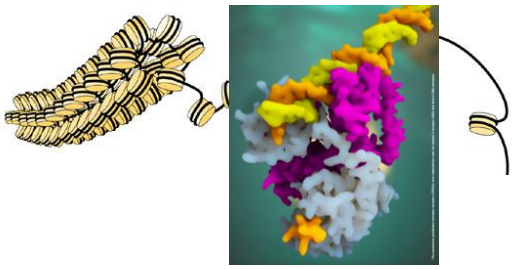


You are what you (have) eat(en)

With nutrigenomics to nutritional science 2.0

Michael Müller

Netherlands Nutrigenomics Centre

& Nutrition, Metabolism and Genomics Group

Division of Human Nutrition

WAGENINGEN UNIVERSITEIT

WAGENINGEN UR

“You are what you eat”

"You are what you eat"

Typical diets
(a) Food for one day on a Paleolithic-style diet
(b) Food for one day on a therapeutic diet
(c) Food for one day on a modern Western diet.

Martin C, et al. 2013.
Annu. Rev. Plant Biol. 64:19–46

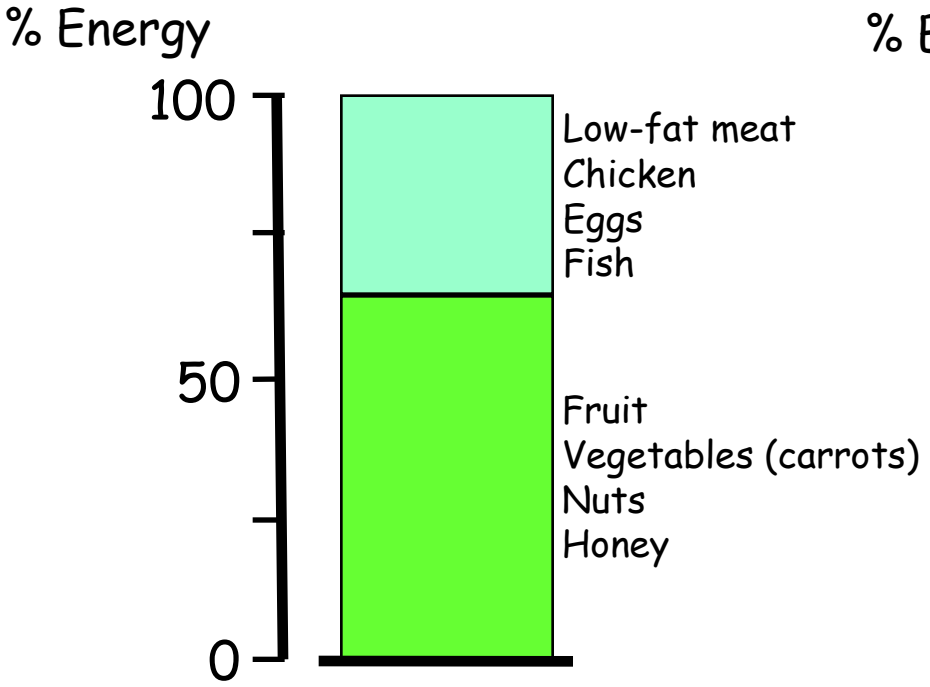
Our "paleolithic" genes + modern diets

Paleolithic era

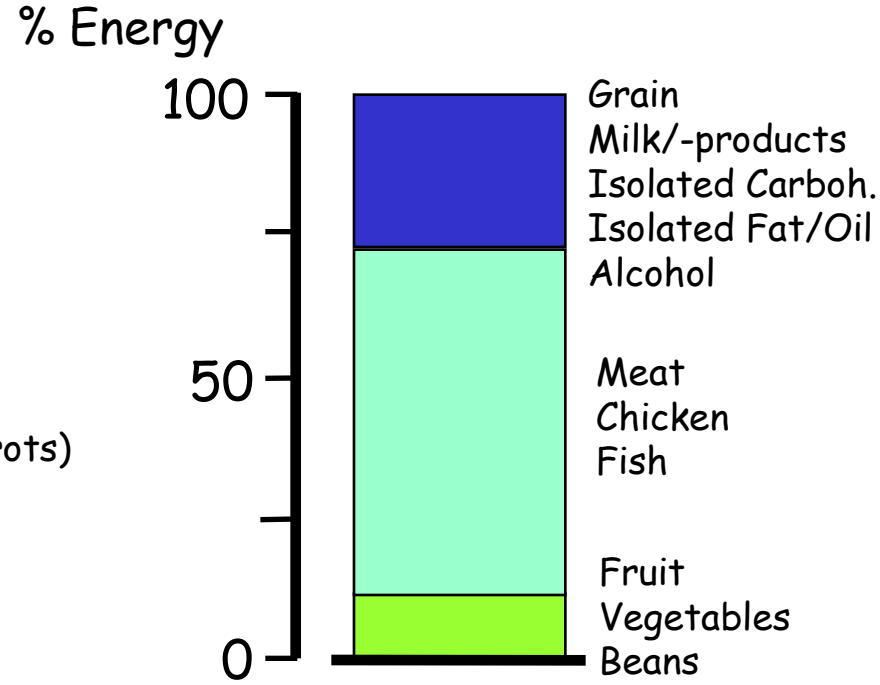
1.200.000 Generations
between feast en famine

Modern Times

2-3 Generations
in energy abundance



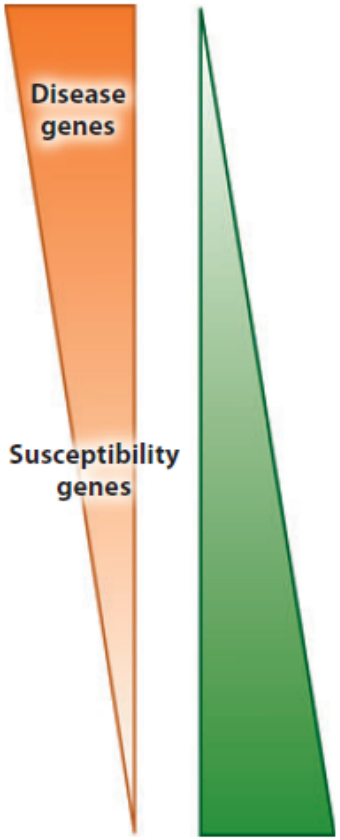
"Unsafe" food = Many challenges



"Safe" food = Less challenges

Genes + Nutrition => Phenotype
It is not that easy!

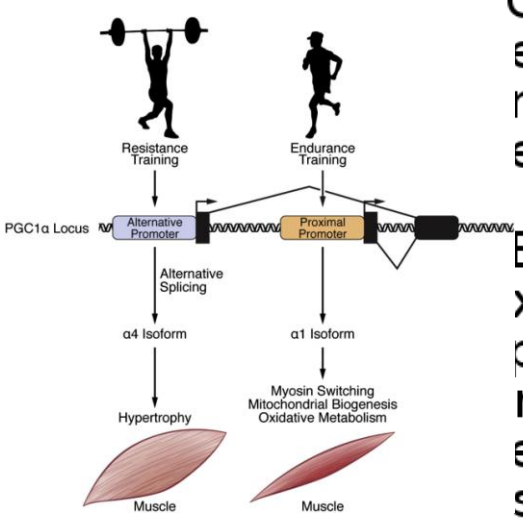
Classification of hereditary diseases

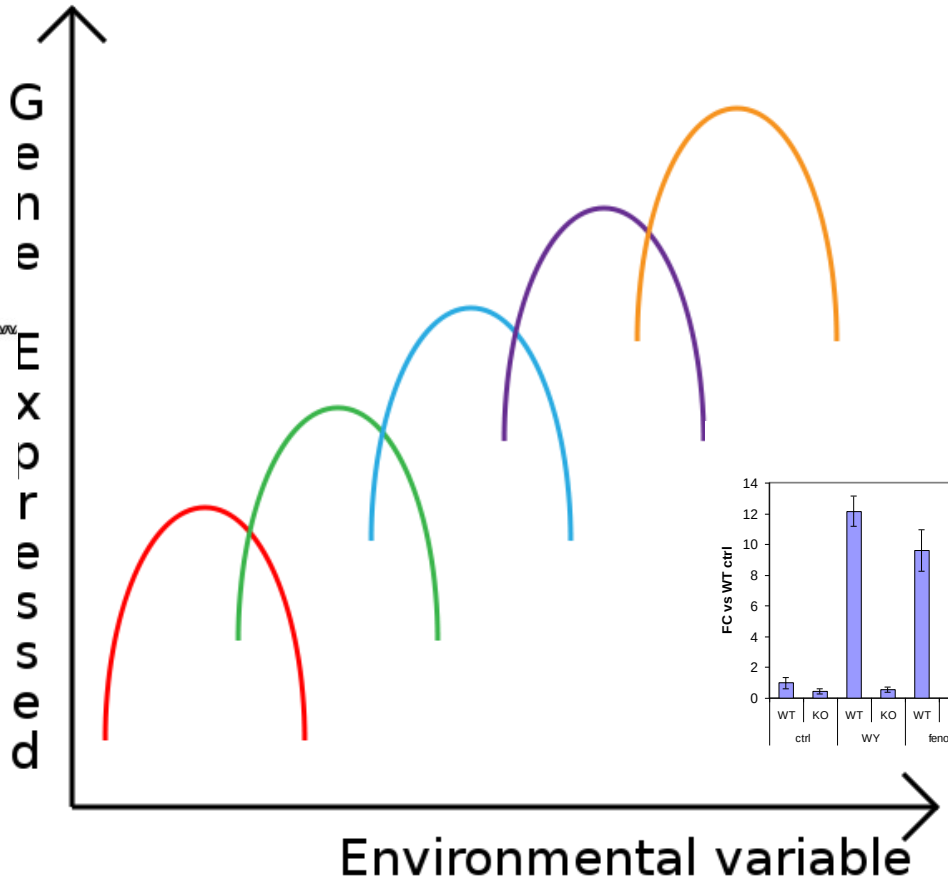


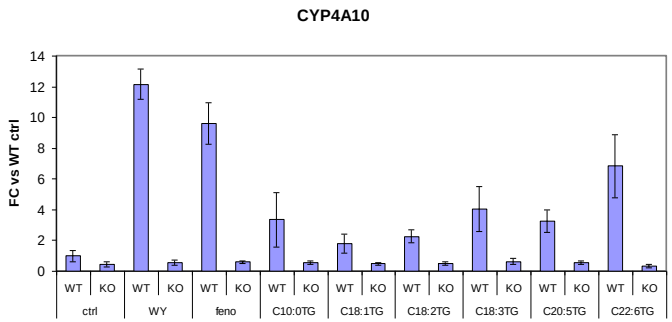
Diseases		Example	Diagnosis
Monogenic diseases Familial Mendelian genetics	High penetrance	Duchenne muscular dystrophy	DNA + clinical picture
		Huntington's disease	DNA + clinical picture
		Congenital hypothyroidism	T4/TSH
		21-hydroxylase deficiency	17-OH-progesterone
		Phenylketonuria	Phenylalanine
Chronic diseases with a single gene component or monogenic variants of complex diseases Familial Mendelian genetics Often genetically heterogeneous	High penetrance with considerable environmental and/or lifestyle influences as well as influences from modifying genes	Familial hemochromatosis	Iron status + DNA
		Familial hypercholesterolemia	LDL cholesterol + DNA
		Familial Mediterranean fever	DNA + clinical picture
		Thrombophilia due to factor V Leiden mutation	Activated protein C activity + DNA
Complex genetic diseases or polygenic multifactorial diseases Familial Non-Mendelian genetics Genetically very heterogeneous	Very low penetrance, mostly of suspected SNPs and overwhelming environmental and lifestyle influences	Type 2 diabetes mellitus	Variety of non-genetic tests
		Hypertension	
		Obesity	
		Osteoporosis	
		Dementia	
		Atherosclerosis	

Phenotype plasticity

Phenotypic plasticity is the ability of an organism to change its phenotype in response to changes in the environment (e.g. nutrition or exercise).





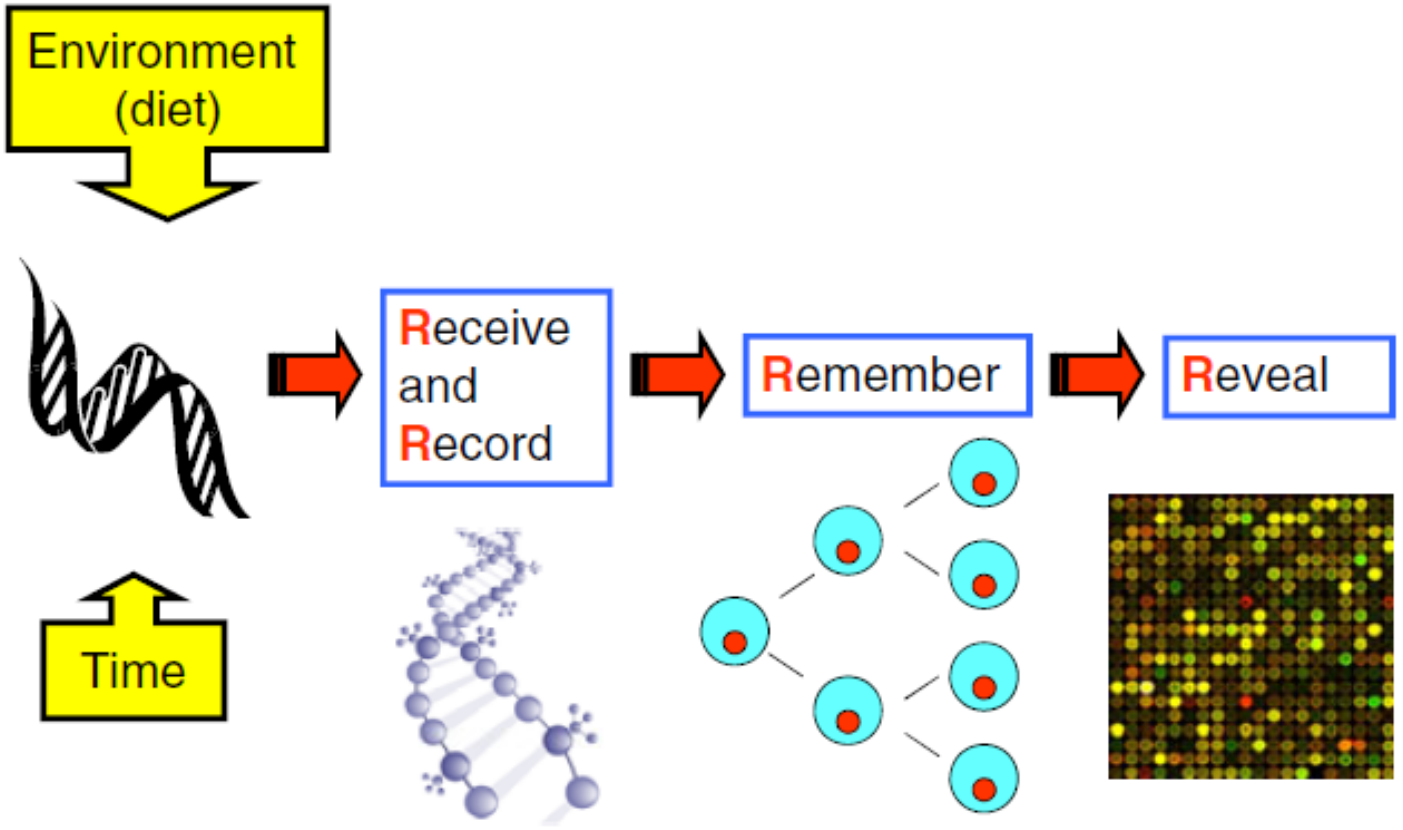


Your are what you eat

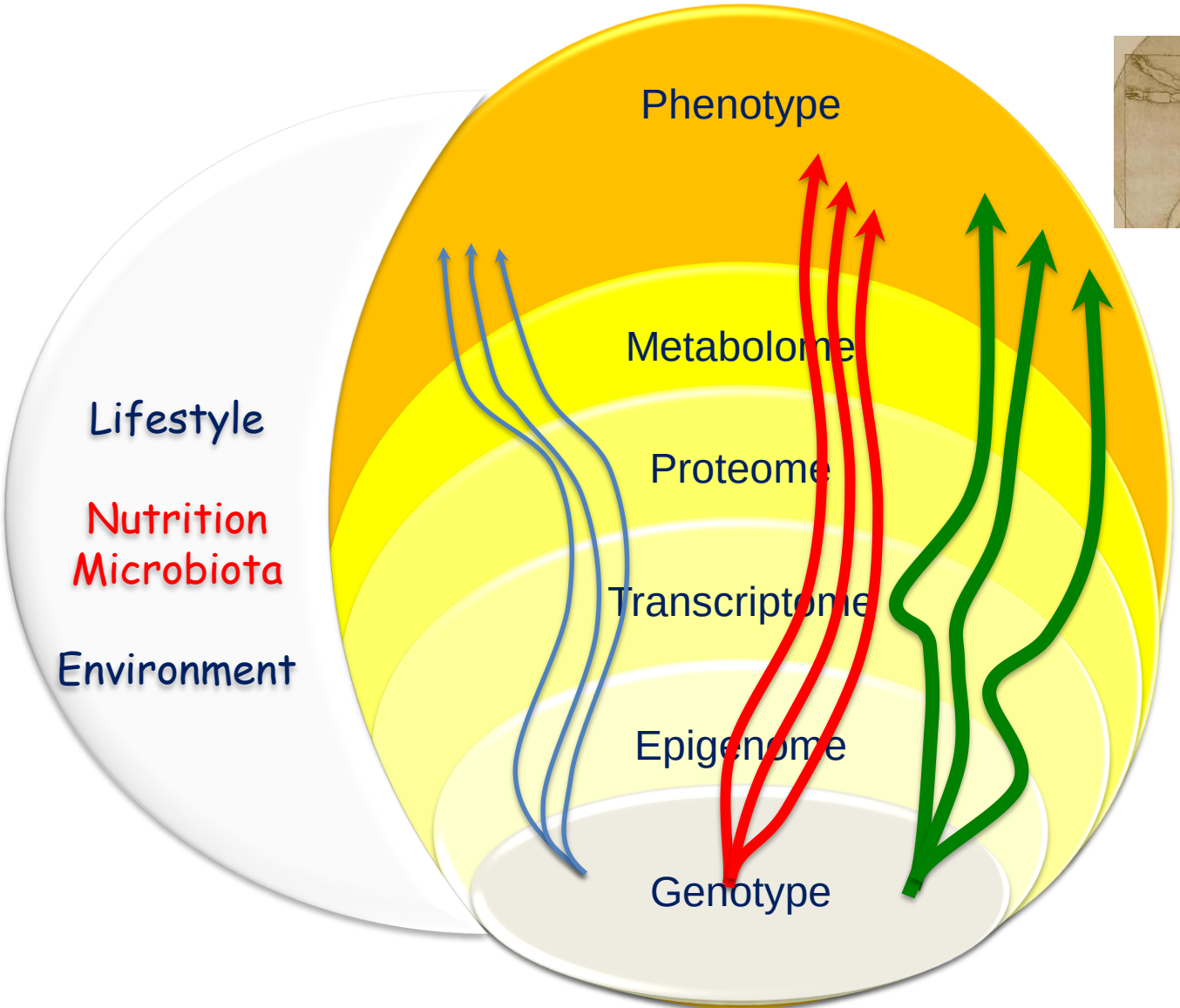
Healthy food (pattern)s have large impact on our gene expression & phenotype

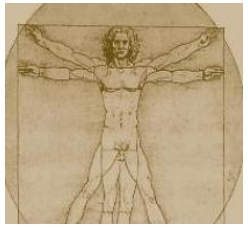
- (Micro & Macro) Nutrients
  - Mono & polyunsaturated fatty acids
  - Vitamines (e.g. vitamin A & D) , minerals (e.g. Zn)
- Microbiota (from foods)
  - Vegetarians / omni- /carnivores => different microbiota
  - “Raw” or fermented food (e.g. diary, cheese) consumption => food-specific microbiota
- Food components (bitter, “toxic”: = “healthy”)
  - Secondary plant metabolites (e.g. resveratrol, glucosinolates, cafestol....)
  - MicroRNA (e.g. rice, milk, plants)?
- Less foods/calories (caloric restriction)
  - “Chromatin exercise”
  - “Cell exercise” (e.g. via autophagy)

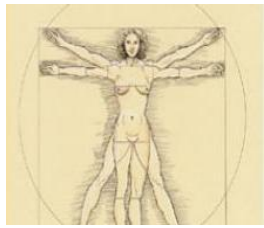
"We are what we eat and have eaten"
Received, Recorded, Remembered & Revealed

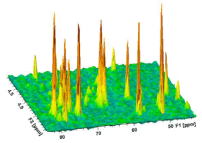


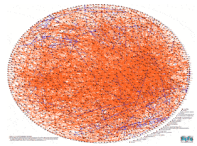
Nutrigenomics enable the quantitative analysis of the nutritional genotype-phenotype relationship

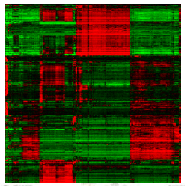


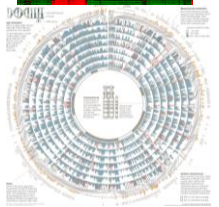


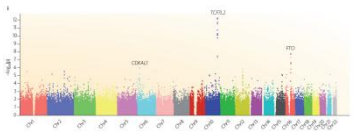






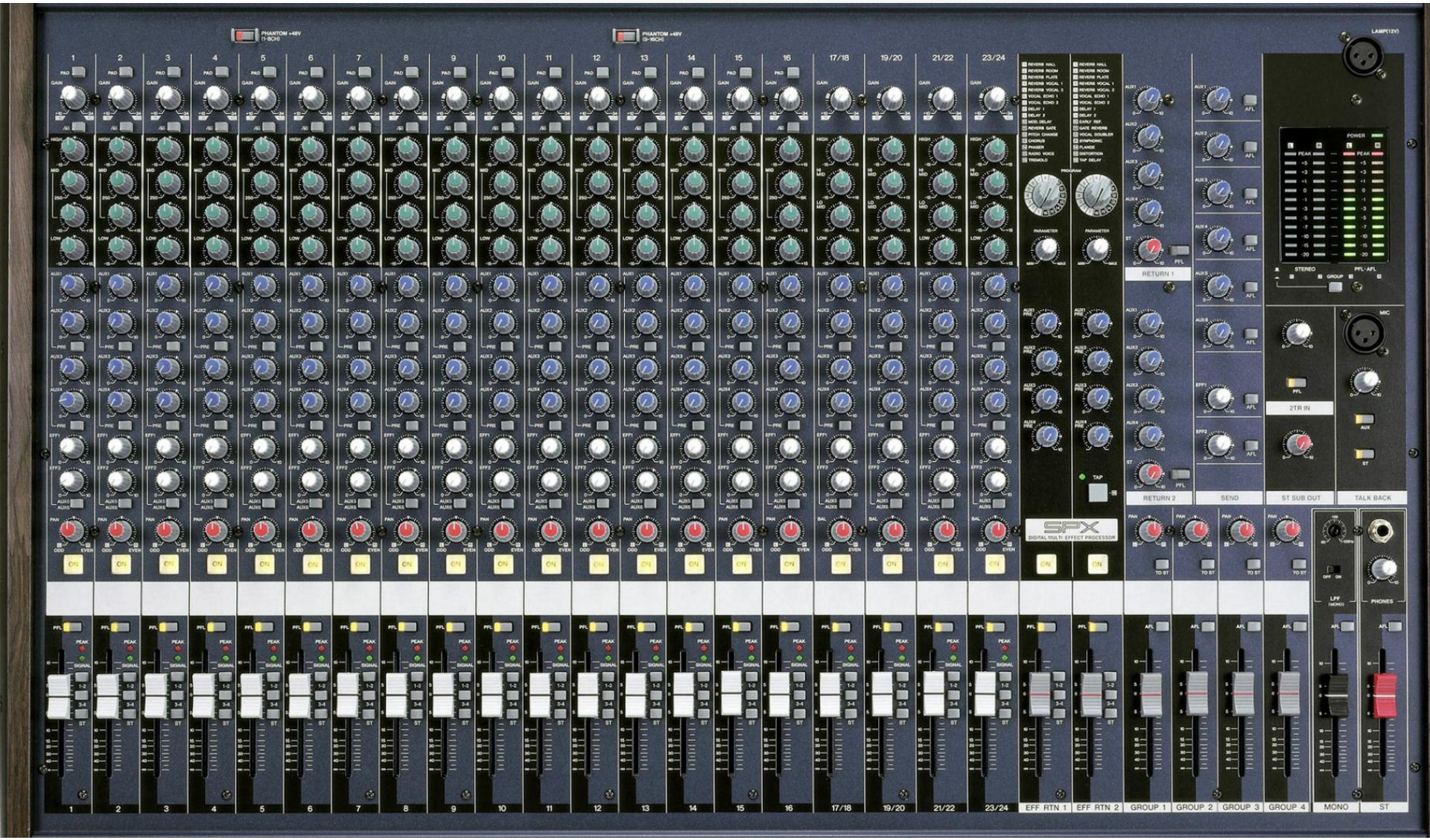




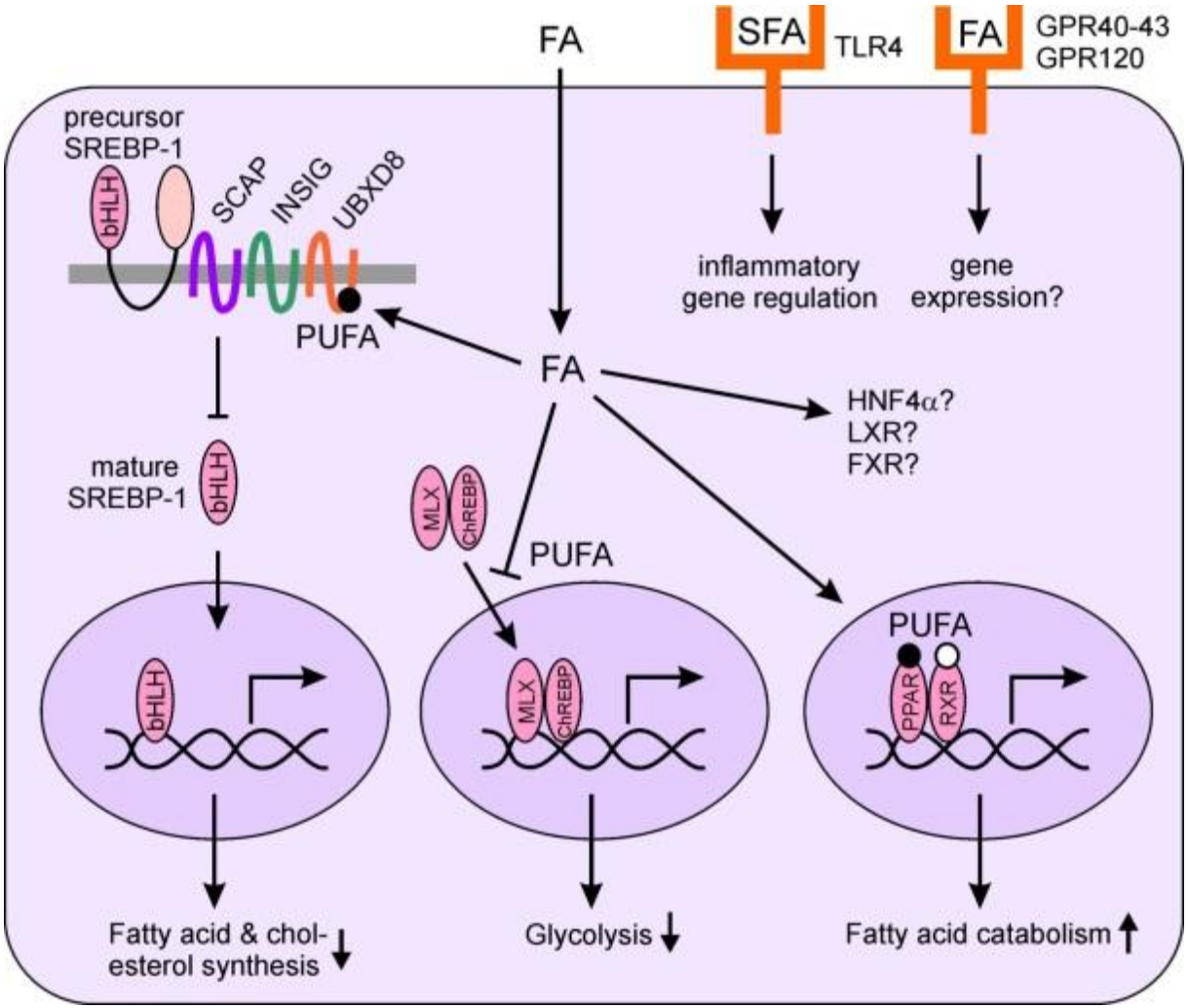


Step 1: Understanding Nutrition

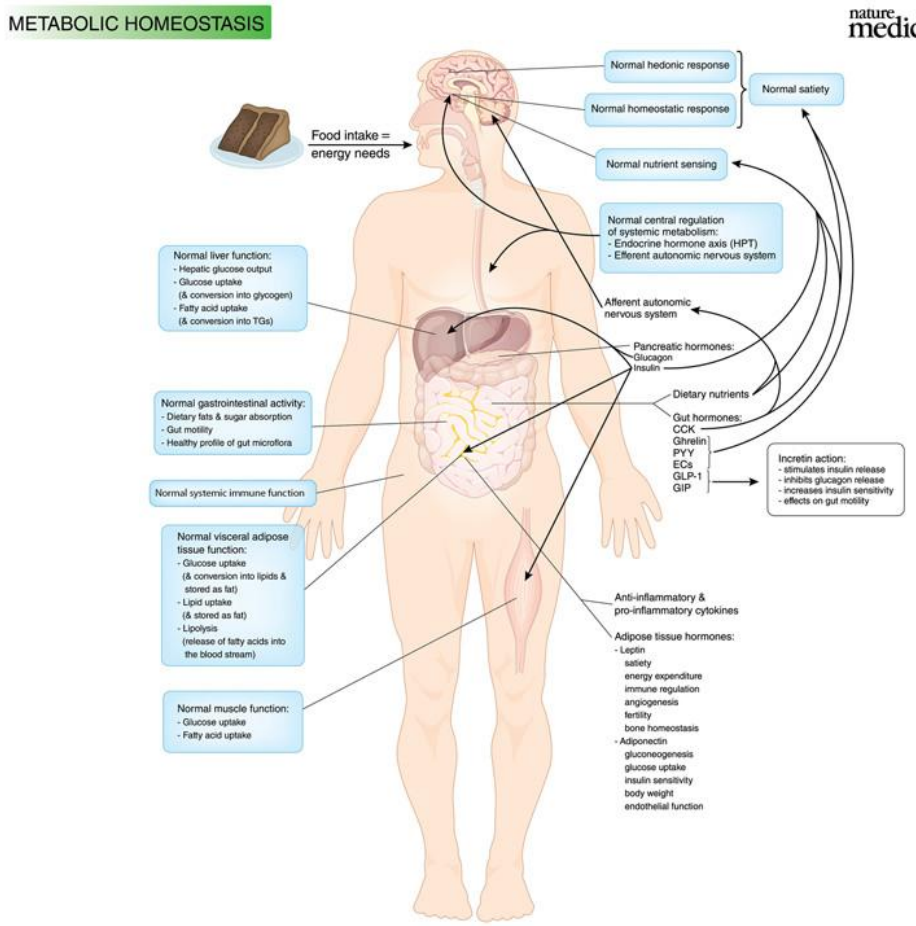
How nutrients regulate our genes - via sensing molecular switches

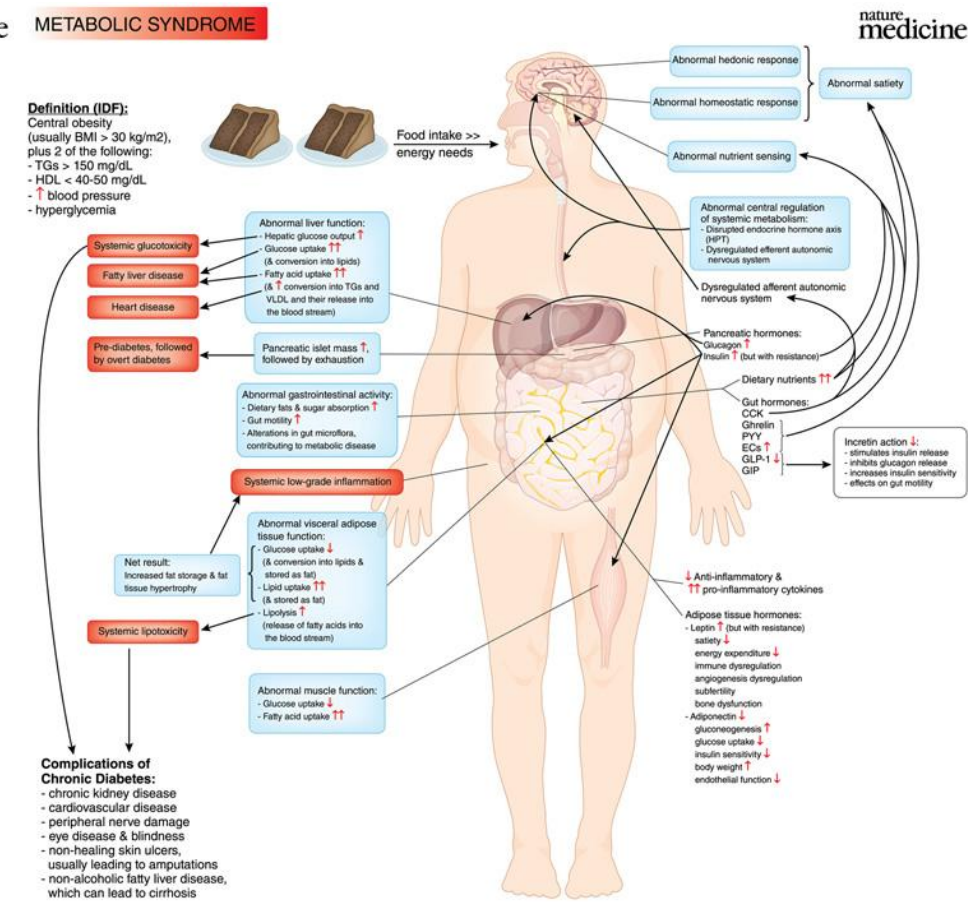


Step 2: Using nutrigenomics & molecular nutrition to define the mechanistic framework

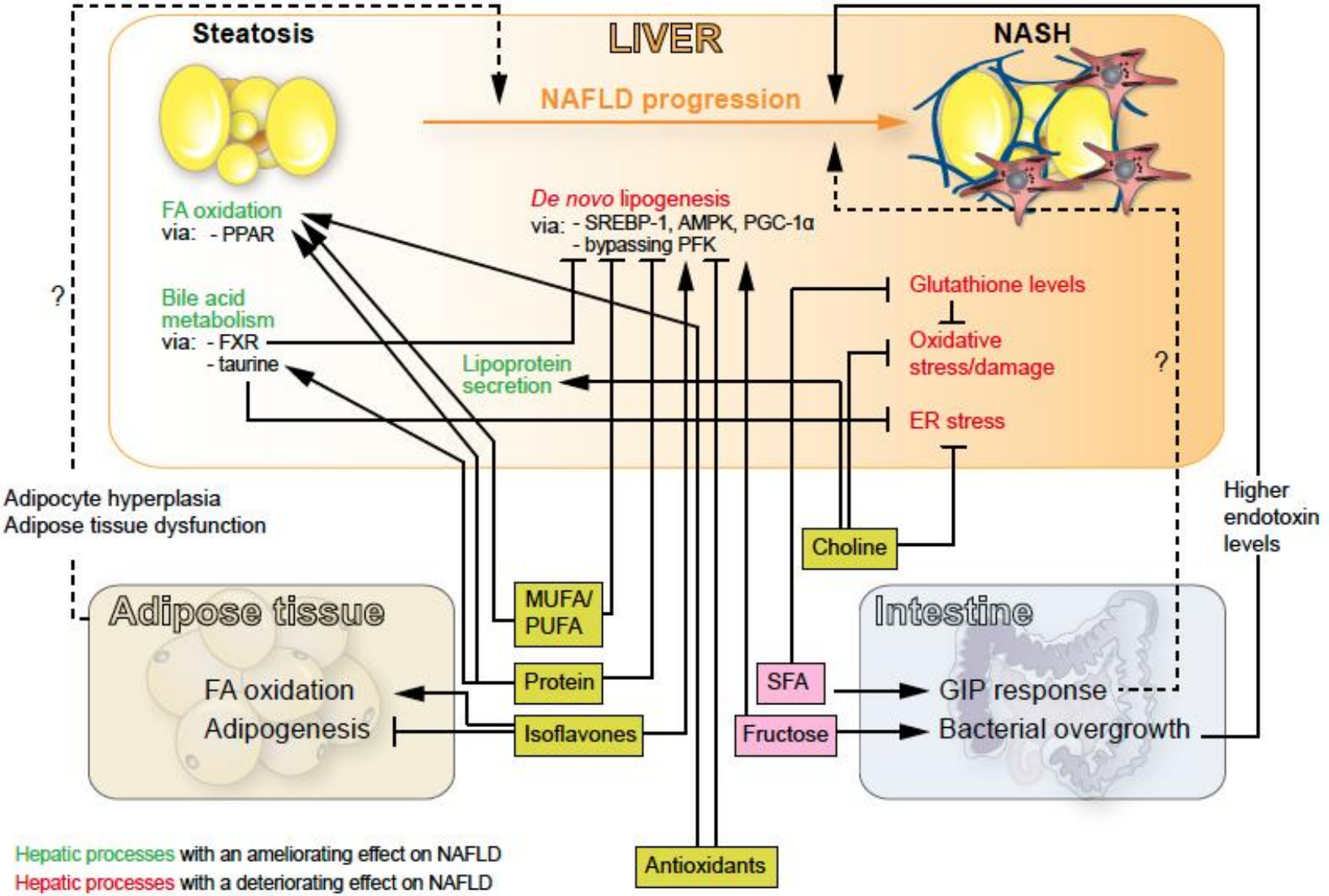


"2 hits" in Metabolic Syndrome
"Too much metabolic & inflammatory stress"
Complex NC diseases are caused by dysregulation





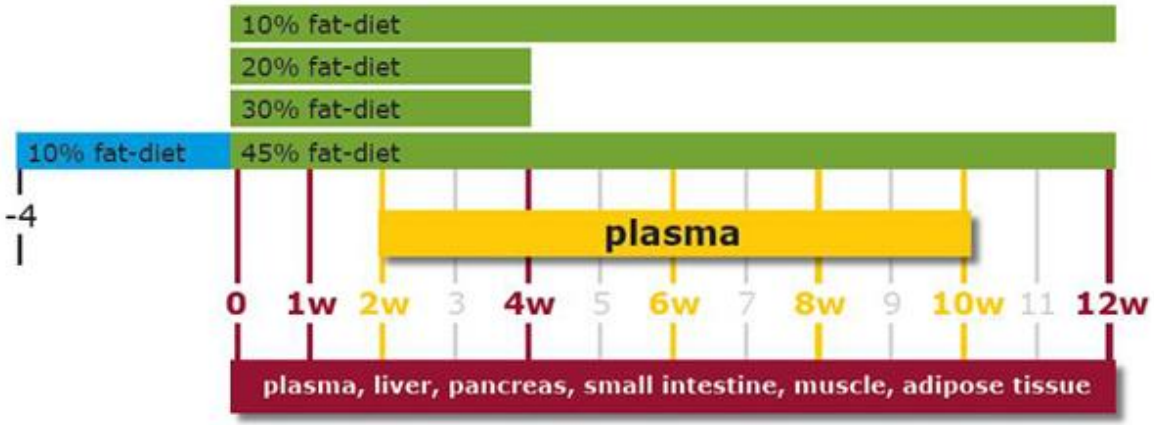
Nature Medicine 2012

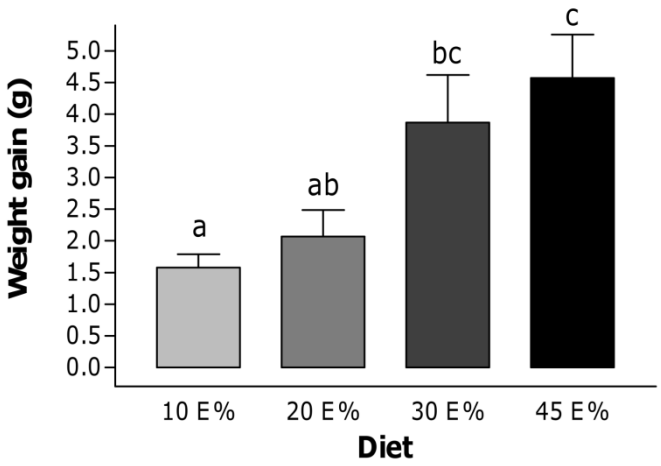


de Wit NJ, Afman LA, Mensink M, Müller M
Phenotyping the effect of diet on non-alcoholic fatty liver disease J Hepatol 2012

Step 3: Understanding organ capacity

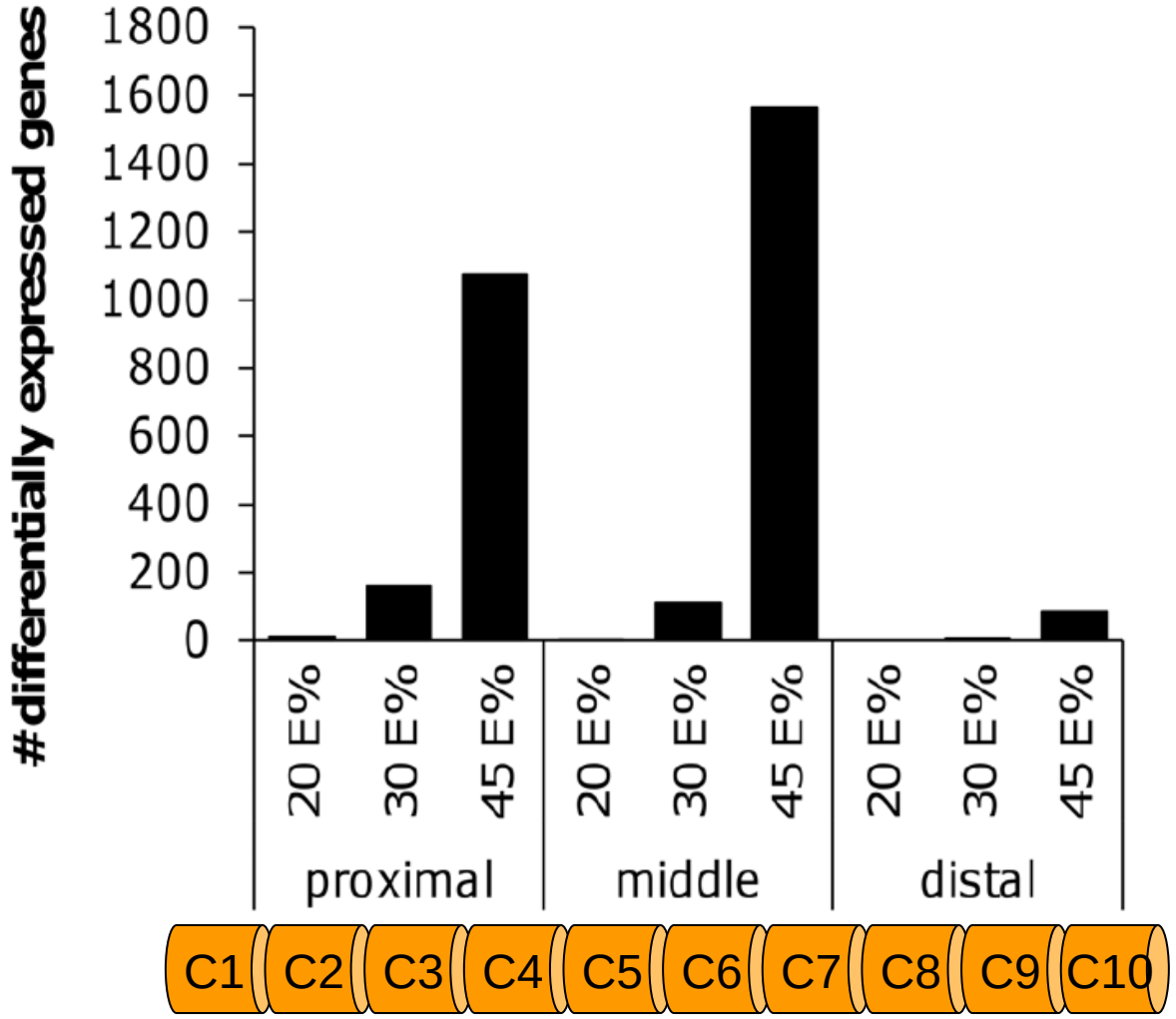
Response to the intestine to different doses of dietary fat





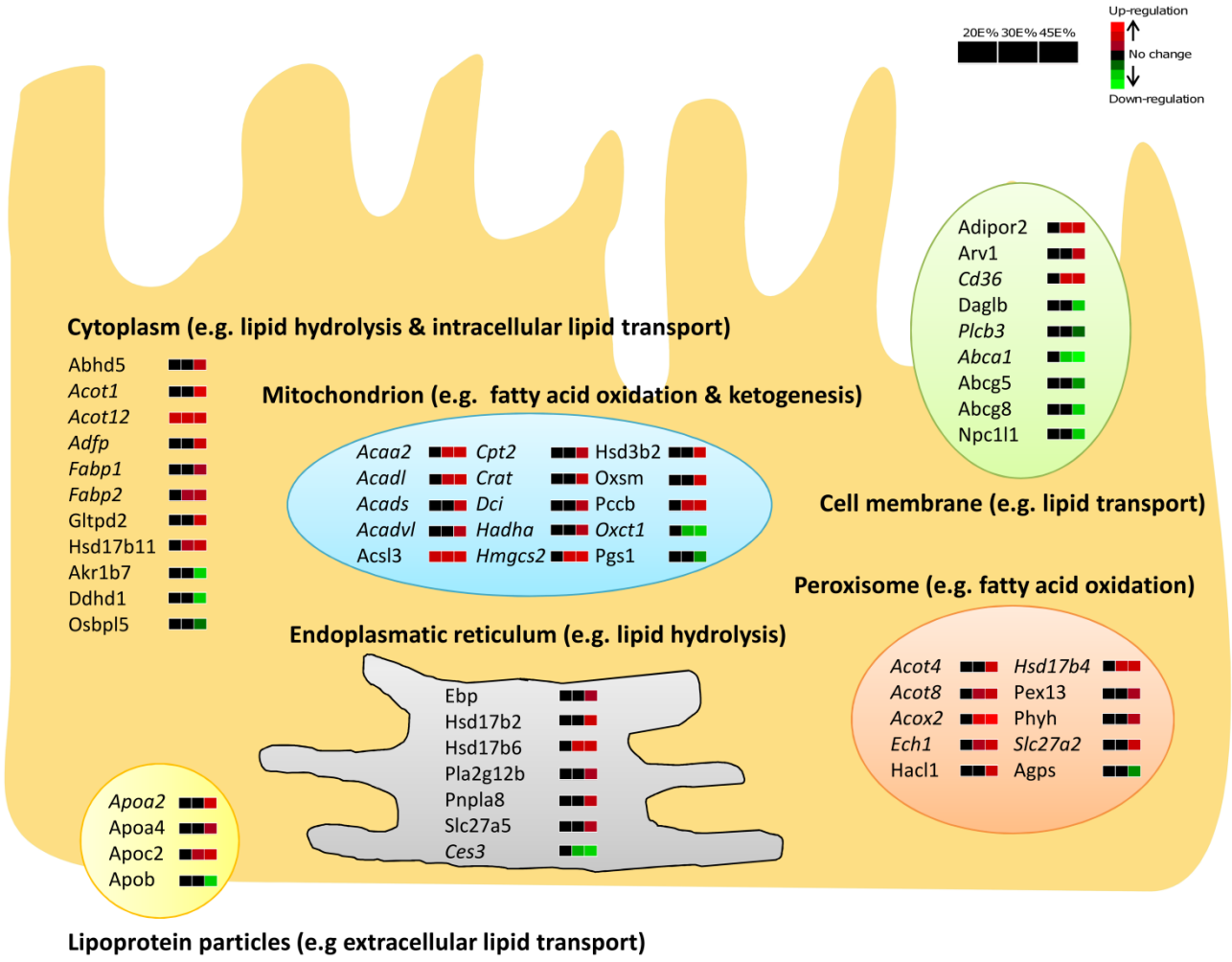
De Wit et al Plos ONE 2011

Robust & concentration dependent effects in small intestine
Differentially regulated intestinal genes by high fat diet



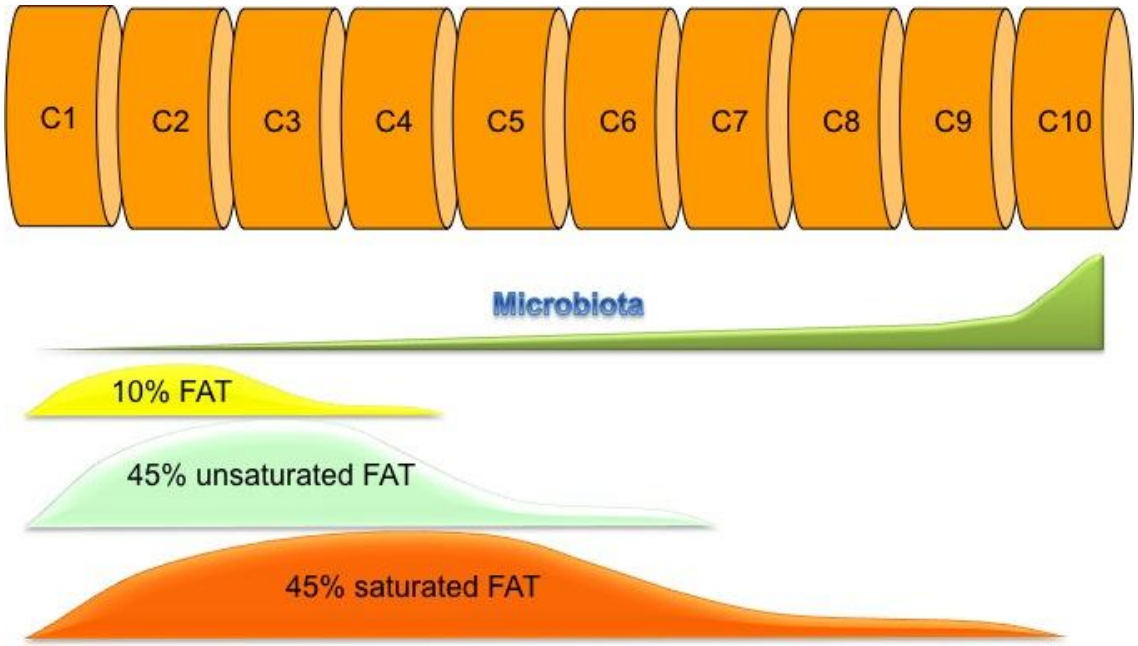
De Wit et al Plos ONE 2011

Cellular localization and specific lipid metabolism-related function of fat-dose dependently regulated genes

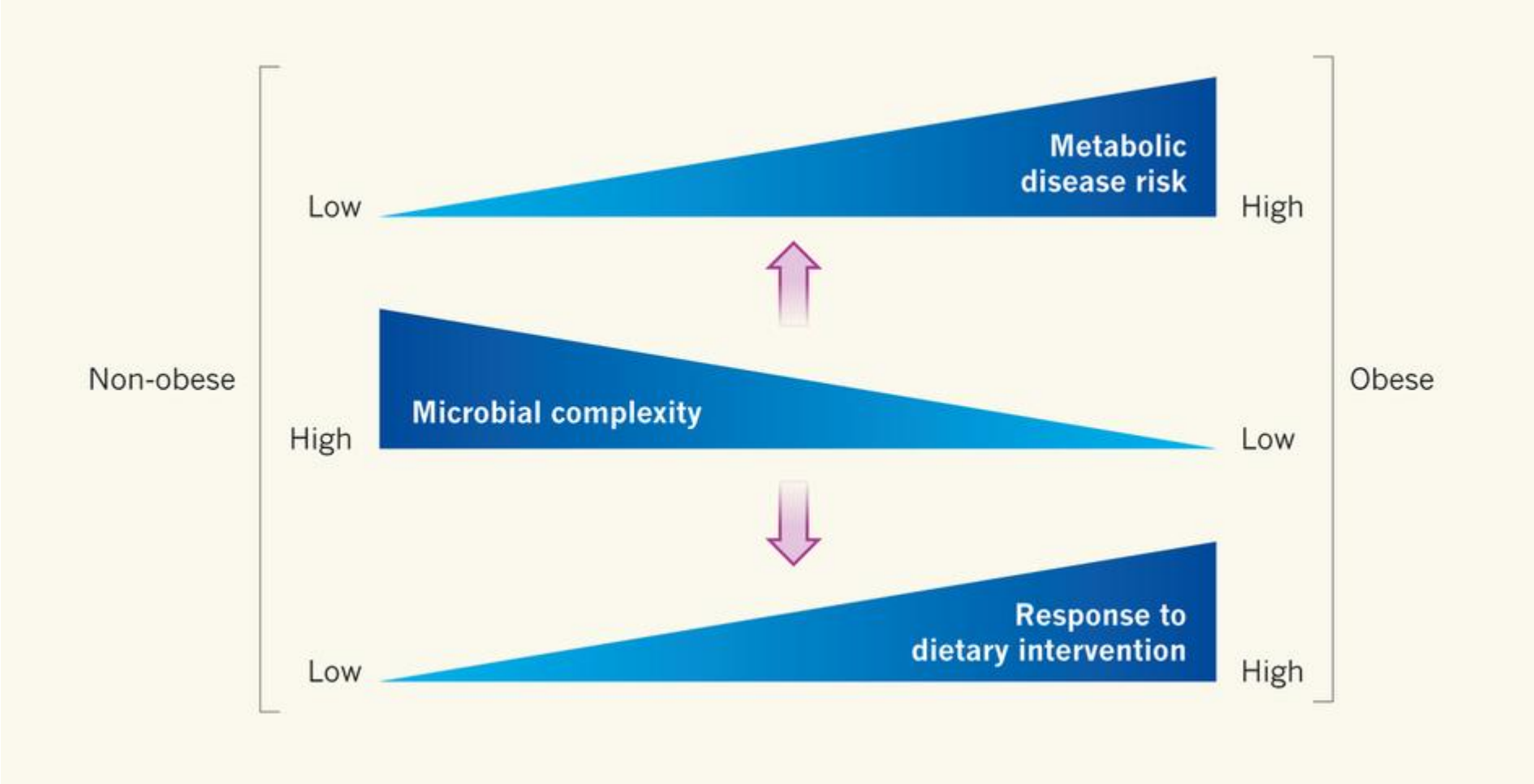


Conclusions

- Saturated fat stimulates obesity and hepatic steatosis and affects gut microbiota composition by an enhanced overflow of dietary fat to the distal intestine.
- Unsaturated fat is more effectively taken up by the small intestine, likely by more efficiently activating nutrient sensing systems (PPARs) and thereby contributing to the prevention the development of early pathology (e.g. NASH).



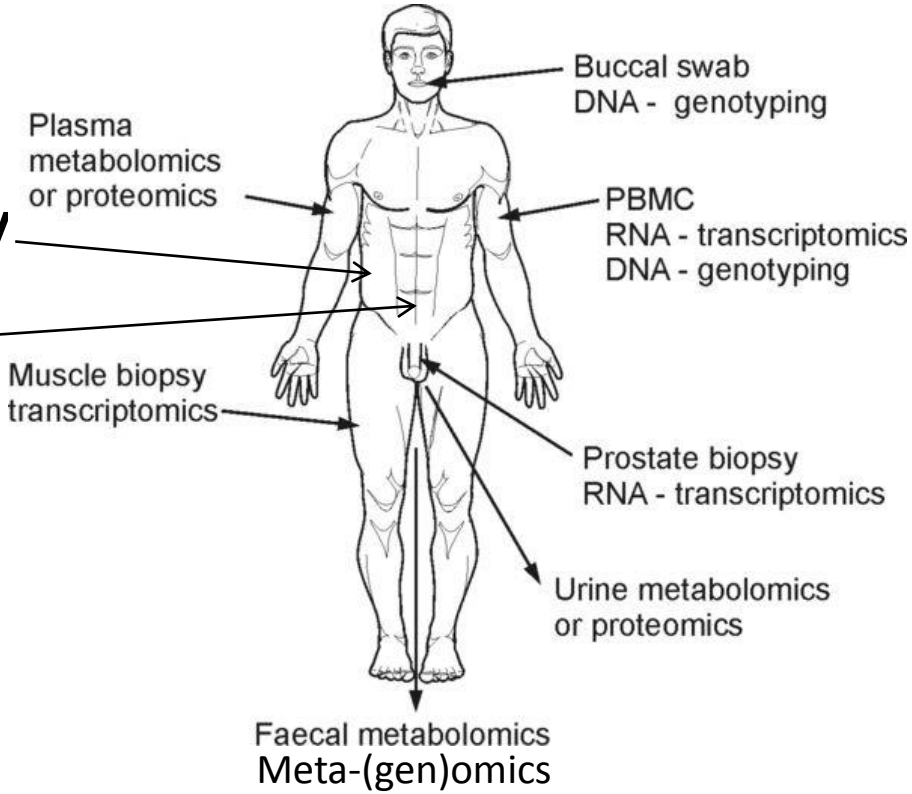
Metabolic plasticity and resilience capacity due to "genetic richness" is an essential feature of health



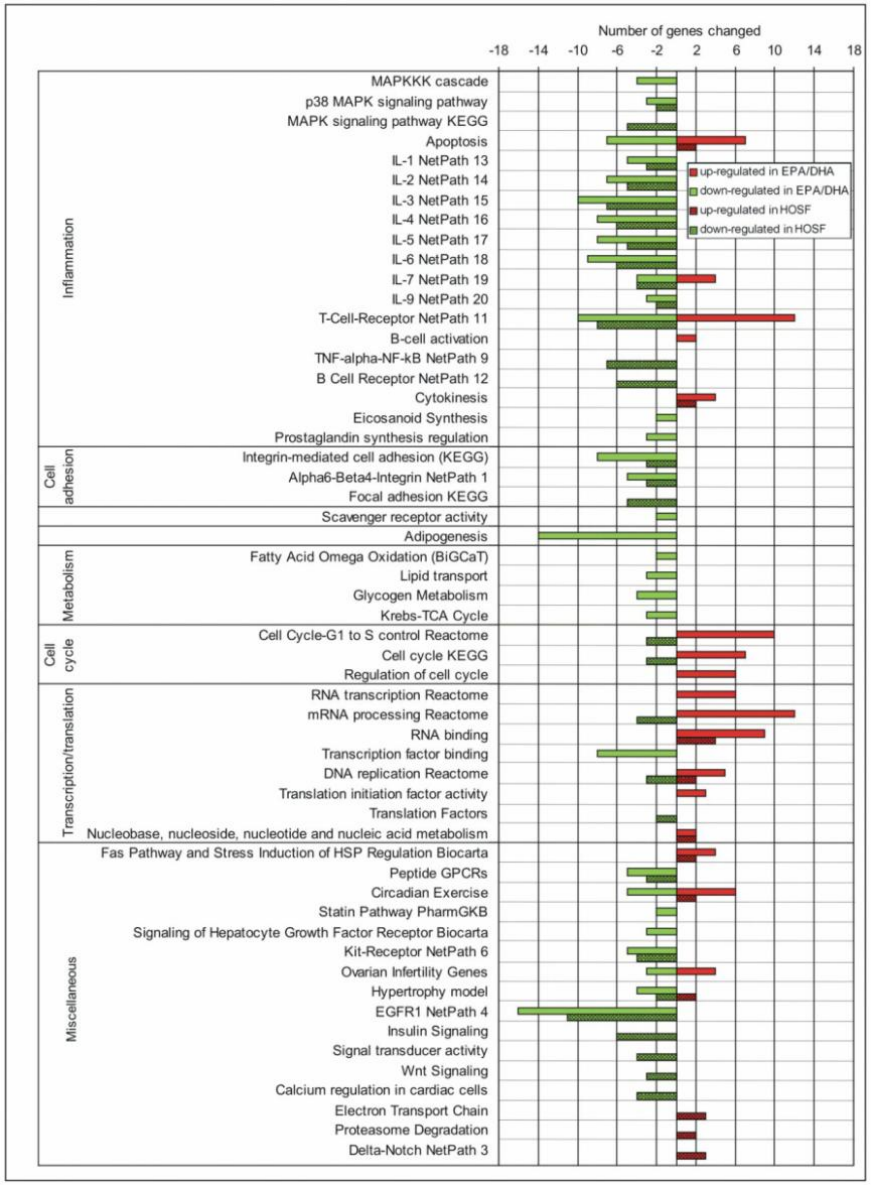
Nature 500, 538–539

Human Nutrigenomics: What is possible?

- ✓Muscle biopsy
- ✓Adipose tissue biopsy
- ✓Intestinal biopsy
- ✓White blood cells



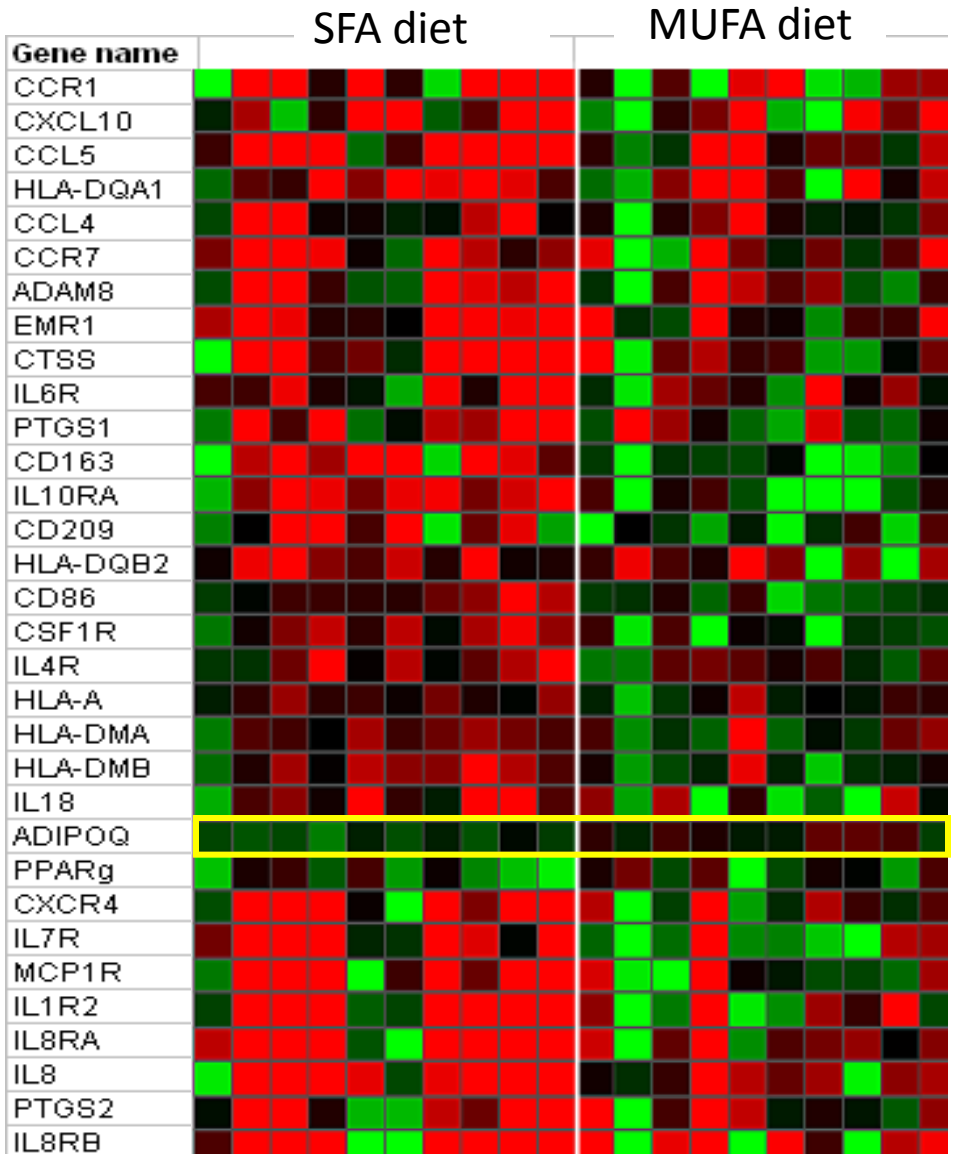
Fish-oil supplementation induces anti-inflammatory gene expression profiles in human blood mononuclear cells



Less inflammation & decreased pro-arteriosclerosis markers = Anti-immuno-senescence

Bouwens et al. Am J Clin Nutr. 2009

'Obese-linked' pro-inflammatory gene expression profile by saturated fatty acids

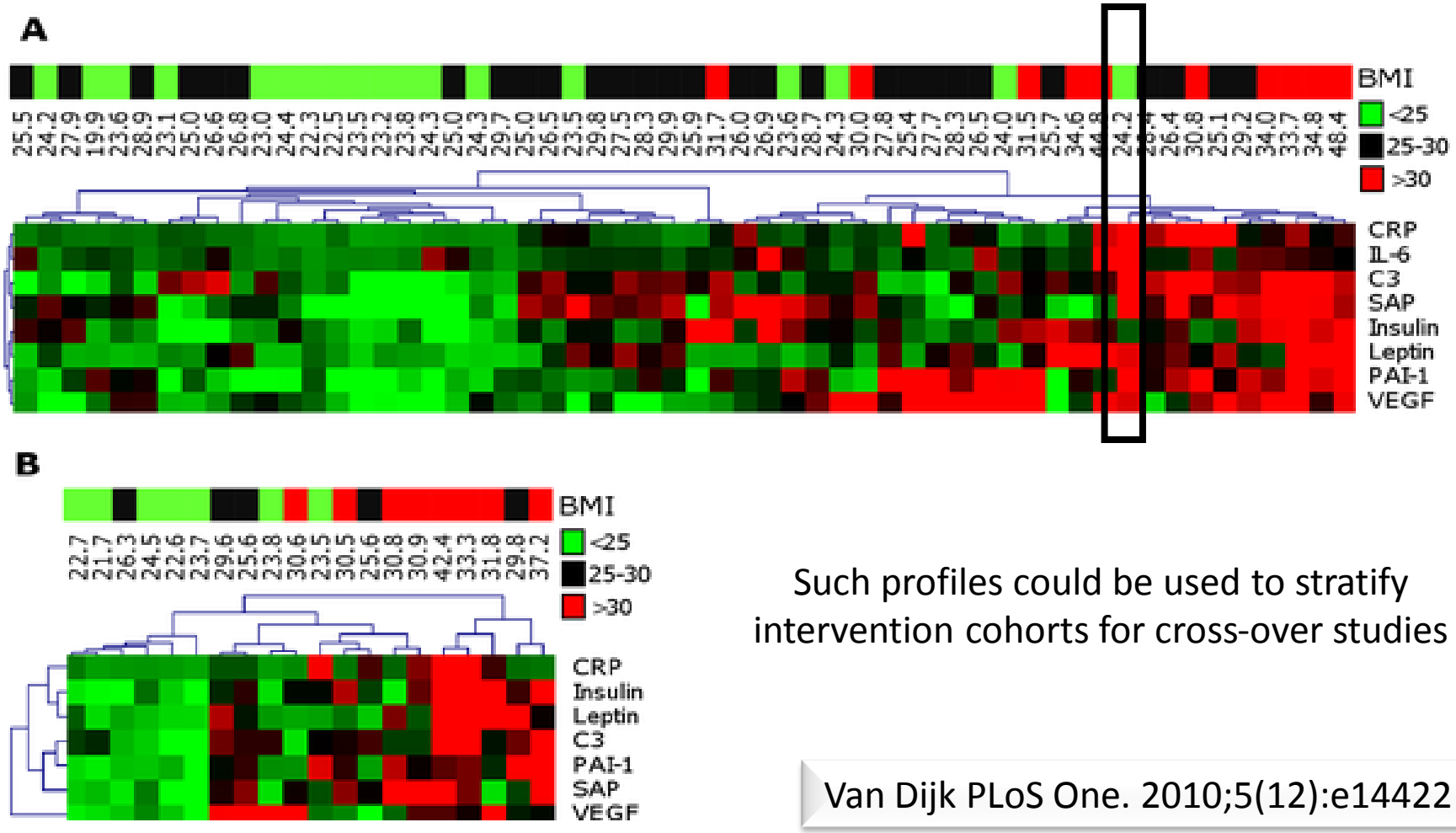


The SFA-rich diet:

- Induces a pro-inflammatory obese-linked gene expression profile
- Decreases expression and plasma level of the anti-inflammatory cytokine adiponectin
- "Personal Transcriptomes"

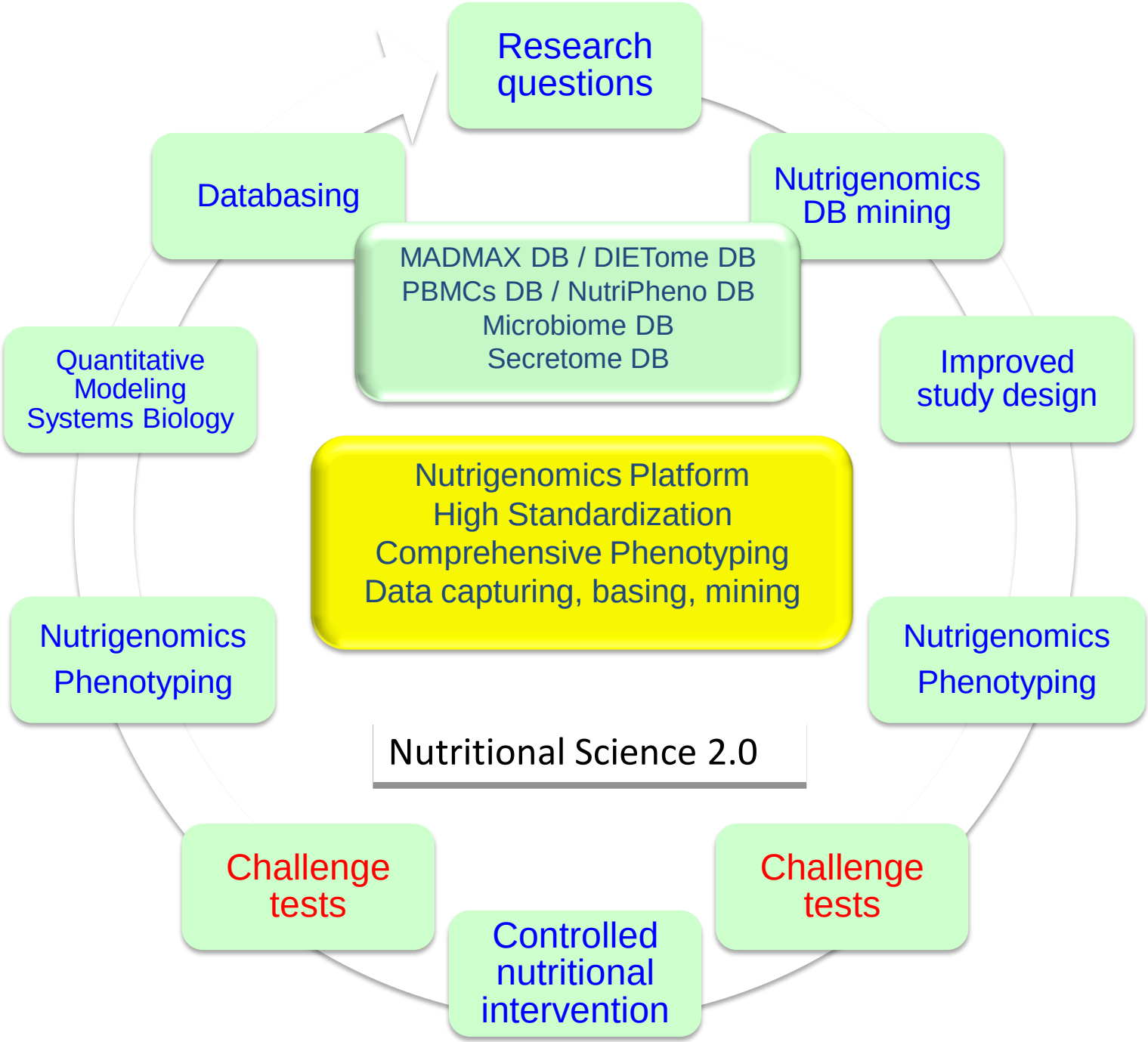
Van Dijk et al. AJCN 2009

Clustering of personal profiles of robustly positively BMI-associated proteins in population I (A) and II (B)



Such profiles could be used to stratify intervention cohorts for cross-over studies

Van Dijk PLoS One. 2010;5(12):e14422


Research questions
Nutrigenomics DB mining
Improved study design
Nutrigenomics Phenotyping
Challenge tests
Controlled nutritional intervention
Challenge tests
Nutrigenomics Phenotyping
Quantitative Modeling Systems Biology
Databasing
MADMAX DB / DIETome DB
PBMCs DB / NutriPheno DB
Microbiome DB
Secretome DB
Nutrigenomics Platform
High Standardization
Comprehensive Phenotyping
Data capturing, basing, mining
Nutritional Science 2.0

Nutrigenomics enables us

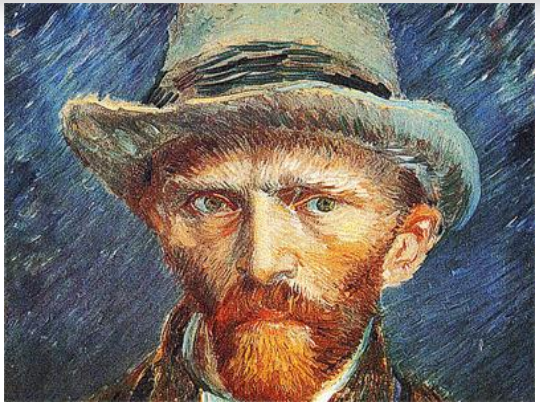
- To define the mechanistic framework of nutrition (evidence-based nutrition);
- To quantify the nutritional needs for optimized fitness at different life stages (“personalized” nutrition);
- To improve early diagnostics of nutrition related disorders (“challenge tests”);
- To support the development of “smart healthy food patterns” for modern mankind (healthy and tasty, sustainable, affordable);
- To enable the transition of nutritional science to nutritional science 2.0.

Its easy to stay healthy (if your genes are ok) 2 Meals a day, work as long as possible & embrace challenges

Walter Breuning (1896 - 2011)

Sander Kersten
Lydia Afman
Guido Hooiveld
Wilma Steegenga
Philip de Groot
Mark Boekschoten
Nicole de Wit
Rinke Stienstra
& many PhDs
e.g. Katja Lange
Danielle Haenen

Christian Trautwein
Folkert Kuipers
Willem de Vos
Michiel Kleerebezem
Ben van Ommen
Hannelore Daniel
Bart Staels
Edith Feskens
Leif Sander
Dirk Haller
Eline Slagboom
Daniel Thome
Mihai Nitea
& many more



Netherlands Genomics Initiative
nutrigenomics consortium
Diabetes Fonds
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nzo nederlandse zuivel organisatie
TI FOOD NUTRITION
MARIE CURIE ACTIONS
NuGO the european nutrigenomics organisation
IDEAL ageing
NuTrTech
WAGENINGEN UNIVERSITEIT
WAGENINGEN UR
Netherlands Nutrigenomics Centre