Deriving the goodness from superfoods - the role of gut microbial metabolism.

Kieran Tuohy
Fondazione Edmund Mach, San Michele all’Adige, Trento, Italy
In the beginning .......... there was man
More than the sum of our genes
Today......super-organism, man and his trillion microbes
Human diet shaped our closely co-evolved gut microbiota

**Human microbiome evolution**

- *A. ardipecerus* 4.5 - 3.8 mya
- *A. ramidus* 2.6 to 1.6 mya
- *A. anamensis* 3.9 to 3.0 mya
- *A. aethiopius* 2.6 to 1.6 mya
- *A. africanus* 2.6 to 1.6 mya
- *A. robustus* 2.3 to 1.0 mya

**Diet changes**

- **Neolithic times:** ~10,000 yrs BP (birth of agriculture)
- **Agricultural/Industrial revolutions:** Late 18th and early 19th century
- **Recent changes:** Over the last 50 yrs (Western-style diet)
## Estimated fiber daily intake in Palaeolithic/Traditional diets and Modern diet

Tuohy et al. (2009) *Current Pharmaceutical Design*

<table>
<thead>
<tr>
<th>Dietary pattern</th>
<th>Fiber content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palaeolithic diet first reported in 1985 (Eaton SB)</td>
<td>45.7g</td>
</tr>
<tr>
<td>Palaeolithic diet modified in 1990 (Eaton SB)</td>
<td>&gt;100g</td>
</tr>
<tr>
<td>Palaeolithic diet reported in 1996/1997 (Eaton SB)</td>
<td>104g</td>
</tr>
<tr>
<td>Rural Chinese diet</td>
<td>77g¹</td>
</tr>
<tr>
<td>Rural African diet</td>
<td>120g²</td>
</tr>
<tr>
<td>Current US diet</td>
<td>10-20g³</td>
</tr>
<tr>
<td>Recommended fiber content in US</td>
<td>25-38g⁴</td>
</tr>
<tr>
<td>Current UK diet</td>
<td>12g⁵</td>
</tr>
<tr>
<td>Recommended fiber content in UK</td>
<td>18g⁶</td>
</tr>
</tbody>
</table>

Total polyphenols (catechin equivalents, mg/100 g)

Gut microbiota differs between children on Western-style diet in Italy and children in rural Africa on traditional diet.

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo, Duccio Cavalieri, Monica Di Paola, Matteo Ramazzotti, Jean Baptiste Poullet, Sebastien Massart, Silvia Collini, Giuseppe Pieraccini, and Paolo Lionetti

De Filippo et al., PNAS (2010)
**Fig. 2.** 16S rRNA gene surveys reveal a clear separation of two children populations investigated. (A and B) Pie charts of median values of bacterial genera present in fecal samples of BF and EU children (>3%) found by RDP classifier v. 2.1. Rings represent corresponding phylum (Bacteroidetes in green and Firmicutes in red) for each of the most frequently represented genera. (C) Dendrogram obtained with complete linkage hierarchical clustering of the samples from BF and EU populations based on their genera. The subcluster located in the middle of the tree contains samples taken from the three youngest (1-2 y old) children of the BF group (16BF, 3BF, and 4BF) and two 1-y-old children of the EU group (2EU and 3EU). (D) Relative abundances (percentage of sequences) of the four most abundant bacterial phyla in each individual among the BF and EU children. Blue area in middle shows abundance of Actinobacteria, mainly represented by *Bifidobacterium* genus, in the five youngest EU and BF children. (E) Relative abundance (percentage of sequences) of Gram-negative and Gram-positive bacteria in each individual. Different distributions of Gram-negative and Gram-positive in the BF and EU populations reflect differences in the two most represented phyla, Bacteroidetes and Firmicutes.
Aberrant gut microbiota associated with Western-style diet

• SCFA about 3-4 fold higher in African children than Italian children
• Abundance of Enterobacteria commonly associated with gastrointestinal disease was higher in EU/Italian children

De Filippo et al., PNAS (2010)
Gut microbiota differs between children on Western-style diet in Italy and children in rural Africa on traditional diet.

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

Carlotta De Filippo\textsuperscript{a}, Duccio Cavalieri\textsuperscript{a}, Monica Di Paola\textsuperscript{b}, Matteo Ramazzotti\textsuperscript{c}, Jean Baptiste Poulet\textsuperscript{d}, Sebastien Massart\textsuperscript{d}, Silvia Collini\textsuperscript{b}, Giuliana Pieraccini\textsuperscript{e}, and Paolo Lionetti\textsuperscript{b,1}

\textsuperscript{a}Department of Preclinical and Clinical Pharmacology, University of Florence, 50139 Firenze, Italy; \textsuperscript{b}Department of Pediatrics, Meyer Children Hospital, University of Florence, 50139 Firenze, Italy; \textsuperscript{c}Department of Biochemical Sciences, University of Florence, 50134 Firenze, Italy; \textsuperscript{d}DNA Vision Agrifood S.A., B-4000 Liège, Belgium; and \textsuperscript{e}Department Interscito Pale di Spettrometria di Massa, University of Florence, 50139 Firenze, Italy

De Filippo et al., PNAS (2010)
The diet of
- **BF rural** children is low in fat and rich in fibers and plant-polysaccharides and predominantly vegetarian
- **BF urban** children maintain the consumption of cereals and legumes but introduces milk, meat, fish, egg and peanuts.
- **EU** is a a typical western diet high in animal protein, sugar, starch, and fat and **low in fiber**.

Nutritional composition of foods is available from [http://www.inran.it](http://www.inran.it) for EU and [http://www.fao.org](http://www.fao.org) for BF.

a) Millet; b) Millet flour; c-d) black-eyed peas, Niebè, e) *Parkia biglobosa* tree (Néré); f) Soumbalà, Nerè fruits fermented.
Quantification of SCFAs in fecal samples from BF and EU populations by SPME-GC-MS.
Gut microbiota….. but not as we know it!
Dietary patterns – Mediterranean diet

**INRAN, FAO** Double Pyramid

**Barilla Centre for Food Nutrition:** Double Pyramid: healthy food for people, sustainable food for the planet

Conclusions: Adherence to an MD pattern is associated with better HRQL. The association is stronger with mental health than with physical health. Dietary total antioxidant and fibre content independently explain this relationship.
Calorie restricted & traditional diets increase life-span and protect against age-associated disease

- Average life span: Okinawa, 83.8 years; Japan 82.3 years, US 78.9 years

- Traditional Japanese diet: high in vegetables, fruit, soy, fish, fibre

- Low calorie intake, negative energy balance at young age, little weight gain with age, lifelong low BMI, low risk of age associated diseases contribute to longevity in Okinawans

Wilcox et al., 2008 Ann NY Acad Sci
Gut microbiota and systemic health

Whole plant foods

- Immune function
- IBD
- Diarrhoea/IBS
- Laxation
- Cancer (CRC)
- Obesity
- Blood glucose
- Satiety
- Lipid metabolism
- Mineral absorption
Gut microbiota and systemic health

Polyphenols

- Cancer (CRC)
- Obesity
- Blood glucose
- Satiety
- Lipid metabolism
- Mineral absorption
- Laxation
- Diarrhoea/IBS
- IBD
- Immune function

Polyphenols affect various health aspects, including cancer (CRC), obesity, blood glucose, satiety, lipid metabolism, mineral absorption, diarrhea/IBS, IBD, and immune function.
Gut microbiota and systemic health

Prebiotics

- Cancer (CRC)
- Obesity
- Blood glucose
- Satiety
- Lipid metabolism
- Mineral absorption
- Laxation
- Diarrhoea/IBS
- IBD
- Immune function

Note: The diagram illustrates the potential impacts of prebiotics on various health conditions and functions.
Gut microbiota and systemic health

- Probiotics
  - Cancer (CRC)
  - Obesity
  - Blood glucose
  - Satiety
  - Lipid metabolism
  - Mineral absorption
  - IBD
  - Diarrhoea/IBS
  - Laxation
  - Immune function
Gut microbiota and systemic health

- Cancer (CRC)
- Obesity
- Blood glucose
- Satiety
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- Mineral absorption
Influence of red wine polyphenols and ethanol on the gut microbiota ecology and biochemical biomarkers

Mariá Isabel Queipo-Ortuño, María Boto-Ordóñez, Mora Murri, Juan Miguel Gomez-Zumaquero, Mercedes Clemente-Postigo, Ramon Estruch, Fernando Cardona Díaz, Cristina Andreís-Lacueva, and Francisco J Tinahones

Influence of red wine polyphenols and ethanol on the gut microbiota ecology and biochemical biomarkers\textsuperscript{1–4}

\textit{María Isabel Queipo-Ortuño, María Boto-Ordoñez, Mora Murri, Juan Miguel Gomez-Zumaquero, Mercedes Clemente-Postigo, Ramon Estruch, Fernando Cardona Díaz, Cristina Andrés-Lacueva, and Francisco J Tínahones}

\begin{table}[h]
\centering
\begin{tabular}{lccccc}
\hline
 & \textbf{Baseline} & \textbf{De-alcoholized red wine period} & \textbf{Red wine period} & \textbf{Gin period} & \textbf{\textit{P}} \textsuperscript{2} \\
 & \textit{(washout period)} & & & & \\
\hline
\textbf{Weight (kg)} & 97.8 ± 21.3 & 97.8 ± 19.4 & 96.4 ± 20.6 & 97.2 ± 19.6 & 0.306 \\
\textbf{Waist (cm)} & 106.7 ± 14.3 & 106.5 ± 14.4 & 105.1 ± 14.5 & 105.7 ± 13.5 & 0.392 \\
\textbf{Hip (cm)} & 111.0 ± 10.4 & 109.0 ± 12.8 & 110.2 ± 11.1 & 110.8 ± 10.3 & 0.908 \\
\textbf{DBP (mm Hg)} & 97.4 ± 15.2\textsuperscript{a} & 91.0 ± 12.9\textsuperscript{a} & 86.5 ± 11.6\textsuperscript{b} & 98.4 ± 14.3\textsuperscript{a} & 0.026 \\
\textbf{SBP (mm Hg)} & 145.4 ± 23.9\textsuperscript{a} & 135.1 ± 24.6\textsuperscript{b} & 129.5 ± 17.6\textsuperscript{b} & 142.7 ± 22.3\textsuperscript{a} & 0.026 \\
\textbf{BMI (kg/m\textsuperscript{2})} & 27.6 ± 3.2 & 27.6 ± 3.1 & 27.5 ± 2.9 & 27.6 ± 2.8 & 0.241 \\
\textbf{Glucose (mg/dL)} & 111.3 ± 23.1 & 104.5 ± 24.2 & 108.5 ± 16.4 & 108.8 ± 17.2 & 0.772 \\
\textbf{Uric acid (mg/dL)} & 5.7 ± 1.1\textsuperscript{a} & 5.3 ± 1.0\textsuperscript{a} & 5.0 ± 0.8\textsuperscript{b} & 5.4 ± 1.5\textsuperscript{a} & 0.018 \\
\textbf{GOT (mg/dL)} & 22.0 ± 7.3\textsuperscript{a} & 14.3 ± 4.0\textsuperscript{b} & 17.6 ± 13.4\textsuperscript{b} & 19.1 ± 8.0\textsuperscript{a} & 0.021 \\
\textbf{GPT (mg/dL)} & 46.4 ± 12.6 & 41.2 ± 7.7 & 42.0 ± 9.3 & 43.1 ± 6.9 & 0.888 \\
\textbf{GGT (mg/dL)} & 36.9 ± 25.6 & 30.1 ± 13.5\textsuperscript{b} & 36.1 ± 16.3 & 38.0 ± 27.7\textsuperscript{a} & 0.012 \\
\textbf{Triglycerides (mg/dL)} & 245.4 ± 231.7\textsuperscript{a} & 171.7 ± 206.7\textsuperscript{b} & 179.4 ± 177.1\textsuperscript{b} & 190.1 ± 222.5\textsuperscript{b} & 0.001 \\
\textbf{Cholesterol (mg/dL)} & 257.5 ± 88.6\textsuperscript{a} & 241.2 ± 94.9\textsuperscript{a} & 188.6 ± 61.6\textsuperscript{b} & 235.3 ± 91.4\textsuperscript{a} & 0.008 \\
\textbf{LDL cholesterol (mg/dL)} & 129.6 ± 41.9 & 123.5 ± 28.1 & 125.7 ± 30.3 & 130.6 ± 22.0 & 0.266 \\
\textbf{HDL cholesterol (mg/dL)} & 58.5 ± 16.7\textsuperscript{a} & 48.8 ± 17.1\textsuperscript{b} & 49.7 ± 14.3\textsuperscript{b} & 52.3 ± 16.5\textsuperscript{a} & 0.001 \\
\textbf{CRP (mg/L)} & 6.9 ± 2.6 & 4.3 ± 2.3\textsuperscript{b} & 4.6 ± 2.5\textsuperscript{b} & 6.8 ± 3.7\textsuperscript{a} & 0.001 \\
\hline
\end{tabular}
\caption{Anthropometric and biochemical variables during the study\textsuperscript{1}}
\end{table}

\textsuperscript{1} All values are means ± SDs; \textit{n} = 10 subjects. Means in a row with different superscript letters are significantly different, \textit{P} < 0.05 (Wilcoxon’s signed-rank test with post hoc Bonferroni test). CRP, C-reactive protein; DBP, diastolic blood pressure; GGT, \textit{γ}-glutamyl transferase; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; SBP, systolic blood pressure.

\textsuperscript{2} Derived by using the Friedman test.
Prebiotic evaluation of cocoa-derived flavanols in healthy humans by using a randomized, controlled, double-blind, crossover intervention study

Xenophon Tzounis, Ana Rodriguez-Mateos, Jelena Vulevic, Glenn R Gibson, Catherine Kwik-Uribe, and Jeremy PE Spencer

The American Journal of Clinical Nutrition

Prebiotic evaluation of cocoa-derived flavanols in healthy humans by using a randomized, controlled, double-blind, crossover intervention study\textsuperscript{1–3}

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**TABLE 3**
Anthropometric and biochemical variables before (Pre) and after (Post) the 4-wk intervention with either the low–cocoa flavanol or high–cocoa flavanol drink (n = 20)\textsuperscript{1}

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low-flavanol cocoa</th>
<th>High-flavanol cocoa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>BMI (kg/m\textsuperscript{2})</td>
<td>23.1 ± 2.02</td>
<td>23.2 ± 2.06</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>71.4 ± 12.95</td>
<td>72.0 ± 11.75</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>107.3 ± 7.81</td>
<td>105.8 ± 11.32</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.70 ± 0.19</td>
<td>4.31 ± 0.1\textsuperscript{2}</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.36 ± 0.08</td>
<td>1.29 ± 0.08</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.63 ± 0.16</td>
<td>2.50 ± 0.14</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.06 ± 0.08</td>
<td>1.05 ± 0.07</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.13 ± 0.10</td>
<td>5.08 ± 0.10</td>
</tr>
<tr>
<td>C-reactive protein (mg/mL)</td>
<td>0.26 ± 0.11</td>
<td>0.31 ± 0.14</td>
</tr>
<tr>
<td>Fecal water TAC (mmol/L Trolox\textsuperscript{4})</td>
<td>479.2 ± 48.3</td>
<td>459.7 ± 41.3</td>
</tr>
</tbody>
</table>

\textsuperscript{1} All values are means ± SDs. BP, blood pressure; TAC, total antioxidant capacity. Significance was calculated by the Tukey-Kramer test after 2-factor repeated-measures ANOVA with time and treatment as the 2 factors.

\textsuperscript{2} Significantly different from baseline, $P < 0.05$

\textsuperscript{3} Significantly different from low–cocoa flavanol interventions, $P < 0.01$.

\textsuperscript{4} Trolox (Sigma Chemical Co, Poole, United Kingdom).
Lb. reuteri selected for Bile Salt Hydrolase activity (2 capsules/day at 2 x 10^9 CFU/capsule) for 9 weeks

Randomized, double-blind, placebo-controlled, parallel-arm, multicenter study

N=127 hypercholesterolemic patients

Probiotic reduced plasma
- TC by 9.14%
- LDL-C by 11.64%
- LDL-C/HDL-C ratio by 13.39%
- Non-cholesterol plant sterols
- Increased circulating deconjugated bile acids

Proposed new cholesterol lowering activity of probiotics via modified absorption of lipids from the gut
Table 1. Cellular actions described for TGR5 in different cell types. *Macrophages include alveolar macrophages, Kupffer cells and THP-1 cells.

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Species</th>
<th>Cellular action</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophages*</td>
<td>Human / Rabbit / Rat</td>
<td>Inhibition of cytokine production</td>
<td>[62, 68]</td>
</tr>
<tr>
<td>Enteroendocrine cells</td>
<td>Human / Mouse</td>
<td>Secretion of GLP-1</td>
<td>[71, 79]</td>
</tr>
<tr>
<td>Brown adipocytes</td>
<td>Mouse</td>
<td>Increase in energy expenditure</td>
<td>[69]</td>
</tr>
<tr>
<td>Skeletal muscle cells</td>
<td>Human</td>
<td>Increase in energy expenditure</td>
<td>[69]</td>
</tr>
<tr>
<td>Sinusoidal endothelial cells</td>
<td>Rat</td>
<td>Regulation of endothelial NO synthase</td>
<td>[67]</td>
</tr>
<tr>
<td>Biliary epithelial cells</td>
<td>Mouse</td>
<td>Promotion of chloride secretion</td>
<td>[65]</td>
</tr>
<tr>
<td>Astrocytes</td>
<td>Rat</td>
<td>Generation of ROS</td>
<td>[101]</td>
</tr>
<tr>
<td>Enteric neurons</td>
<td>Mouse</td>
<td>Release of NO and suppression of intestinal motility</td>
<td>[70]</td>
</tr>
<tr>
<td>Gallbladder smooth muscle cells</td>
<td>Mouse</td>
<td>Decrease of gallbladder smooth muscle cell function</td>
<td>[73]</td>
</tr>
</tbody>
</table>
Increasing fruit and vegetable intake *in vivo* – FLAVURS project

**Flavonoid-rich F&V**

+2  |  +4  |  +6

**Flavonoid-poor F&V**

+2  |  +4  |  +6

**Habitual diet**

Wk 0  |  Wk 6  |  Wk 12  |  Wk 18
Visit 1  |  Visit 2  |  Visit 3  |  Visit 4
High Flavonoid group

Apple crumble
Dried cranberries/ blueberries

Fruit smoothies
(Strawberry and raspberry/ Blackberry and blueberry)

Fruit juices
(Blackcurrant /apple/cranberry /orange )

Roasted peppers
Pepperdew cherry peppers

All fruits and vegetables contain ≥ 15mg/100g of flavonoids
## Low Flavonoid group

<table>
<thead>
<tr>
<th>Item</th>
<th>Flavonoids (mg/100g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhubarb crumble</td>
<td>＜5</td>
</tr>
<tr>
<td>Dried fruits (raisins, currants, mango)</td>
<td>＜5</td>
</tr>
<tr>
<td>Fruit smoothies (tropical mix)</td>
<td>＜5</td>
</tr>
<tr>
<td>Fruit juices (mango/pineapple)</td>
<td>＜5</td>
</tr>
<tr>
<td>Guacamole</td>
<td>＜5</td>
</tr>
<tr>
<td>Houmous</td>
<td>＜5</td>
</tr>
<tr>
<td>Soups (Carrot &amp; coriander/broccoli &amp; stilton)</td>
<td>＜5</td>
</tr>
<tr>
<td>Canned chopped tomatoes</td>
<td>＜5</td>
</tr>
</tbody>
</table>

All fruits and vegetables contain ＜5mg/100g of flavonoids.
**Dietary intake:** HF dose dependent increase
HF higher vs LF & CT +2,+4,+6
Time x treatment (P=0.006)

**Biomarker:** 24h urinary flavonoid & metabolites
HF dose dependent increase
HF higher vs LF & CT +2, +4, +6
Time x treatment (P=0.0001)
**Dietary intake:** HF & LF dose increase
HF & LF vs CT higher +2, +4, +6
Time x treatment (P=0.0001)

**Biomarker:** Plasma vitamin C
HF & LF dose increase
HF & LF vs CT higher +2, +4, +6
Time x treatment (P=0.0001)
**Dietary intake**: LF dose dependent increase
HF & LF higher CT all points
Time x treatment (P=0.001)

**Biomarker**: Total plasma carotenoids
LF dose dependent increase
HF & LF higher CT all points
Time x treatment (P=0.0001)
Non-starch polysaccharide (NSP) changes

HF & LF higher than the CT all time points
LF dose dependent increase
Time x treatment interaction (P=0.0001).
F&V impact on arterial stiffness measured by PWA

HF and LF attenuated increase shown in CT group
Time x treatment P=0.009 when standardised for HR75 P=0.03
Other blood parameters

Total plasma nitrate/nitrite
HF higher than LF & CT +6
Time x treatment (p=0.03)

Plasma FRAP
HF dose dependent increase
LF higher +4 & +6 vs baseline
Time x treatment (P=0.009)
High fruit and veg diet appears to stimulate intestinal Actinobacteria

HF: high flavonoids group, n=19 ; LF: low flavonoids group, n=20 C: control group, n=20. Means ± s.e.m
Fruit and veg increase numbers of butyrate producing Firmicutes

Eubacterium rectale group (Erec482)

Faecalibacterium prausnitzii (Fpra655)

HF: high flavonoids group, n=19; LF: low flavonoids group, n=20; C: control group, n=20. Means ± s.e.m.
Fruit and veg increase numbers of butyrate producing Firmicutes

**Ruminococci**
(Rbro730/Rfla729)

**Lactobacilli/enterococci**
(Lab158)

HF: high flavonoids group, n=19; LF: low flavonoids group, n=20; C: control group, n=20. Means ± s.e.m
Untargeted urine metabolomics

- Urine dilution 1:5
- HPLC Analysis on RP column in positive and negative ionization mode
- XL Orbitrap in Full Scan MS and MS/MS within high resolution and mass accuracy
- Approaches
  - Substances considered as biomarkers when $p<0.005$ (t-test)
  - Annotation of metabolites:
    - Mass accuracy of precursor ion $[M+H]^+$ (< 3 ppm error)
    - Isotopic pattern distribution
- Databases used for annotation: In-house data base, Human Metabolome Database, Metlin, MAssBank, LipidMaps
Metabolomics workflow

Sample preparation: extraction of all analytes

Separation on LC column

Biomarker identification

Statistical analysis

Untargeted HR mass spectrometry

Samples: urine, plasma, fecal water
ALLIGNMENT OF CHROMATOGRAMS, BATCH CORRECTIONS, PEAK PICKING
UNIVARIATE ANALYSIS with XCMS

Data processing - XCMS using the “matchedFilter” peak picking method with Spectra Filter Window Mower function. For each mass feature two linear mixed models were fitted, diet-time interaction and time alone.

Both models were adjusted for baseline. p values for all features were corrected for multiple testing according to the two-stage Benjamini and Hochberg step-up false discovery rate (FDR).
<table>
<thead>
<tr>
<th>Rt</th>
<th>Annotation; Elemental Composition, MW, adjusted p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.10</td>
<td>ProlineBetaine; MMW: 143.0946, p 0.002 ↑Diet A;</td>
</tr>
<tr>
<td>2.20</td>
<td>N-acetyl-S-(2-hydroxypropyl) cysteine, MMW: C8H15NO4S; p</td>
</tr>
<tr>
<td>3.80</td>
<td>Hydroxy Hippuric Acid (isomer); MMW: 195.0531, p 0.02 ↑Diet A;</td>
</tr>
<tr>
<td>4.40</td>
<td>Hydroxy Hippuric Acid (isomer); MMW: 195.0531, p 0.002 ↑Diet A,</td>
</tr>
<tr>
<td>4.82</td>
<td>Vanilloylglycine, MMW: 225.0637; p 0.03 ↑ Diet A, B;</td>
</tr>
<tr>
<td>5.70</td>
<td>Hippuric Acid, MMW: 179.0582; p 0.002 ↑Diet A</td>
</tr>
<tr>
<td>5.89</td>
<td>Phenylacetylglutamine, MMW: 264.1110, p 0.04 ↑Diet A;</td>
</tr>
<tr>
<td>6.15</td>
<td>Ferulic Acid Sulfate , MMW: 274.0731, p 0.04; ↑Diet B</td>
</tr>
<tr>
<td>6.26</td>
<td>Dihydroxyphenyl-γ-valerolactone-O-sulphate MMW: 288.0306 p 0.0003 ↑Diet A;</td>
</tr>
<tr>
<td>6.56</td>
<td>Dihydroxyphenyl-γ-valerolactone-O-methyl-O-GLC, p 0.01 ↑ Diet A;</td>
</tr>
<tr>
<td>7.14</td>
<td>Cresol-Glucuronide, MMW: 284.0896; p 0.001 ↓Diet A;</td>
</tr>
<tr>
<td>7.35</td>
<td>Hydroxy Hippuric Acid (isomer), MMW: 195.0531, p 0.01 ↑ Diet A;</td>
</tr>
<tr>
<td>7.76</td>
<td>Hydroxy-tridecenoic acid GLC, MMW: 404.2046, p 0.001 ↑ Diet A;</td>
</tr>
<tr>
<td>12.38</td>
<td>Iberin N-acetyl-cysteine MMW: p 0.0001 ↑ Diet A &amp; p 0.001↑ Diet B</td>
</tr>
</tbody>
</table>
Health effects of apples

- Cancer (CRC)
- Obesity
- Blood glucose
- Satiety
- Lipid metabolism
- Immune function
- IBD
- Diarrhoea/IBS
- Laxation
- Mineral absorption
Microbiota modulation - *in vitro* faecal batch cultures

- 4 commercial apples
- Simulated gastric and small intestinal digestion
- Fermentation pH and temperature controlled anaerobic faecal batch cultures
- FISH microbial enumeration
- Profile of microbial polyphenol catabolites
In vitro bifidogenic effect of apples

Change in bifidobacteria over 24 h (FISH)

log10 bac/g sample

Blank
Positive Control
Neg Control
Gold Rush
Renetta
Golden Delicious
Pink Lady
Measuring the effect of apples (2 per day) on the gut microbiome and heart health.

...from Trentino with love!
Effect of apples consumption on lipid levels, gut health and vascular function in a group of 40 hypercholesterolemic subjects.

Biological samples
- Blood
- Urine
- Faecal sample

Measurements
- Anthropometrical
- % body fat composition,
- Blood pressure,
- Vascular stiffness (pulse wave analysis, PWA)
- And vascular reactivity (laser Doppler imaging, LDI).

Athanasios Koutsos, Joint PhD student
Dietary patterns – Mediterranean diet

INRAN, FAO Double Pyramid

Barilla Centre for Food Nutrition: Double Pyramid: healthy food for people, sustainable food for the planet

Adherence to Mediterranean diet (or other healthy eating patterns) reduces risk of chronic disease and increases healthy microbiota activities e.g., SCFA, polyphenol catabolites, BA deconjugation, immune homeostasis, gut barrier, nutrient absorption, K and B vitamins, lipid biohydrogenation.

GUT MICROBIOTA PYRAMID

Western diet or low adherence to Mediterranean diet increases risk of chronic human disease and is associated with aberrant microbiota profiles and harmful activities e.g., TMA, TMAO, leaky gut, inflammation, BCFA, 2° BA, genotoxins, carcinogens.

CHRONIC DISEASE PYRAMID
Thank you: FOOD MATTERS LIVE and Prof Anne-Marie Minihane

Fulvio Mattivi, Duccio Cavalieri and Roberto Viola, FEM-IASMA

NN Group: Lorenza Conterno, Francesca Fava, Elena Franciosi, Carlotta de Filippo, Athanasios Koutsos, Ilaria Carafa, Florencia Ceppa, Andrea Mancini

University of Reading, Glenn Gibson, Bob Rastall, Julie Lovegrove, Parveen Yaqoob, Christine Williams, Ian Rowland, Michael Connolly

Chris Gill, University of Ulster
When to drink red wine, the French paradox revisited?

Red wine prevents the postprandial increase in plasma cholesterol oxidation products: a pilot study

F. Natella\textsuperscript{1*}, A. Macone\textsuperscript{2}, A. Ramberti\textsuperscript{1}, M. Forte\textsuperscript{1}, F. Mattivi\textsuperscript{3}, R. M. Matarese\textsuperscript{2} and C. Scaccini\textsuperscript{1}

\textsuperscript{1}National Research Institute on Food and Nutrition, Via Ardeatina, 546, 00178 Rome, Italy
\textsuperscript{2}Department of Biochemical Sciences, University La Sapienza, Rome, Italy
\textsuperscript{3}Fondazione Edmund Mach, IASMA Research and Innovation Centre, Via E. Macb 1, 38010 San Michele all’Adige, Italy

(Received 24 June 2010 – Revised 23 November 2010 – Accepted 29 November 2010)

“the modality of drinking wine (during the meal) could represent a decisive factor”