WELCOME
to the ILSI Europe Workshop

BIOMARKERS OF INFLAMMATION:
TOWARDS GUIDANCE FOR FUTURE NUTRITION STUDIES

14-15 May 2012, Seville (SP)
Dr Stéphane Vidry
ILSI Europe

The European branch of the International Life Sciences Institute
To improve public health and safety through advancement of science
ILSI Mission

Academia

Neutral Forum

Industry

Government
European branch of the worldwide International Life Sciences Institute (ILSI)
http://europe.ilsi.org
ILSI Europe’s Portfolio

Assessment of Benefits & Risks
• Addition of nutrients to food
• Emerging Technologies
• Food intake methodology
• Functional foods
• Novel foods and Nanotechnology
• Risk analysis in food microbiology
• Risk assessment of chemicals in food
• Risk assessment of genotoxic carcinogens
• Threshold of toxicological concern

Societal Aspects
• Consumer science

Diet, Health & Disease
• Dietary carbohydrates
• Eating behaviour and energy balance
• Food allergy
• Metabolic imprinting
• Metabolic syndrome
• Nutrient requirements
• Nutrition and immunity in man
• Nutrition and mental performance
• Prebiotics
• Probiotics
• Weight management in public health

Food Chain
• Emerging Microbiological Issues
• Environment & health
• Packaging materials
• Process-related compounds and Natural Toxins
## ILSI Europe Membership in 2012

### 60 Members

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<th>Category</th>
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<td>H J Heinz, Institut Mérieux, International Nutrition Company</td>
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<td>Ajinomoto Europe</td>
<td>Kellogg Europe, Kikkoman Foods Europe, Kraft Foods Europe, Luigi Lavazza</td>
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<td>Barilla G. &amp; R. Fratelli</td>
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<td>Bayer CropScience BioScience</td>
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Workshop supported by

Nutrition and Immunity Task Force

Danone
Institut Mérieux
Merck
Nestlé
Pfizer Consumer Healthcare
Royal FrieslandCampina
Unilever
Yakult Europe
MONITORING IMMUNE MODULATION BY NUTRITION IN THE GENERAL POPULATION

A collaboration of the Nutrition and Immunity and Probiotics Task Forces
16-17 April 2012, Nice (FR)
The aim of the activity is to arrive at:

• Criteria for the selection of markers of immune function

• Ranked list(s) of markers that best describe (modulation of) immune functions in the general population

• Reference to normal values and ranges established in laboratory medicine and daily clinical practice for selected markers

• Rational approaches for the design of studies, selection of markers and interpretation of changes observed in those markers due to exogenous factors such as nutrition
Focus on EFSA-defined functional domains indicating distinct physiological functions of the immune system:

A. Defence against pathogens
B. Mitigation of hypersensitivity (e.g. allergy)
C. [Reduction of symptomatic inflammation]**
D. Reduction of asymptomatic (low-grade, metabolic) inflammation

**The immune modulation project focuses on asymptomatic inflammation only**
Scenarios for changes in markers

- Upper reference value
- Lower reference value
- Value of biomarker(s)
- Time

Reference range of generally healthy population
Reference range of less favorable (sub)population
Reference range of less favorable (sub)population
Flow chart to aid interpretation of immune modulation in nutrition studies

**Significant modulation of marker(s) indicative of immune function?**
- Yes
  - **Is marker by itself indicative of biological / clinical relevance?**
    - Yes
      - Scenario 1, 2 & 4 beneficial modulation of immune function (scenario 1, 2 & 4)
    - No
      - Scenario 1, 2, 3 & 4 No modulation of immune function (scenario 1, 2 & 4)
  - No
    - **Is marker known to be associated with health improvement in (sub)populations?**
      - Yes
        - Scenario 1 interpretation NOT possible (scenario 1, 2 & 4)
      - No
        - Scenario 2 & 4 beneficial modulation of immune function (scenario 1, 2 & 4)

**Significant modulation of other marker(s) indicative of biological / clinical relevance?** (in same or similar study)
- Yes
  - Scenario 3 potentially undesired modulation of immune function (scenario 1, 2 & 4)
- No
  - Scenario 3 potentially undesired modulation of immune function (scenario 1, 2 & 4)

**Level of markers**
- Level A: Relevance AND involvement of immune functions (e.g. response to vaccination)
- Level B: Relevance BUT NOT necessarily involvement of immune functions (e.g. diarrhea)
- Level C: Involvement of immune functions BUT NOT necessarily relevance (in all population) (associated with clinical endpoints in specific (sub)populations, e.g. NK cell activity)
- Level D: Mechanistic insights BUT NOT directly associated to clinical outcomes (e.g. production of specific cytokines)
**Broad overall agreement on the approach**

**Additional points for action by the EG:**
- Improve consistency throughout the manuscript
- Several suggestions for inclusion of markers
- Modify marker rating system, including changing from quantitative to semi-quantitative (e.g. *** or +++)
- Incorporate language so the framework remains open to future developments (e.g. omics)
- More systematically reference the selected markers
- Addition of 5th scenario on maintenance of optimal function (e.g. prevention of movement outside optimal range)

**Next steps:**
- Refinement and finalization of draft
- Submission to JACI by early 2013
Background

- ILSI Europe coordinated many EU-funded projects related to markers, like FUFOSE, PASSCLAIM, BRAFO, EURRECA
- Gap has been identified in nutrition research: lack of criteria to evaluate markers
- The lack of criteria makes comparing results from various studies difficult and jeopardizes future development of evidence-based nutrition
- ILSI Europe started in 2011 a 3-year initiative, called the Marker Initiative in Nutrition Research

Objectives

- Identify criteria for evaluating markers in nutrition research
- Identify examples of adequate markers in each field of nutrition research
- Produce a peer-reviewed journal supplement
Marker Initiative in Nutrition Research

**Approach A**
Review of existing validation criteria
Done by a selected EG through a literature search covering all fields of nutrition research

**Approach B**
Identification of validation criteria for markers based on broadly used markers in the various fields of nutrition research

- Dietary Carbohydrates
- Nutrient Requirements
- Probiotics
- Functional Foods
- Nutrition and Mental Performance
- Eating behaviour and Energy Balance
- Nutrition and Immunity
- Metabolic Imprinting
- Addition of Nutrients to Food

Workshop 27-29 June 2012
Together, these projects move the field of Nutrition and Immunity toward:

More conscientious selection and rational interpretation of markers for nutrition intervention studies
1. In the generally healthy population
2. In inflammation-related disease conditions [this workshop!]
Objective:
To develop principles and guidance that could be universally applied to the discovery, development, use, and interpretation of current and new biomarkers.
**INSPIRE Goals:**
Review what is known about the interaction and impact of inflammation (from infection or other causes) on selection, use and interpretation of biomarkers specifically and nutrition more broadly.

**Discuss**
– Basic biology to explain mechanisms of nutrition/inflammation interactions
– Implications to our ability to utilize and interpret biomarkers of nutritional status
– Implication to biomarker development, monitoring and evaluation of interventions

**Define** a targeted research agenda that could include:
– Identification of biomarkers that reflect the full range of inflammatory conditions (infections, chronic illness, obesity etc.)
– Assessing what difference may exist in the impact of different inflammatory response on biomarkers of nutrition
Have a fruitful workshop!

Acknowledgement:
• Marie Latulippe
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