IUNS 21st ICN
International Congress of Nutrition
“From Sciences to Nutrition Security”

Buenos Aires, Argentina, 15-20 October 2017

Sheraton Buenos Aires Hotel & Convention Center
Conflict of Interest Disclosure

I have no conflict of interest to report in relation to this presentation.
The role of microbiota in nutrient metabolism and bioavailability

Dr. Fabrice Vaillant
Importance of microbiota

Proximal GI tract

Adsorption

Stomach

Duodenum

Jejunum

Colon

Distal GI tract

Gut microbiota

Lactobacillus

Veillonella

Helicobacter

Bacilli

Streptococcaceae

Actinobacteria

Actinomycinaeae

Corynebacteriaceae

Lachnospiraceae

Bacteroidetes
Definition of bioavailability in nutrition science

There are many different definitions of bioavailability in nutritional science, that differs from the accepted definition in pharmacology.

The concept of bioavailability incorporates: (i) availability for the absorption or “bioaccessibility”; (ii) absorption; metabolism (iii), tissue distribution (iv) bioactivity (v) and excretion (vi). Stahl et al., Molecular Aspects of Medicine, 2002, 23, 39

ADME concept: Absorption, distribution, metabolism, and excretion (ADME) patterns of the main plant food bioactives

Microbiota enhance bioavailability of some food nutrients

The contribution of gut microbiota to human nutrition, through the production of more bioavailable food compound is essential
Synthesis of short chain fatty acids (SCFAs) from dietary fibres

Are dietary fibbers bioavailable? At least partially

The importance of the conversion into SCFA depends on microbiota composition and as a consequence there is a high inter-individual variability.
In-vivo metabolism of Isoflavones

Daidzin (an isoflavone)

Conjugated metabolites

Liver Conjugation

Primary metabolites

Colonic bacteria

Secondary metabolites

Colonic bacteria

Daidzein

Equol

O-desmethyl-angolensin (O-DMA)
Equol and O-DMA metabotype

(Kenneth D. R. Setchell and Carlo Cleric; Equol: History, Chemistry, and Formation, *J Nutr*. 2010 Jul; 140(7))

O-desmethyl-angolensin (O-DMA)
Gut-microbial phenotypes from Daizin

Gut metabotypes with specific polyphenol metabolism patterns can be differentiated

Probably up to 4 metabotypes for Daizin metabolism

1-ODMA and Equol-producer
2-No-ODMA- producer and Equol Producer
3-ODMA producer and no-Equol Producer
4- No-ODMA and equol producer

The interindividual differences in metabolizing the isoflavone daidzein to equol or O-desmethyl-angolensin (ODMA) might explain the discrepancy of the soy/isoflavones effects on human health (cardiovascular, obesity, bone density, etc.).
In-vivo metabolism of ellagitannins
Urolithin excretion: High inter-individual variability

After one single shot of Andean blackberry juice

Large inter-individual variability, low intra-individual variability

Clustering according to urolithin metabotype explains the interindividual variability in the improvement of cardiovascular risk biomarkers in overweight-obese individuals consuming pomegranate: A randomized clinical trial.

González-Sanfeliú A1, García-Villalba B1, Ronco-Vaquero M1, Alcalayar C2, Crema A1, Zahilla P2, Tomás-Barberán FA1, Salma MV4, Espín JC1.

PUBLIC RELEASE: 27-APR-2017

Amazentis announces successful phase 1A/1B study results for urolithin A in healthy elderly subjects


Urolithin B, a newly identified regulator of skeletal muscle mass.

Rodríguez J1,2, Pierre N1, Naslain D1, Bon temps F3, Ferreira D4, Priem F2, Delicigue L1, Francaux M1.

Spain: Tomás- Barberán et al. 2014
Bioconversion of lignan by gut microbiota
List of some bioactive compounds known to be metabolized by gut microbiota

<table>
<thead>
<tr>
<th>Dietary compound</th>
<th>Main food source</th>
<th>Gut microbial metabolite</th>
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<tbody>
<tr>
<td>Dietary fibbers</td>
<td>Whole grains</td>
<td>Short Chain Fatty Acids (SCFA) (butyrate, propionate, etc…)</td>
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<tr>
<td>Isoflavone</td>
<td>Soybean</td>
<td>Equol, 0-DMA</td>
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<tr>
<td>Ellagitannins</td>
<td>Blackberry, walnuts, pomegranate</td>
<td>Urolithin A and B</td>
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<tr>
<td>Secoisolariciresinol</td>
<td>Flaxseed, sesame</td>
<td>Enterolactone, enterodiol</td>
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<tr>
<td>Linoleic acid</td>
<td>Vegetable oil</td>
<td>Conjugated linoleic acid (CLA)</td>
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<tr>
<td>Isoxanthohumol</td>
<td>Hop (beer)</td>
<td>8-prenylnaringenin</td>
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<tr>
<td>Resveratrol</td>
<td>Grape skin</td>
<td>dihydro-resveratrol</td>
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<tr>
<td>caffeoylisocitric acid</td>
<td>Amaranth</td>
<td>Hydroxyphenyl-propionic acid</td>
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<tr>
<td>Etc………</td>
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Characterization of gut microbiota

- From the taxonomic viewpoint (metagenomic)
- From the functional viewpoint (metabolomic)
How phenotyping and stratifying individuals according to gut-microbiota functionality

Designing challenging tests

At the University of Costa Rica, was developed a standardized food supplement that contains blackberries (Ellagitanins), Soy flour (isoflavones) and flaxseed (lignan).

Test: After ingestion of 100 ml of the standardized beverage during 3 days, urinary excretion of equol, urolithin, enterodiol and enterolactone is monitored on a fasting spot of urine on the 4th day. According to concentration (measured by UPLC-MS), individuals could be stratified according to each metabotypes.

Try to correlate health status with gut metabotype of world's longest-lived people in a blue zone, Nicoya, Costa Rica.
conclusion

- The stratification of volunteers according to their microbiota metabotype could reduce the large variability of “health biomarkers” often observed in clinical trials assessing functional food effects.

- Functional stratification in addition to phylogenetic stratification of gut-microbiota profile is required.

- Challenge test approach should allow stratifying individual according to microbiota metabotype.

Thank you