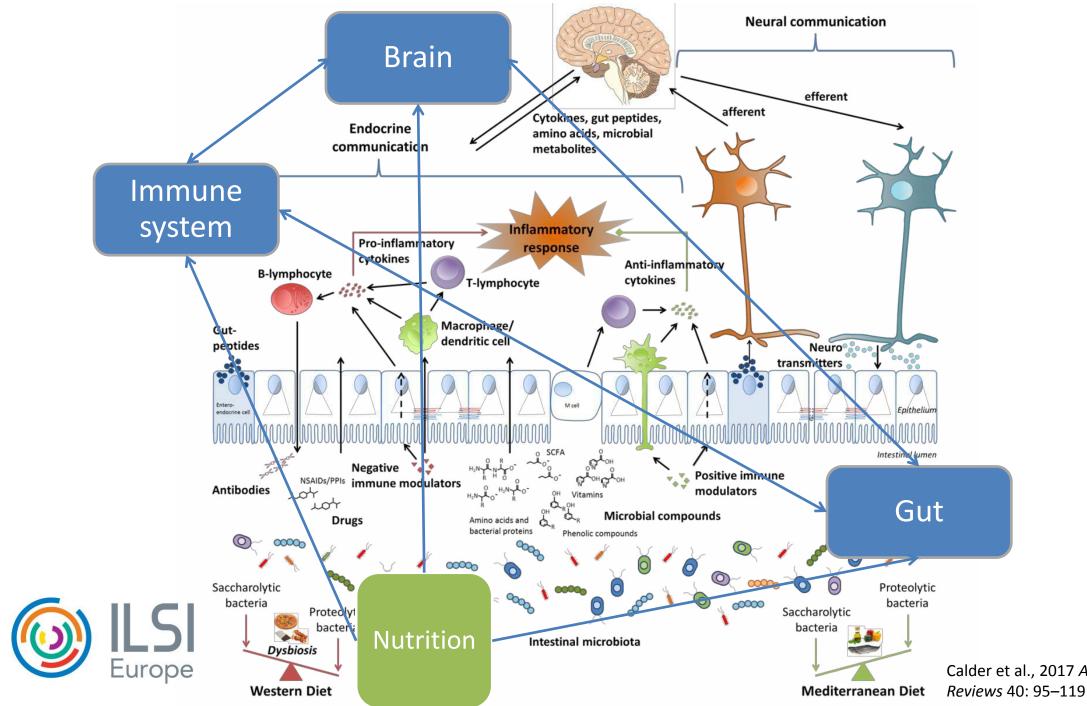
### Prebiotics

- - Barrier Function
  - Mechanisms of Probiotic Action

 Tolerable Risk in Food Allergy EU Project iFAAM



Calder et al., 2017 Ageing Research Reviews 40: 95–119



Calder et al., 2017 Ageing Research

### **Schematic representation** of the gut brain axis Controller of basic homeostatic processes Brain Coordinates the responses to internal and external threats $\rightarrow$ Ensures survival of the organism Nutrition

- Defence machinery to fight pathogens
- Key role in regulating homeostasis
- → part of fundamental physiological processes and a close crosstalk with other body systems

Immune

system

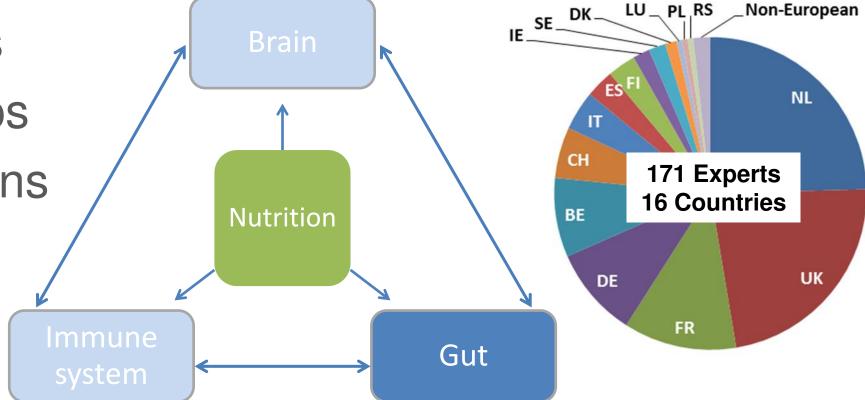
• An unhealthy gut contributes to a wide range of diseases

Gut

• The gut microbiota plays a major role in gastrointestinal health

# **Gut related activities**

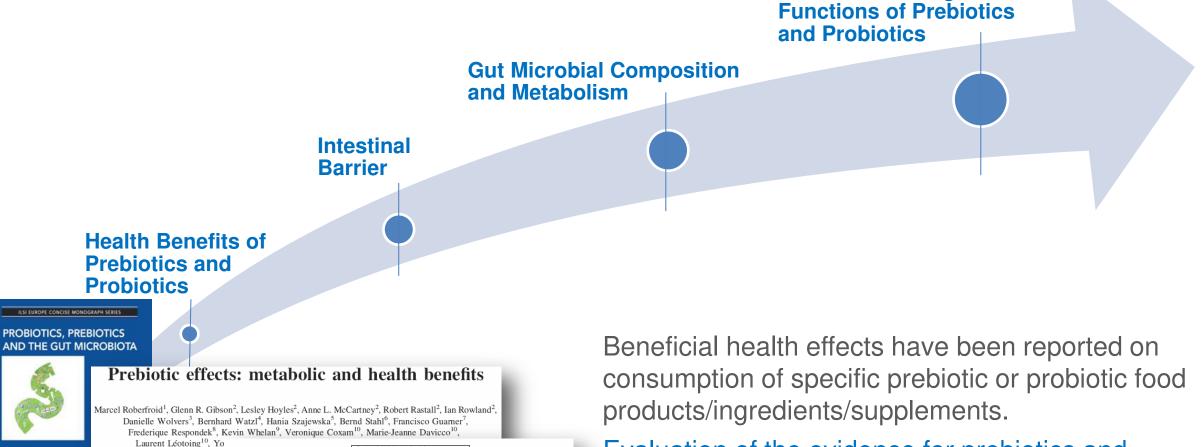
- 12 Activities
- 3 Workshops
- 9 Publications



- An unhealthy gut contributes to a wide range of diseases
- The gut microbiota plays a major role in gastrointestinal health



# **Gut related activities**



The Journal of Nutrition

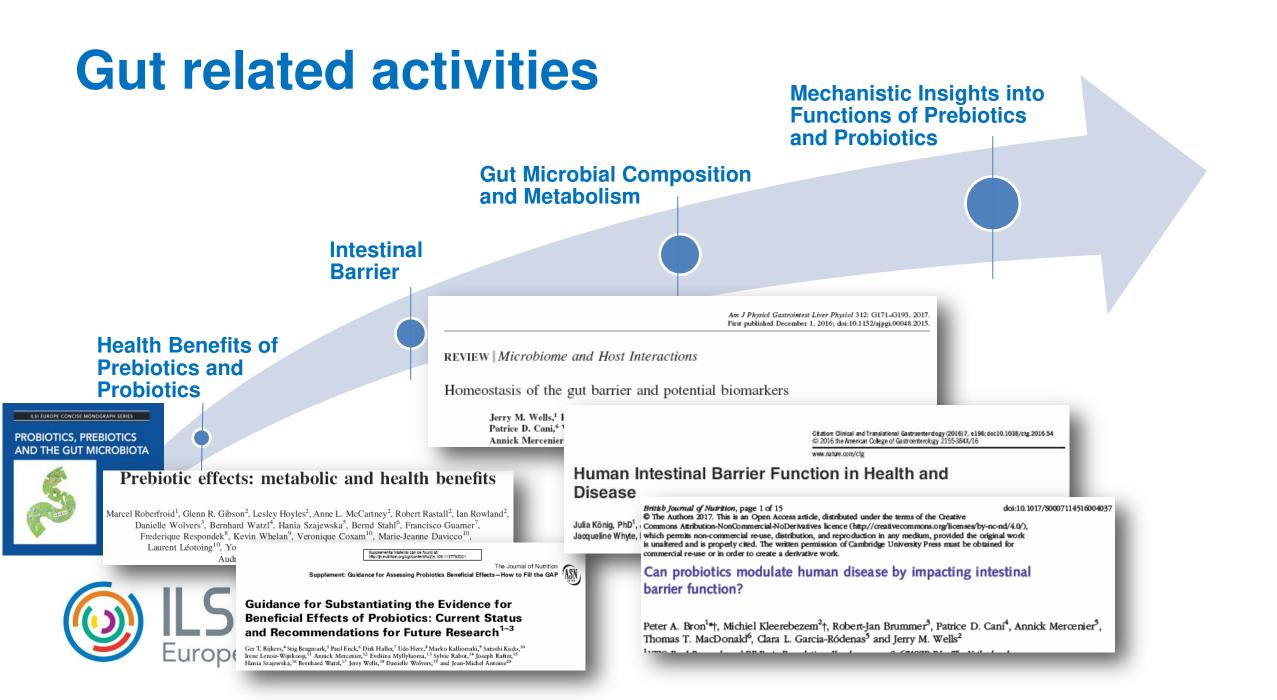
Material can be found at: morpicolicontent/full/in.109.113779/DC1

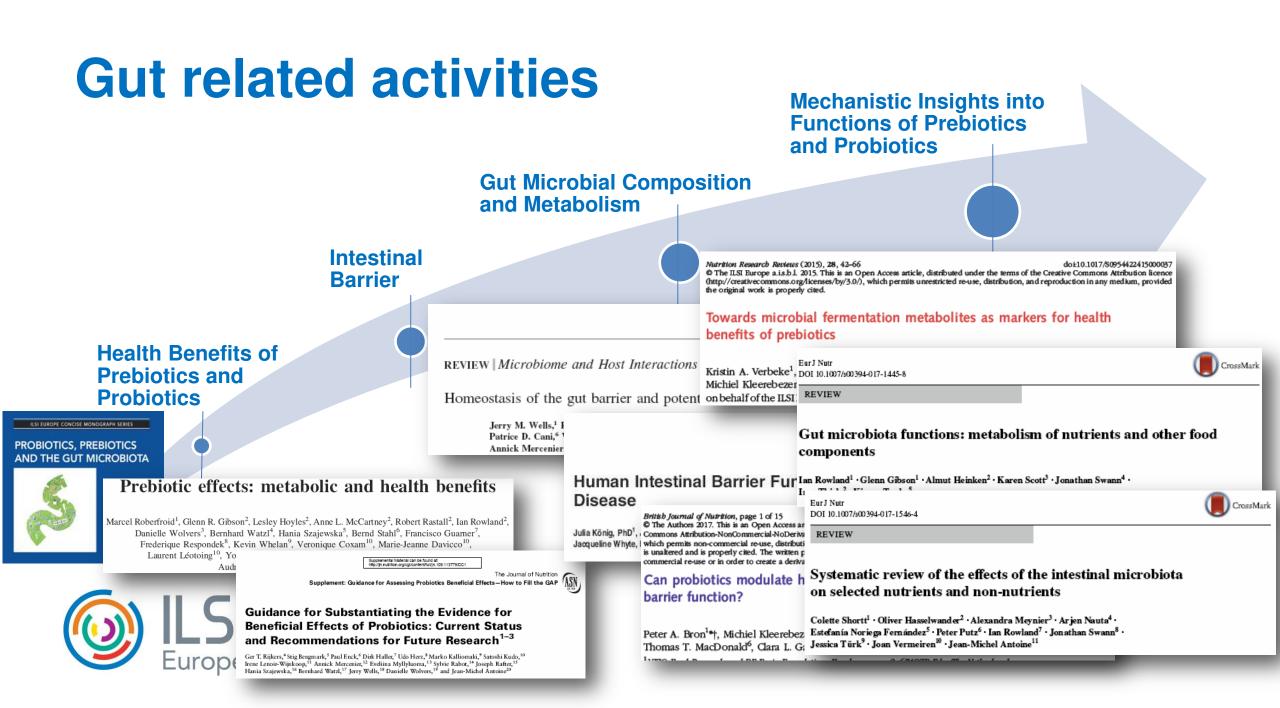
#### Guidance for Substantiating the Evidence for Beneficial Effects of Probiotics: Current Status and Recommendations for Future Research<sup>1-3</sup>

Aud

Ger T. Rijkers,<sup>4</sup> Stig Bengmark,<sup>5</sup> Paul Enck,<sup>6</sup> Dirk Haller,<sup>7</sup> Udo Herz,<sup>8</sup> Marko Kalliomaki,<sup>9</sup> Satoshi Kudo,<sup>10</sup> Irene Lenoir Wijnkcoo,<sup>11</sup> Annick Mercenier,<sup>12</sup> Evelinia Myllytuoma,<sup>13</sup> Sylvie Rabot,<sup>14</sup> Joseph Rafter,<sup>13</sup> Hania Szajewska,<sup>16</sup> Bernhard Watzl,<sup>7</sup> Jerrey Wells,<sup>16</sup> Daniel Wolvers,<sup>13</sup> and Jean-Michel Antoine<sup>20</sup> Evaluation of the evidence for prebiotics and probiotics' functionality in several areas of application like inflammatory conditions or metabolism and energy homeostasis

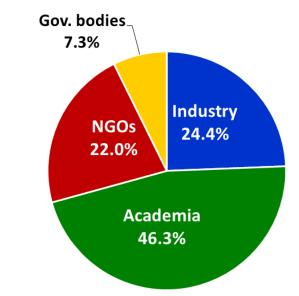
**Mechanistic Insights into** 





# **Gut Microbial Composition and Metabolism**





### Stakeholder Workshop, on 3-4 December 2015

- Gut microbiota metabolism extends metabolic flexibility of host to process a wide range of substrates
- Microbial metabolites of nutrients and non-nutrients can be important cell signaling molecules (SCFA, bile acids) and have impacts on health (SCFA, TMA, phenolics)
- Large inter-individual variation in microbiota → potential consequences for metabolism of dietary compounds and health

# Mechanistic Insights into Functions of Prebiotics and Probiotics

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### Mechanisms of Probiotic Action

- Investigate and evaluate current knowledge about the mechanisms of probiotic action
- Link health benefit, physiological function and probiotic mechanism;

explain

Molecular mechanism of cross-talk at mucosal level

Cellular responses in the mucosa (local)

Cellular / physiology effect in host (mucosal and systemic)

Clinical benefit (meta-analysis)

### Structure-Function Relation of Prebiotics

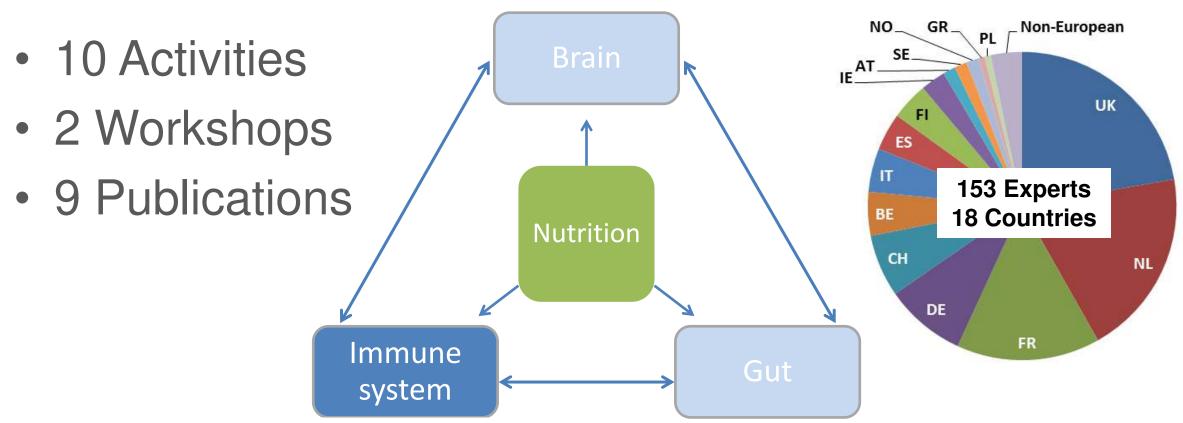
- Prediction how a specific core structure of a carbohydrate compound impacts the gut microbiota, and subsequently the host
- → This activity is a first step in defining structure-function relations

Oligofructose  $(Fru\beta2\rightarrow1)_nFru\beta2\leftrightarrow1\alpha Glc$ Soy oligosaccharides  $(Gal\alpha1\rightarrow6)_{1-3}Glc\alpha1\leftrightarrow2\beta Fru$ Galacto-oligosaccharides  $(Gal\beta1\rightarrow4/6)_nGlc$ 

Acetate Propionate Butyrate

Rastall, 2017 *Designing next generation prebiotics for lifelong health?* Presentation at IPC2017

## Immune system related activities



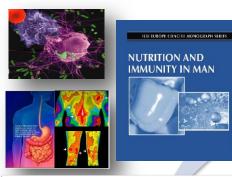
- Defence machinery to fight pathogens
- Key role in regulating homeostasis
- → part of fundamental physiological processes and a close crosstalk with other body systems

# Immune system related activities

Understanding the health relevance of immune modulation and the role of nutrition

Understanding the impact of nutrition on immune functions

Understanding the complexity of the immune system and its role in maintaining health



British Journal of Nutrition (2005), 94, 452-481

© ILSI 2005



Monitoring immune modulation by nutrition in the general population: identifying and substantiating effects on human health

Ruud Albers<sup>1</sup>, Raphaëlle Bourdet-Sicard<sup>2</sup>, Deborah Braun<sup>3</sup>, Philip C. Calder<sup>4</sup>, Udo Herz<sup>5</sup>,

#### Inflammatory Disease Processes and Interactions with Nutrition

P. C. Calder<sup>1</sup>, R. Albers<sup>2</sup>, J.-M. Antoine<sup>3</sup>, S. Blum<sup>4</sup>, R. Bourdet-Sicard<sup>3</sup>, G. A. Ferns<sup>5</sup>, G. Folkerts<sup>6</sup>,

Markers to measure immunomodulation in human nutrition intervention studies<sup>†</sup>

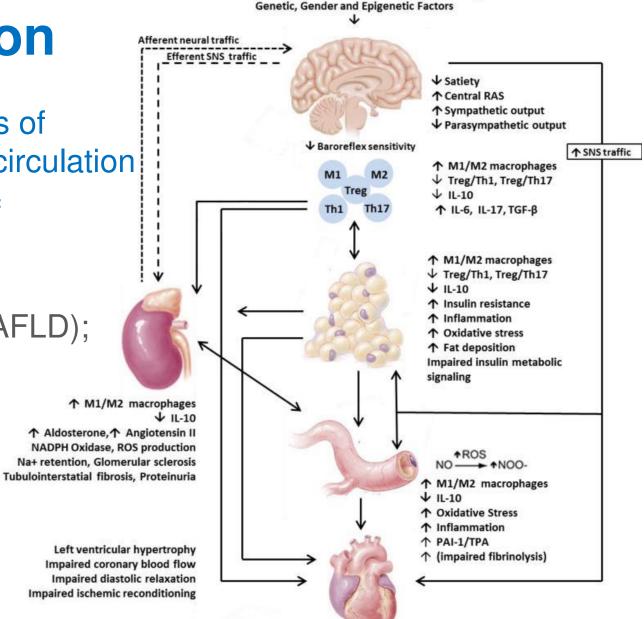
Ruud Albers<sup>1</sup>, Jean-Michel Antoine<sup>2</sup>, Raphaëlle Bourdet-Sicard<sup>2</sup>, Philip C. Calder<sup>3</sup>, Michael Gleeson<sup>4</sup>,

A Consideration of Biomarkers to be used for Evaluation of Inflammation in Human Nutritional Studies

P.C. Calder<sup>1</sup>, N. Ahluwalia<sup>2</sup>, R. Albers<sup>3,4</sup>, N. Bosco<sup>5</sup>, R. Bourdet-Sicard<sup>6</sup>,

# Low-grade inflammation

- Characterised by raised concentrations of inflammatory markers in the systemic circulation
- Pathological feature of a wide range of chronic disease conditions:
  - $\rightarrow$  Metabolic syndrome (MetS);
  - $\rightarrow$  Non-alcoholic fatty liver disease (NAFLD);
  - $\rightarrow$  Type 2 diabetes mellitus (T2DM);
  - $\rightarrow$  Chronic kidney disease (CKD);
  - $\rightarrow$  Cardiovascular disease (CVD);
  - $\rightarrow$  Cognitive decline.



Environmental (Western Diet and physical activity)

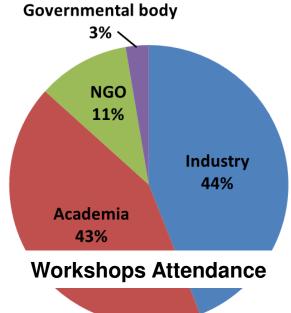


Aroor et al.,2013 Metabolism 62(11):1543–1552



In collaboration with ILSI Brazil, ILSI North America, ILSI Southeast Asia Region

- Highlighted the importance of low-grade inflammation in health and disease;
- Reviewed and interpreted the extensive literature on the dietary modulation of lowgrade inflammation by macronutrients, micronutrients and non-nutrients (such as fibre and other plant bio-actives);
- Provided a comprehensive overview of the hierarchy of inflammatory markers as biomarkers of risk of the metabolic syndrome, diabetes, cardiovascular disease, cognitive and gut health;
- Focused on issues relevant to the translation of research findings into health claims.
  - → Controlling inflammation a key future preventative and therapeutic target



# Low-grade inflammation and diet

### Dietary factors and low-grade inflammation in relation to overweight and obesity

Philip C. Calder<sup>1</sup>, Namanjeet Ahluwalia<sup>2</sup>, Fred Brouns<sup>3,21</sup>, Timo Buetler<sup>4,22</sup>, Karine Clement<sup>5</sup>, Karen Cunningham<sup>6</sup>, Katherine Esposito<sup>7</sup>, Lena S. Jönsson<sup>8</sup>, Hubert Kolb<sup>9</sup>, Mirian Lansink<sup>10</sup>, Ascension Marcos<sup>11</sup>, Andrew Margioris<sup>12</sup>, Nathan Matusheski<sup>13</sup>, Herve Nordmann<sup>14</sup>, John O'Brien<sup>4</sup>, Giuseppe Pugliese<sup>15</sup>, Salwa Rizkalla<sup>5</sup>, Casper Schalkwijk<sup>16</sup>, Jaakko Tuomilehto<sup>17</sup>, Julia Wärnberg<sup>11,18</sup>, Bernhard Watzl<sup>19</sup> and Brigitte M. Winklhofer-Roob<sup>20</sup>

#### Low-grade inflammation, diet composition and health: current research • FOCUS on the latest research findings in evidence and its translation

Anne M. Minihane<sup>1</sup>, Sophie Vinoy<sup>2</sup>, Wendy R. Russell<sup>3</sup>, Athanasia Baka<sup>4</sup>, Helen M. Roche<sup>5</sup>, Kieran M. Tuohy6, Jessica L. Teeling7, Ellen E. Blaak8, Michael Fenech9, David Vauzour1, Harry J. McArdle<sup>3</sup>, Bas H. A. Kremer<sup>10</sup>, Luc Sterkman<sup>11</sup>, Katerina Vafeiadou<sup>12</sup>, Massimo Massi Benedetti13, Christine M. Williams14 and Philip C. Calder15,16

- Explains the nature of chronic low-grade inflammation in the context of overweight and obesity;
- Describes the factors that might influence it, in particular those related to diet.

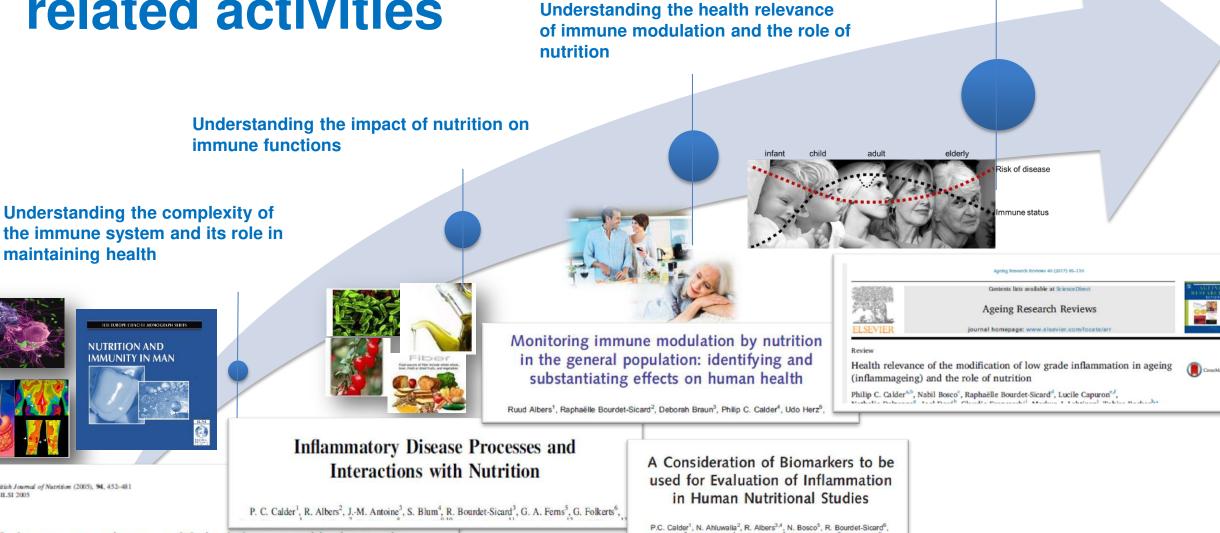
the areas of inflammation and cardiometabolic, cognitive and gut health,

• Reviews how early-life nutrition as well as the macronutrient and plant bioactive composition of the adult diet influence inflammatory processes.



# Immune system related activities

Understanding immune modulation across lifespan



Markers to measure immunomodulation in human nutrition intervention studies†

British Journal of Nutrition (2005), 94, 452-481

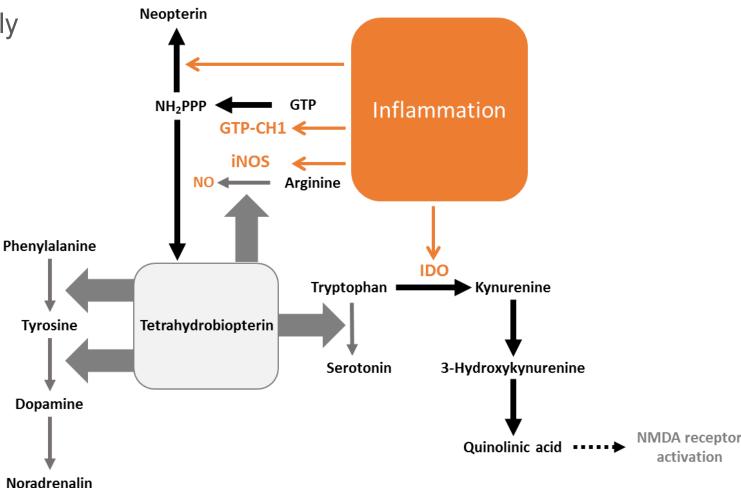
© ILSI 2005

Ruud Albers<sup>1</sup>, Jean-Michel Antoine<sup>2</sup>, Raphaëlle Bourdet-Sicard<sup>2</sup>, Philip C. Calder<sup>3</sup>, Michael Gleeson<sup>4</sup>,

# Low Grade Inflammation mediated alteration of brain functions

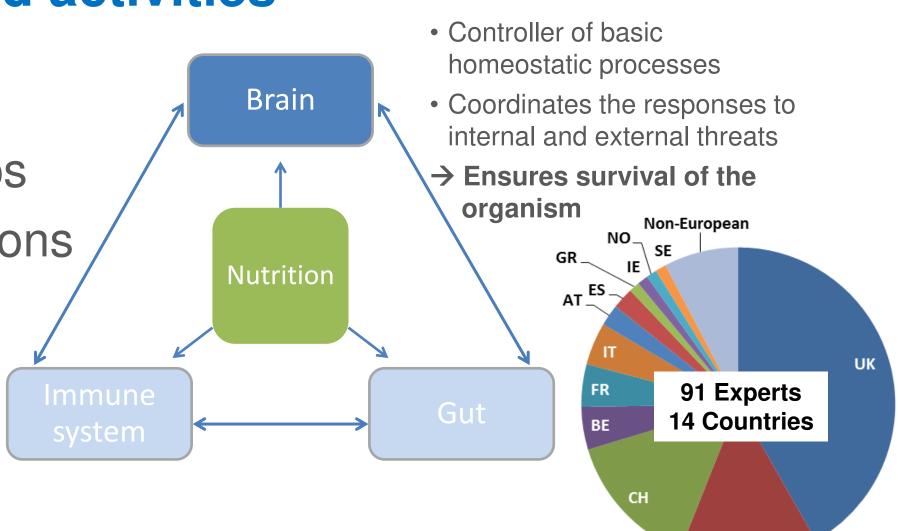
- Pro-inflammatory cytokines potently modulate the activity of the neuroendocrine system → chronic inflammation could result into dysregulation of the HPA axis
- Pro-inflammatory cytokines significantly modulate neural plasticity and neurogenesis
- Pro-inflammatory cytokines have potent effects on neurotransmitter metabolism and function





# **Brain related activities**

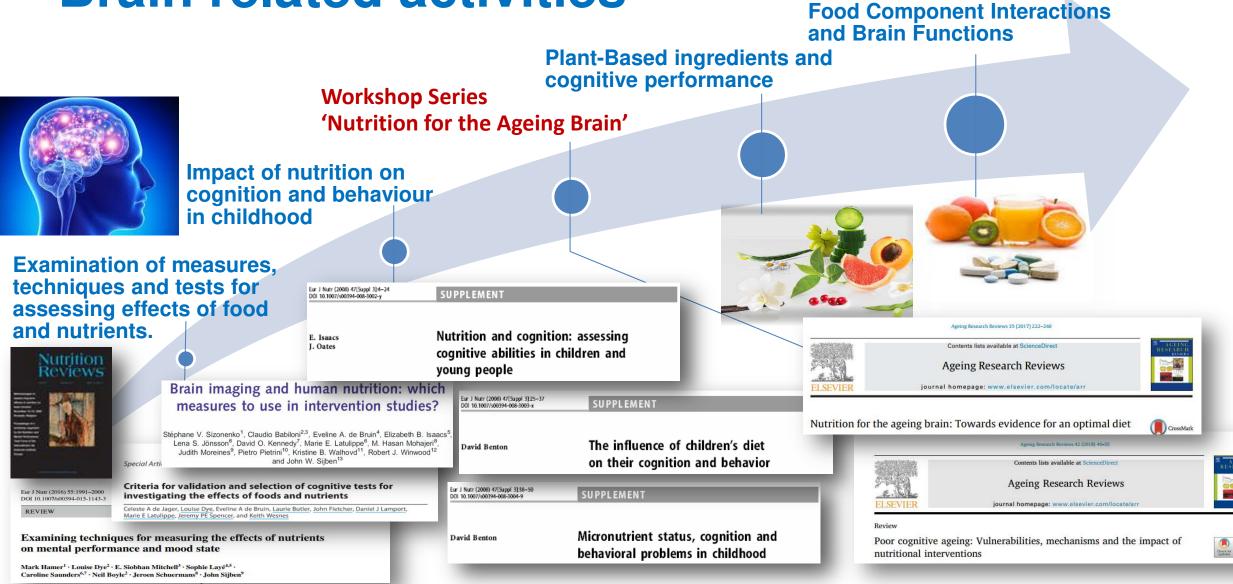
- 7 Activities
- 4 Workshops
- 10 Publications



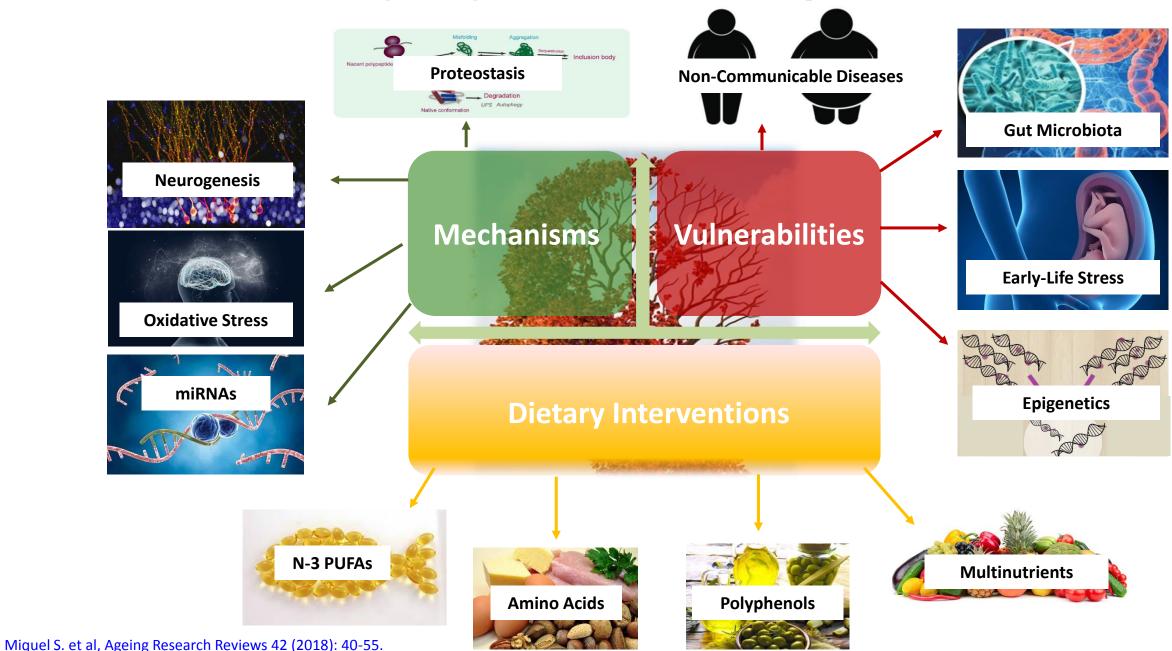
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## **Brain related activities**



### **Nutrition for the Ageing Brain Workshops**



### **Nutrition for the Ageing Brain Workshops**

New

### Upcoming 3rd Workshop

'Nutrition for the Ageing Brain: Moving Towards Clinical Applications' 30 – 31 August 2018, Madrid, ES

### **Objectives**

- 1. Debate the potential for maintaining cognitive function through dietary intake.
- 2. Focus on clinical aspects and novel strategies developed to determine whether diet and nutrients have efficacy in individuals affected by cognitive decline.

### **Main themes**

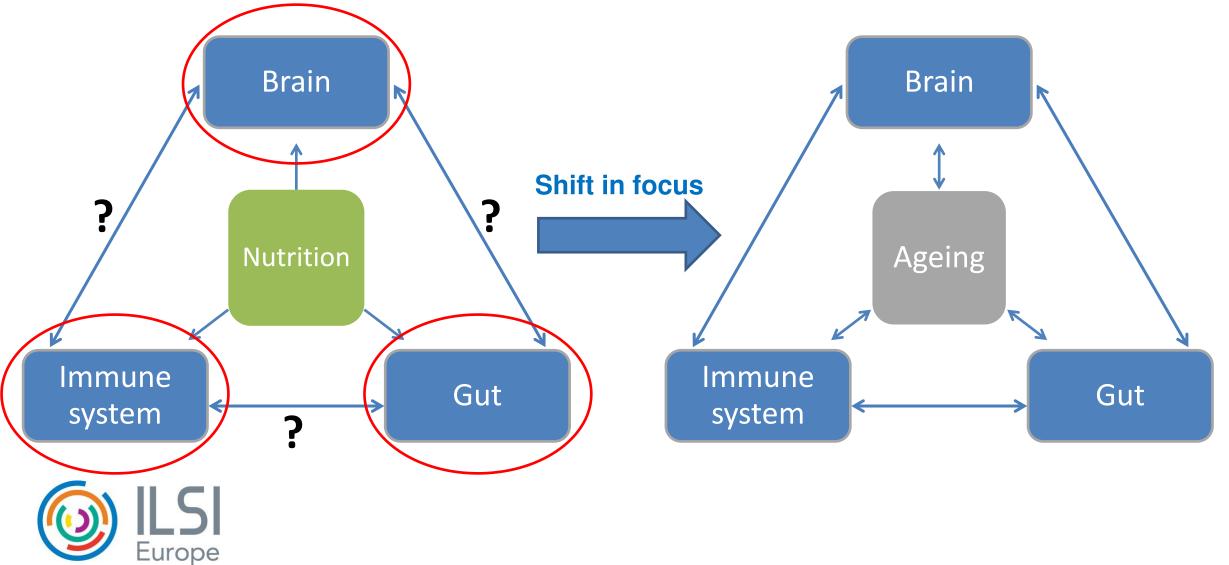
- Impact of nutrition on brain functions using neuroimaging technologies;
- Microbiome and immune status: impact on brain function;
- Biomarkers of food intake and cognitive health;
- Sleep deprivation: effects on diet and cognitive performance;
- New methodologies applied to dementia and how nutrition could play a role.

Industry Academia 57% 34%

### **Workshops Attendance**

**Governmental body 9%** 

### In brief: Research from gut to brain



## In brief: Research from gut to brain

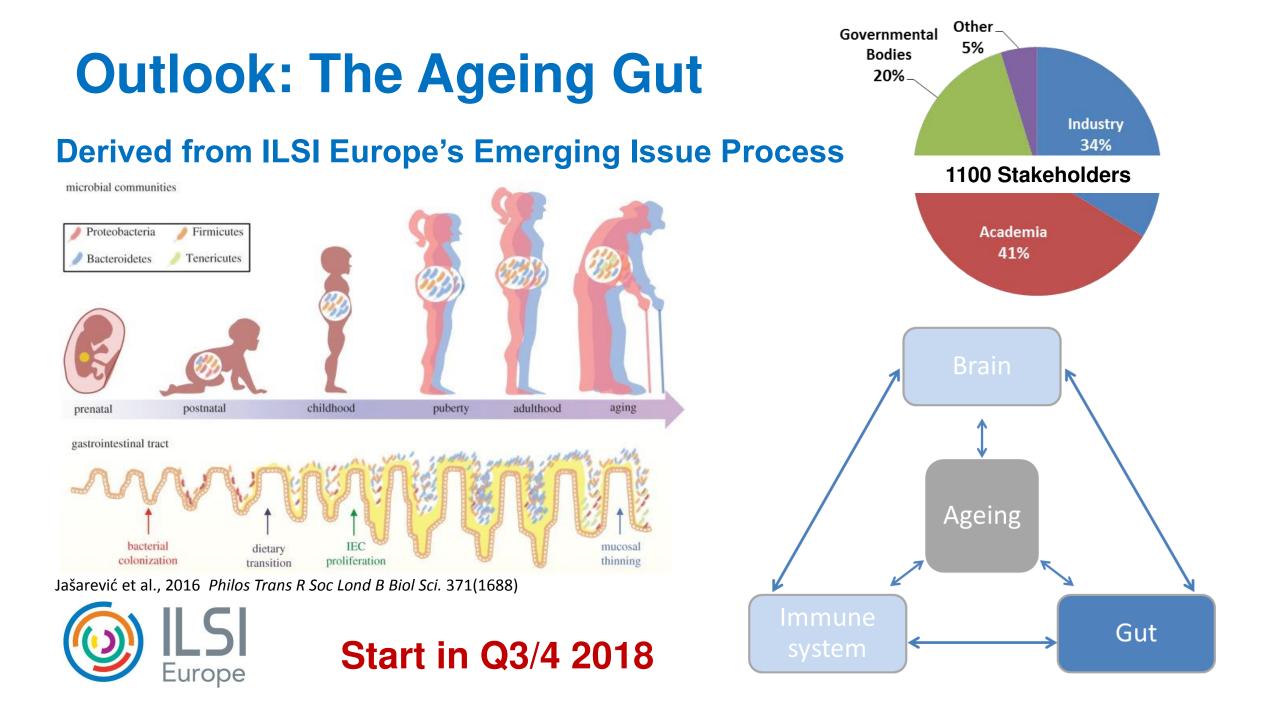


Europe

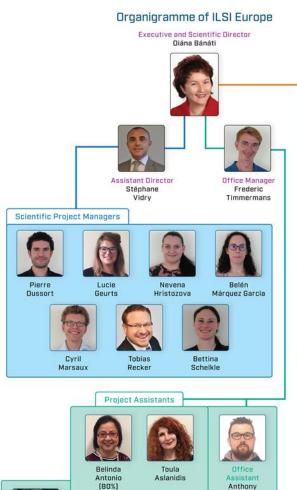
### In brief: Research from gut to brain







# Thank you.



Adam

Coventry

Maryline

Tubiermont

(on leave)



Communication

Manage

Accounting

Manager

Jonathan Karekezi

Accounting

Assistant

Karen Maniraho (80%)

Regan

Isobel Head



ADM Ajinomoto Arla Foods Barilla G&R Fratelli BASF SE Caelus Health Cargill Chr. Hansen Cosucra Groupe Warcoing Danone Dow Europe DSM DuPont Nutrition & Health Firmenich FrieslandCampina General Mills Givaudan International Indoor Biotechnologies Institut Mérieux Johnson & Johnson EAME Kabi Fresenius Kao Corporation

Abbott Nutrition

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