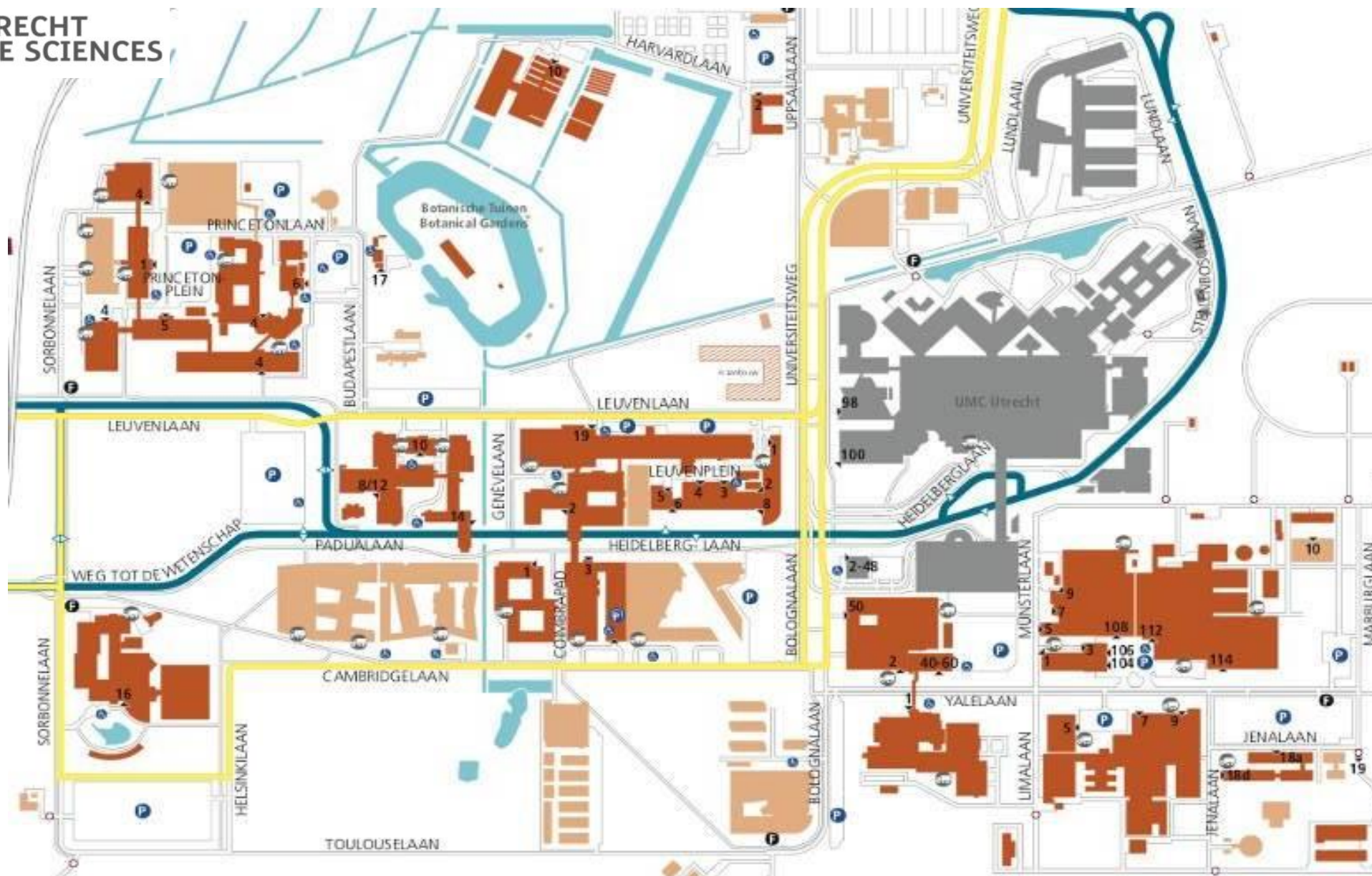


Bruggen bouwen voor innovatie in onderzoek en onderwijs: food pharma als een voorbeeld

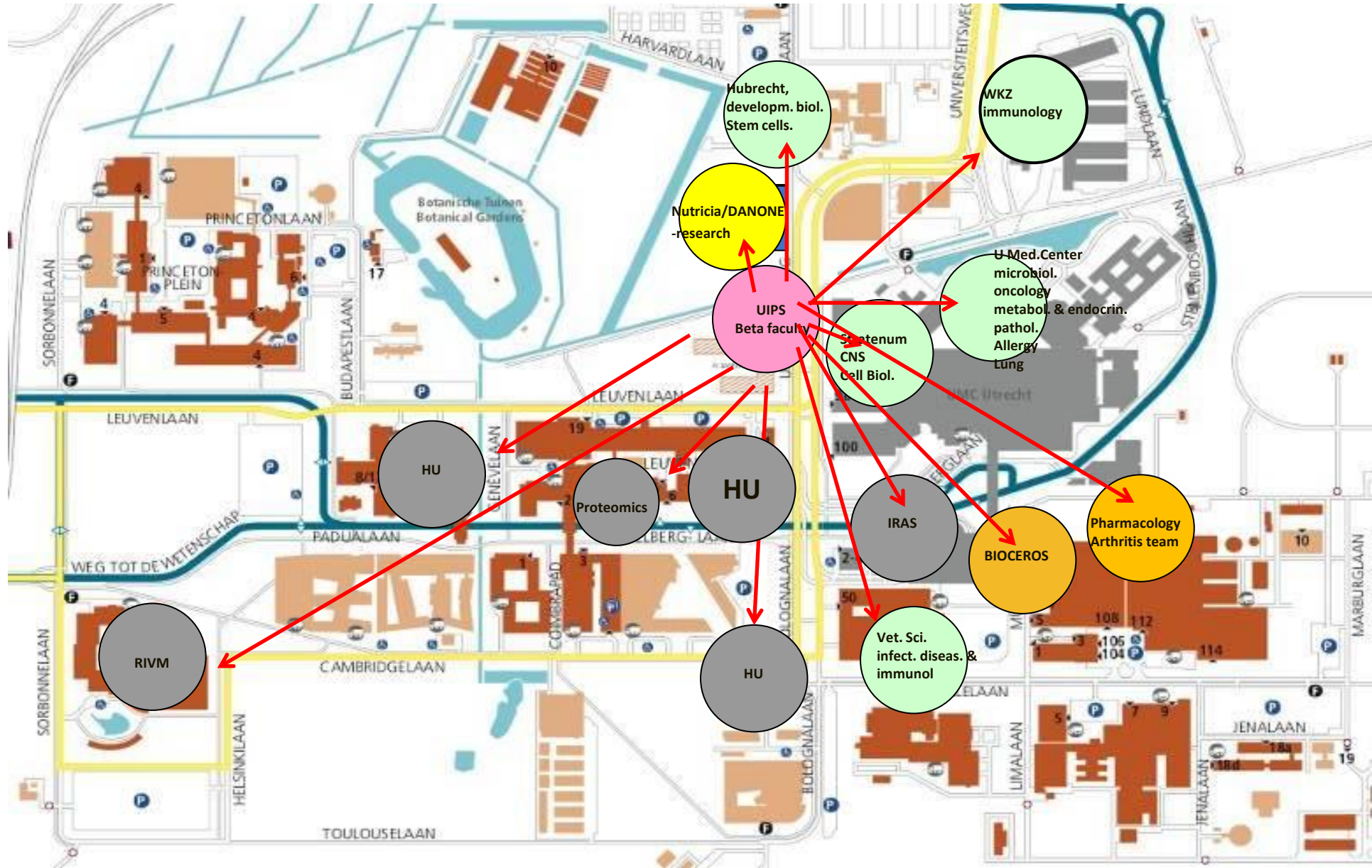
Prof. Johan Garssen, MD, PhD
Head Pharmacology, Beta Faculty, Utrecht University
Chief Scientific Advisor Danone-Nutricia-research

A bit about myself/conflicts of interest

- **Medicine and Medical Biology, Free University Amsterdam (1987)**
- **PhD Pharmacy, Utrecht University, several postdoc projects (Netherlands/USA)**
- **RIVM/VWS (1994) (drugs, food, exposome...)**
- **2002 NUMICO**
- **2005part-time Utrecht University - program leader immunopharmacology**
- **2006NUTRICIA and DANONE....research moved to Utrecht some years later**
- **WHO global health task force//Ad boards HUBRECHT; NWO; DSM; Nutricia medical; RDLV; *EUREKA*; international government business/innovation missions; Chair Future Food Utrecht research hub**



Embedding in Life Sciences Utrecht (present collaborations)



Some highlights together with this unique school/university of applied sciences:

3Rs: alternative for animal testing in the area of allergy. Methods used and accepted by several industries. A standard within Danone Nutricia for cows milk allergy

Systems biology: focus on immune

NWO grants for teachers working on a PhD

Healthy volunteer studies (exercise, immune markers.....PhD thesis almost finalized)

Lectures/Workshops/Internships/Research grants



Brainstorm session EU summit on innovation for health (2019, Brussels)

- World is changing.....**digital (r)evolution**.....
- A need for **translational** medicine-
from ingredient/molecule to health benefit
(prevention/treatment)- what is health?
- Multi-national/**Diversity**: different cultures, regulations,
reimbursement, funding
- Research and teaching/**communication**
- Alliances: Industries vs Universities (**dirty or needed?**)
- University of **Applied** Sciences for **translation**

Fast changing environment



Luca Bruno / AP

Fast changing environment



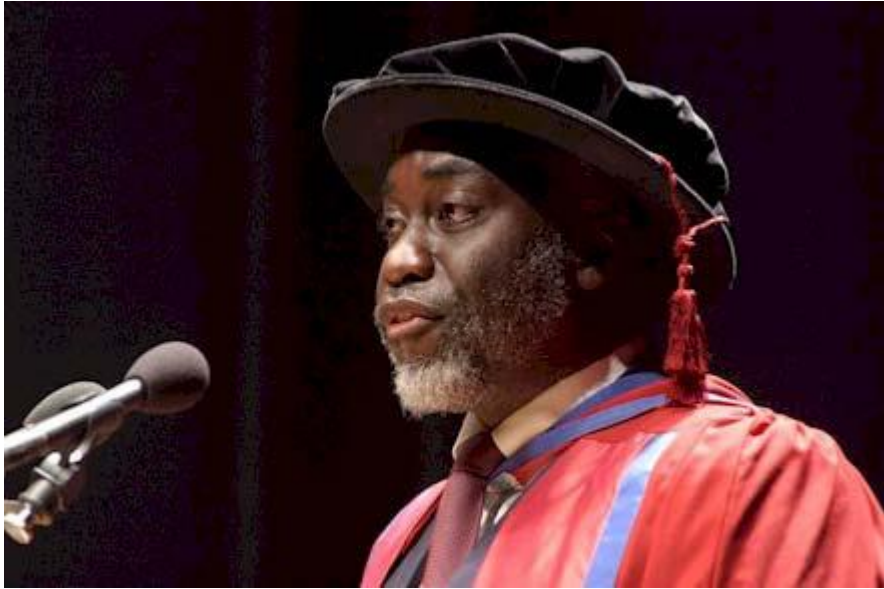


Mauritsschool, 1970, Papendrecht



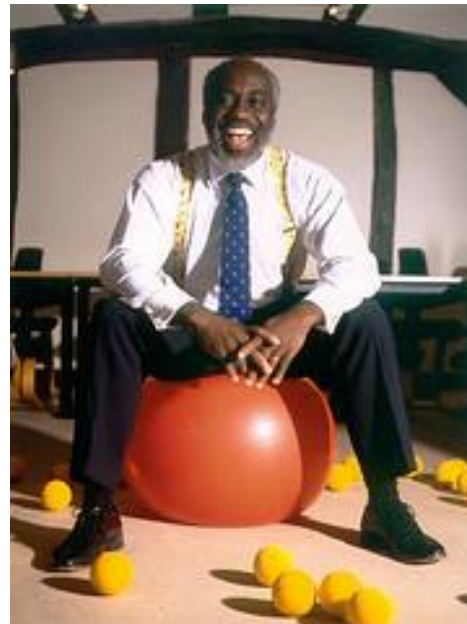


WORLD AFTER MIDNIGHT (WAM)



Prof.dr. Eddie Obeng

"We have moved as a world, from an age when we could learn faster than our local environments change to one where the local environment of individuals, organisations, and governments changes faster than we can learn."



Verbinden (oud en nieuw)

Verbinden van mensen

Verbinden van culturen

Verbinden van onderzoekers, expertises

Verbinden van onderwijs en onderzoek

Verbinden van food en pharma

Verbinden van public en private

DIVERSITEIT



Bridging (life sciences) between different cultures/continents



Bridging life sciences between profit and non-profit organisations [valorisation]



UIPS: Translational medicine

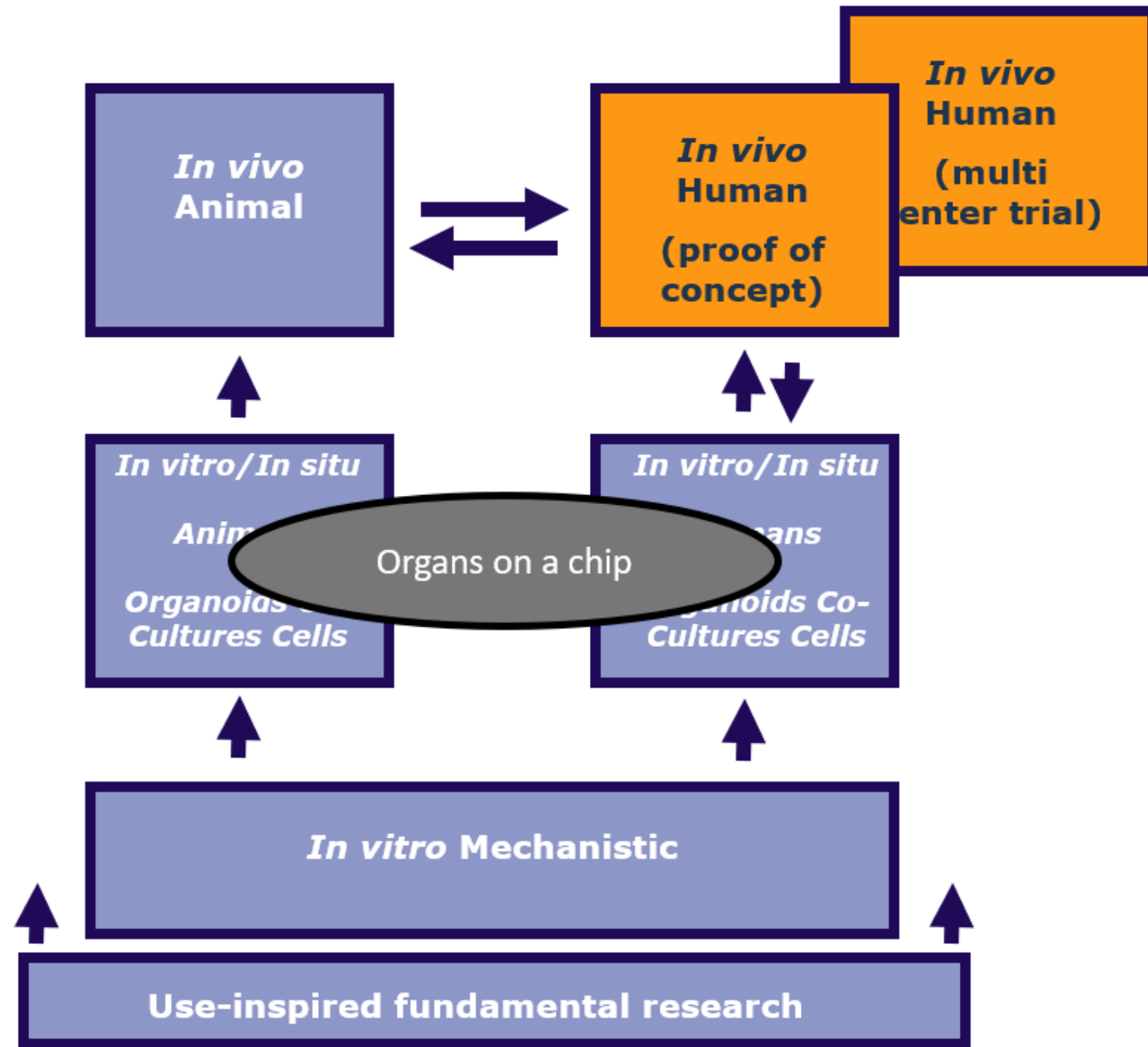
Disease



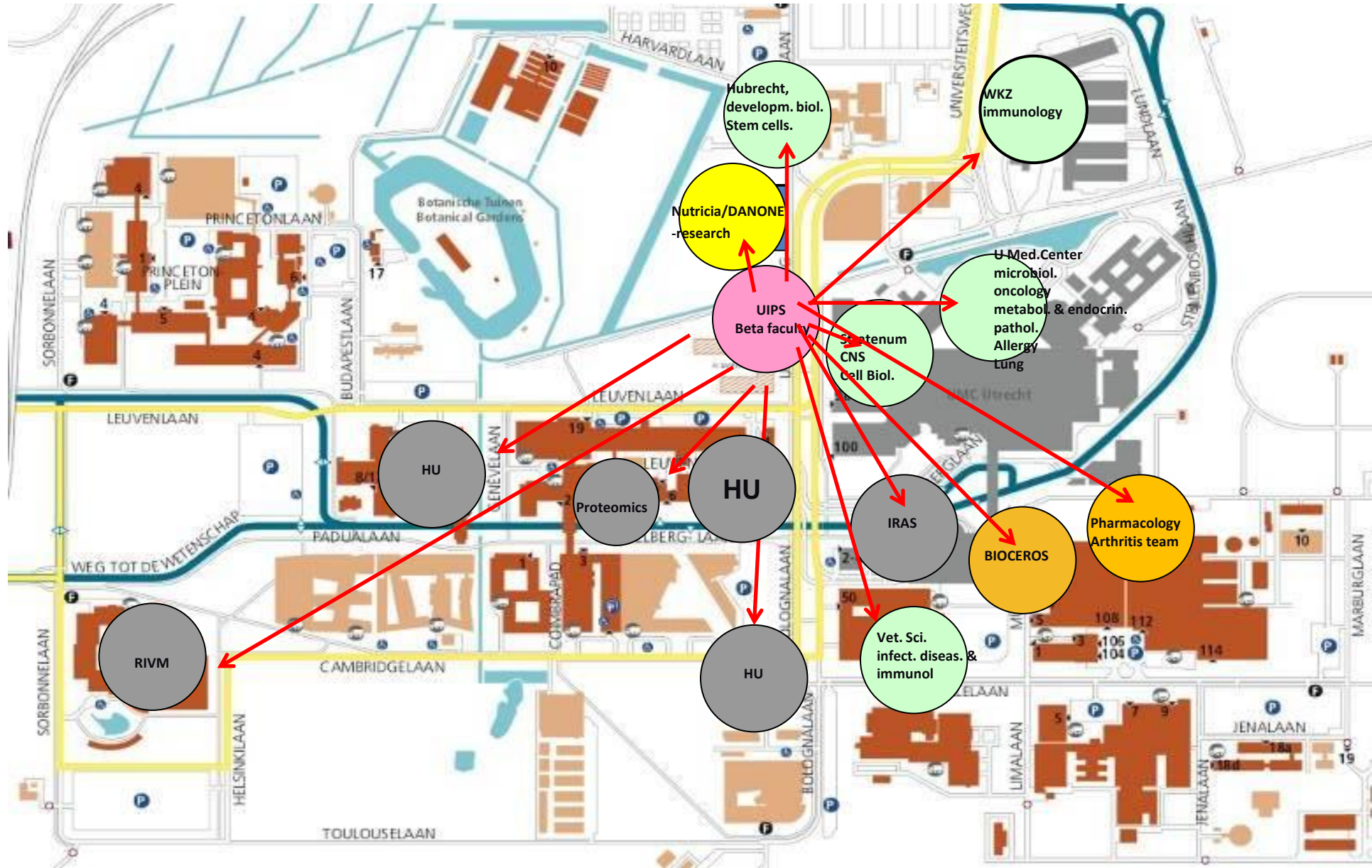
**Drugs/Specialised nutrition
Therapy and Prevention**

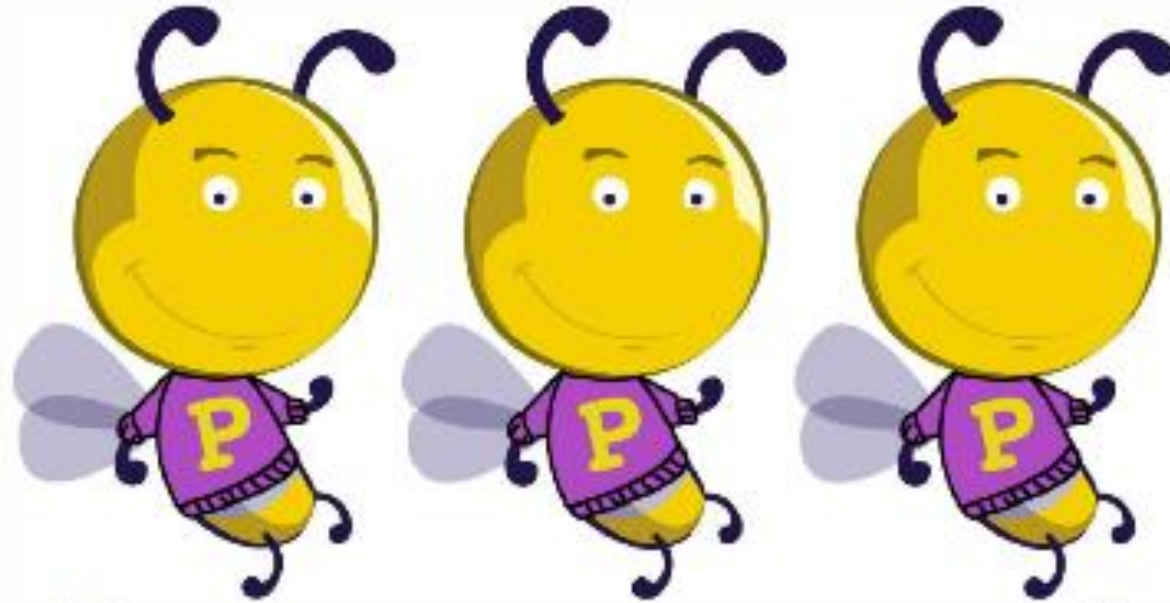
Mission: From bench/molecule to bedside

Translational medicine/research



Embedding in Life Sciences Utrecht (present collaborations)





Public Private: Perfect!

Translational Medicine
from bench to bedside



TI PHARMA



NCDS ARE THE LEADING CAUSE OF DEATH GLOBALLY

While global health resources are currently focused largely on infectious diseases, Non-Communicable Disease (NCDs) affect more people and are a “silent epidemic” in middle-income countries.



OF ALL
GLOBAL
DEATHS
ARE CAUSED
BY

NON-COMMUNICABLE DISEASES

• Cardiovascular • Cancer • Chronic Lung • Diabetes

80% OF DEATH OCCUR IN LOW AND MIDDLE-INCOME COUNTRIES

Why are NCDs (including allergies) so increasingly common?

No change in genes/mutations!!

- Altered environmental diversity (dysbiosis)?
- Altered lifestyle?
- Industrial technologies?
- Altered antigen/allergen
- Pollution?
- Dietary
- Microbiome hypothesis?
- Change in infectious triggers?
- ???

change in our exposome

Key role for immune system!!

**WHO global health (Washington 2013):
there is a need for better preventive and
therapeutic protocols in order to manage
our modern diseases (*NCDs*: immune
related disorders, brain disorders,
metabolic disorders)**



**Multidisciplinary and integrated approach
(Specialized) Nutrition, Pharma, Lifestyle, Define groups at risk
(breaking down the silos)**

WHO Goal “25 by 25”

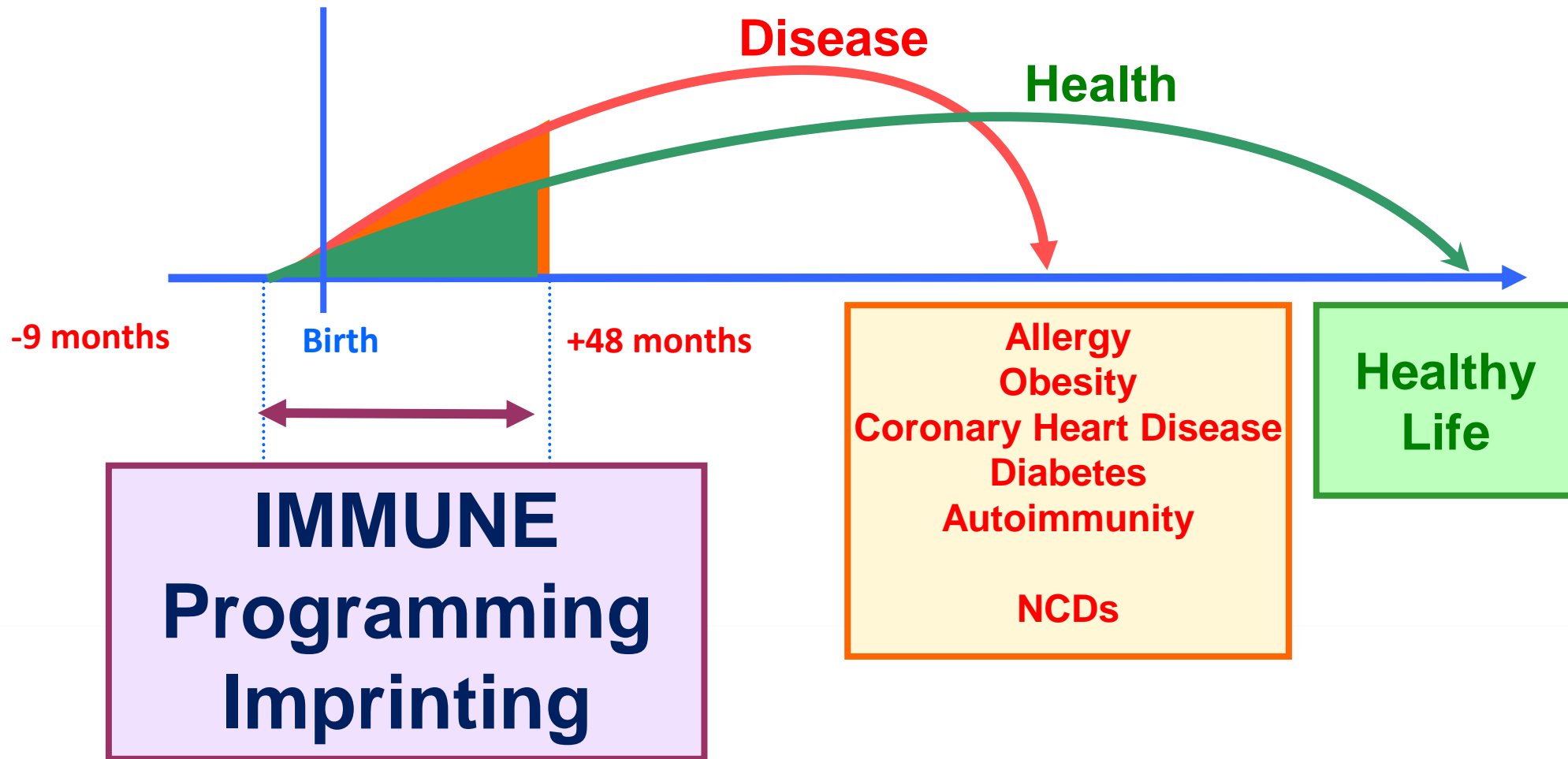
25% reduction by 2025 in mortality from non-communicable disease in persons ages 30 to 70 (prevention + treatment).

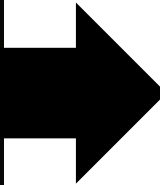


World Health Organization

PREVENTION of NCDs

Early life: Setting the Right Course for Later Life





WHO definition of health

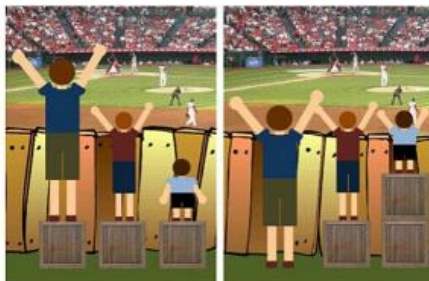
- *“Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”*



The ability to adapt

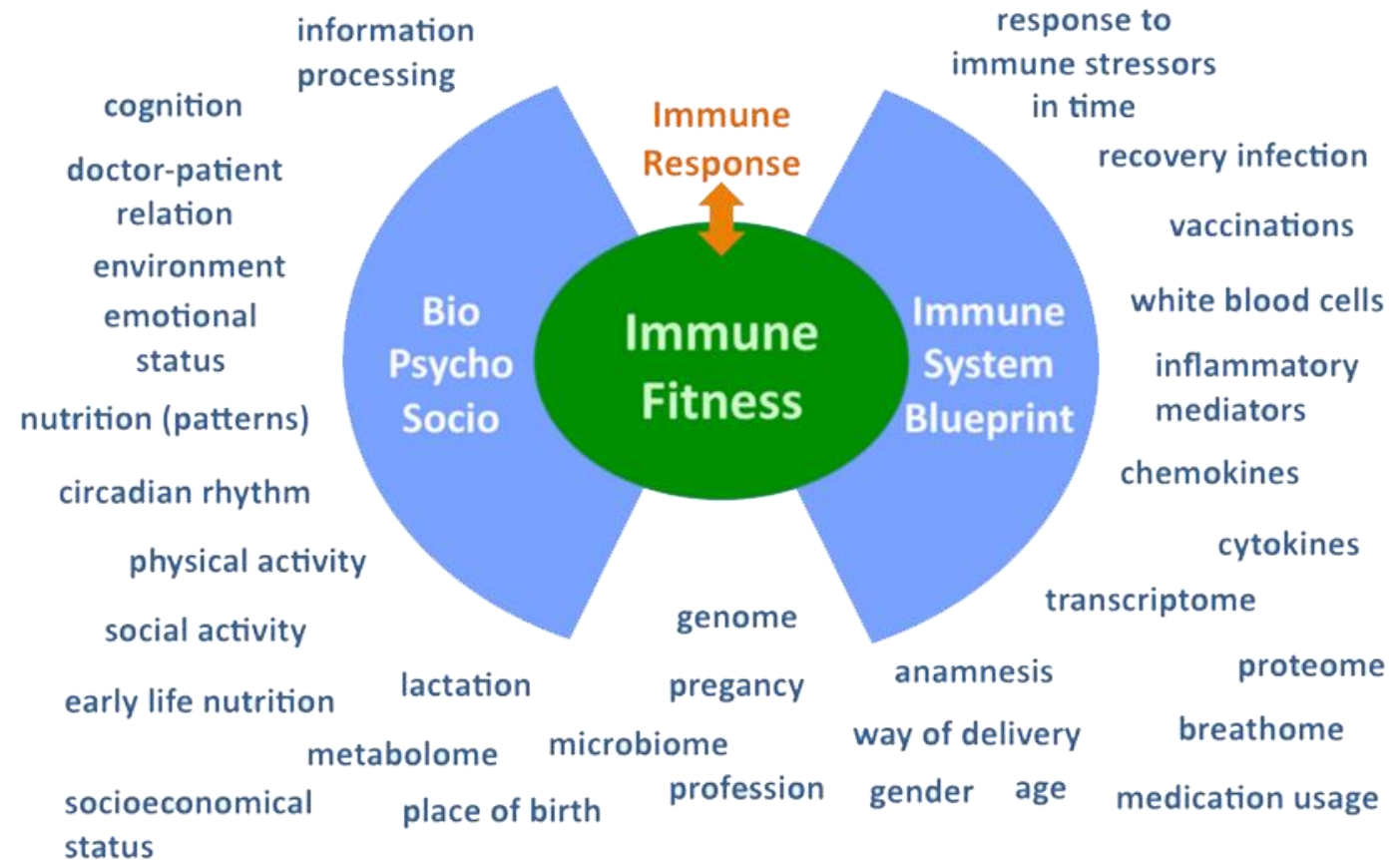
re·sil·ience:

the ability to bounce back when faced with stress or pressure.



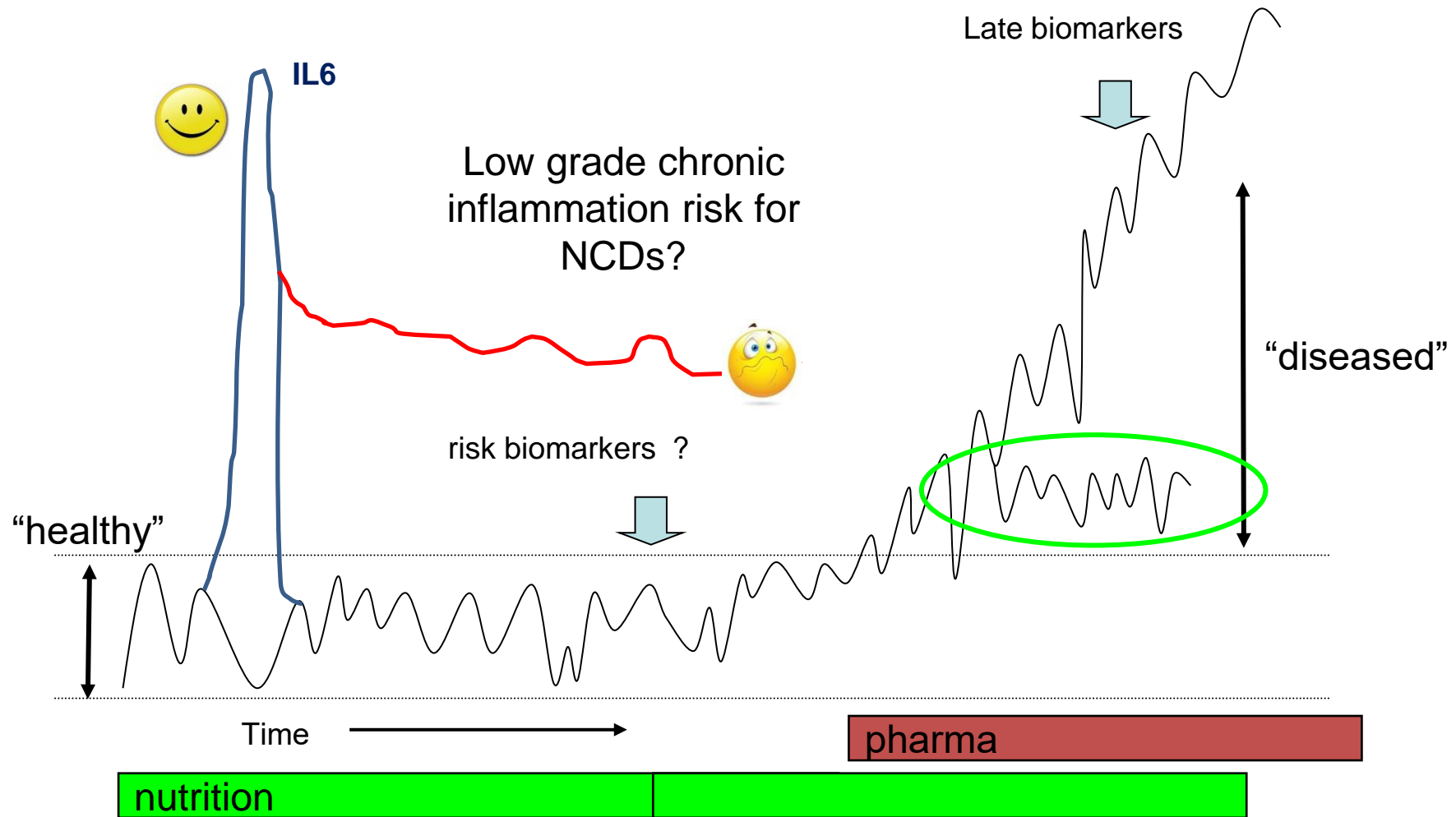
Immune fitness: are we fit to fight for health

Immune fitness refers to a ***resilient*** immune system with an **inbuilt capacity to adapt to challenges by establishing, maintaining and regulating an appropriate immune response**



Te Velde et al, dec. 2016; Renz et al, dec. 2017

From Healthy to Diseased: Loss of resilience

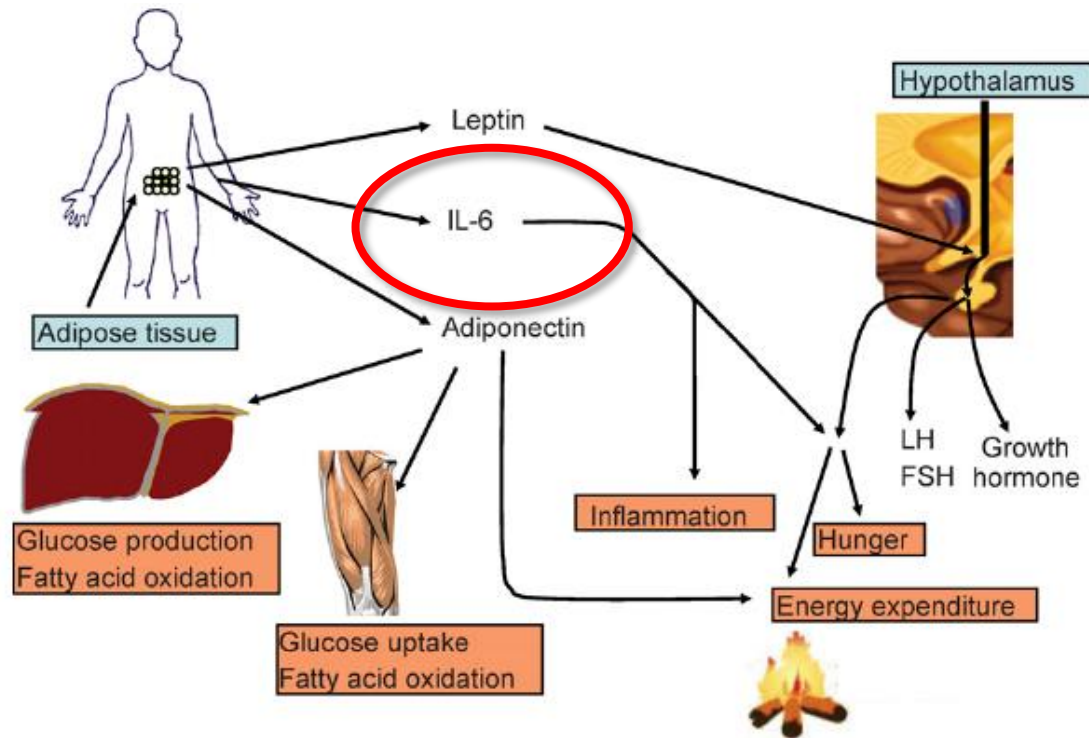


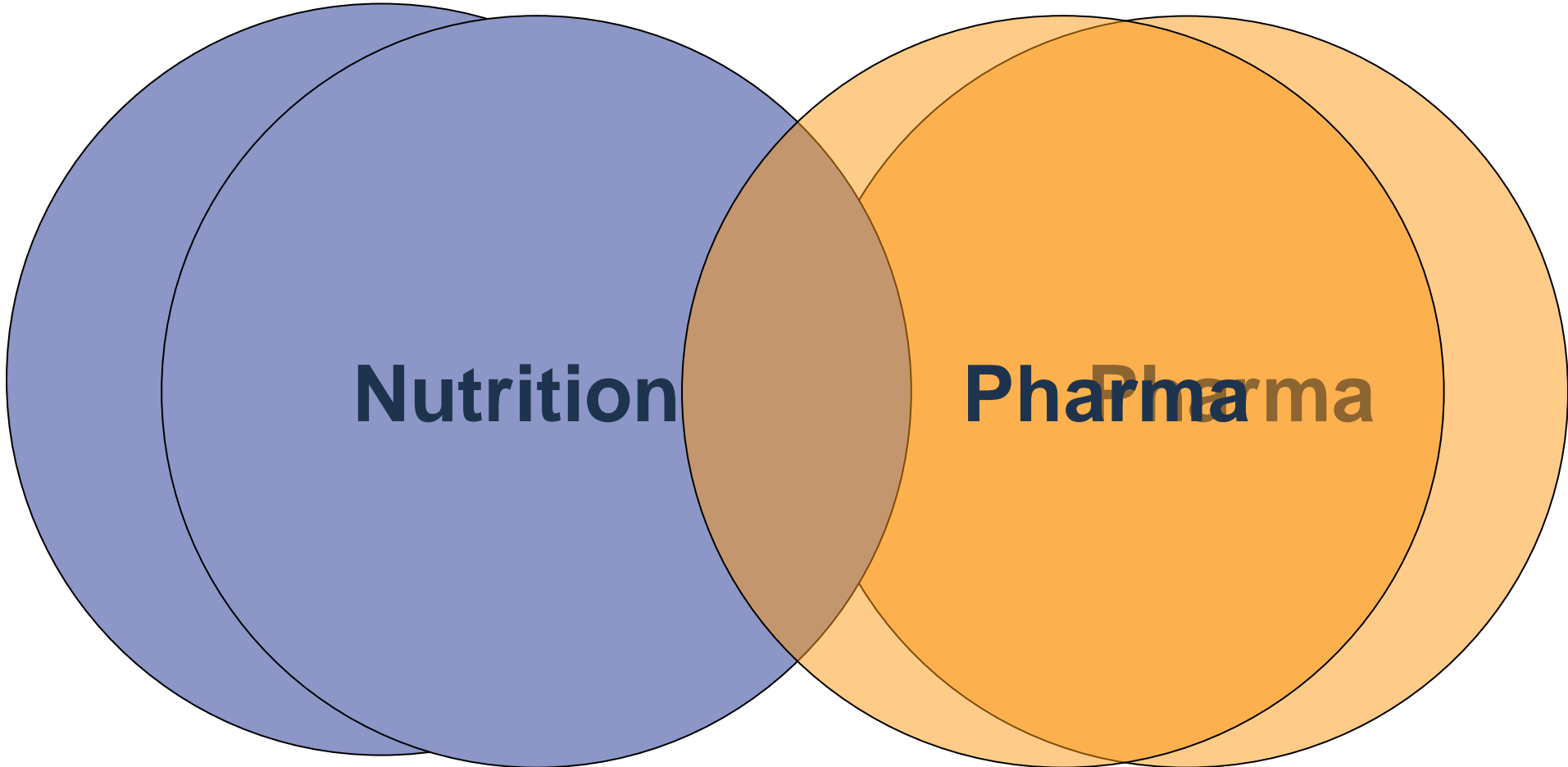
Preliminar data (proof of concept study):

Universities Leiden/Utrecht

80 Females BMI 40+

Abdominal fat monocytes. **increased IL6 predictive** for the onset of insulin resistance/diabetes within 2 years, not predictive for BMI changes

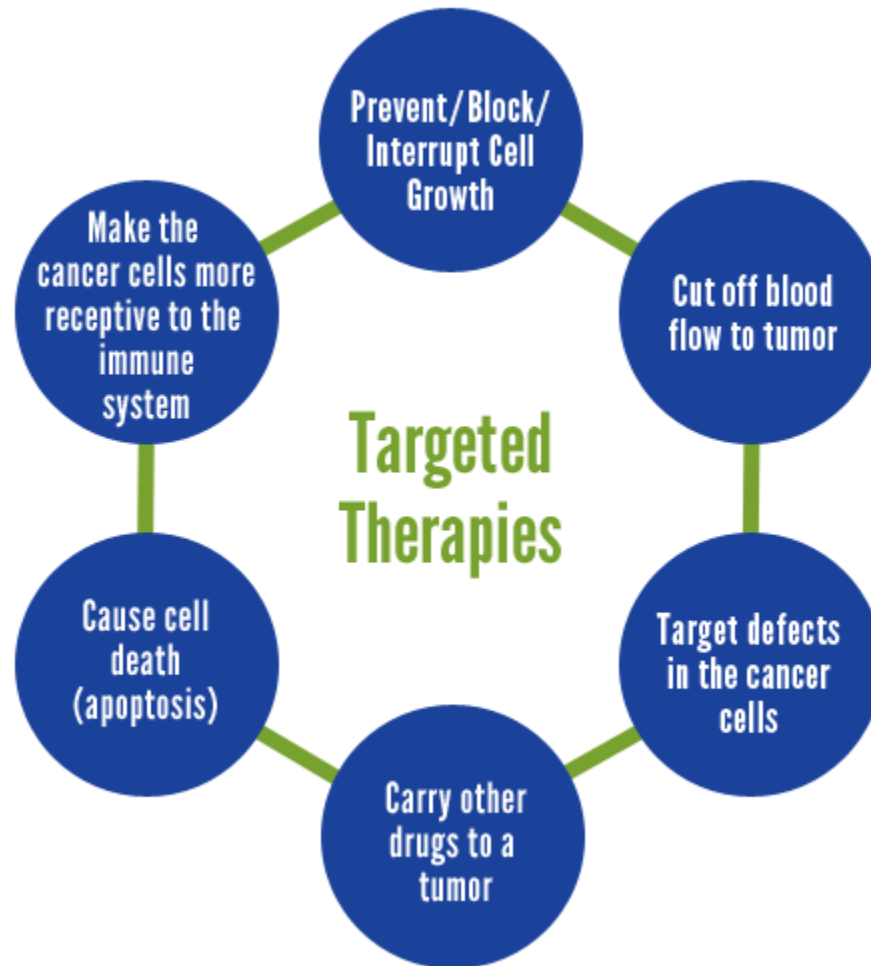




Nutrition

Pharma

From single towards multitarget approaches
(cancer)



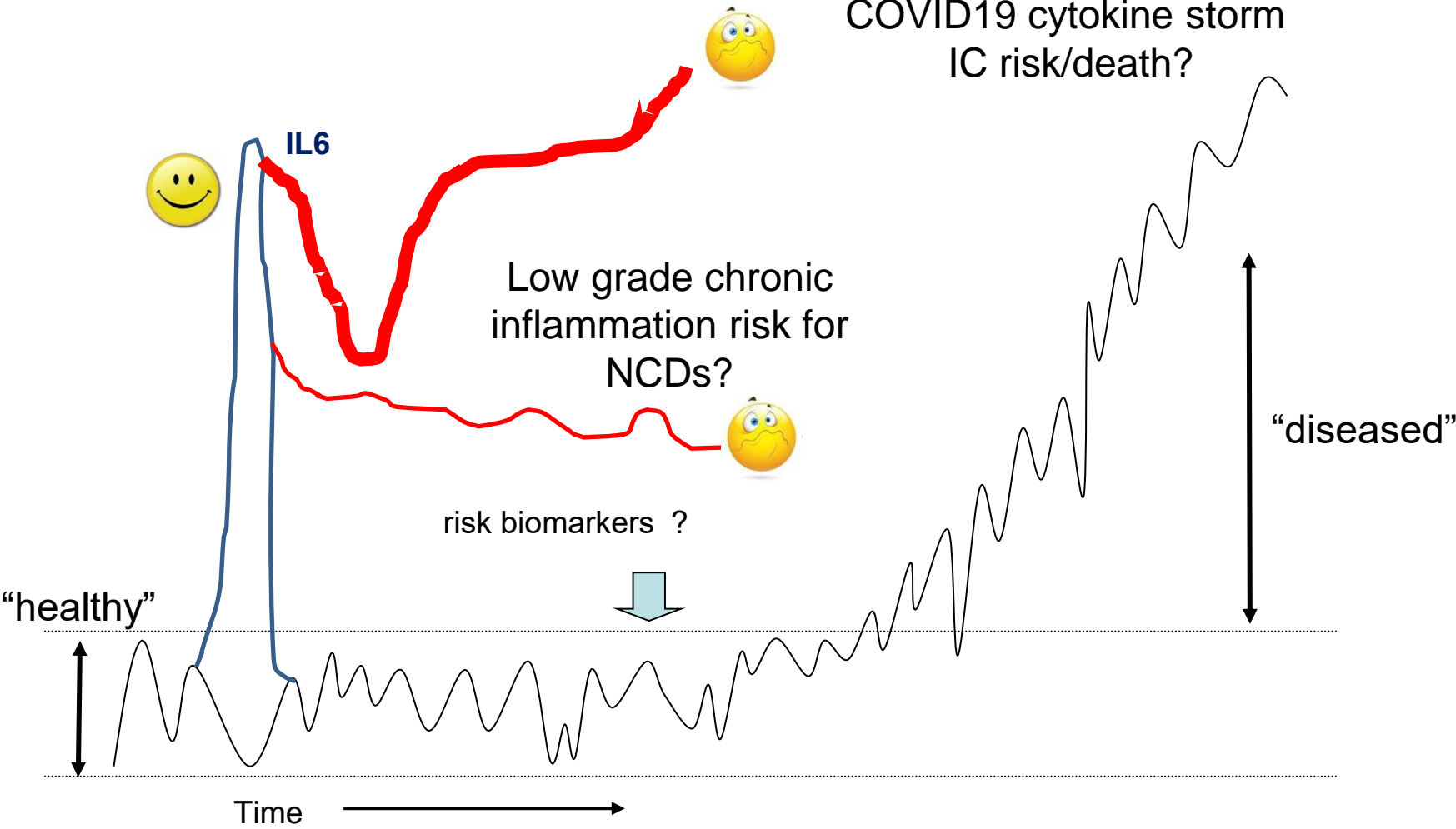
Cachexia
Malnutrition
Fatigue
Systemic inflammation
Infections
Mucositis

...



MEDICAL NUTRITION

From Healthy to Diseased: Loss of resilience



Immune disorders and NCDs

Hyper immune- responsiveness:

Allergy

Autoimmunity

Chronic inflammation

Hypo immune- responsiveness:

Infections

Metastasis

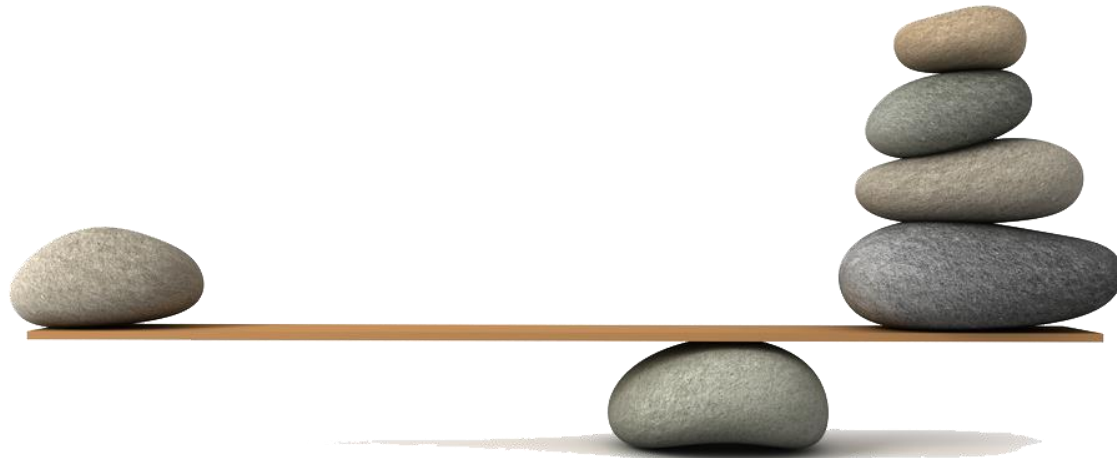


Role in metabolic disorders: **Metabolism**

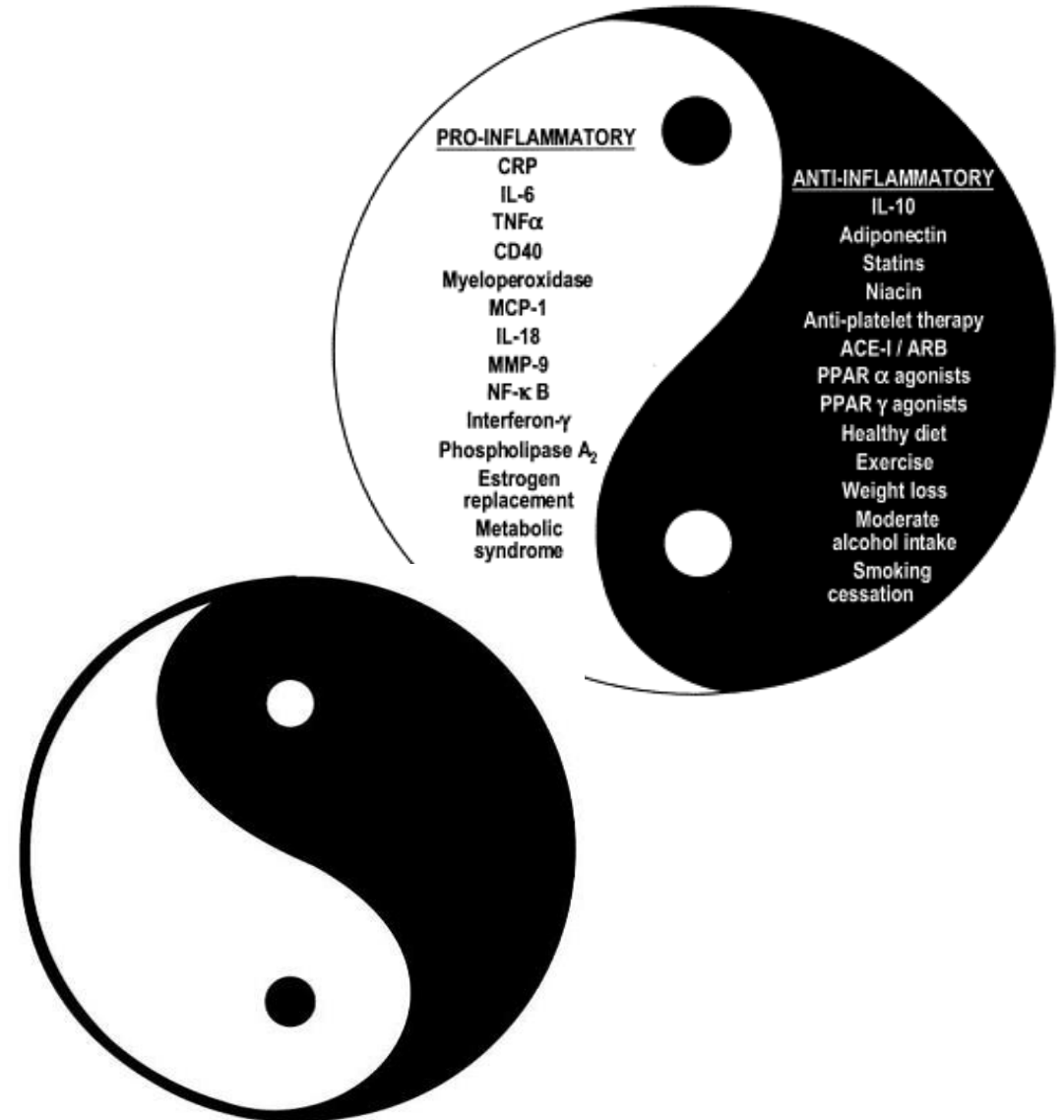
Role in cachexia/sarcopenia

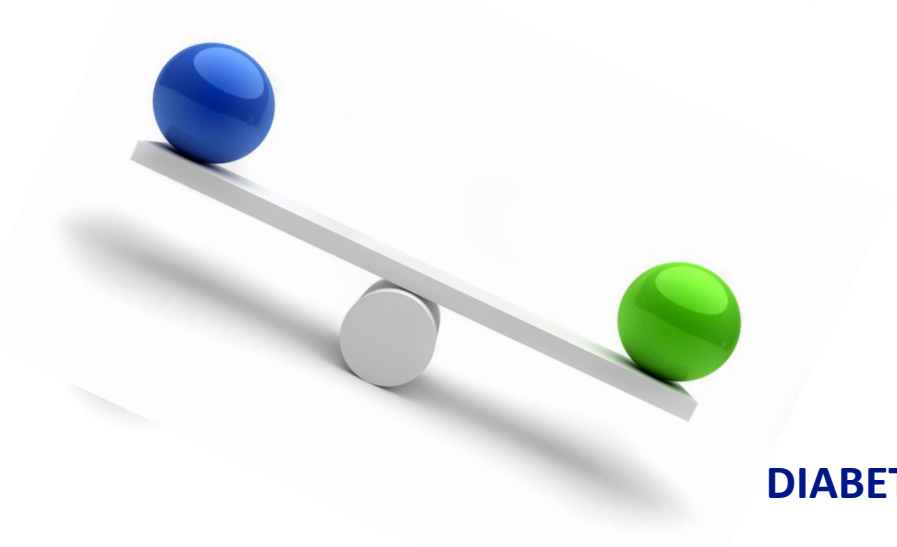
Role in neurological disorders: Autism, Alzheimer, Depression, Hyperactivity Syndrome, ...

Immune fitness a healthy balance and resilience



INFLAMMATION MANAGEMENT

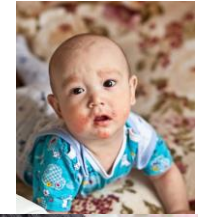




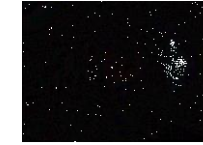
INFECTIONS



ALLERGIES



DIABETES, OBESITY

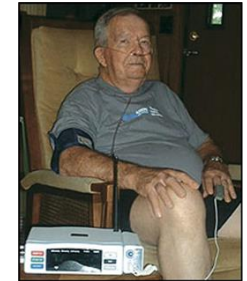


COPD

NEC



**CANCER
CACHEXIA**



IMMUNOSENESCENCE



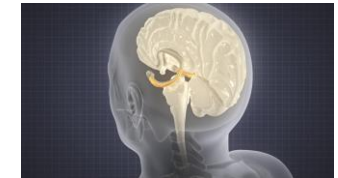
ALZHEIMER

ARTHRITIS



PARKINSON

AUTISM



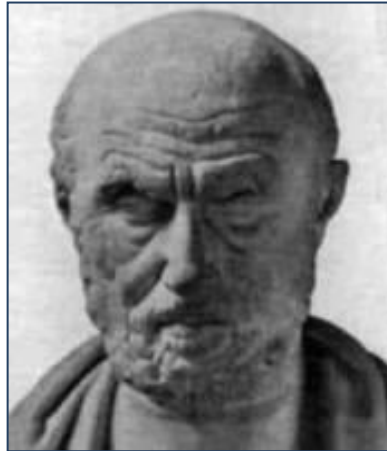
NCDs are the leading cause of death globally in high, middle and even low-income countries. Estimations indicate > 60%

THE Gut as an important part of our immune system

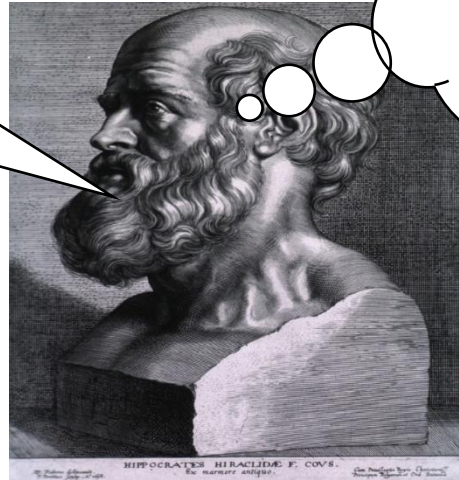


***“Let medicine be thy food,
and food be thy medicine (food for health)”***

Hippocrates of Cos, Greece
460-377 B.C.



*"let food be thy
medicine and
medicine be thy
food"*



*Did I ever say that?
Sorry, but I really
can't recall*
Actually I don't even
agree !*

* Cardenas, E-SPEN Journal 8 (2013) e260ee262

Immune regulation in the gut CROSS TALK

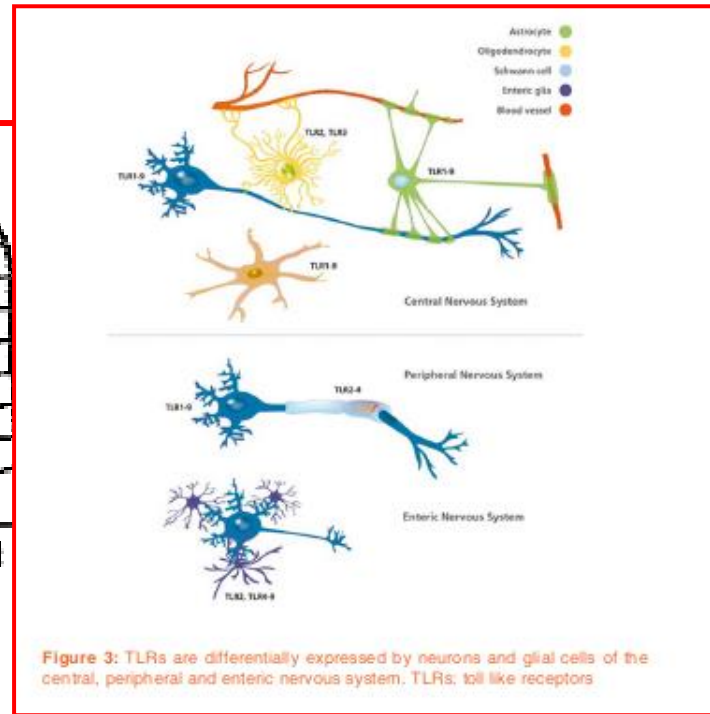
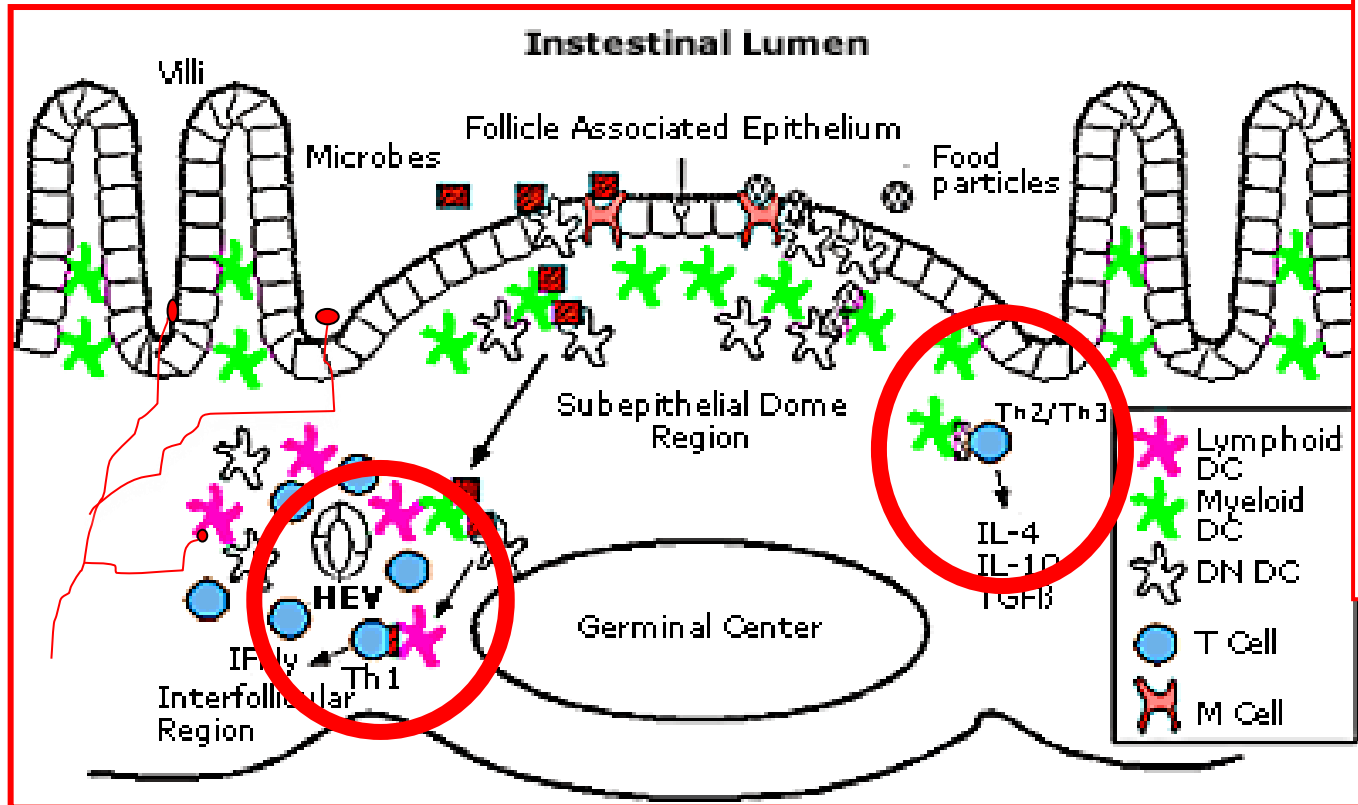


Figure 3: TLRs are differentially expressed by neurons and glial cells of the central, peripheral and enteric nervous system. TLRs: toll like receptors

Kraneveld, Nijkamp and Garssen 2009, EJP

Rietdijk, van Wezel, Garssen and Kraneveld 2016, Neuroimmunology Neuroinflammation

Th1 and Th2 activity as function of age

- Genes
- Hygiene
- Microbiota
- C-section
- Antibiotics
- **Drugs**
- Diets
- Stress
- Hormones
- Infections
- C...



Early life antibiotic use and the risk of asthma and asthma exacerbations in children

ERS 2016, PAI 2017, Allergy 2018
F Ahmadizar et al.

5 10 40 50 60 70 80 90 years

Allergy

Infections

Johan Garssen: Breast milk: components with immune modulating potential and their role in disease resistance. In Dietary Components and Immune Function, Series: Nutrition and Health. ... Zibadi, Sherma; Preedy, Victor R. 2011



Shaping the Gut Microbiota by Breastfeeding Promotes Allergy

Allergy. 2019 Mar 19. doi: 10.1111/all.13787. [Epub ahead of print]

Gut microbiota from infant with Cow's Milk Allergy promotes clinical and immune features of atopy in a murine model.

Mauras A^{1,2}, Wopereis H^{3,4}, Yeop I⁵, Esber N¹, Delannoy J^{1,2}, Labelle C^{1,2}, Revgnier J¹, Kapel N^{1,2,6}, Slump R³, van Eijndhoven T³, Rutten L³, Knol J^{3,4}, Garssen J^{3,7}, Harthoorn LF^{2,8}, Butel MJ¹, Bajaj-Elliott M⁵, Hartog A^{3,7}, Waliqora-Dupriet AJ^{1,2}.

Author information

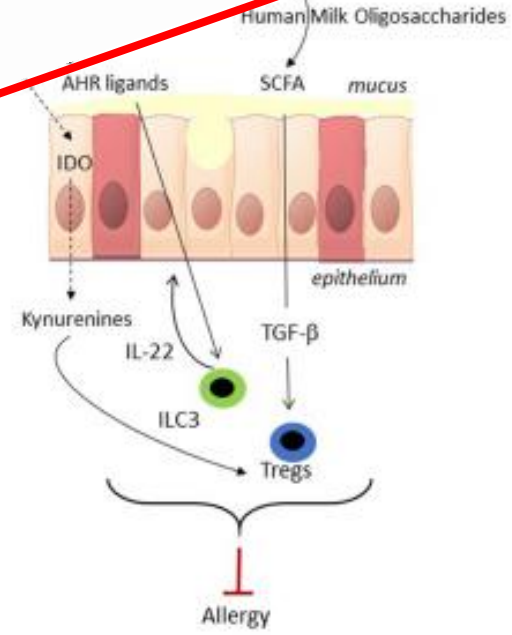
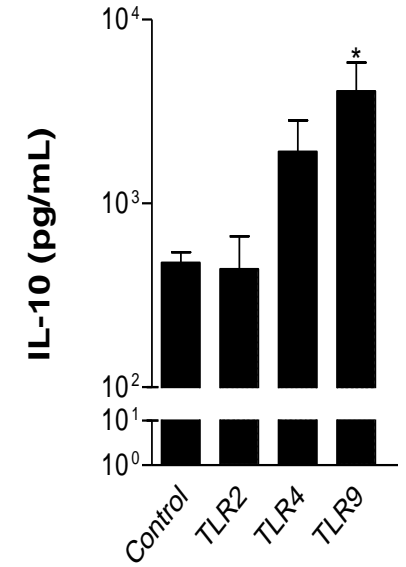
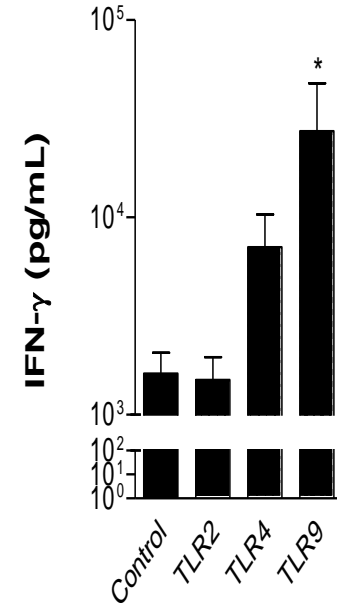
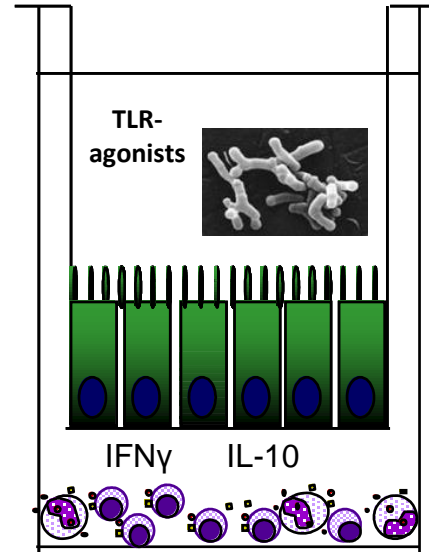
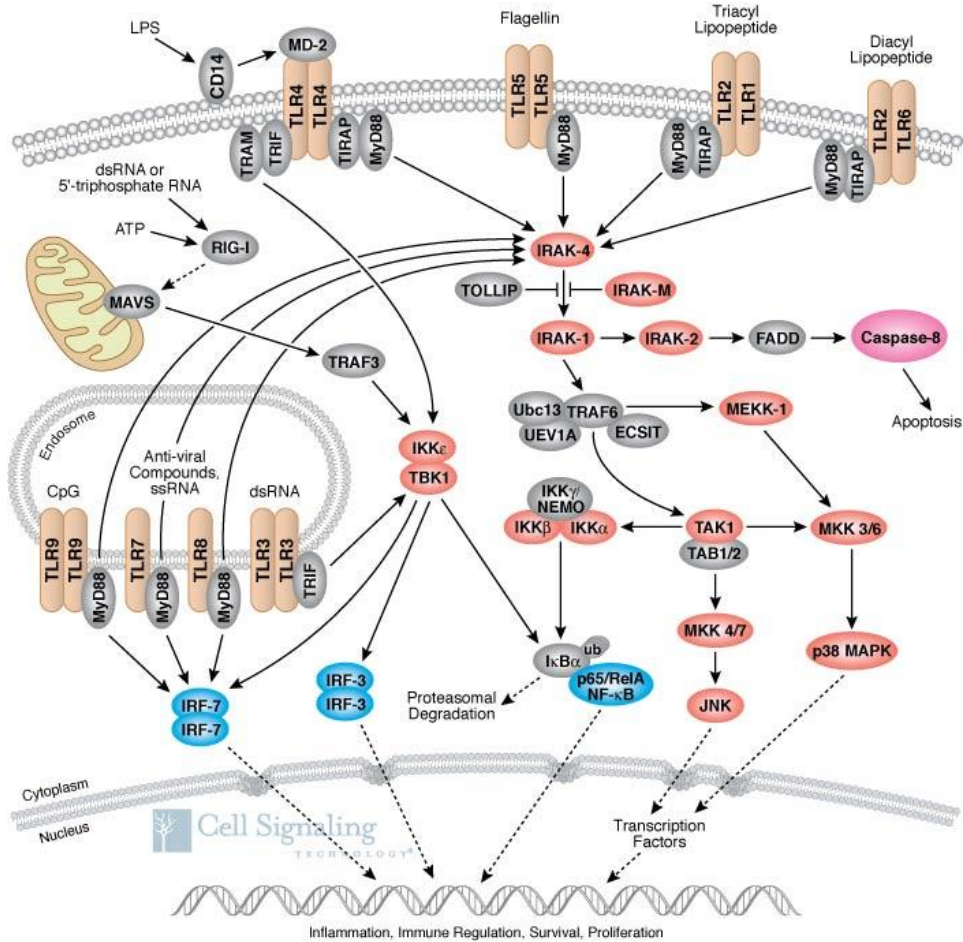
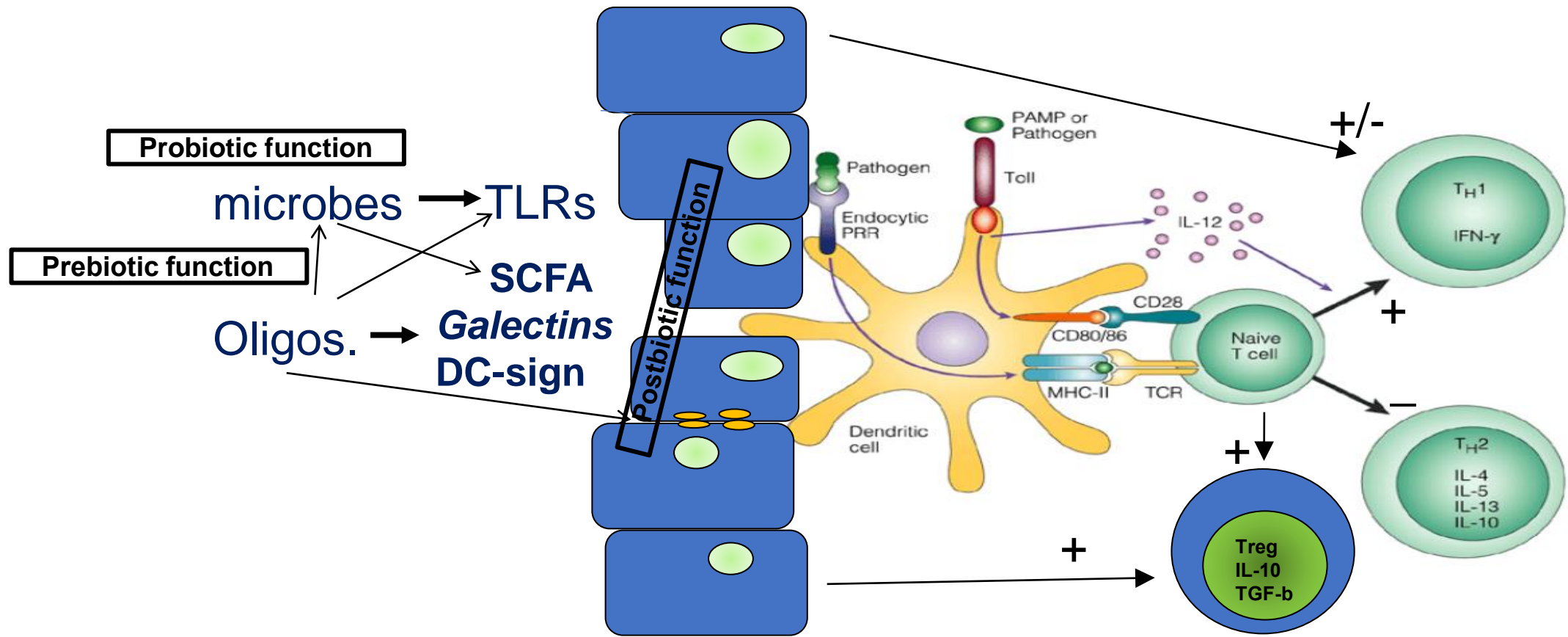


FIGURE 1 | The potential of breastmilk to prevent allergic disease by shaping of the neonatal gut microbiota. Breastmilk contains microbes as well as factors that indirectly shape the gut microbiota of the neonate. Breastmilk can direct the early microbiota composition, i.e., favor the growth of Bifidobacteria and Lactobacillus, and affect microbiota metabolic function, which subsequently can impact on immune development and maturation. The gut microbiota in early life impacts on immune maturation via microtranslumen-associated molecular patterns (MAMPs) signaling (not shown in the figure) and via microbiota metabolites, such as short-chain fatty acids (SCFA).

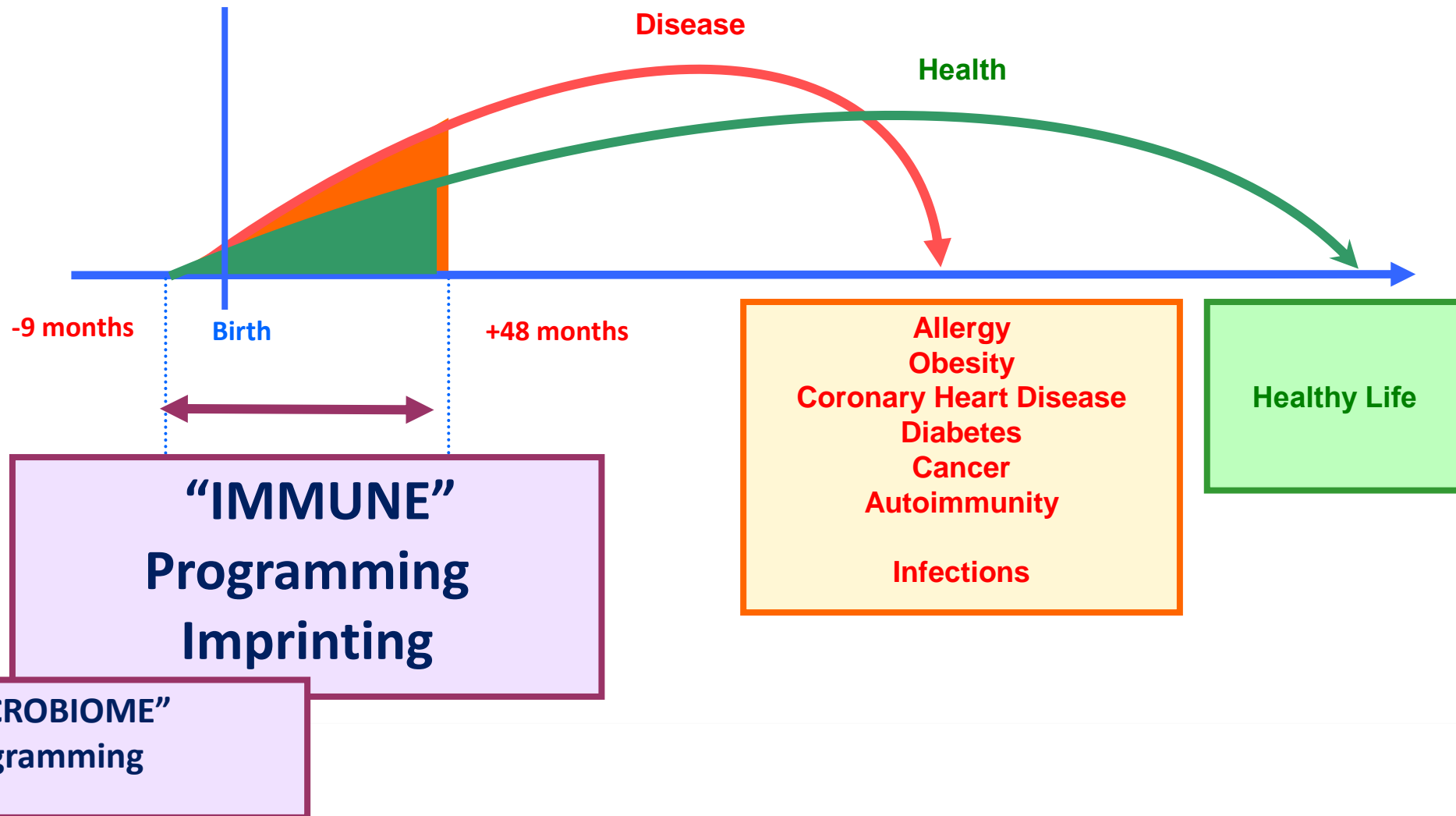
Receptors at the interface between innate and adaptive immunity (TLRs)





Preparing for “immune” health

Early life is setting the Right course for later life



***“There is a reason behind everything
in nature.”***

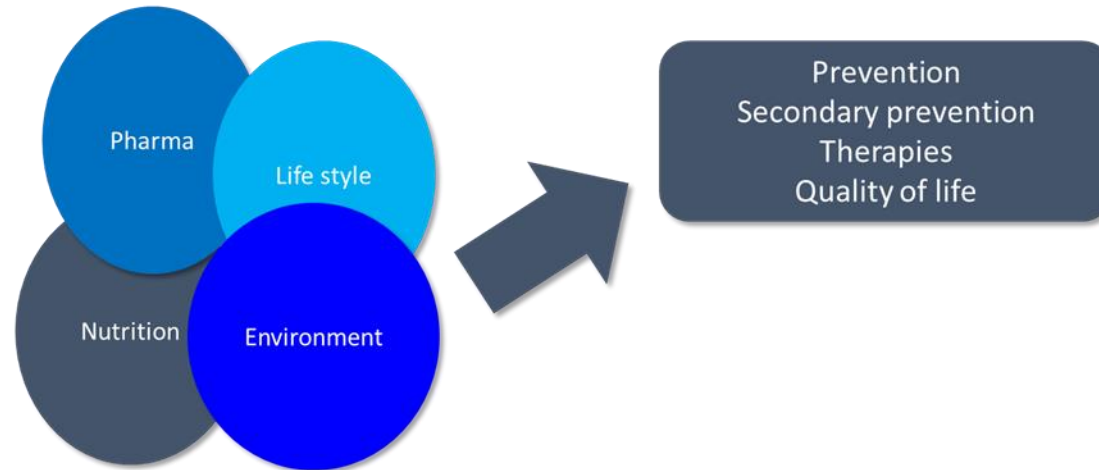


Aristoteles



CONCLUSION

- Nutritional ingredients such as oligosaccharides, unique microbes and “tolerizing” epitopes, can promote a fit immune system
- Immune system is under development at all ages: first few years essential
- Food immunology is the cutting edge between pharma and food: from quackery towards evidence based life sciences, a need for translational medicine.
- A need for integrated medicine/care



- We need translational research and involvement of the university for applied sciences
- Working together without borders/barriers
- Linking teaching with research....tell and explain our stories
- Systems biology/Machine learning-mathematics/models
- Explorative studies with human volunteers
- 3Rs
- Regulation/Guidelines involvement

Bruggen bouwen voor innovatie in onderzoek en onderwijs: food
pharma als een voorbeeld

Een oceaan van mogelijkheden

Prof. Johan Garssen, MD, PhD
Head Pharmacology, Beta Faculty, Utrecht University
Chief Scientific Advisor Danone-Nutricia- research