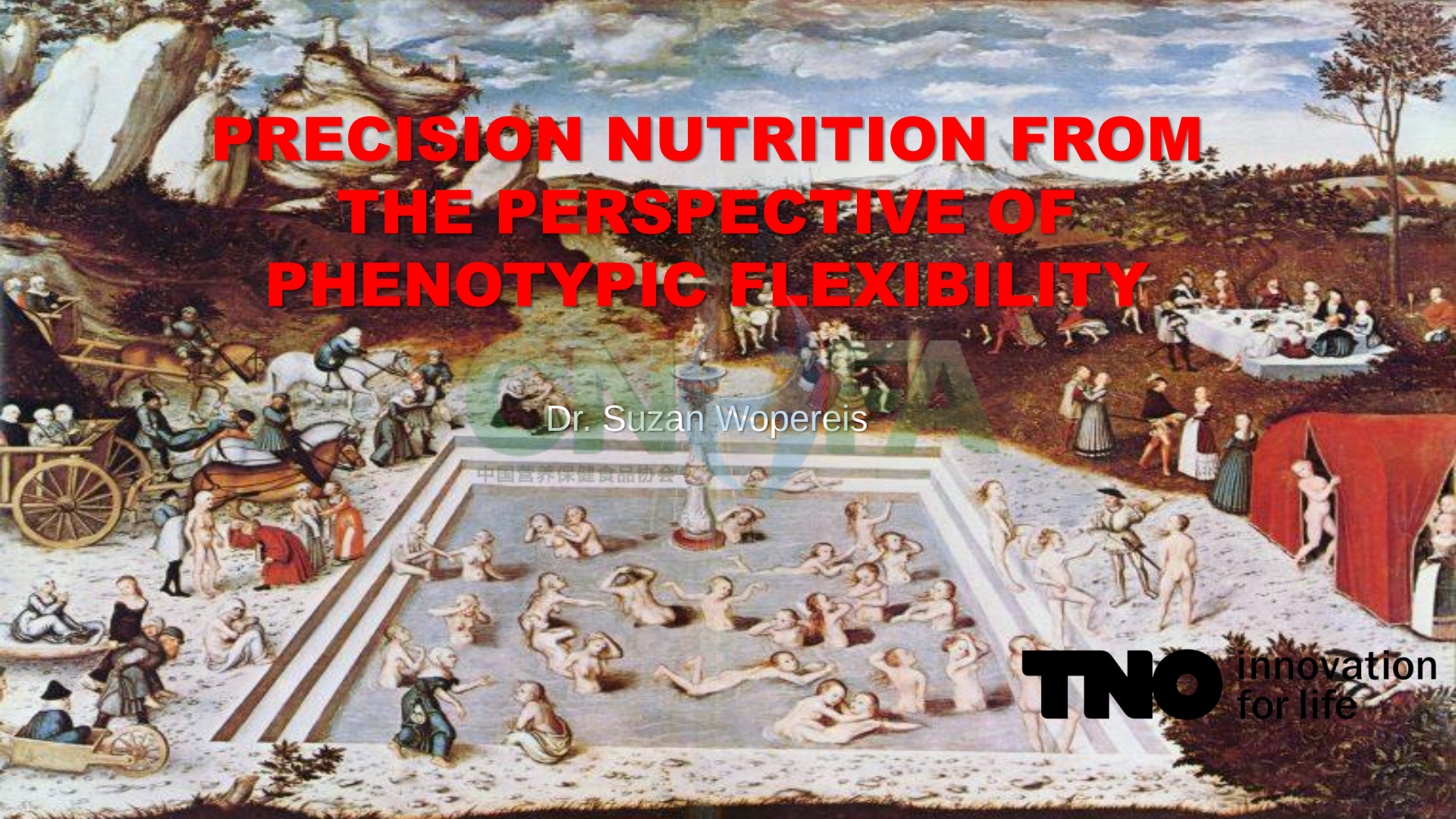


PRECISION NUTRITION FROM THE PERSPECTIVE OF PHENOTYPIC FLEXIBILITY

Dr. Suzan Wopereis

中国营养保健食品协会

TNO innovation for life

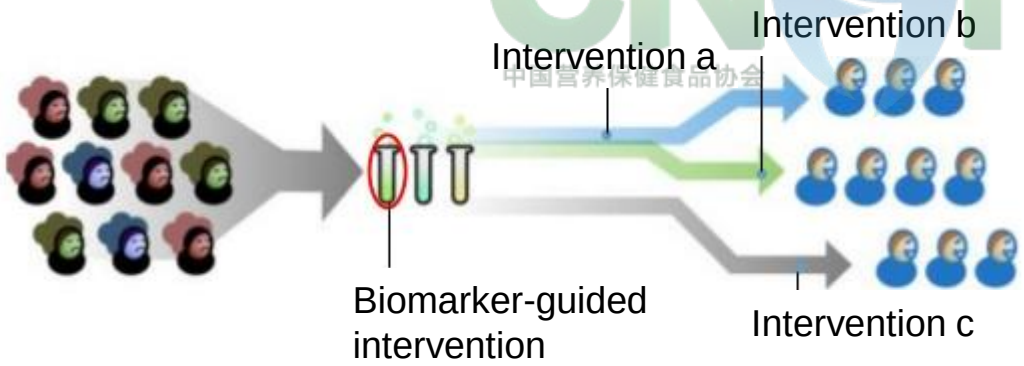
TNO - Better world through applied research

- Research and Technology Organisation
- Independent, not for profit
- Founded by law (1932)
- > 3000 employees

TNO connects people and knowledge to create innovations that boost the sustainable competitive strength of industry and well-being of society

Outline of presentation

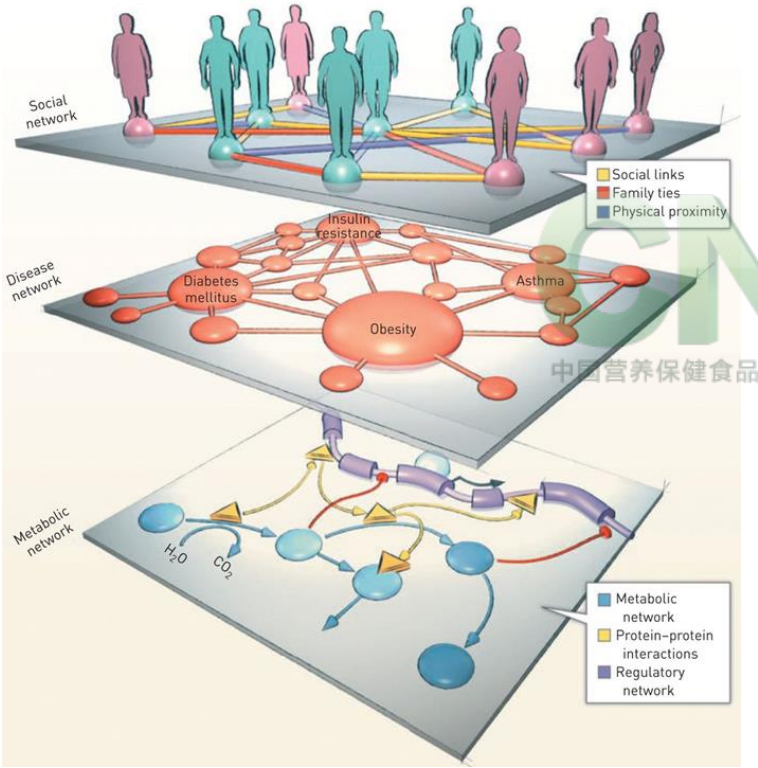
- Introduction to Phenotypic flexibility
- One size fits all: added value of Phenotypic Flexibility
- Responders vs Non-responders: the example from Nutritech
- Towards Precision Nutrition: the example from Cordioprev



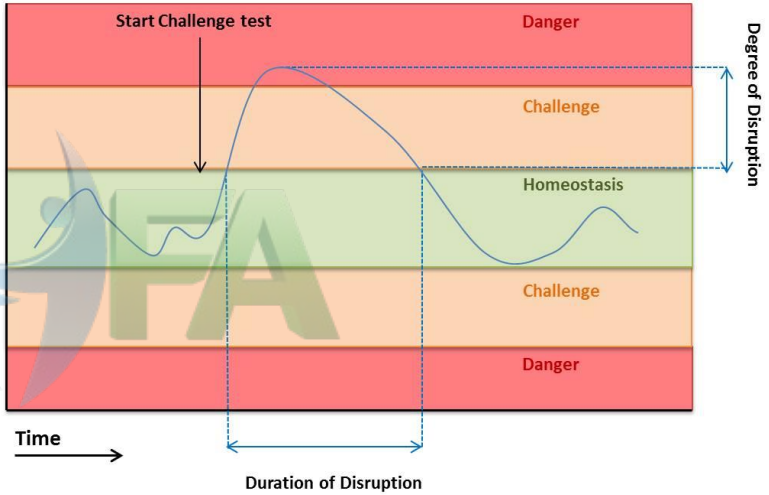
- Two Precision Nutrition Initiatives: Habit and PhenFlex-2

The two TNO pillars: systems & flexibility

1 – HEALTH IS A SYSTEM

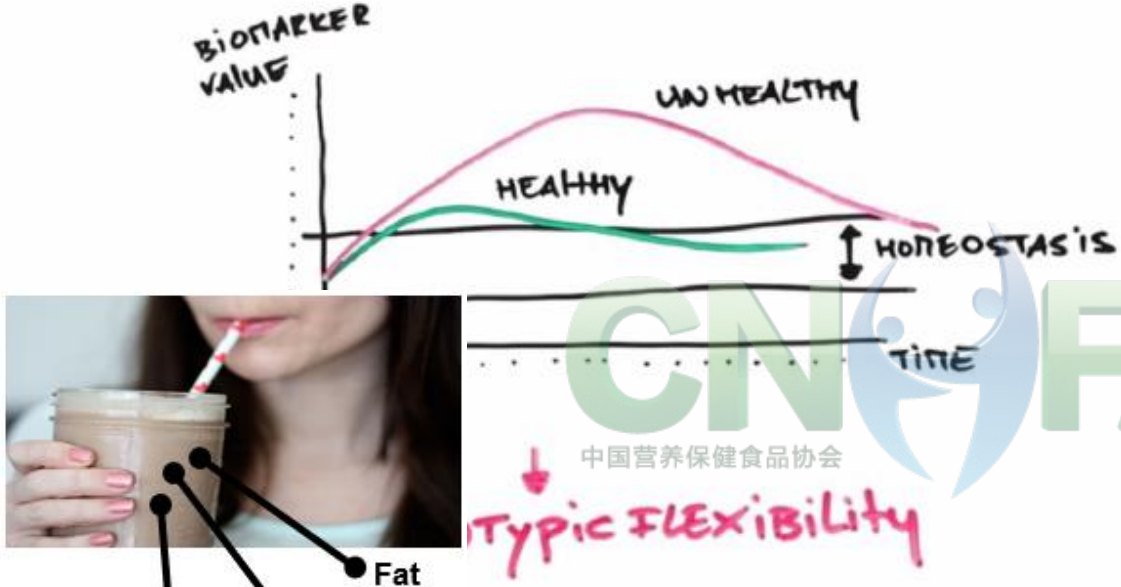


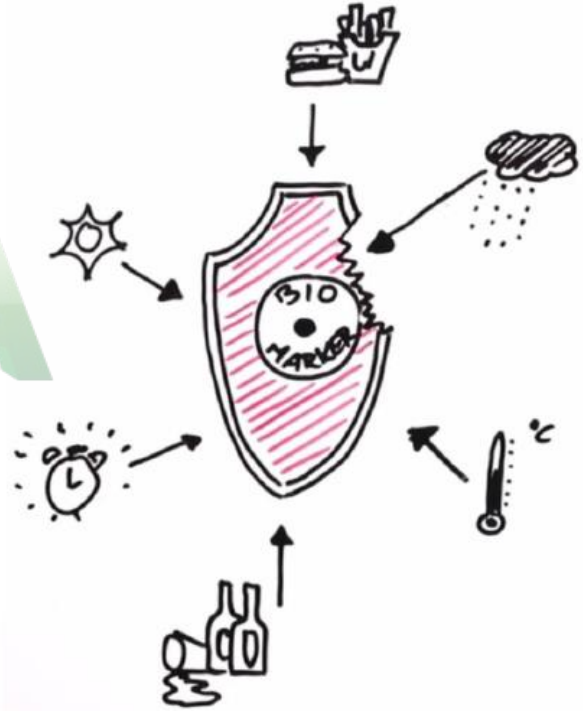
2 – HEALTH IS RESILIENCE

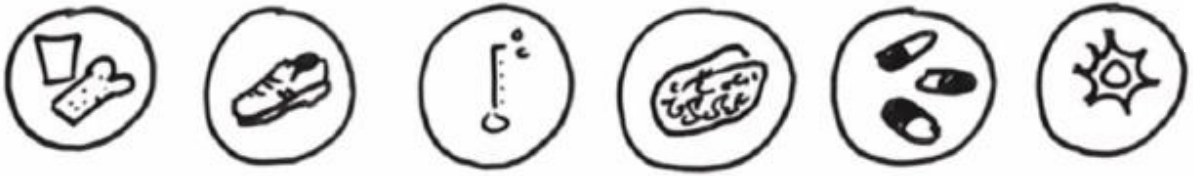


- From care to cure: reversible diseases
- Prevention & wellbeing: precision nutrition

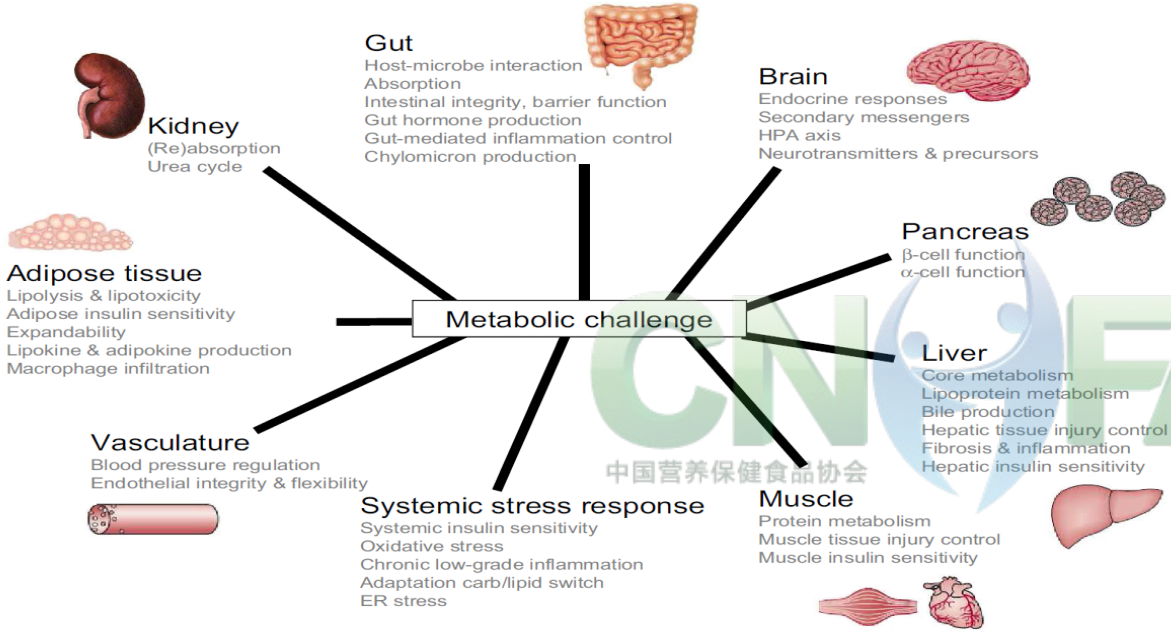
Phenotypic flexibility: next generation biomarker for health!







Phenflex challenge test:



Fat

Sugar

Protein

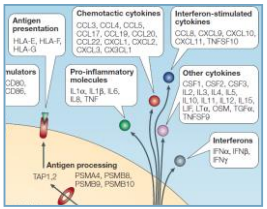
- 320 ml tapwater
- 60 grams palm olein
- 75 grams of glucose
- 20 grams of Protifar
- 0,5 gram / 20 droplets of artificial aroma

Genes Nutr (2015), 10:13

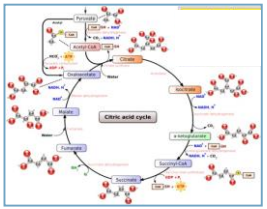
Time course studies to monitor challenge test response

Blood sampling at multiple time points after challenge, up to 10 hours

clinical chemistry



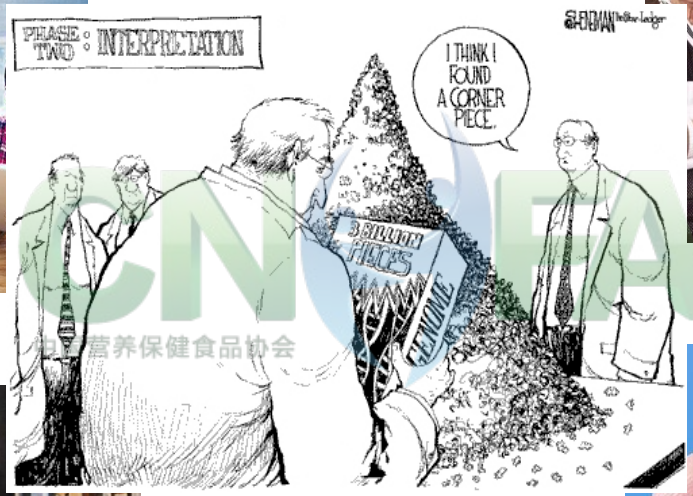
proteome



metabolome

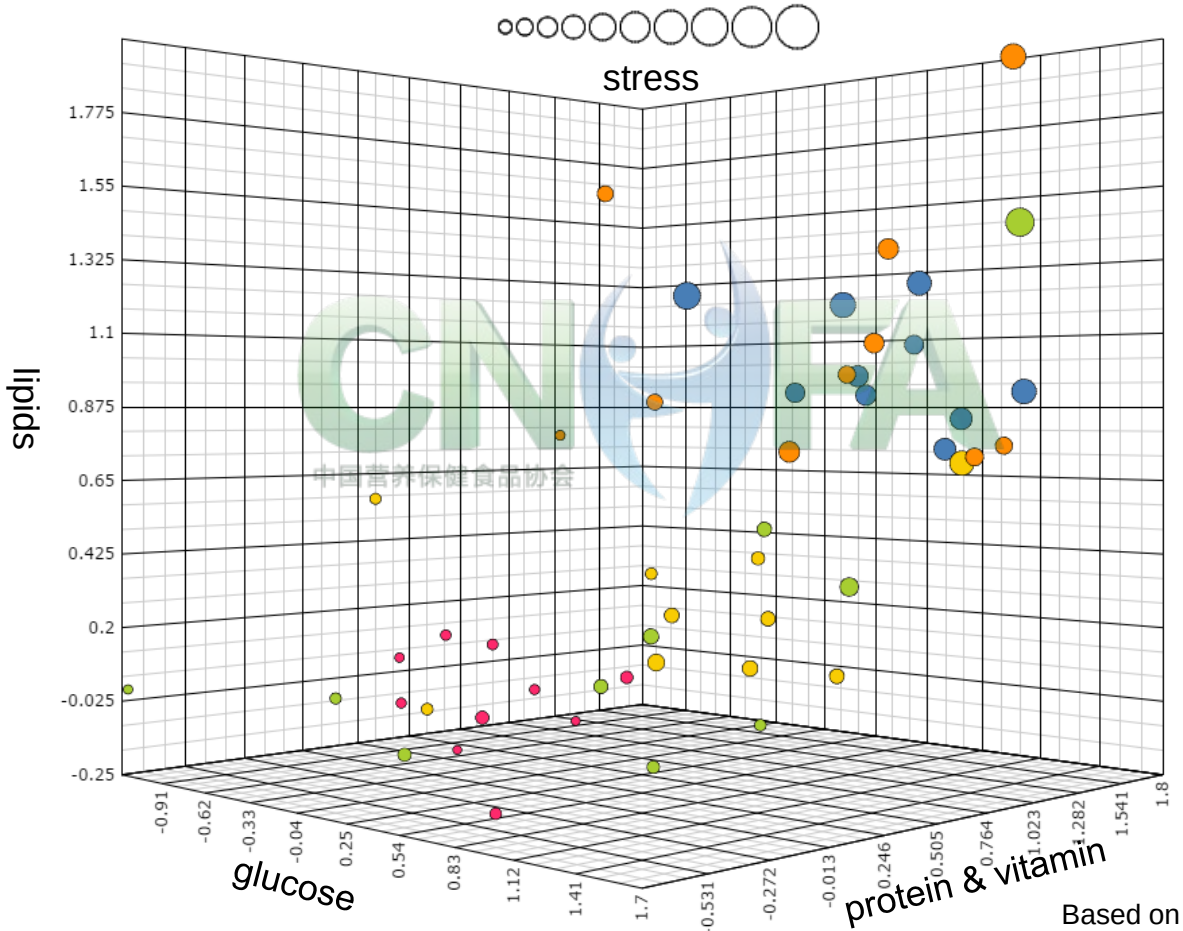
transcriptome

Measuring a total of ~150 different markers representing ~25 health related processes



Genes Nutr. 2017;12:21
Genes Nutr. 2017;12:32

Variation in phenotypic flexibility in healthy subjects



Age 20-29, L-N
Age 60-69, N-H

Age 30-59
LOW FAT%
NORMAL FAT%
HIGH FAT%

Based on ~160 markers

First publications that showed health effect of nutritional intervention by using a challenge test

- 36 overweight male elevated CRP
  5 weeks supplement mix
  cross-over design

Bakker et al. Am J Clin Nutr. 2010; 91:1044-59.
Pellis et al. Metabolomics. 2012; 8(2):347-359.
Bouwman et al. BMC Med Gen. 2012; 6;5:1.

- 10 healthy male
  before and after 4 weeks overfeeding
  (1300 kcal/day extra)

Kardinaal et al. FASEB J. 2015;29(11):4600-13.

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- 18 MetS (male & female)
  12 weeks HMUFA diet before and after

Cruz-Teno et al. Mol. Nutr. Food Res. 2012;56:854–865

- 29 healthy overweight middle-aged men
  double-blind crossover study
  effects of 4 wk high flavonol chocolate (HFC) vs normal dark chocolate (NFC)

Esser et al. FASEB J. 2014;28(3):1464-73

Plasma metabolome analysis identifies distinct human metabotypes in the postprandial state with different susceptibility to weight loss–mediated metabolic improvements

Jarlei Fiamoncini,*,[1] Milena Rundle,[†] Helena Gibbons,[‡] Louise Thomas,[§] Kerstin Geillinger-Kästle,* Diana Bunzel,[¶] Jean-Pierre Trezzi,[‖,#] Yoana Kiselova-Kaneva,** Suzan Wopereis,[††] Judith Wahrheit,[‡‡] Sabine E. Kulling,[¶] Karsten Hiller,[§§,¶¶] Denise Sonntag,[††] Diana Ivanova,** Ben van Ommen,[††] Gary Frost,[†] Lorraine Brennan,[‡] Jimmy Bell,[§] and Hannelore Daniel*

*Department Food and Nutrition, Technische Universität München, Freising-Weihenstephan, Germany; [†]Division of Diabetes, Endocrinology and Metabolism, Department of Medicine, Imperial College London, London, United Kingdom; [‡]University College Dublin (UCD) School of Agriculture and Food Science, Institute of Food and Health, Dublin, Ireland; [§]Research Centre for Optimal Health, Department of Life Sciences, University of Westminster, London, United Kingdom; [¶]Department of Safety and Quality of Fruit and Vegetables, Max Rubner Institut, Karlsruhe, Germany; [‖]Integrated Biobank of Luxembourg, Dudelange, Luxembourg; [#]Centre for Systems Biomedicine, Esch-sur-Alzette, Luxembourg; **Department of Biochemistry, Molecular Medicine and Nutrigenomics, Medical University Varna, Varna, Bulgaria; [††]Department of Microbiology and Systems Biology, Netherlands Institute for Applied Scientific Research (TNO), Zeist, The Netherlands; [‡‡]Biocrates Life Sciences, Innsbruck, Austria; and [§§]Braunschweig Integrated Centre of Systems Biology, University of Braunschweig, Braunschweig, Germany; and [¶¶]Department of Computational Biology of Infection Research, Helmholtz Centre for Infection Research, Braunschweig, Germany

ABSTRACT: Health has been defined as the capability of the organism to adapt to challenges. In this study, we tested to what extent comprehensively phenotyped individuals reveal differences in metabolic responses to a standardized mixed meal tolerance test (MMTT) and how these responses change when individuals experience moderate weight loss. Metabolome analysis was used in 70 healthy individuals. with profiling of ~300 plasma metabolites during an MMTT over 8 h. Multivariate analysis of plasma markers of fatty acid catabolism identified 2 distinct metabotype clusters (A and B). Individuals from metabotype B showed slower glucose clearance, had increased intra-abdominal adipose tissue mass and higher hepatic lipid levels when compared with individuals from metabotype A. An NMR-based urine analysis revealed that these individuals also to have a less healthy dietary pattern. After a weight loss of ~5.6 kg over 12 wk, only the subjects from metabotype B showed positive changes in the glycemic response during the MMTT and in markers of metabolic diseases. Our study in healthy individuals demonstrates that more comprehensive phenotyping can reveal discrete metabotypes with different outcomes in a dietary intervention and that markers of lipid catabolism in plasma could allow early detection of the metabolic syndrome.—Fiamoncini, J., Rundle, M., Gibbons, H., Thomas, L., Geillinger-Kästle, K., Bunzel, D., Trezzi, J-P., Kiselova-Kaneva, Y., Wopereis, S., Wahrheit, J., Kulling, S. E., Hiller, K., Sonntag, D., Ivanova, D., van Ommen, B., Frost, G., Brennan, L., Bell, J. Daniel, H. Plasma metabolome analysis identifies distinct human metabotypes in the postprandial state with different susceptibility to weight loss–mediated metabolic improvements. FASEB J. 32, 000–000 (2018). www.fasebj.org

FASEB J (2018) fj201800330R

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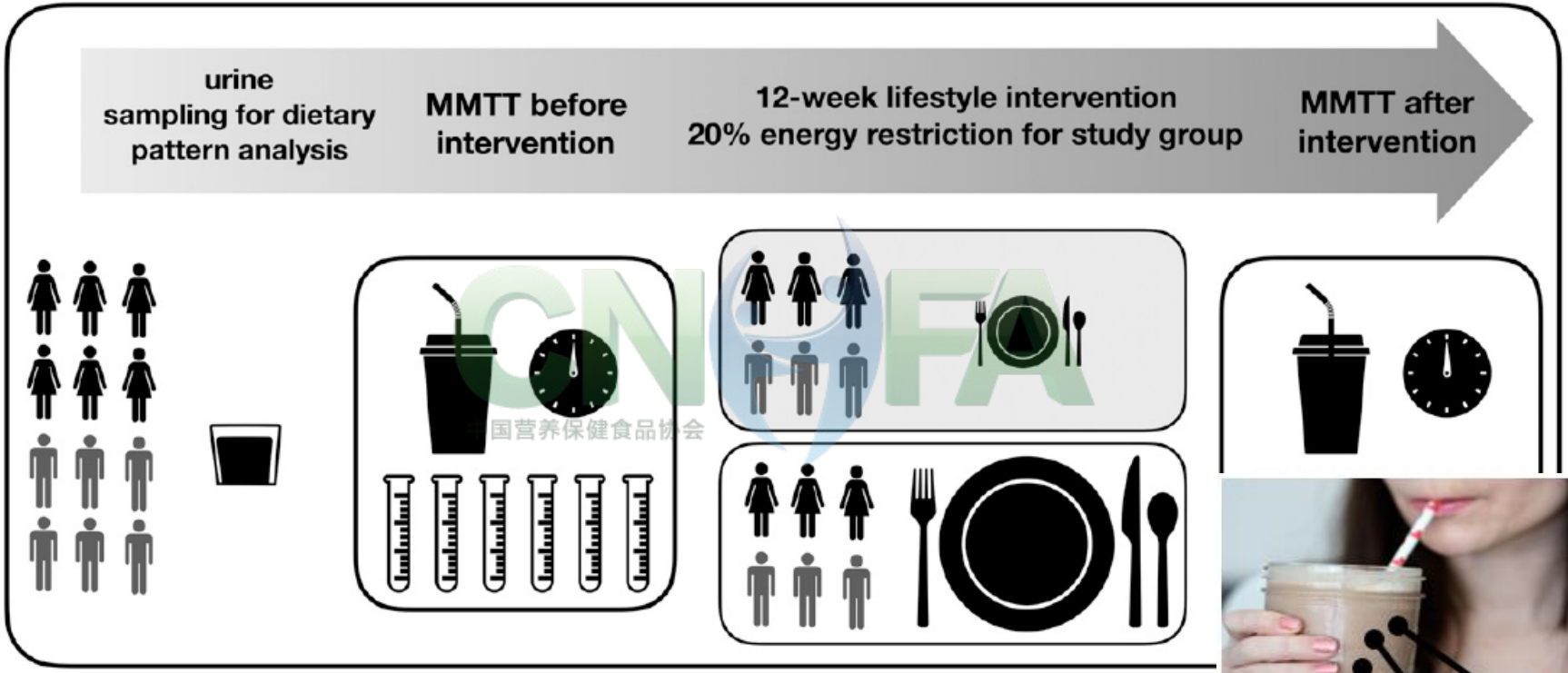
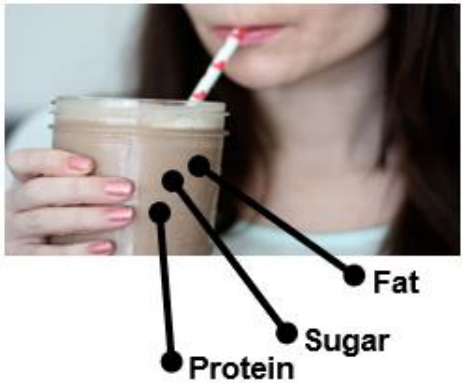
NuTriTech

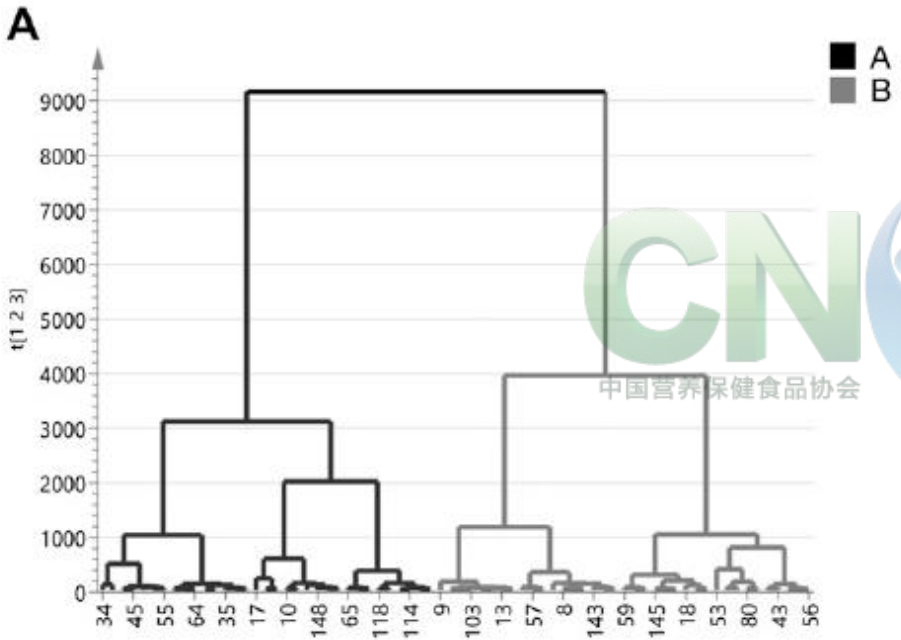
Study design

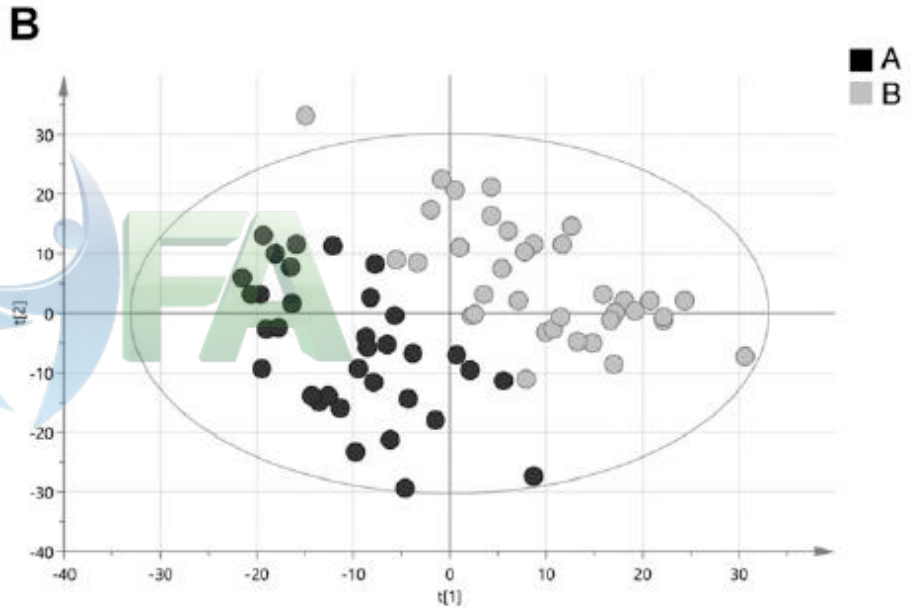


n= 72 male and female



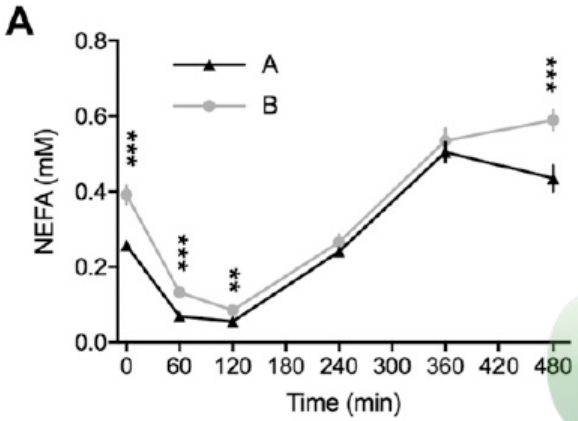
Two distinct ‘metabotypes’ were identified

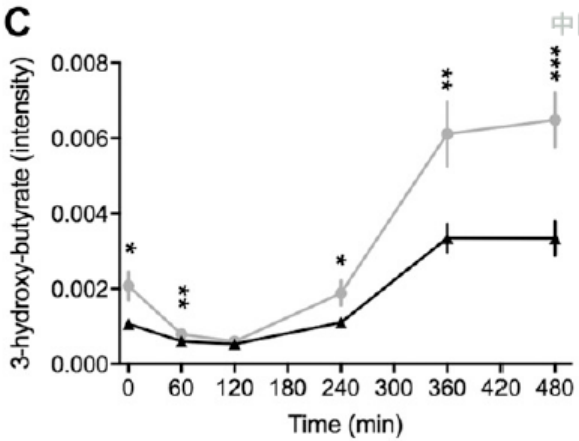




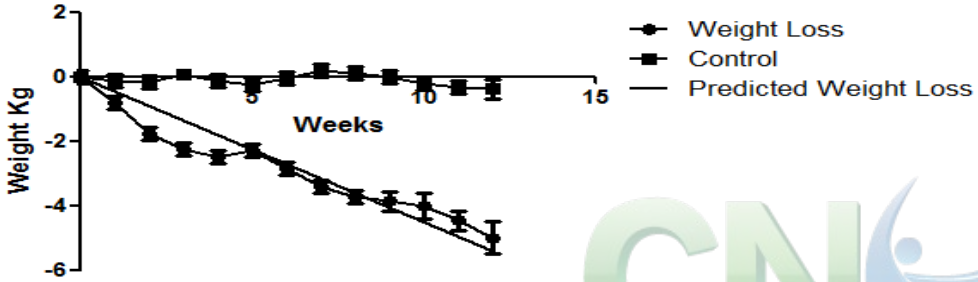
n=34 in group A; n=36 in group B

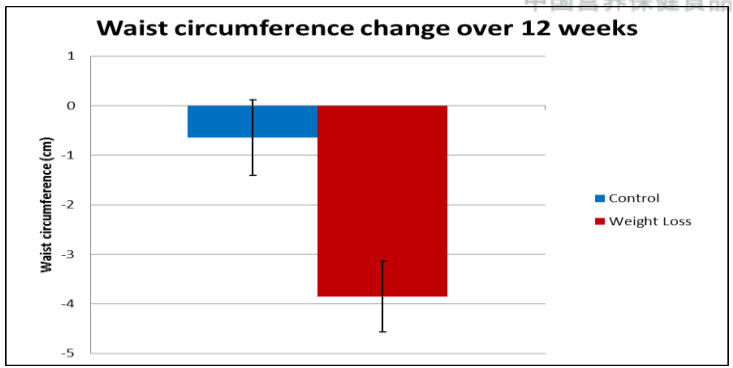
Metabotype A is more flexible as compared to Metabotype B

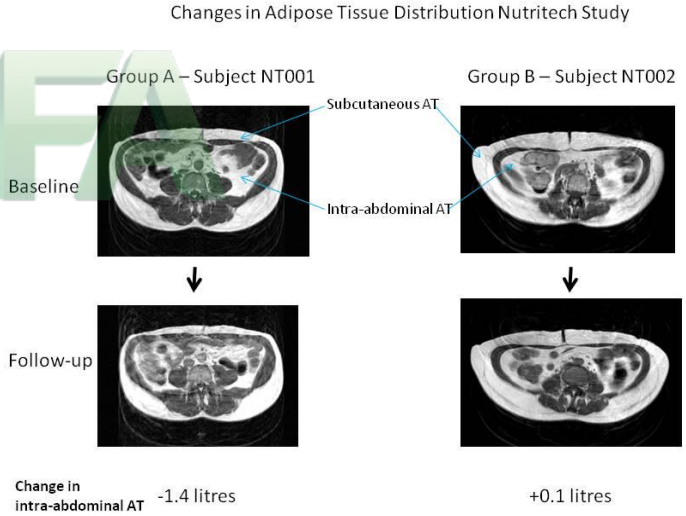




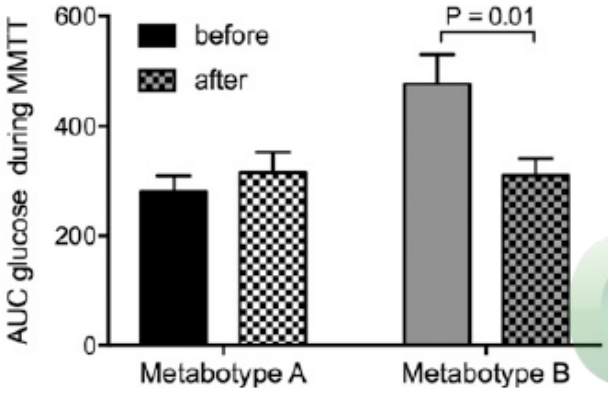
The intervention was successful in terms of weight loss

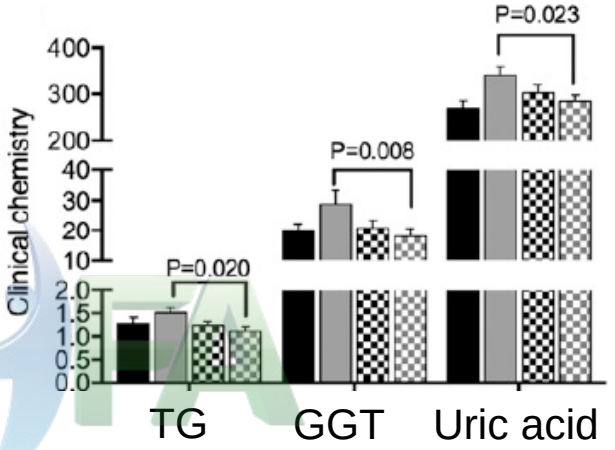


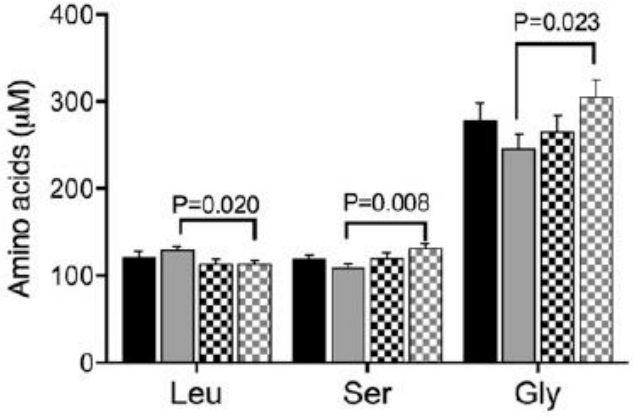


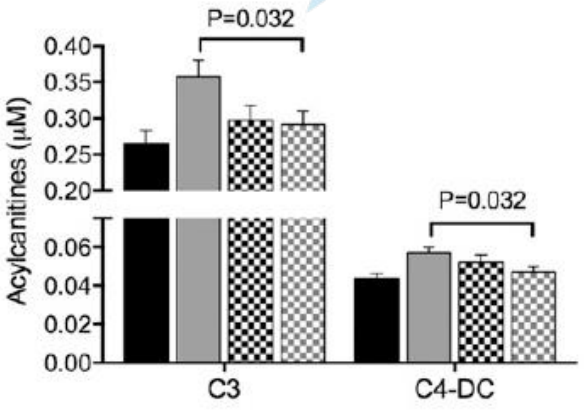


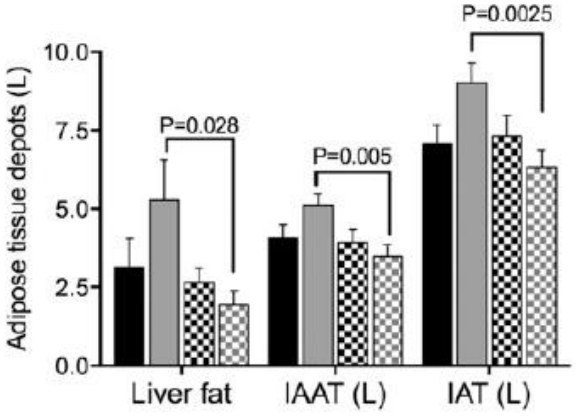
Only inflexible subjects (group B) improved metabolic health!











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Towards Precision Nutrition….

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Type 2 (pre)diabetes subgroups react differently on different diets

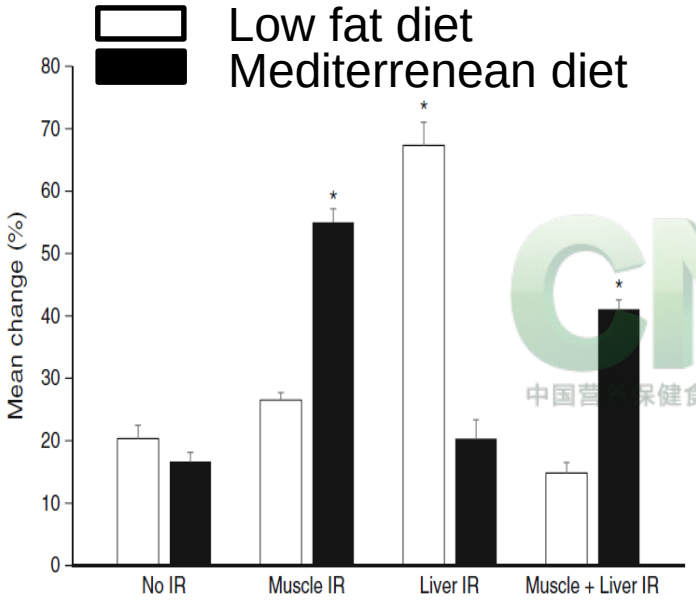
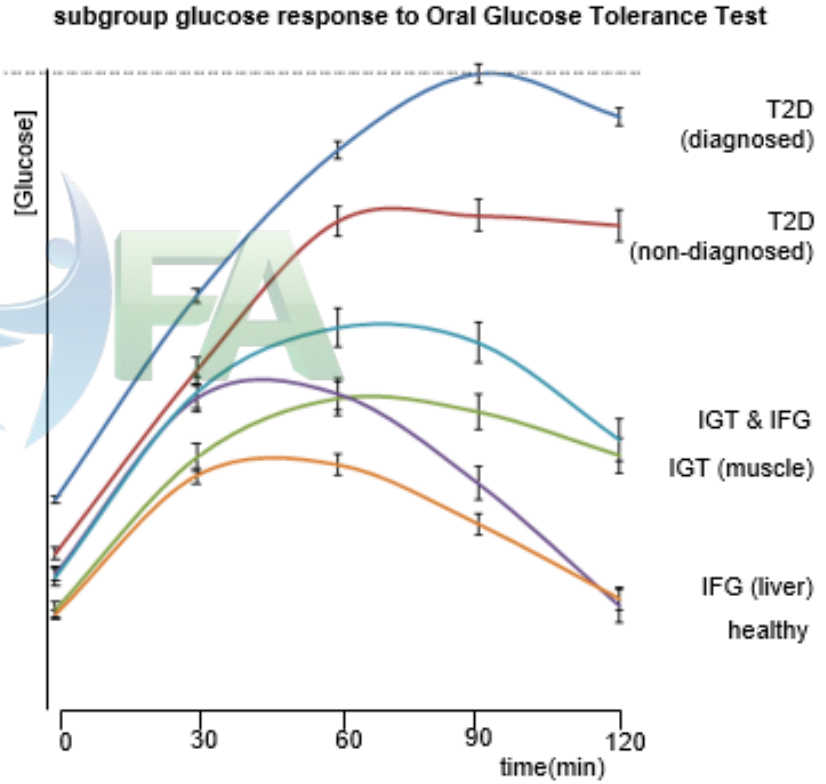


Fig. 1 Mean percentage change in values of disposition index between baseline and after 2 years of follow-up by IR phenotype. *$p<0.05$ between low-fat diet (white bars) and Mediterranean diet (black bars) in each IR subgroup analysed using a univariate model adjusted for age, sex, baseline BMI and change in weight



Blanco-Rojo, Diabetologia, Oct 2015

This initiated two precision nutrition initiatives

from the perspective of phenotypic flexibility

TNO innovation for life

1

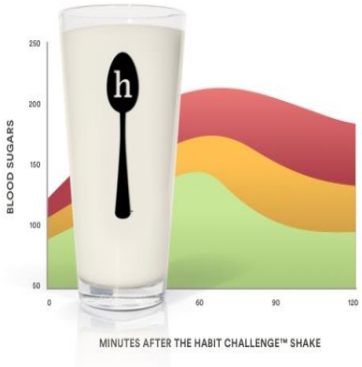
habit
FOOD, PERSONALIZED

2

PHENFLEX2

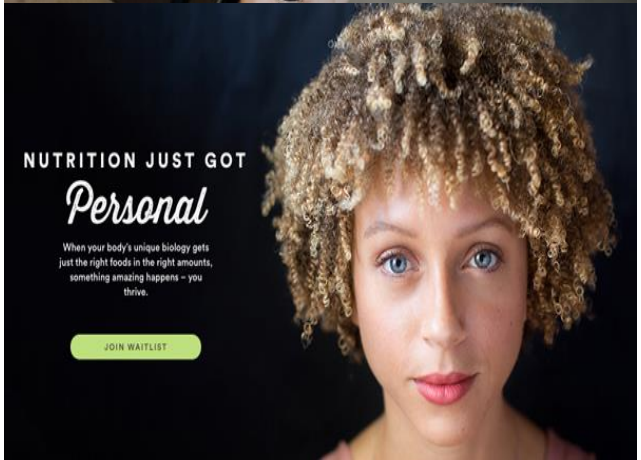
1 Precision nutrition in healthy range of US population

habit
FOOD, PERSONALIZED



THE HABIT CHALLENGE™ SHAKE

To help determine the ratio of carbs, fats, and protein that may be best for you, you are given a metabolic challenge beverage that is nutritionally equivalent to a large American breakfast. A lab measures indicators in your blood using samples you collected at different points before and after you drank the shake. Your results show us how your body responded to carbs, fats, and protein during the testing process.



中国营养保健食品协会

Nutrition reviews
2017;75(8):579-599.

Feature Article

Systems biology of personalized nutrition

Ben van Ommen, Tim van den Broek, Iris de Hoogh, Marjan van Erk, Eugene van Someren, Tanja Rouhani-Rankouhi, Joshua C. Anthony, Koen Hogenelst, Wilrike Pasman, André Boorsma, and Suzan Wopereis

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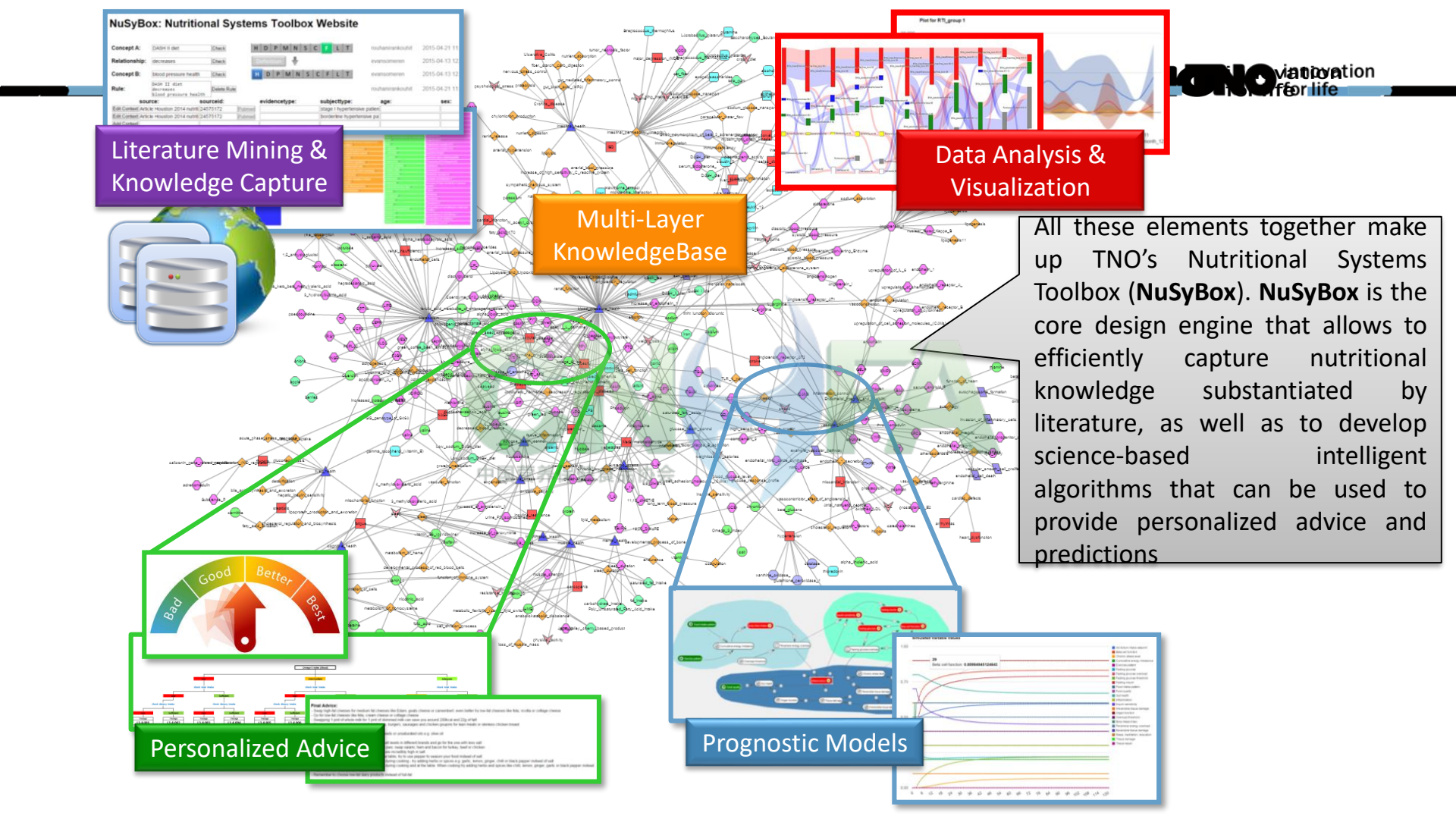
Personalized nutrition is fast becoming a reality due to a number of technological, scientific, and societal developments that complement and extend current public health nutrition recommendations. Personalized nutrition tailors dietary recommendations to specific biological requirements on the basis of a person's health status and goals. The biology underpinning these recommendations is complex, and thus any recommendations must account for multiple biological processes and subprocesses occurring in various tissues and must be formed with an appreciation for how these processes interact with dietary nutrients and environmental factors. Therefore, a systems biology–based approach that considers the most relevant interacting biological mechanisms is necessary to formulate the best recommenda-



All these elements together make up TNO's Nutritional Systems Toolbox (**NuSyBox**). **NuSyBox** is the core design engine that allows to efficiently capture nutritional knowledge substantiated by literature, as well as to develop science-based intelligent algorithms that can be used to provide personalized advice and predictions

To demonstrate that a healthy or optimal diet in an intervention study can improve “metabolic age” and “metabolic stress”, which are composite biomarkers by quantifying phenotypic flexibility, within a healthy population. These composite markers validate previous findings from other intervention studies using phenotypic flexibility and could be the next generation biomarkers.

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BY-HEALTH

BASF We create chemistry

ciro

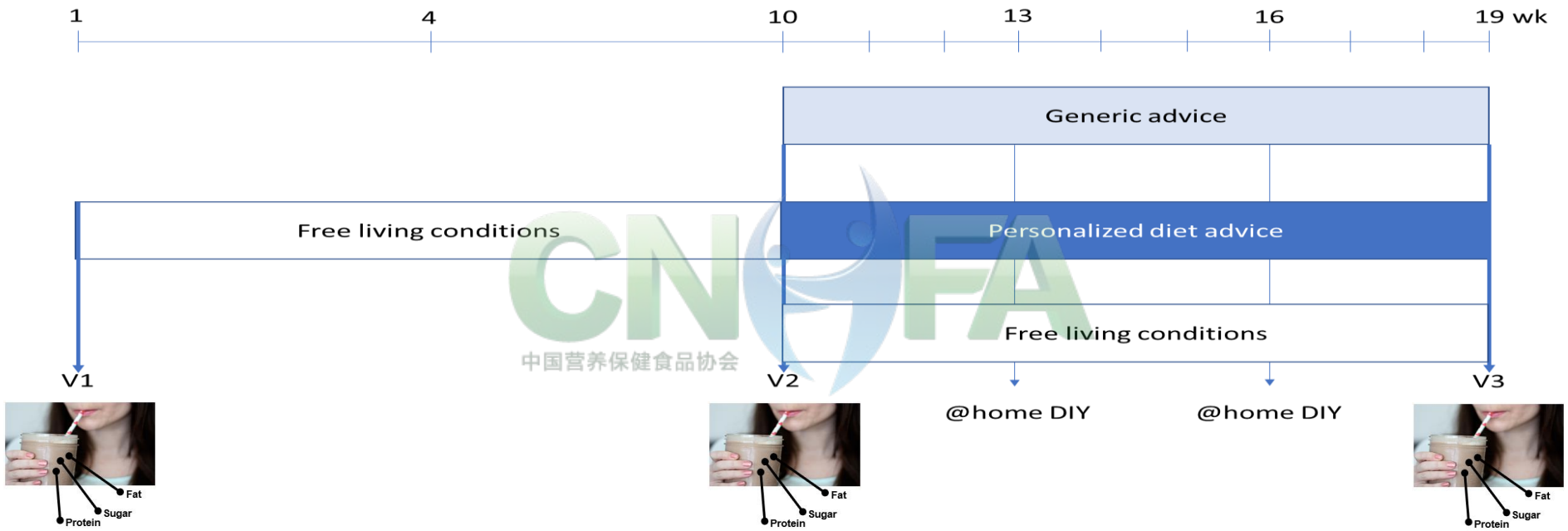
ILSI Europe

Pfizer Consumer Healthcare

BIOFORTIS INNOVATION SERVICES

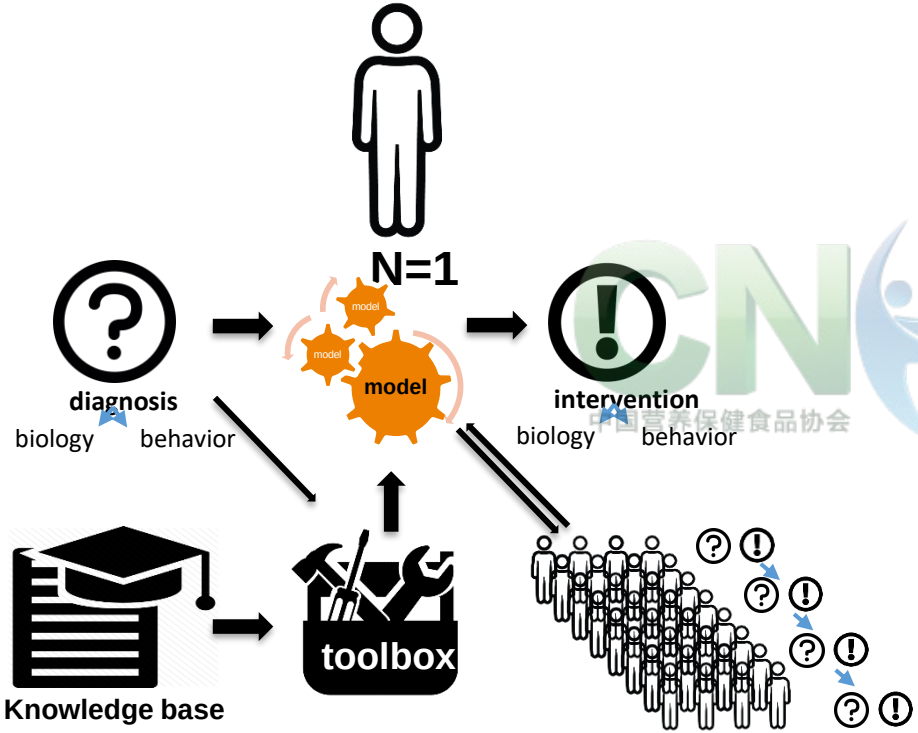
MERIEUX NutriSciences

2 Study design PhenFlex-2 study



To show additional advantages of **personalization** / tailoring of dietary recommendations over general dietary recommendations. PhenFlex-2 delivers the scientific evidence that a healthy diet is beneficial for your health specially when this is tailored to the (nutritional) needs of a person.

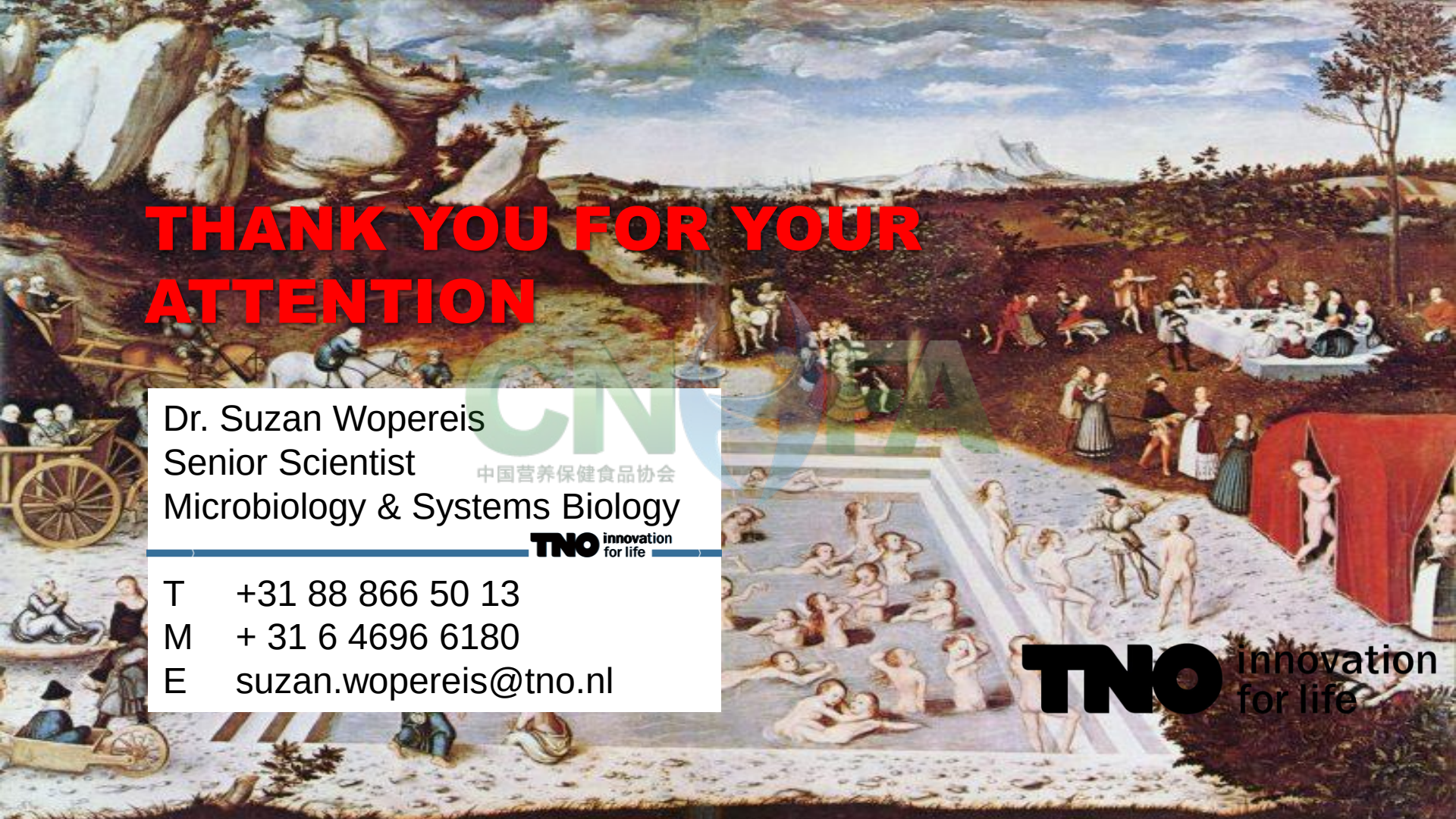
So how will nutrition look like in 10 years?



1. It is personal
2. The intervention or advice is based on a diagnosis, i.e. my personal health data.
3. A (science based) model is used to translate diagnosis into advice
4. The model is tailored to specific conditions and goals from a large toolbox
5. The toolbox is continuously and systematically updated with all relevant scientific knowledge
6. Exploit/use information from large numbers of personal health data

Take home message

- For diagnosis of health effects of nutrition we need resilience markers of health rather than biomarkers of disease
- The PhenFlex challenge discriminates between different states of health and is superior to measurements in fasted state to quantify health effects of nutrition
- Only subjects with reduced metabolic resilience in healthy range of population show improved health
- Subgroups of DT2 patients have a personal response to nutritional interventions
- In this way we can quantify subtle personal health effects of nutrition!



THANK YOU FOR YOUR ATTENTION

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