Nutrigenomics and the Future of Nutrition: Personalized Nutrition in the real world-where do we stand?

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Nutrigenomics for the practicing physician

- Nutrigenomics was proposed on the evaluation of genetic and epigenetic alterations in response to specific dietary components, perhaps leading to changes in disease status (Sales, Pelegrini, & Goersch, J Nutr Metab 2014)
- Studies suggest that communicating genetic risk makes patients more ready to accept changes in behavior (Meisel SF et al, Obesity 2015;23:305).
- 2,500 or more genetic tests available, but few studies are informative about influencing clinical behavior in nutrition, e.g. in obesity management (Bray MS et al, Obesity 2016;24:14).
- Studies will be difficult, requiring isolation of individual gene/food effects, and including adequate control arms.
- Studies will also be difficult because proving causation from associations (e.g. using Hill criteria) is especially difficult in the field of nutrition.

Hill criteria for causal association are difficult to achieve in nutrition-related disorders

Criterion	Nutritional data
• Strong association	often not present
• Association constant	often one or a few studies
• 1 cause - 1 effect	dietary as well as metabolic complexity
• dose-response relationship	difficult for SNPs
• Scientific justification	present, but often based on in vitro and animal data
• Coherence with other data	other data often relatively limited
• RCTs	difficult to perform; not many done with interventions

Adapted from Bruemmer B et al, J Am Diet Assoc 2009;109:1728

The cause(s) of the phenotype of adult malnutrition is often uncertain

- Consensus criteria, ASPEN, Acad Nutr Dietetics (White JV et al, JPEN 2012;36:275):
  - Insufficient energy intake, weight loss, loss of muscle mass/subcut fat, decreased function (hand grip)
- In clinical practice, overlap of causes can occur (Jensen GL et al, JPEN 2010;34:156):
  - Pure chronic starvation without inflammation (e.g. anorexia nervosa)
  - Chronic diseases with sustained superimposed mild/moderate inflammation (e.g. obesity, rheumatoid arthritis, cancer, COPD, IBD
  - Acute disease or injury with marked inflammation (e.g. trauma, major infection, burns)
- Disorders in which genomic links have been sought:
  - Obesity, cancer, diabetes type 2, pregnancy, aging
  - Most of these conditions have a component of inflammation
  - Only conditions without inflammation respond in a clear manner to nutrient supplementation
- Therefore, studies linking genomics (single gene/single nucleotide polymorphism) to malnutrition (or altered nutrition) may be difficult, as a change in clinical phenotype may be due to nutrients only in part.

Scientific approaches linking genomics to nutrition have identified changes in cells or in metabolic tests, but not clinical outcomes

- In vitro and in vivo animal studies support the rationale
  - Cancer prevention targets
- Human data, when present, are often less suggestive
  - Caffeine metabolism, omega-3 FA
  - Anti-oxidant pathways and theory of pathogenesis of human disease
- Some genetic factors are not sensitive enough
  - HLA subtypes for celiac disease
- Other genetic factors are not yet additive to clinical information
  - Lactose intolerance
- Many chronic diseases are related to the phenotype of malnutrition or altered nutrition (e.g. obesity)
  - Management with SoC nutritional advice is difficult by itself and often not implemented
- Are we ready for nutrigenomics in 2017?
  - We can expect a long lag before strong data are available
  - Will probably happen one disease or disease component at a time, as data become available
- Need for definite clinical effects before implementing commercially

Current and future directions of personalized nutrition

- Use of personalized internet services (Gibney MJ, Walsh MC, Proc Nutr Soc 2013;72:219)
  - Based on analysis of a person's dietary pattern, often biased
  - Meal-based vs food component-based information
  - Mobile-phone technology, adolescent>>adult
- Personalized nutrition based on phenotypic data: examples
  - Monitoring urine Na, decrease Na-containing foods and BP (Yamasue K et al, J Hum Hypertens 2006;20:596)
  - Monitoring wrist-watch accelerometer to deliver physical activity (Horling R et al, J Internal Med Res 2007;9:e7)
  - Blood spot analysis for metabolites, development of metabolic profile, vit D supplementation without effect (O'Sullivan A et al, Mol Nutr Food Res 2011;5:1018).
- Personalized nutrition based on genomic data
  - Observational studies link dietary patterns with SNP pattern of a given gene: not enough by itself
  - MTHFR SNPs and homocysteine levels showed role of riboflavin in TT variants only (McNulty H et al, Circulation 2006:113:74)
- Difficult to predict extent to which potential users will want a one-off result or will maintain a service long term
- Food4Me studies are developing data on consumer responses
  - Knowledge of FTO gene risk carrier for obesity led to more weight loss in 6 months, but mean differences were <0.3 kg, and there was no non-genomic motivation for the control group (Celis-Morales C et al, AJCN 2017;105:1204)