Personalised nutrition and gut microbiome: opportunities and challenges

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Diet & Lifestyle changes through human evolution

- Over nutrition with foods high in fat, processed meat, sugars, salt and refined grains
- Low in fruit and vegetables
- Limited physical activity

Starting in the early 1980s, rapid increases in the prevalence of overweight and obesity began in high income countries.

- Global pandemic of obesity, type 2 diabetes, NAFLD
- 30,000 early deaths due to obesity; 6% of all deaths in the UK (National Obesity Forum 2018)

Hochberg et al. (2018) Trends in Endocrinology & Metabolism
Campaigns have successfully made people aware of healthy eating (reached 99% of mothers with children <10y)

But the message is generalised (eg healthy vs unhealthy foods)

Successful in educating, but does it translate to effect?
Is there a clear message for consumers?

Effect of Low-Fat vs Low-Carbohydrate Diet on 12-Month Weight Loss in Overweight Adults and the Association With Genotype Pattern or Insulin Secretion: The DIETFITS Randomized Clinical Trial.

A carbohydrate-reduced high-protein diet acutely decreases postprandial and diurnal glucose excursions in type 2 diabetes patients

No grains or legumes (low fibre)

Increased satiety in healthy (Bligh et al., 2015)/improved glucose tolerance in obese (Frassetto et al., 2009)

Does a clear message even exist?

N=307 obesity patients
• 2y later **no difference in weight loss**

...BUT
Baseline fasting plasma glucose and insulin were strong predictors of weight loss
• High FI: lost more on low-fat diet
• Low FI: lost more on low-carb

Hjorth et al. (2019) Int. J. Obesity. 2:e188102
A personalized approach... is it necessary?

**Inter-individual** variability in glycemic response to the same meal

**Inter- & intra-individual** variability in glycemic response to the same food

Mendes-Soares *et al.* (2019) JAMA Network Open. 2:e188102

Sources of variability

• GENETICS (SNPs, Mutations, CNVs)
  • EPIGENETICS
    • ENVIRONMENT & LIFESTYLE (Exercise, Sleep, Stress)
      • GUT MICROBIOTA
The human microbiota: we are home to highly diverse and dynamic microbial communities

- Are we more human or microbial?
  - Human cells \((3.0 \times 10^{13})\) vs. bacterial cells \((3.8 \times 10^{13})\)
    - estimate \(B/H = 1.3\)
    - BUT if counting only nucleated cells
      - ratio \(B/H = 10.1\)


- Microbiome contains **150X** more unique genes than human genome
The gut microbiota

- Mammalian intestine most densely colonised microbial habitat found in nature
- 1000+ bacterial species capable of colonising colon
- Broad range of physiological conditions
  - creates distinct niches for colonisation

Also Virome & Mycobiome!
Function of the gut microbiota – energy harvest

Nutrient metabolism

Fermentation of CHO and glycans such as resistant starch, inulin, lignin, pectin, cellulose and fructo-oligosaccharides

Butyrate
- main energy source for human colonocytes
- activates intestinal gluconeogenesis | beneficial effects on glucose and energy homeostasis
- prevents gut microbiota dysbiosis

Propionate
- regulates gluconeogenesis and satiety signalling through interaction with the gut fatty acid receptors

Acetate
- essential metabolite for the growth of other bacteria
- reaches peripheral tissues where it is used in cholesterol metabolism and lipogenesis,
- plays a role in central appetite regulation.
Function of the gut microbiota – other

**Nutrient metabolism**
- Protein metabolism (e.g., conversion of L-histidine to histamine)
- Synthesis of vitamin K and several components of vitamin B

**Non-nutrient metabolism**

*Polyphenols*

*Glucosinolates*


Cortes-Martin *et al.* (2018) Food & Function
Diet modifies gut microbiota

**Hadza** community of hunter-gatherers
- wild foods (meat, honey, baobab, berries and tubers)
- High fibre

- **Matses** | remote hunter-gatherer population from the Peruvian Amazon | tubers, plantain, fish, limited game
- **Tunapuco** | traditional agricultural community from the Andean highlands | stem tubers (potatoes, oka, mashua), fruit, meat
- **Norman, Oklahoma, US** | typical US urban-industrialized lifestyle | processed foods, bread and prepackaged meals

Matses and Tunapuco are enriched in genus *Treponema*, an efficient carbohydrate metaboliser

*Obregon-Tito et al.* (2015). Nat Communications, 6:6505

*Schnorr et al.* (2014). Nat Communications, 5:3654
Can the gut microbiome modulate response to diet?

Indirect evidence

• Obese individuals show decreased bacterial diversity and gene richness

• Composition of the gut microbiota has the potential to affect energy harvest (capacity for fibre-utilization)

• Secretion of hormones affecting appetite (gut-brain axis)

How can we use information on gut microbiota to understand WHICH foods are doing WHAT to WHOM?

New sequencing technologies allow TAXONOMIC and METAGENOMIC analysis
Evidence from human studies (RCTs) – Taxonomic information

Obese individuals stratified by **Prevotella**–to–**Bacteroides** (**P/B**) ratio (n=52) on low calorie diets (500 kcal/d) for 24w

- **Prevotella** | high CHO and fibre diets
- **Bacteroides** | high protein and animal fat

Hjorth et al. (2019). Int. J. Obesity, 43:149-157
Using taxonomic AND functional information
Not just what is present but what they are doing

In healthy (n=20) **no difference** in metabolic or clinical parameters

When only gut microbiota were used in a classification algorithm they could predict the bread that induced lower glycemic response

Challenges for integrating gut microbiome in PN solutions

- Requires individuals to be engaged
- Multiple sample collection and analyses is costly
- RCTs are necessary to show efficacy above and beyond existing personalised interventions (e.g., with a professional)
- Healthy vs diseased
- Requires multidisciplinary approaches
- Evidence for sustained effect is yet to be demonstrated

...just because we can measure all doesn’t mean we should...
Clinical nutrition, big data and Digital Health for PN

Opportunities for academia – industry collaborations

Mendes-Soares et al. (2019) JAMA Netw. Open 2:e188102
Quality Information Services and Dietary Advice for Personalized Nutrition in Europe (Quisper)

**Aim**: design a platform to support companies/health professionals in Europe in creating evidence-based and effective personalised nutrition services for their clients/consumers.
Partners with

Quadram Institute (UK) – Project Leader
Technical University Munich (DE)
University of Reading (UK)
PepsiCo (UK)
ShiftN (BE)
The Hyve (NL)
EuroFIR AISBL (BE)
The platform principle

Food, nutrition and health resources

Data Providers

Data Users

feedback from users to enhance products

translation of research into practice

translational research

feedback from users to enhance products

operational costs
Thank you for listening....

Paul Finglas
Jenny Plumb
Hannah Pinchen
Daniela Segovia Lizano
Lindsay Hall