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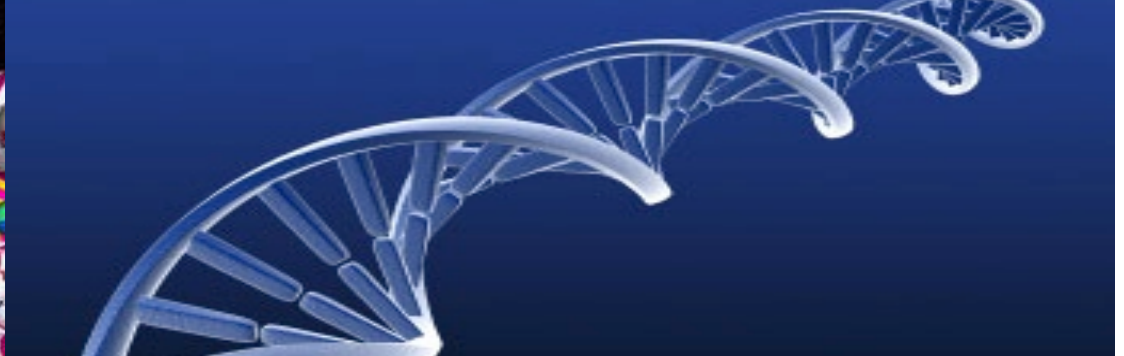
Nutrigenomics, health's new ally

NTU/LKC Medicine – NHG Research Seminar
Population Health
15 August 2014

Walter Wahli



Is there a **DIRECT** link between nutrition and gene activity ?



What is the natural diet for a human being?

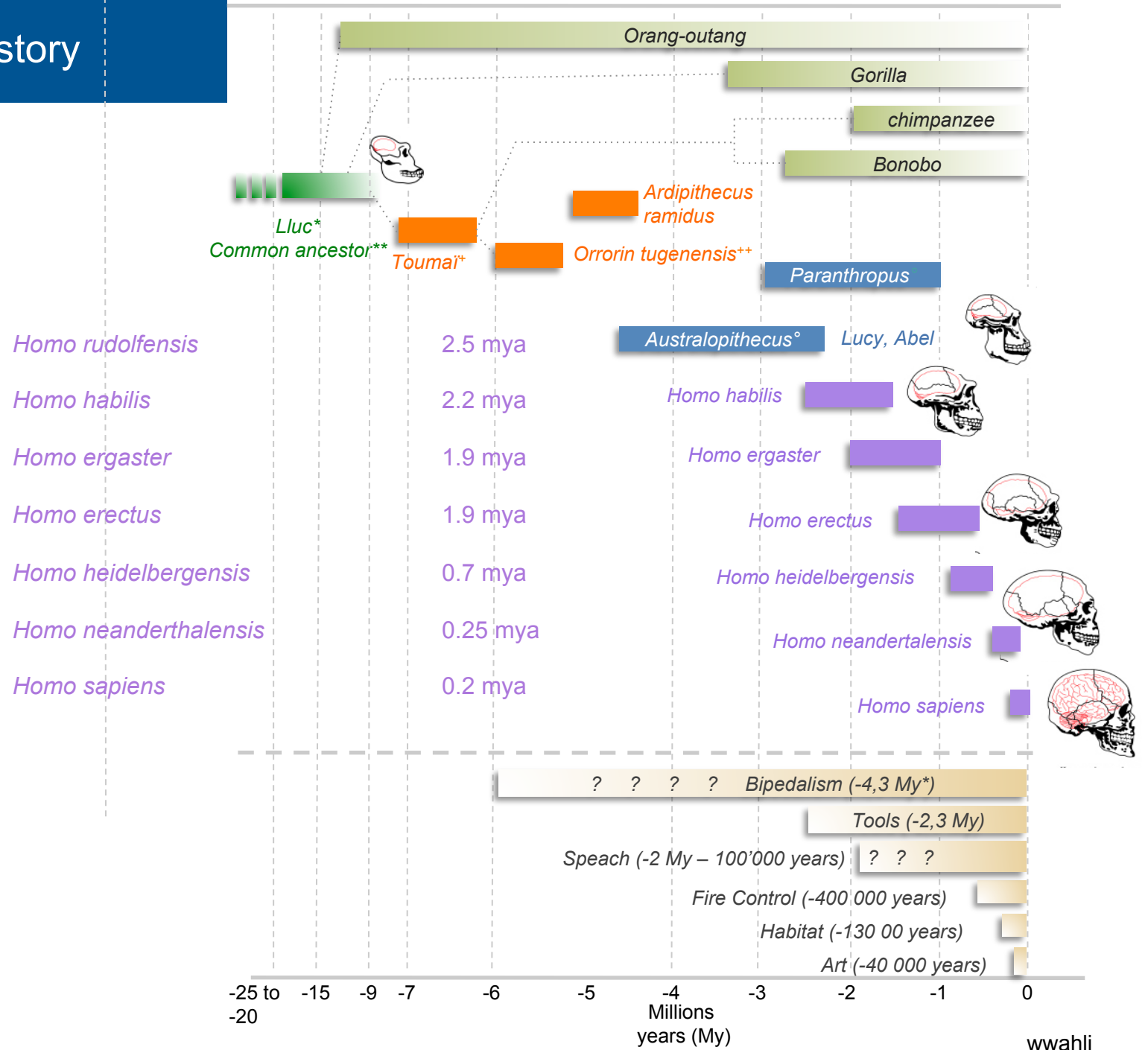


- What can an evolutionary / natural history perspective offer?



Our natural history

- Common ancestor(?)
- Apes
- Most ancient pre-humans
- Biped pre-human primates
- Humans
- Important developments

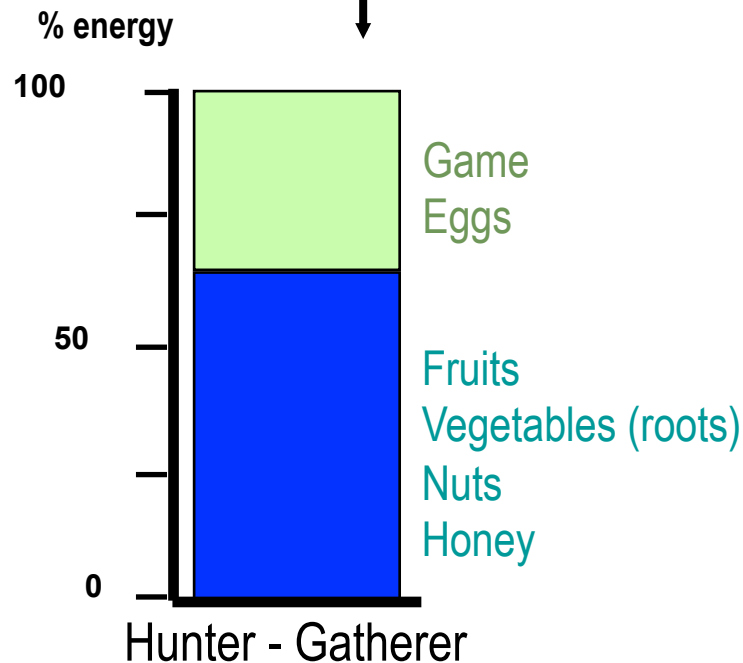


Environment – gene interactions

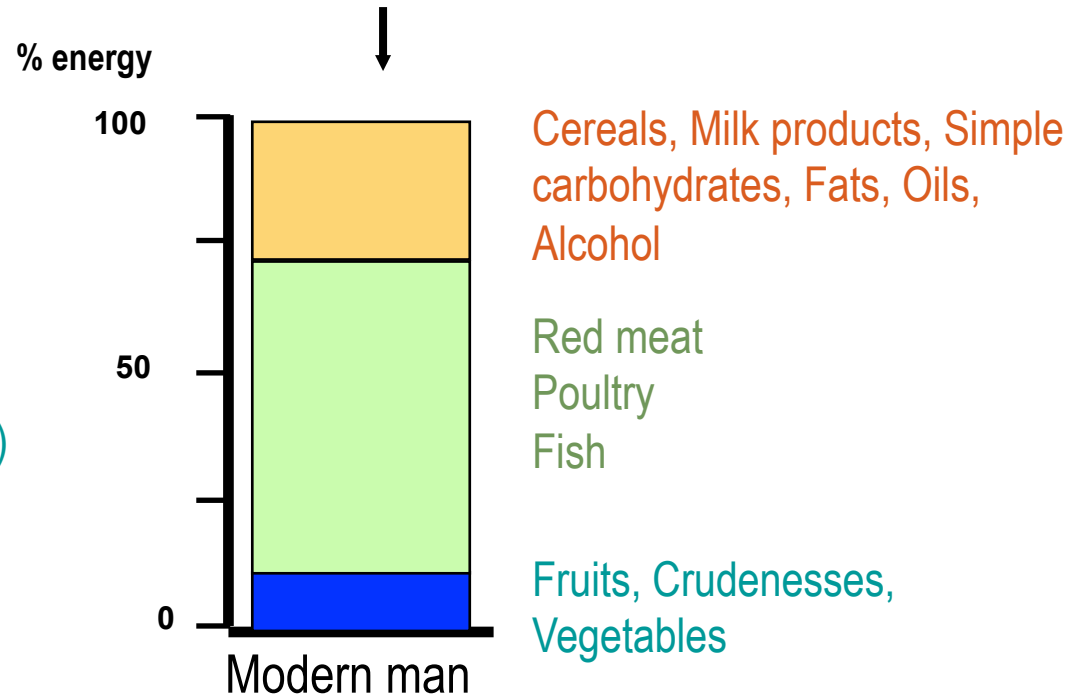
Genome stability vs huge food composition changes
- from Homo habilis to you and me -



From *Homo habilis* to you and me,
100'000 ~130'000 generations



Modern times
2 generations of plenty of food and
sedentary lifestyle



Evolution of the genome : ~ 0.3 % per MY → from 10'000 years ago (Neolithic period) = 0.003 %

The overweight pandemics and the prevalence of diabetes

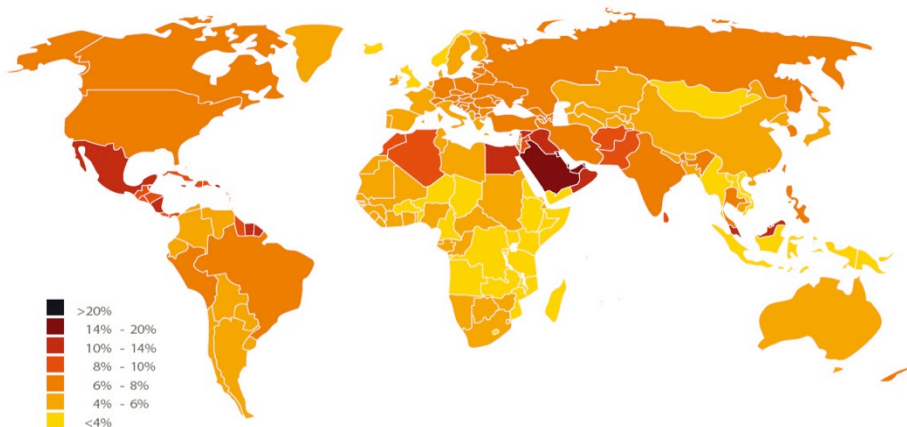
2.1 billion people obese or overweight

The obesity pandemic is not the consequence of mutations in our genome

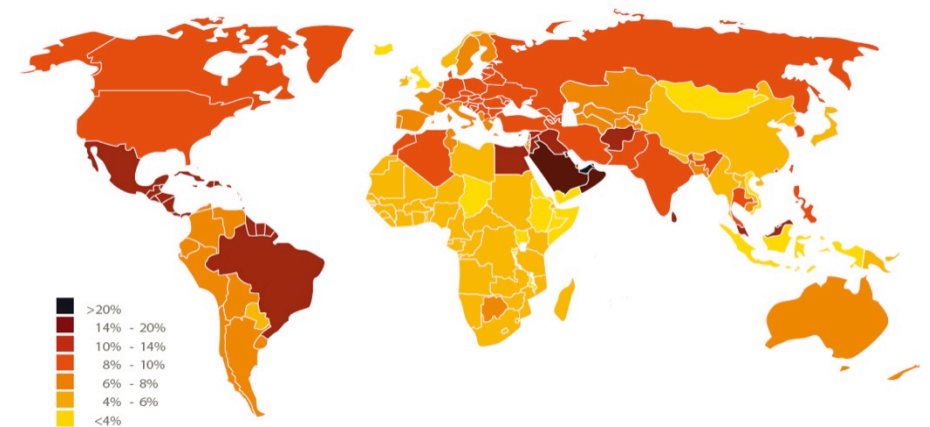
The obesity pandemic reflects the mismatch between modern diet, a sedentary lifestyle and our genetic inheritance



Prevalence estimates of diabetes, 2007



Prevalence estimates of diabetes, 2025



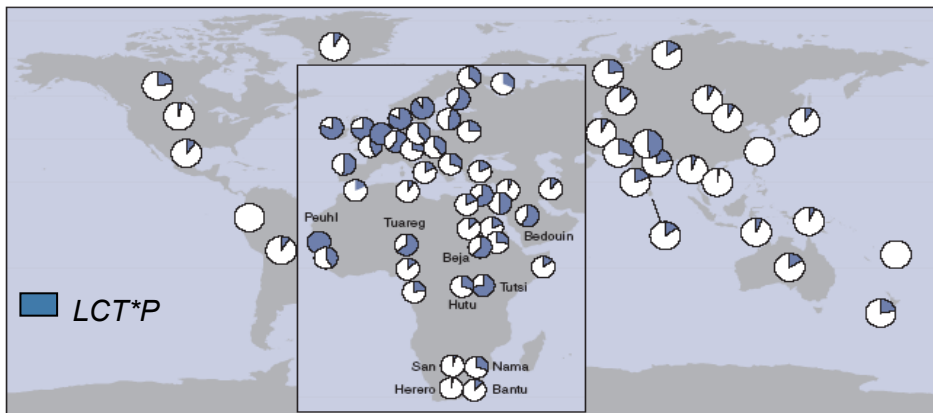
An estimated 285 million people, corresponding to 6.4% of the world's adult population, lived with diabetes in 2010. The number is expected to grow to 438 million by 2030, corresponding to 7.8% of the adult population.

The total cost of diabetes in the United States jumped from \$174 billion in 2007 to \$245 billion in 2012 wwahli

Lactase persistence

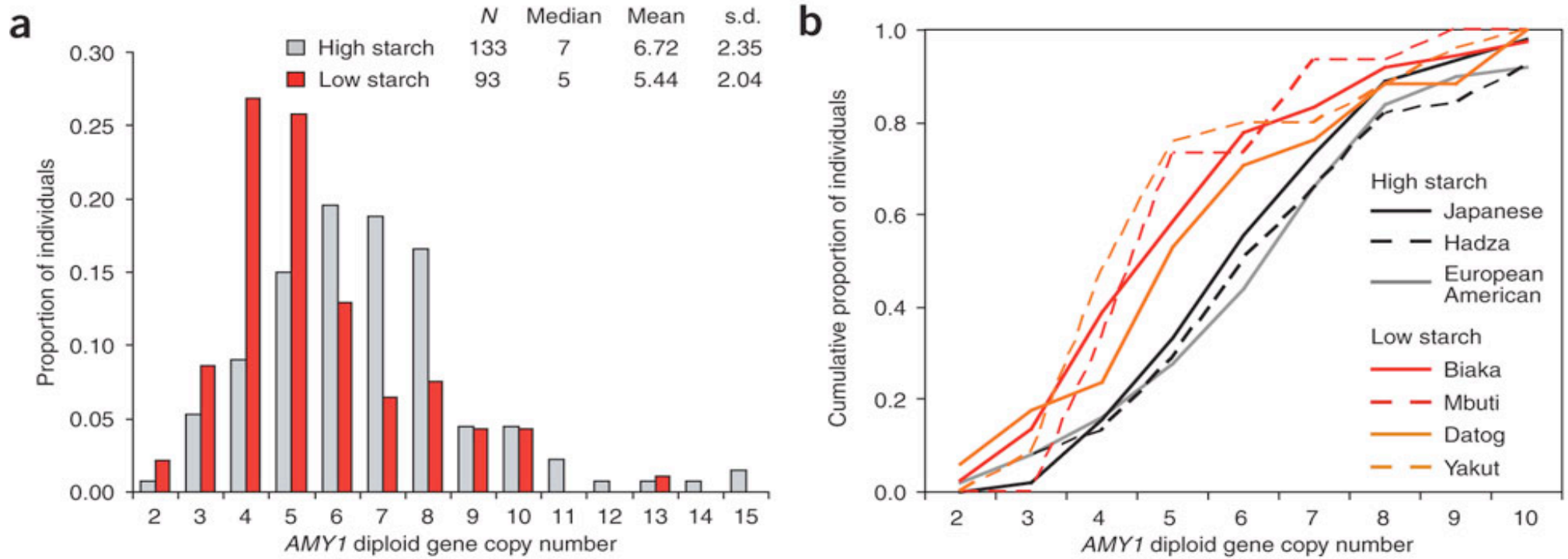
A strong selection occurred within the past 5,000–10,000 years, consistent with an advantage to lactase persistence in the setting of dairy farming.

- * All infants have high lactase enzyme activity to digest the sugar lactose in milk.
- * In most humans, activity declines after weaning, but in some it persists.
- * Lactase level is controlled by a cis-acting element. Association of lactase persistence with the T allele of a T/C polymorphism 14 kb upstream of the lactase gene.



Enattah *et al.* (2002) *Nature Genet.* **30**, 233-237
Besaglieri *et al.* (2004) *Am J Hum Genet.* 74(6):1111-20.

Starch rich diet and amylase gene copy number variation



Perry et al. Nat Genet. 2007 Oct;39(10):1256-60.

wwahli



Population Genomics Reveal Recent Speciation and Rapid Evolutionary Adaptation in Polar Bears



Polar bears and brown bears diverged less than 500,000 years ago.

Genes on the polar bear lineage have been **under stronger positive selection** than in brown bears;

9 of the top 16 genes under strong positive selection are associated with **cardiomyopathy and vascular disease**, implying important reorganization of the cardiovascular system.

One of the genes showing the strongest evidence of selection, **APOB**, encodes the primary lipoprotein component of low-density lipoprotein (LDL).

Functional mutations in **APOB** may explain how polar bears are able to cope with life-long elevated LDL levels that are associated with high risk of heart disease in humans.

Healthy preventive nutrition

Do nutrients control gene expression ?

A balanced ENERGY providing fraction -
Macronutrients

Carbohydrates

from diverse and complex plant products
Low amounts of purified sugars

Proteins from diverse
animal and plant origins

Lipids

Rich in monounsaturated fatty acids
and
balanced ratio of omega-3 and omega-6
fatty acids

Complex REGULATORY
Fraction - Micronutrients

Vitamins (group B, C, A, D, E, K)

Minerals (K, Ca, Mg, ...)

Oligo-elements

(Fe, Zn, Cu, Se, Cr,...)

Protective micronutrients

Carotenoids

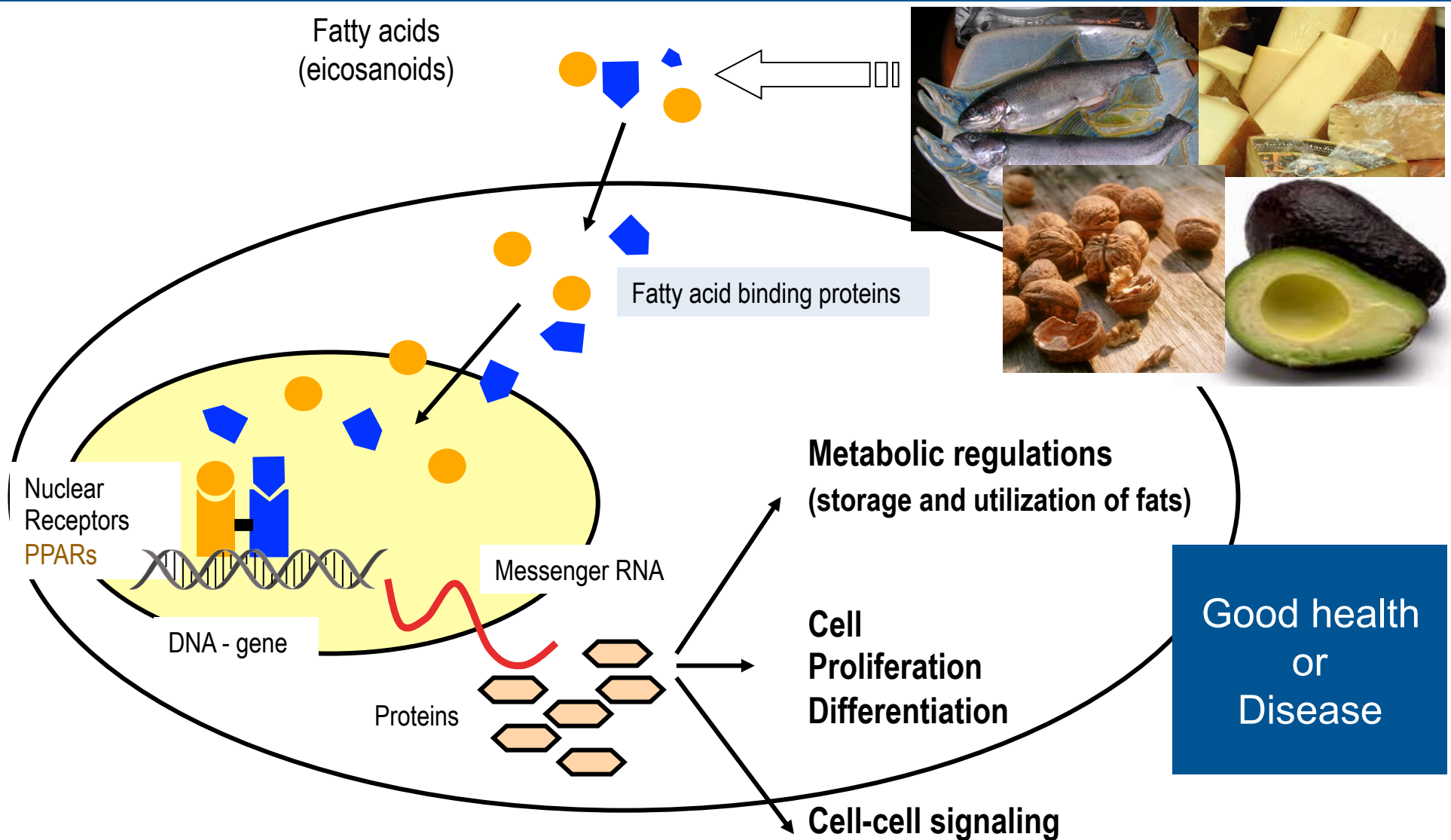
Polyphenols

Phytosterols

...

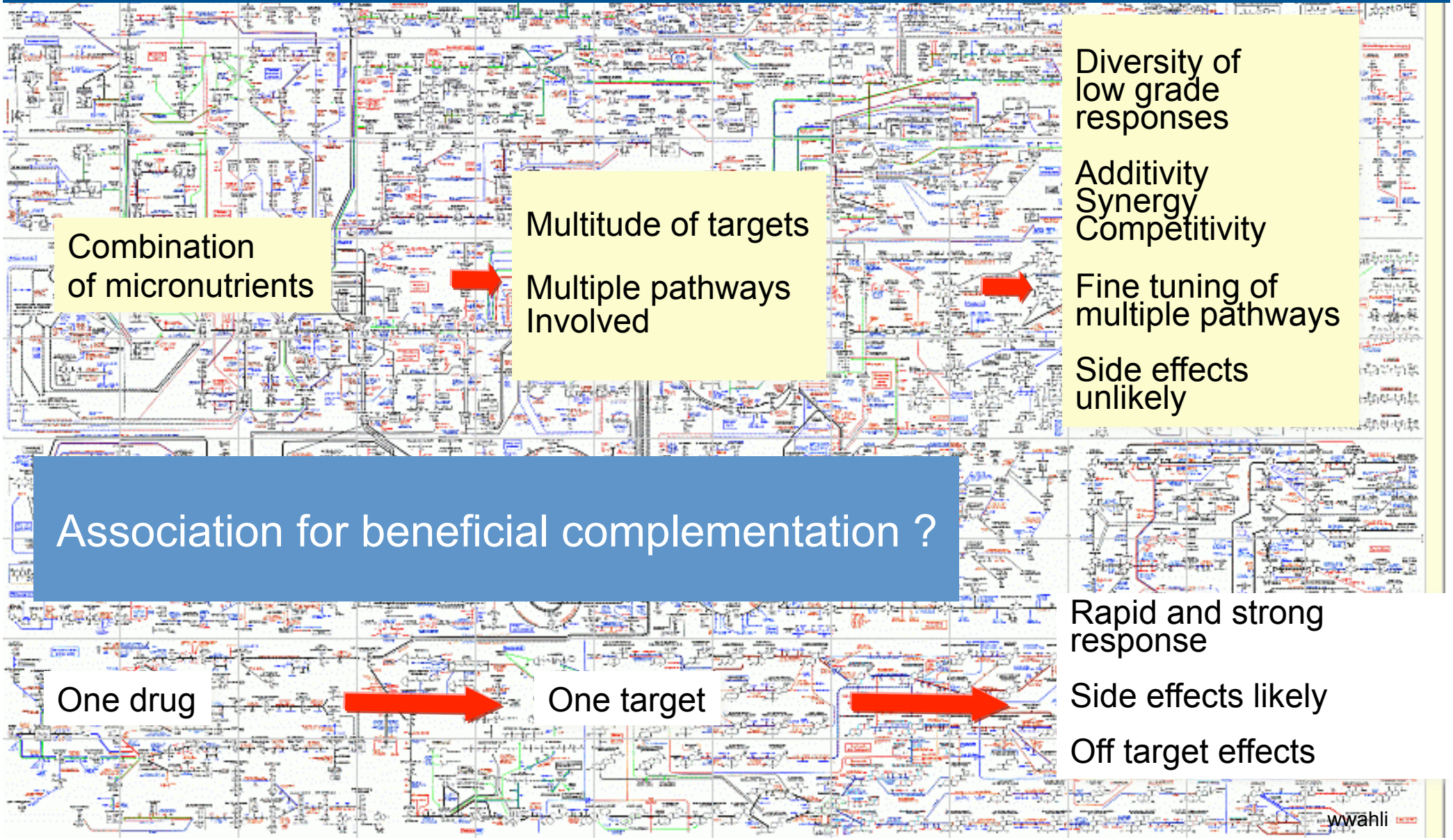
Alimentary fibers (30g/day)

Fatty acids modulate gene expression through PPARs



Micronutrients also modify the epigenetic profile of genes (DNA methylation, histone modifications) (folate, choline, methionine, betaine)

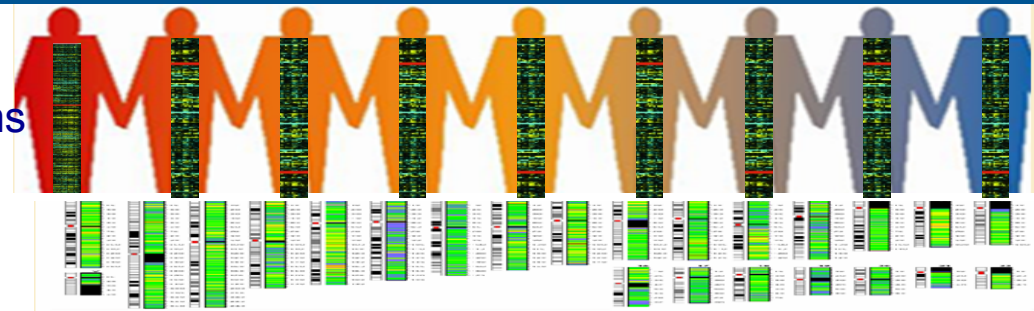
One drug - one target
Multiple micronutrients - multiple targets



Does one size fit all - Personalized nutrition - Fine tuning nutrients

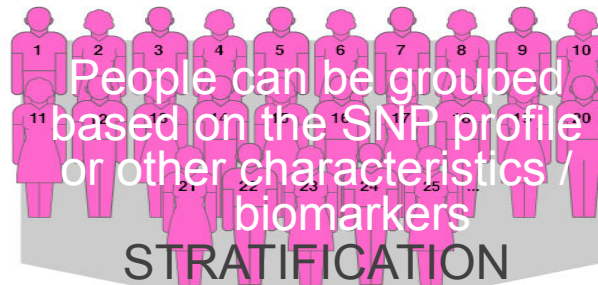
WELLNESS - PREVENTION & DELAY IN DISEASE PROGRESSION - AGING

Not everyone responds similarly to foods.
 People / Patients are “different” by polymorphisms
 (SNP, CNV, Epigenetic marks)



Disease prevention
 Early phase of a disease

Promotion and maintenance
 of good health

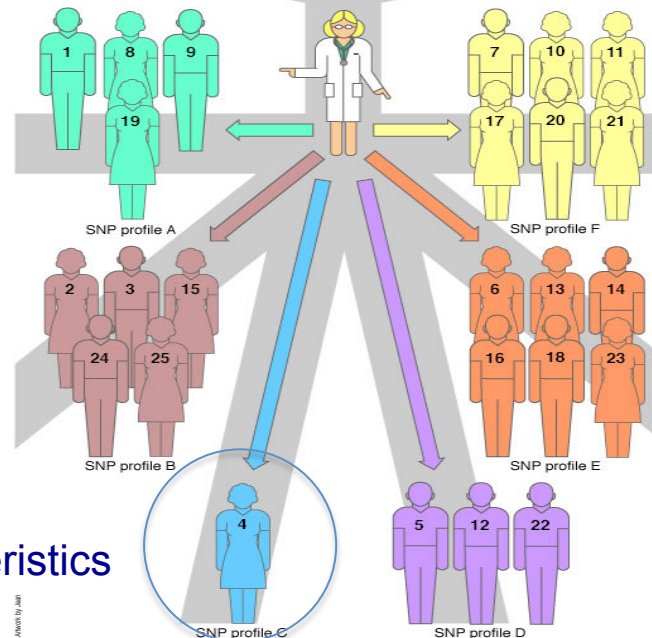


Mixed hyperlipidemia

Predisposition for
 Type 2 diabetes

Inborn Errors of Metabolism

Unique characteristics



Age
 Gender

Sedentary lifestyle
 Regular physical activity

Ethnic background

Personalized Nutrition : time has come to develop it !

Science

Human genome elucidated
High throughput techniques and
“Omics” technologies developed
Nutritional genomics

Medicine

Therapeutic nutrition

Individuals / Patients

Health awareness

Society

Drive towards prevention

Food industry:

Novel market niches
Business opportunities

SNP's and nutrition



Food science
Communication



“Prêt-à-manger”
Foods
and/or
Personalized
nutrition

