Can ‘personalized nutrition’ be informed by population-based approaches?

Murielle Bochud, MD, PhD
Division of chronic diseases
Institute for Social and Preventive Medicine (IUMSP)

September 22, 2016
Choose the foods that are right for you!

Discover the right foods for you, by measuring your genetics, microbes, and personal glucose response to food.
Personalized nutrition: novel perspectives

- High interpersonal variability in post-meal glucose.
- Accurate prediction of glucose response using personal and microbiome features.
- Added value compared to current practice.
- Successful short-term personalized interventions.

Zeevi et al, Cell 2015; 163: 1079
TOBACCO vs MEAT WHAT’S THE RISK?

The EVIDENCE that processed meat causes cancer is as strong as the evidence for tobacco, but the RISK from tobacco is much higher...

CANCERS CAUSED BY TOBACCO

- 86% OF LUNG CANCERS
- 19% OF ALL CANCERS

CANCERS CAUSED BY PROCESSED AND RED MEAT

- 21% OF BOWEL CANCERS
- 3% OF ALL CANCERS

THE NUMBER OF CANCERS PER YEAR IN THE UK THAT COULD BE PREVENTED IF...

NO-ONE SMOKE

64,500 FEWER CASES

NO-ONE ATE ANY PROCESSED OR RED MEAT

8,800 FEWER CASES

Cancer Research UK

Source: cruk.org/cancersfacts
Mechanisms linking foods to colorectal cancer

Song, Gastroenterology 2015
Microbial metabolites from diet and the environment involved in initiation or progression of colorectal cancer

<table>
<thead>
<tr>
<th>Dietary and environmental compounds</th>
<th>Microbial products</th>
<th>Known effect on host</th>
</tr>
</thead>
</table>
| Non-digestible carbohydrates        | SCFAs             | • Microbiota modulation  
                                      • Cellular differentiation; apoptosis  
                                      • Inflammation |
| Phytochemicals                      | Phenolic acids; isothiocyanates | • Xenobiotic detoxification  
                                      • Microbiota modulation  
                                      • Cellular differentiation; apoptosis  
                                      • Inflammation |
| Protein                             | NOCs; ammonia      | • ROS production; genotoxicity |
|                                     | Polyamines         | • Inflammation  
                                      • ROS production; genotoxicity |
|                                     | Hydrogen sulphide  | • Inflammation  
                                      • ROS production; genotoxicity |
| Fat → Bile acids                    | Taurine            | • Microbiota modulation  
                                      • Cellular differentiation; apoptosis  
                                      • ROS production; genotoxicity |
|                                     | Secondary bile acids |                                      |
| Xenobiotics                         | Carcinogens        | • ROS production; genotoxicity |
| Ethanol                             | Acetaldehyde       | • ROS production; genotoxicity |

Louis, Nat Rev Microbiol 2014
Microbiome, diet and precision medicine

Zmora et al, Cell Host Micr 2016.
Classical methods to capture exposure to diet

<table>
<thead>
<tr>
<th>Category</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-report</td>
<td>24h recall</td>
</tr>
<tr>
<td></td>
<td>7-day food record</td>
</tr>
<tr>
<td></td>
<td>Food frequency questionnaire (FFQ)</td>
</tr>
<tr>
<td></td>
<td>Food propensity questionnaire (FFP)</td>
</tr>
<tr>
<td>Biomarker</td>
<td>Blood (serum, plasma, cells)</td>
</tr>
<tr>
<td></td>
<td>Urine (spot, 24-hour collection)</td>
</tr>
<tr>
<td></td>
<td>Hair, nails</td>
</tr>
<tr>
<td></td>
<td>Stool</td>
</tr>
<tr>
<td></td>
<td>Biopsy (tissue biomarker)</td>
</tr>
</tbody>
</table>
Urine metabololomics

- Intestinal microbiome
- Drug monitoring
- Neurodegenerative diseases
- Disease diagnostic
- CVD
- Metabolic state
- Toxic exposure
- Dietary exposure

Sample collection
Metabolite extraction
Metabolites analysis
Exposome concept

- Integrating all exposures over the life of an individual, including fetal stage and encompassing exposures to chemical, physical, or biological agents, diet, infection, but also psychological and socioeconomical stresses.

Life-course perspective for nutrition

- Conception
- Childhood
- Adolescence
- Adulthood
- Death

- Birth

- Breast feeding
- Learning of nutritional habits and taste
- Early metabolic changes

- Homeostasis

- Biomarkers of diseases

- Intrauterine exposure
- Maternal nutrition
Towards a personalized pyramide?

CYP1A2, CYP2E1, CYP2D6; CYP3A2 ALDH2

PPARγ; APOE; 5-LO

LCT; SLC2A9, VDR, CUB; CYPs, CASR

TAS2R38; GSTM1/GSTT1

CYP1A2, CYP2C9, ADORA2A, AHR

Idris Guessous
Selected GWAS results provide insight into nutrigenomics

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Loci (gene)</th>
<th>Dietary factor</th>
<th>Publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>CYP1A2/CYP1A2</td>
<td>Caffeine intake</td>
<td>Erhet, Nature 2011</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ehret, Nat Genet 2016</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Guessous, HMG 2012</td>
</tr>
<tr>
<td>Serum calcium</td>
<td>CASR, DGKD, GCKR, GATA3, CYP24A1</td>
<td>Calcium intake</td>
<td>O’Seaghdha, PLoS Genet 2013</td>
</tr>
</tbody>
</table>

Diet induces the expression of selected genes in different tissues
Age-related renal function decline in CoLaus

11.4% with rapid decline among participants without CKD at baseline


Geographical location of SKIPOGH participants

P. Vuistiner
Omic’s information in the population-based SKIPOGH cohort (N=1100)

Genomics: Illumina Omni2.5 chip, N=1100.

Epigenomics: N=750

Steroidomics: N=750

Blood & urine metallomics, N=1100

Urine metabolomics (ongoing)
Omic’s information in the population-based SKIPOGH cohort (N=1100)

Genomics: Illumina Omni2.5 chip, N=1100.

Epigenomics: N=750

Steroidomics: N=750

Urine metabolomics (ongoing)

+ smartphone-based longitudinal nutrition assessment

+ assessment of a large panel of objective nutrition biomarkers

Urine metalloomics, N=1100
Conclusions

• Diet represents a major complex modifiable protective factor for non-communicable diseases. No single approach is sufficient; interdisciplinarity is needed.
• We are not all equal in response to food intake (dietary choices and health consequences).
• Part of these differences are attributable to genetic factors, to the microbiome, with complex interactions between diet and other environmental exposures.
• Methodological developments and innovative study designs are needed to more adequately capture long-term exposure to diet.
• Non-targeted dietary recommendations remain a useful affordable public health tool to be complemented by targeted approaches.